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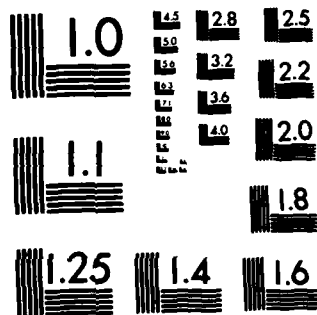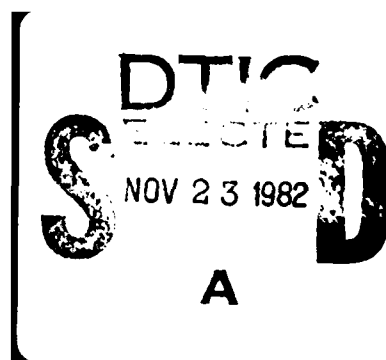
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The polyether 18-Crown-6 catalyzes a phase-transfer reaction between solid potassium cyanide, aromatic diazonium tetrafluoroborate salts in dichloromethane to produce high yields of aromatic azocyanides. The azocyanides are potent dienophiles, undergoing high-yield cycloaddition (Diels-Alder) reactions with a variety of dienes.

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The Azocyanide Functional Group

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The Pennsylvania State University

The Graduate School

Department of Chemistry

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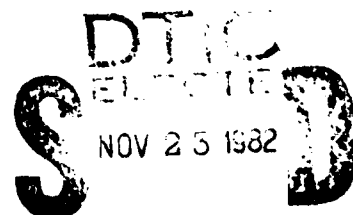
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Chemistry

by

Michael Francis Ahern

Submitted in Partial Fulfillment
of the Requirements
for the Degree of

Master of Science

August 1979

To Elaine and our Family

The signatories below indicate that they have read and approved the thesis of Michael Francis Ahern.

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ABSTRACT

The reduced reactivity of aryldiazonium ions solubilized
in non-polar media through complexation by macrocyclic polyethers
led to an investigation of arylazocyanides (Ar-N=N-CN) as pro-
tected diazonium ions. Formed by the reaction between aryldia-
zonium and cyanide ions, arylazocyanides are stable, covalent
compounds which can undergo dissociation into the corresponding
ionic species. Although arylazocyanides had been first prepared
by Hantzsch in 1895, and had figured prominently in the debate
over azo-compound isomerism, classical methods for their syn-
thesis were generally unsatisfactory.

Accordingly, the polyether 18-crown-6 has been found to
catalyze a phase-transfer reaction between solid aryldiazonium
tetrafluoroborate salts and solid potassium cyanide in non-polar
solvents. This reaction has been used to synthesize 4-substi-
tuted arylazocyanides in higher yields than any previously-
reported method. Several variations of this basic reaction have
been carried out, utilizing different solvent/catalyst systems.
The results of these investigations suggest a complex role
played by crown ether in the phase-transfer reaction system.
Additionally, arylazocyanides were subjected to hydrolysis,
reduction, and aromatic substitution reactions, which demonstrate

an altered reactivity for the arylazocyanides compared with other azo compounds and the corresponding aryldiazonium ions.

Although azodicarboxylate esters and azodicarbonyl compounds are known to be effective dienophiles in (2 + 4)-cycloaddition reactions, an analogous dienophilic reactivity has not been demonstrated for either aromatic azo compounds or aryldiazonium ions. Arylazocyanides, however, have been found to undergo facile (2 + 4)-cycloaddition reactions with a variety of acyclic and cyclic dienes to form novel N-aryl-N'-cyano reduced pyridazines. ^{13}C-nmr spectroscopy has been used to elucidate the structures of the cycloadducts formed from arylazocyanides and unsymmetrical dienes; the regioisomer distributions of these unsymmetrical adducts have been correlated with the arylazocyanide ring substituents using Hammet-type inductive constants (σ_I). Finally, kinetic measurements have been carried out on the cycloaddition reaction between 4-chlorophenylazocyanide and 2,3-dimethyl-1,3-butadiene. The derived activation parameters for the reaction were found to be similar to those reported for other potent azo and all-carbon dienophiles.

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LIST OF ABBREVIATIONS

BTEAC	Benzyltriethylammonium chloride
DMBD	2,3-Dimethyl-1,3-butadiene
THF	Tetrahydrofuran
TMAC	Tetramethylammonium chloride

ACKNOWLEDGEMENTS

I. INTRODUCTION

Since their discovery by Griess in 1858,[1] aryldiazonium ions have evidenced both synthetic utility and commercial importance.[2-4] The aromatic diazonio group may serve as a precursor to cationic, anionic, and radical intermediates formed by both thermal and photolytic reactions.[5] However, this extreme and diverse reactivity can introduce complications: the dry salts are notoriously unstable, and exploitation of potential reactions in other parts of the molecule has never been completely successful.

Because of these competing reactivity effects, several types of "stabilized," or "protected" diazonium ions have been developed. Both the diazotate salts (Ar-N=N-O$^-$M$^+$) and diazoamino compounds (Ar-N=N-NH-Ar') are stable species which can be safely handled and stored, but which form diazonium ions when treated with acid. The diazonium ions regenerated in this manner can undergo coupling reactions with suitable substrates to form azo dyestuffs. Thus, these types of "protected" diazonium ions have seen widespread industrial use in textile dying and printing processes.[6]

The use of diazonium ions paired with complex anions such as hexafluorophosphate and tetrafluoroborate has become increasingly common for synthetic purposes. Such salts are readily prepared in a pure form, and are relatively safe and stable.[7,8] These diazonium salts are, by themselves, soluble only in highly polar

media such as acetone, dimethylsulfoxide, and dimethylformamide.
Such solvents often react with the diazonium ion as well, leading
to undesirable by-products.[9,10] These salts can, however, be
solubilized in non-polar media such as chloroform and dichloro-
methane by complexation with appropriately sized crown ethers.[11]
Through this reversible complexation process, the crown ether also
acts as a protecting group for the diazonium ion in solution
(equation 1).
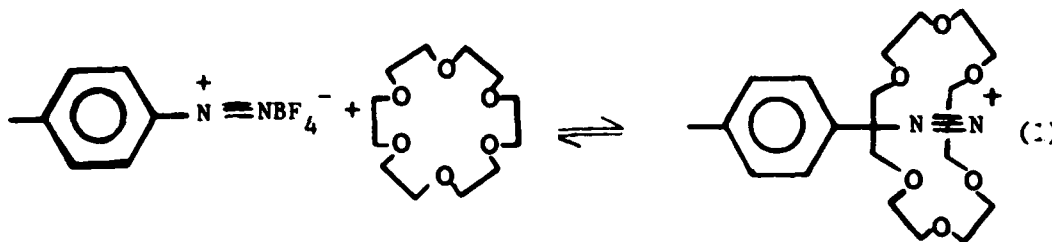
The efficiency of this protection has been aptly demonstrated
by Bartsch and coworkers, who showed that both thermal and photo-
lytic decompositions of diazonium ions (via the Schiemann reaction,
equation 2) were dramatically slowed in the presence of crown
ethers.[12] However, crown ether solubilization and protection of

$$Ar\text{-}N_2^+ BF_4^- \xrightarrow{\Delta \text{ or } h\nu} Ar\text{-}F + N_2 + BF_3 \qquad (2)$$
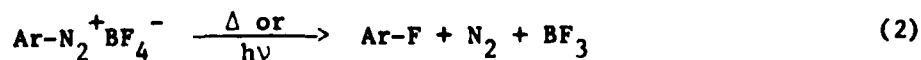
the diazonium ion is attended by a significant decline in its
desirable reactivity. The rate of the coupling reaction of crown-
complexed diazonium ions with N,N-dimethylaniline is significantly

lower than in the uncomplexed case.[13] Further, the resulting

attenuation of the diazonium ion positive charge appreciably

reduces its efficacy as an activating group for nucleophilic

substitutions at other sites in the molecule.[14] Thus, crown-

complexation affords the desired protection, but retards desir-

able transformations.

Arylazocyanides (Ar-N=N-CN) were first prepared by Hantzsch

in 1895.[15] Although isolated as stable, covalent compounds,

the arylazocyanides also underwent ionization in polar

solvents, dissociating into diazonium and cyanide ions,

(equation 3). Thus, the arylazocyanides could also conceivably

function as protected diazonium ions. Although figuring prominently

$$Ar-N=N-CN \rightleftharpoons Ar-\overset{+}{N}\equiv N + CN^- \qquad (3)$$
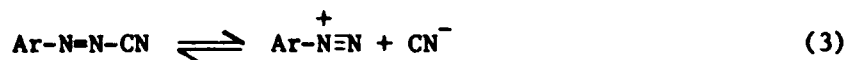
in the debate over cis, trans-isomerism of azo compounds during the

late 1930's and 1940's,[2] the arylazocyanides had not been exploited

as useful, synthetic intermediates.

Our interest in the arylazocyanides was stimulated by a few

preliminary reactions,[16] which showed that these compounds might

be easily prepared from stable diazonium tetrafluoroborate salts

in a crown-mediated phase-transfer reaction with solid KCN in

non-polar solvents (equation 4). The yields from these preliminary

reactions exceeded those generally afforded by literature proce-

dures. Thus, we first intended to perfect this synthetic method.

$$Ar-N_2^+BF_4^- + KCN \xrightarrow[\text{CH}_2\text{Cl}_2]{\text{18-crown-6}} Ar-N=N-CN + KBF_4 \qquad (4)$$
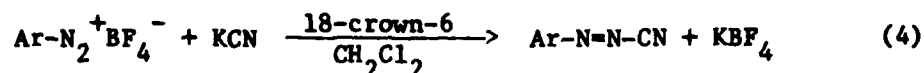
We next proposed to investigate the utility of arylazo-cyanides as synthetic intermediates in two primary roles, namely, as cycloaddition partners with dienes, and as substrates for ortho-directed metallation by palladium.

Although azodicarbonyl compounds had been known as effective dienophiles since 1925,[17] an analogous dienophilic activity had not been reported for aromatic azo compounds. Further, the few reports of cycloaddition reactions involving diazonium ions themselves (equation 5) indicated their dienophilic activity to be far from general.[18,19] If arylazocyanides were to undergo (2 + 4)-cycloaddition reactions, removal of the cyano group of the resulting cycloadduct (2) would afford the same product (1) as that derived from aryldiazonium ions (equation 6).
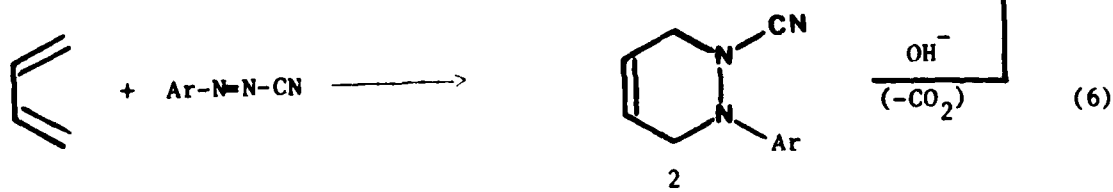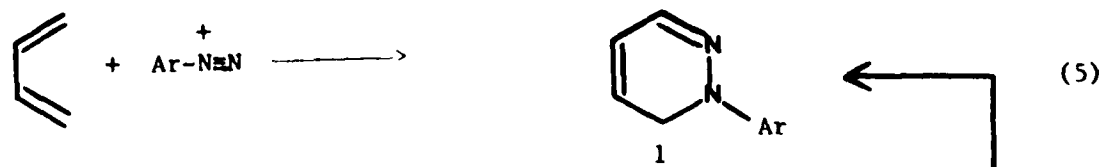
Cope and Siekman had shown that azobenzene formed on ortho-metallated complex (3) when treated with Pd(II) salts (equation 7).[20] In recent years, a large number of similar ortho-metallated complexes have been prepared, using various aromatic ligands and other transition metals.[21] Thus, it seemed reasonable that arylazocyanides might undergo the same reaction with Pd(II), to afford the complex 4.

We further expected that 4 might prove to be an interesting substrate for alkylation reactions, several of which are known for carbon-palladium sigma-bonded complexes.[22,23] After alkylation, the azocyanide linkage should be susceptible to reduction, either directly or through dissociation to a diazonium ion, followed by protodediazoniation (reduction). The proposed reaction sequence (equation 8) can formally be regarded as a regioselective arylation reaction.

(7)

(3)
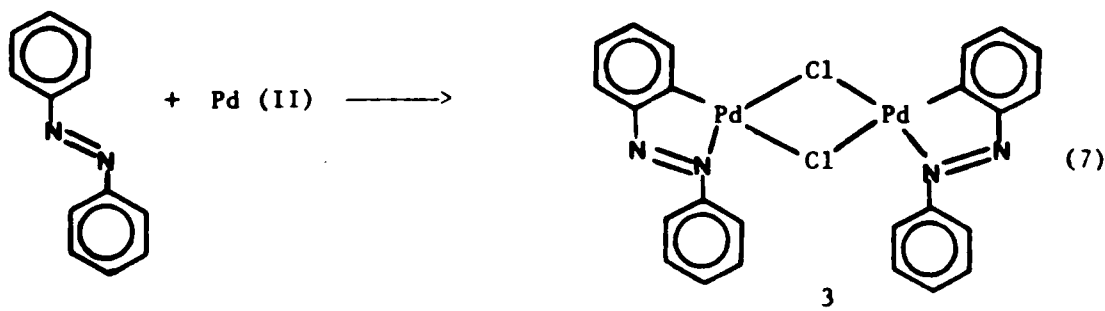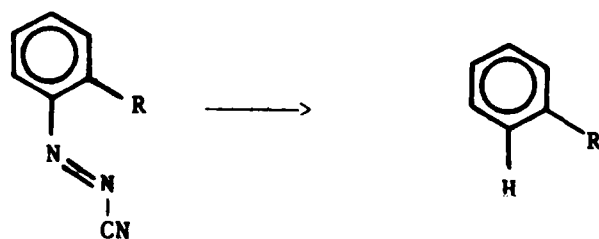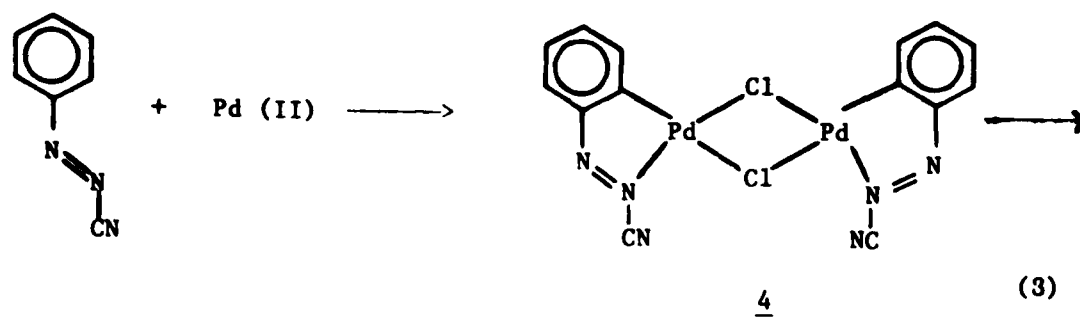
II. PHASE-TRANSFER SYNTHESIS OF ARYLAZOCYANIDES

A. Introduction

Although the stereoisomerism of aromatic oximes was first recognized by Hantzsch and Werner in 1890,[24] the concept of similar isomerism occurring in the azo compounds did not gain immediate acceptance. With the discovery by Schraube and Schmidt that diazotate salts ($Ar-N=N-O^-M^+$) could be isolated in both a labile and a stable form,[25] Hantzsch theorized that the concept of stereoisomerism could be extended to all azo compounds.[26]

In order to defend his hypothesis from those who argued in favor of _structural_ rather than _stereo_isomerism,(notably Bamberger, v. Pechmann, and more recently, Hodgson and Marsden),[27] Hantzsch attempted to isolate other azo compounds which could exist in distinct isomeric forms. Accordingly, he successfully synthesized two distinct forms of aromatic azosulfonates, ($Ar-N=N-SO_3^-M^+$), to which he also assigned a stereoisomeric relationship.[28] Finally, by adding aqueous KCN to a diazotized solution of 4-chloroaniline, Hantzsch isolated an aromatic azocyanide, ($4-Cl-C_6H_4-N=N-CN$).[15]

The pale-orange solid (mp 29°C) first isolated from the reaction mixture proved to be extremely reactive. In polar, ionizing solvents such as ethanol, it precipitated silver cyanide when treated with silver nitrate, and readily formed an azo-dye coupling product with β-napthol. This behavior suggested its facile dissociation into diazonium and cyanide ions (equation 9).

$$Ar-N=N-CN \xrightleftharpoons[\text{solvents}]{\text{ionizing}} Ar-N_2^+ + CN^- \qquad (9)$$
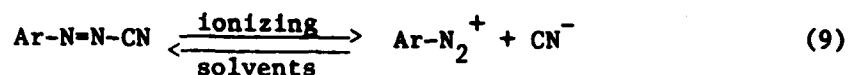
The azocyanide also underwent a copper powder catalyzed decomposition reaction, in which nitrogen was evolved; the products of this decomposition suggested that phenyl radicals were involved (equation 10).[29]

$$Ar-N=N-CN \xrightarrow{\text{Cu}} Ar^\bullet + CN^\bullet + N_2 \qquad (10)$$
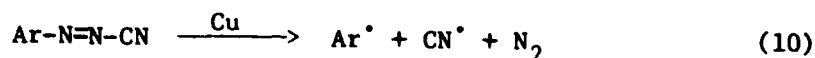
The reactive azocyanide could easily be converted into a higher-melting (mp 105°C) form simply by dissolving in a non-polar solvent such as benzene or petroleum ether, and evaporating to a red-orange residue. This higher-melting form was extremely stable, and did not undergo the dissociation or decomposition reactions. Again postulating a stereoisomeric relationship, Hantzsch assigned a cis- or Z-structure to the more labile form, and a trans- or E-structure to the stable isomer (Figure 1).

This structural assignment based upon stereoisomerism was quickly challenged by Orton,[30] and some years later by Hodgson and Marsden, who had earlier maintained that Hantzsch's alleged cis- and trans-azosulfonates were actually structural isomers, namely, azosulfites and azosulfonates, respectively.[31] The latter
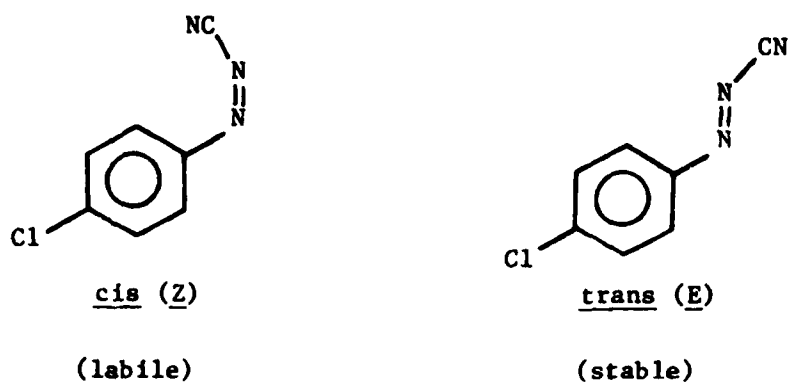
Figure 1. Stereoisomers of 4-Chlorophenylazocyanide.

workers now argued in a similar fashion with respect to the aryl-azocyanides, claiming that the labile and stable forms were re-lated as isocyanide and cyanide (Figure 2). In promoting the
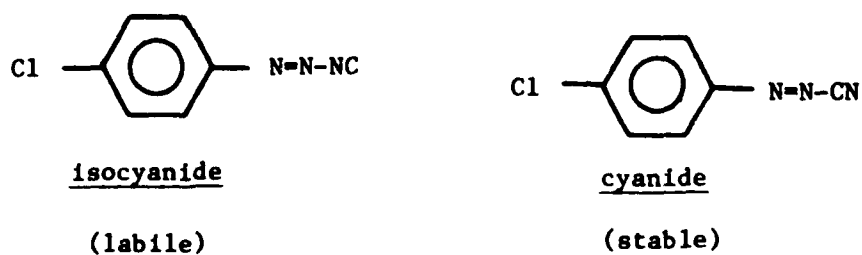
Figure 2. Proposed Structural Isomers of 4-Chloro-phenylazocyanide.

structural isomerism theory, Hodgson and Marsden argued primarily from the energy differences between carbon-carbon and carbon-nitrogen bonds, and by analogy to the known chemistry of iso-cyanides and isocyanates.[32]

The stereoisomerism theory, on the other hand, was championed primarily by LeFevre and his coworkers. Their measurements of molecular dipole moments, rates of isomerization, optical rotary powers, and diamagnetic susceptibilities of the two isomeric forms all tended to corroborate Hantzsch's original assignment,[33-36] although the earliest infrared spectra were not entirely unequi-vocal.[37-39]

Since the bulk of the evidence tended to support the stereo-isomeric structures, and as numerous examples of such isomerism among the aromatic azo compounds were discovered,[40-43] Hantzsch's theory generally became acceptable as fact. However, it was not until the relatively recent synthesis of the elusive arylazo-isocyanide, (which was shown to have vastly different physical and spectral properties from either of the isomeric cyanides), that the structural isomerism argument could be conclusively dismissed.[44] Some recently-reported ^{13}C-nmr spectra of three isomeric pairs of arylazocyanides also support the geometrical isomerism viewpoint.[45]

With the exception of the isomerism controversy, the arylazo-cyanides have received relatively little recent attention. Several patent applications claim potent fungicidal activity for

both the arylazocyanides, their N-oxides, and the corresponding

carboxamides.[46] Reactions between arylazocyanides and diphenyl-

ketene have afforded (2 + 2)-cycloaddition adducts, (Section IV).[47,48]

In addition, Huisgen and coworkers have reported the formation of

some novel addition compounds from arylazocyanides and diazoal-

kanes.[49]

B. Synthesis of Arylazocyanides from Aryldiazonium Tetra-
     fluoroborate Salts in Non-Polar Media.

Although a large number of arylazocyanides have been character-

ized during the course of these investigations, with one exception

the synthetic procedure first utilized by Hantzsch for their pre-

paration has undergone little improvement or change since 1895.

The procedure most often used and reported[33] requires the slow

addition of aqueous KCN to a freshly prepared and filtered diazotized

solution of the appropriate aromatic amine at -10°C; the diazoti-

zation is normally carried out with conc HCl and $NaNO_2$. The pro-

duct precipitates, and can be collected by filtration. The arylazo-

cyanide thus formed is the cis-isomer; it may be purified as such,

or alternatively, converted into the more stable trans-isomer by

dissolving in a non-polar solvent (equation 11).

Except for a very recent modification reported by Huisgen,

this procedure has been the only synthetic route to the arylazo-

cyanides, and it has some serious shortcomings. In general, the

yields are poor. High conversions (i,e., 90%) have been reported

only for electron-rich 4-dimethylaminoaniline;[50] the few yields

$$Ar-NH_2 \quad \frac{1)\ \underline{aq\ HCl}}{2)\ NaNO_2} \rightarrow \quad Ar-N_2^+Cl^- \quad \xrightarrow{\ \underline{aq\ KCN}\ } \rightarrow$$

(11)

$$\underset{cis}{\overset{\displaystyle Ar-N}{\underset{\displaystyle NC-N}{\parallel}}} \quad \frac{non\text{-}polar}{solvent} \rightarrow \quad \underset{trans}{\overset{\displaystyle Ar-N}{\underset{\displaystyle N-CN}{\parallel}}}$$
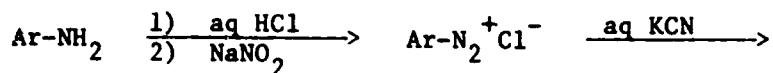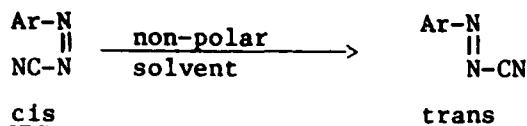
reported in the literature for other substituted anilines range from 17-25%.[35,46] Our attempts to prepare 4-bromophenyl- and 4-chlorophenylazocyanide by the classical method resulted (in both cases) in yields of 11%. Further, the method necessitates some potentially hazardous procedures. Particular care must be exercised in manipulating the potentially explosive diazonium chloride solutions. Additionally, the formation of some free HCN during the course of the reaction must always be assumed, since the method involves addition of KCN to the strongly acidic diazonium ion solution, and stringent ventilation precautions must be taken.

The Huisgen modification[49] involves diazotization of the anilinium chloride salt in glacial acetic acid using either sodium or ethyl nitrite, followed by the usual addition of aqueous KCN. This modification afforded somewhat improved yields, but was of exceptional value in only one case, $(4\text{-}Cl\text{-}C_6H_4\text{-}N{=}N\text{-}CN$, 65-71%). Thus, although this method shows promise, its generality remains to be demonstrated.

The fact that 18-crown-6 polyether effectively complexes and solubilizes aryldiazonium tetrafluoroborate salts in non-polar

solvents (such as dichloromethane and chloroform),[11] and also functions as an effective phase-transfer catalyst for solid potassium cyanide in the same media,[51] suggested that the aryl-azocyanides could be synthesized by a crown-mediated phase-transfer reaction (Scheme 1). Since the aryldiazonium tetra-fluoroborate salts can be readily prepared in high yields from the appropriate anilines[8] (Table 11), this scheme offered an attractive synthetic alternative to the procedure of Hantzsch.

$Ar-N_2^+BF_4^-$ (solid)

K^+CN^- (solid)

+ Crown (sol'n)

$(Ar-N_2 \cdot Crown)^+ BF_4^-$ (sol'n)

$(K \cdot Crown)^+ CN^-$ (sol'n)

$Ar-N{=}N-CN$ (sol'n) $\longleftarrow$ $Ar-N_2^+CN^-$ (sol'n) +

KBF_4 (solid) + 2 Crown
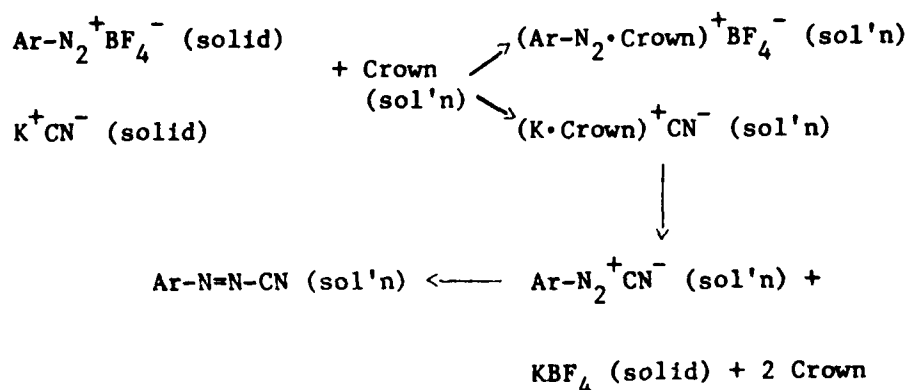
Scheme 1. Phase-Transfer Synthesis of Arylazocyanides.

Accordingly, when solid KCN (2 equiv) was added to a stirred mixture of 4-bromobenzenediazonium tetrafluoroborate (5) (0.1 M in CHCl$_3$) and a catalytic amount (10 mol-%) of 18-crown-6, trans-4-bromophenylazocyanide (6) was isolated in 60% yield (equation 12).

$$4\text{-Br-}C_6H_4\text{-N}_2{}^+BF_4{}^- + KCN \xrightarrow[\text{CHCl}_3]{\text{18-crown-6}} 4\text{-Br-}C_6H_4\text{-N=N-CN} \quad (12)$$

$$\underline{5} \qquad\qquad\qquad\qquad 0°C \qquad\qquad\qquad \underline{6}$$
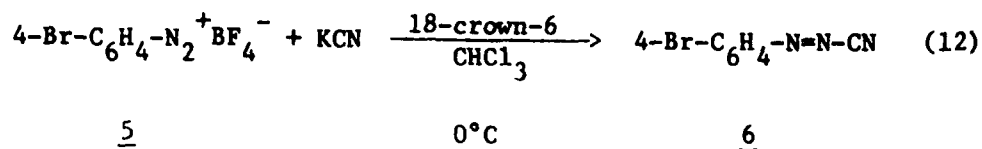
When the reaction was carried out in a similar fashion at 0°C using only one equivalent of KCN, 5 mol-% of 18-crown-6, and dichloromethane as the solvent, crude azocyanide (6) was obtained in 84% yield. Further, when the reaction was carried out at ambient temperature as opposed to 0°C, an identical yield (84%) was obtained. This latter method (1 equiv KCN, 5 mol-% 18-crown-6, 5 h stirring at ambient temperature) was therefore adopted as the standard synthetic procedure. The arylazocyanides prepared by this method are summarized in Table 1.

Reaction times of five hours were generally sufficient to achieve high yields of azocyanides for reactions conducted on scales of 3-6 mmoles of diazonium salt. After reaction, the deep red-orange to red-brown mixtures were filtered to remove residual solids (mostly KBF$_4$). The solid residue thus obtained could be qualitatively tested for the presence of unreacted diazonium salt by extracting a portion with acetone and adding a few drops of N,N-dimethylaniline. The 18-crown-6 used as a catalyst remained in solution along with the product; most of the former could be removed by washing the solution with aq KOAc (10%) w/w). After drying over Na$_2$SO$_4$ in the dark for _ca_. 24 h, the solvent was then removed _in vacuo_ to yield the crude _trans_-product.

Table 1

Preparation of E-Arylazocyanides (X-Ar-N=N-CN); 3-6 mmol Reaction Scale[a]

Cpd No.	X	% Crude Yield Based Upon		% Purified Yield[b]	Purif. Method[c]	Obsd. mp[d] (°C)	Lit. mp (°C)
		$ArN_2^+BF_4^-$	Starting Aniline				
6	4-Br	78-84	70-76	55-71	S	124-128	132[44]
8	4-Cl	75-91	62-76	53-77	S	101-104	105[44]
9	4-F	92	71	71	S	60-61	Note 52
10	4-MeO	87-91	71-75	87-91	N/A	117-122	121-122[44]
11	4-NO_2	80-91	73-83	48-55	E	82-85	86[43]
12	4-H[e]	95	83	15	D[f]	29	Note 53
13	2-Cl[g]	44	38	--	--	--	78[43]
14	2,4-Cl_2[g]	15	--	--	--	--	--

[a] All reactions were carried out at ambient temperature, with a stirring time of five hours, in accordance with the general procedure described in the Experimental Section.

[b] Based upon diazonium salt, using the purification method listed.

[c] S = sublimation; E = extraction; D = distillation; N/A = no further purification required.

Table 1 (continued)

^{d}The mp reported is for material purified as indicated and having the appropriate spectral properties. Literature mp's could be obtained, but compounds with the reported mp's were sufficiently pure for all further reactions.

^{e}Results of a single reaction carried out on a 40-mmol scale, using 2 equiv KCN, 10 mol-% 18-crown-6, and 18 h stir time.

^{f}Results of a single purification attempt using vacuum distillation.

^{g}No purification attempted.

The crude products so obtained were typically red-orange or red-brown solids, with melting points ca. 5-10°C below the literature values for the pure trans-compounds. The compounds were spectroscopically pure (ir and [1]H-nmr) except for small amounts of residual crown ($\leq$ 2 mol-% by [1]H-nmr).

In addition to traces of residual crown, the crude products generally contained some oligomeric material. The cyano group of arylazocyanides is known to undergo facile addition reactions by a variety of nucleophiles, including cyanide ion. Further addition of cyanide to the azocyanide product (in the presence of a proton source) results in the formation of an arylazo-iminoacetonitrile (15, equation 13), a few examples of which have been reported.[54]

$$Ar-N{=}N-CN \xrightarrow{\ CN^-\ } Ar-N{=}N-\underset{\underset{CN}{|}}{C}{=}N^- \xrightarrow{\ H^+\ } Ar-N{=}N-\underset{\underset{CN}{|}}{C}{=}NH \qquad (13)$$

$$\underline{15}$$
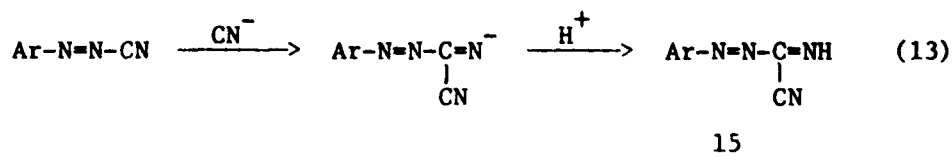
In aprotic reaction media, further addition of cyanide ion to the product should be reversible, but also provides an oligo-merization pathway, since the initial anionic addition product can react further (equation 14).

When a dichloromethane solution of pure 4-chlorophenylazocyanide and 18-crown-6 (5 mol-%) was treated with solid KCN (2 equiv), the bright orange solution immediately turned red-brown. The azocyanide recovered from this reaction was darker brown in color than the pure

$$\text{Ar-N=N-CN} \underset{}{\overset{\text{CN}^-}{\rightleftharpoons}} \underset{\underset{\text{CN}}{\overset{|}{\text{Ar-N=N-C=N}^{(-)}}}}{} \underset{}{\overset{\text{Ar-N=N-CN}}{\rightleftharpoons}}$$

(14)

$$\text{Ar-N=N-}\underset{\underset{\text{CN}}{\overset{|}{\text{C}}}}{\text{C=N-}}\left(\underset{\underset{\text{N=N-Ar}}{\overset{|}{}}}{\text{-C=N}}\right)_n$$
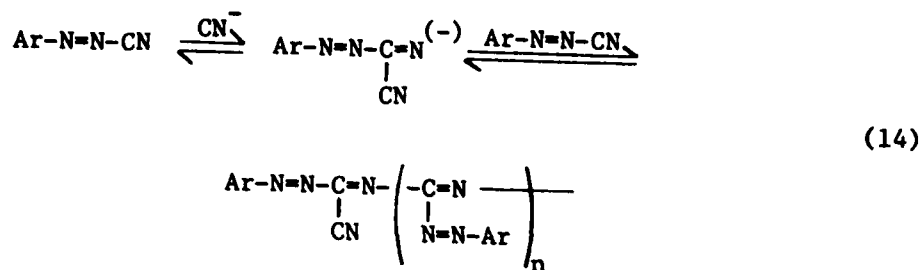
starting material, and its mp was lower by 3°C, although its ir spectrum was unchanged. Obviously, these observations do not conclusively demonstrate that further addition of CN^- can occur under phase-transfer conditions, since no addition product was isolated and characterized. However, they at least suggest that some further reaction can occur.

Interestingly, when solid KCN was added to an identical crown-azocyanide solution which also contained an equivalent of KBF_4, no color change was observed. The solution remained bright orange and the azocyanide recovered from this mixture was identical to the pure starting material in color, mp, and ir spectrum.

The presumably inert BF_4^- ion could be serving a crucial function in our reaction system. As the reaction proceeds and product concentration increases, a second addition of cyanide becomes more probable. Note, however, that KBF_4 is formed as a by-product. The $(crown \cdot K)^+$ complex is a soft cation in the Pearson sense, and tends to ion-pair with the softer BF_4^- anion than with cyanide. The result is an effective poisoning of the 18-crown-6 catalyst as the reaction proceeds, since the increasing amounts of KBF_4 make it less likely that the crown will continue to transfer cyanide ion.

Many cases of such "catalyst poisoning" have been observed
for nucleophilic displacement reactions under phase-transfer
conditions, particularly when the nucleofuge is a soft species
such as iodide or tosylate.[55] However, in our reaction system,
BF_4^- may be fortuitously moderating the catalytic effect in such
a way that the desirable reaction takes place, but further addi-
tion of cyanide ion becomes more difficult and the undesired
side reaction is slowed.

The crude products can be purified by a variety of methods.
Vacuum sublimation was particularly effective for the para-
halogen arylazocyanides, affording highly crystalline, pure
compounds with typical recoveries of 70-85% from crude material.
4-Nitrophenylazocyanide (11) was purified by extraction of the
crude material with boiling hexane-THF (4:1, v/v) solution;
recoveries using this method were typically 60%. 4-Methoxyphenyl-
azocyanide (10) was obtained from the reaction in a highly-
crystalline state, often containing negligible amounts (0-0.3
mol-%) of residual crown; this product could be used without
further purification. Phenylazocyanide (12) is a very low-melting
(mp 29°C) solid, and was purified only with difficulty on one
occasion by vacuum distillation.

The pure trans-compounds are brilliant orange or red-orange
compounds. With the exception of phenylazocyanide (12), which
decomposed in refrigerated storage over a few months, all were
stable indefinitely when stored in a dessicator at ambient
temperature. The compounds generally melt below 130°C without
decomposition, and have a pungent, acrid odor. They are readily

soluble in chlorocarbon and aromatic solvents, and in polar solvents such as acetone, acetonitrile, and ethanol. They are somewhat soluble in saturated hydrocarbon solvents, and relatively insoluble in water.

18-Crown-6 is clearly functioning as a phase-transfer catalyst in the reaction system. Thus, when 4-chlorobenzene-diazonium tetrafluoroborate (7) was stirred (5 h, ambient temperature, CH_2Cl_2) with solid KCN (1 equiv) in the absence of 18-crown-6, only a 5% yield of 4-chlorophenylazocyanide (8) was obtained, compared to yields of 75-91% using 5 mol-% 18-crown-6 (Table 1). Using a large excess (5 equiv) of KCN and stirring for five days in the absence of crown increased the yield of 8 to 34%. When 7 was reacted with NaCN in the presence of 15-crown-5, (6 mol-%), which effectively complexes Na^+ but whose cavity is too small to complex the diazonio group, 8 was obtained in only 24% yield.

The catalytic effect of crown is further demonstrated by the reduced reactivity of diazonium salts having ring substituents in the ortho-position. In general, such diazonium salts afforded reduced yields of azocyanides. Indeed, CPK-models clearly demonstrate that complexation (and thus lipophilization) of the diazonio group by crown ether is sterically hindered by even relatively small ortho-substituents such as chlorine. The fact that the para-substituted azocyanide (8) can be obtained (albeit in poor yield) in the total absence of crown, and that not-insignificant yields can be obtained from ortho-substituted salts

suggests the presence of a slight, purely heterogeneous reaction between the solid diazonium salt and solid KCN. This "heterogeneous" reaction, however, may actually be due to the presence of adventitious water in the system, affording an aqueous microphase in which both KCN and (to a very slight extent) the solid diazonium salt dissolve. The product azocyanide, itself only slightly soluble in water, would then be continuously extracted into the organic phase as it is formed.

As stated previously, the more labile cis-arylazocyanide is the isomer formed in the aqueous acid reaction, but the products so obtained can be very easily converted into the more stable trans-structure. This thermal cis-to-trans isomerization occurs in the dark even in the solid state. Thus, when a sample of cis-6 prepared according to this method was stored in the dark, the melting point underwent a gradual transition from 41-42°C to 125-130°C over a six-day period (Lit. mp °C: cis-isomer 42-43; trans-isomer 132). Similar solid-state isomerization has been reported by other workers.[33]

Isomerization in solution is much more facile, occurring quantitatively in the dark in non-polar solvents. An activation energy of ca. 22 kcal/mole has been reported for the cis-to-trans isomerization of 8 in chloroform; this value is similar to that reported for the cis-to-trans thermal isomerization of azobenzene.[33] Additionally, LeFevre and others have extensively studied the effect of ring substituents and solvent dielectric upon isomerization rate.[36]

The reverse isomerization, that of _trans_-to-_cis_, occurs
photolytically (also similar to azobenzene), but has not been
extensively studied. For azocyanide _6_, the photostationary state
is reported to be 20:80 _cis_:_trans_ for a benzene solution in normal
daylight at ambient temperature.[41]

When Ignasiak and Suszko published the first unequivocal
infrared spectra of the _cis_-arylazocyanides, they also demonstra-
ted that the _cis_-to-_trans_ isomerization could be measured quanti-
tatively by infrared spectroscopy.[44] This measurement relies
upon a surprising difference in the infrared spectra between the
two isomers (Figure 3). The cyanide stretching vibration (v_{CN})
of the _cis_-isomer is reported to be an extremely weak absorption
in the region 2175-2150 cm^{-1}, but is readily observed as a strong
band at 2190-2195 cm^{-1} in the _trans_-compound.[56] Other absorption
bands in the spectrum become sharper and stronger as isomeri-
zation proceeds, particularly a band at _ca_. 1400 cm^{-1} which has
been assigned to a ring skeletal vibration.

Although spectral measurements and melting points indicated
that the products ultimately isolated from the phase-transfer
synthesis were the _trans_-isomers, we were interested in ascer-
taining whether such isomers were being formed initially, or
were resulting from the facile isomerization of an initially-
formed _cis_-compound in the non-polar solvent. Accordingly, when
4-bromophenyldiazonium tetrafluoroborate in CH_2Cl_2 was stirred
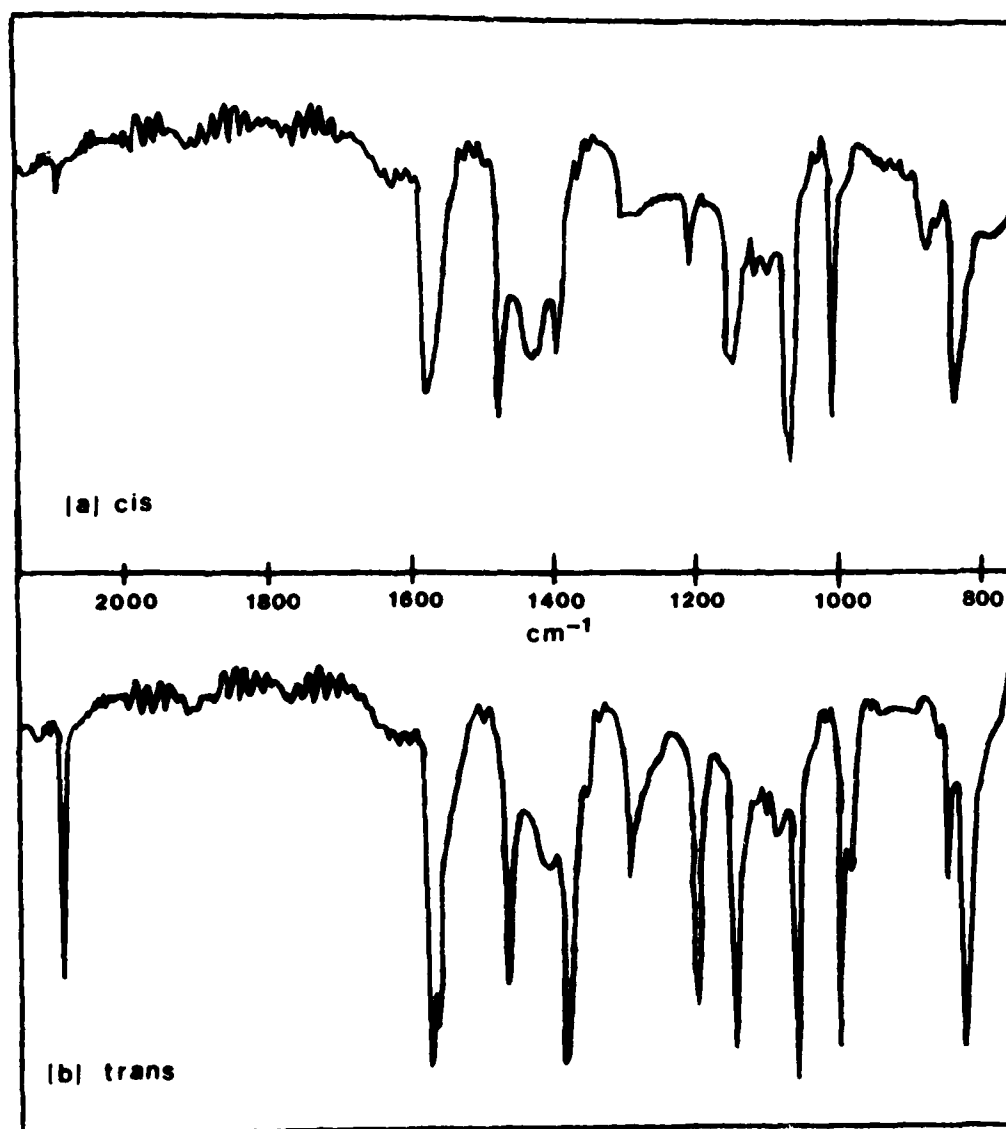
Figure 3. Infrared Spectra of 4-Bromophenylazocyanide (ca. 0.1 M in CH_2Cl_2): a) = cis; b) = trans.

with KCN (1 equiv) and crown (5 mol-%) for only two h at 0°C,

a CH_2Cl_2 solution of the product immediately obtained showed

an infrared spectrum essentially characteristic of the cis-

isomer. Both the characteristic cyanide (2191 cm^{-1}) and ring

(1395 cm^{-1}) vibrations were weak, but slowly increased in intensity

over a period of 21 h until both bands were sharp and prominent.

Similar results were obtained using 4-chlorobenzenediazonium

tetrafluoroborate in an identical reaction at ambient temperature.

It was thus concluded that even at ambient temperature in the

non-polar solvent, the cis-isomer is initially formed, just as

in the aqueous acid system.

The cis-compounds can be isolated from the aqueous system

because they are insoluble in the reaction medium and therefore

do not undergo immediate and facile isomerization. In the non-

polar solvent of the phase-transfer system however, the solubility

of the cis-compounds allows isomerization to commence immediately

in the reaction mixture. Even though the half-lives for the

isomerization of para-halogen-substituted arylazocyanides are

typically 9-10h,[36] the total reaction times necessary to achieve

high product yields make the phase-transfer method unsatisfactory

for the deliberate preparation of the cis-isomers. Conversely,

the drying of reaction solutions over Na_2SO_4 during workup is

best carried out in the dark for ca. 24 h, in order to insure

complete isomerization to the trans-isomer. Products which

are isolated immediately tend to be less crystalline with slightly
lower melting points, perhaps attributable to a small amount of
cis-isomer.

Although a reaction time of 5 h was nearly always sufficient
for small-scale (3-6 mmol) reactions, larger scale reactions
(30-300 mmol) generally did not proceed to completion during this
time. This phenomenon was common to larger-scale syntheses of
4-chloro-, 4-methoxy-, and 4-nitrophenylazocyanides, and persisted
in spite of precautions to insure reproducible reaction conditions.
Since our interests rested primarily in the chemistry of these
compounds as protected diazonium groups, only a minimal effort
was undertaken to understand and alleviate this problem. However,
a sufficient number of larger-scale syntheses were performed
(primarily of 4-chlorophenylazocyanide) to permit some general-
izations (Table 2).

The progress of these reactions could be qualitatively
estimated by the color of the reaction mixture, which darkened
from an initial pale yellow to a deep red-orange or red-brown
as the highly colored product was formed. Poor-yield reactions
terminated after only a minimal (5 h) reaction time were typically
yellow or very pale orange. The reaction residues of such low-
yield syntheses always contained unreacted diazonium salt, as
indicated by infrared spectra and formation of a colored solution
with N,N-dimethylaniline. In fact, unreacted diazonium salt could
be recovered in such cases from the residue simply by extracting

Table 2

Effect of Reaction Variables on the Yield of 4-Cl-Ar-N=N-CN

Exper. No.	Scale (mmol)	KCN (eq)	18-Crown-6 (mol-%)	Stir Time (h)	Crude[a] Yield %	Notes
1	6	1	5	5	91	
2	30	1	5	5	42	
3	288	1	5	5	25	
4	60	1	5	16	66	
5	150	1	5	20	40	
6	150	1	5	20	22	b
7	83	1	20	20	83	c
8	50	4	2	5	15	
9	50	4	5	5	34	
10	50	4	10	5	48	
11	50	4	5	20	75	
12	50	4	5	30	86, 100	d
13	50	4	5	5	99	e
14	50	4	2	5	99, 100	d,e

[a] Results of a single reaction unless otherwise indicated. Yields listed are based upon diazonium salt, figuring the isolated material as pure compound, and have not been corrected for varying amounts (0-7 mol-%) of 18-crown-6 contaminant in the crude products.

[b] Reaction fitted with sintered-glass delivery tube for nitrogen purge, and contained 10 g added silica gel.

[c] Product contaminated by 7 mol-% 18-crown-6.

[d] Results of two separate reactions.

[e] $4-NO_2-C_6H_4-N=N=CN$.

with acetone and re-precipitating with ether. Further, the products isolated from low-yield reactions were identical, both spectroscopically and in mp, to those from high-yield reactions. Thus, the lower yields are apparently due to a kinetic retardation of the phase-transfer reaction, rather than to a competing reaction of the diazonium ion or further reaction of product. Satisfactory yields could always be obtained simply by extending the reaction times (Table 2, Exper. 1-4).

For preparative convenience, however, it was desirable to keep the reaction time as short as possible. Increasing the available surface area by nitrogen purge through a sintered-glass delivery tube and the addition of silica gel to the reaction actually decreased the yield (Table 2, Exper. 6). Increasing the amount of 18-crown-6 (from 5 to 20 mol-%, Exper. 7) was effective in accelerating the reaction, but the larger amount of crown was correspondingly more difficult to remove from the crude product. An increase in the amount of KCN used (from 1 to 4 equiv., Exper. 8-10) was not in itself effective, but use of more KCN in conjunction with a longer stirring time (ca. 30 h, Exper. 12) afforded reproducibly high yields in 50-mmol syntheses of 4-chlorophenylazocyanide. With an identical excess of KCN, high yields of 4-nitrophenylazocyanide were obtained with a short reaction time (5 h), even when the amount of 18-crown-6 was reduced to 2 mol-% (Exper. 13-14).

Although the problems associated with large-scale synthesis were circumvented, the origin of these problems remains obscure. An explanation may eventually be found in some role played by adventitious water. Several precedents exist which show that water can exhibit an ambivalent effect on phase-transfer reactions. A minute amount may be required to assist the crown in overcoming crystal lattice forces of the solid KCN; such an effect has been observed for the solvation of $KMnO_4$ in benzene by dicyclohexyl-18-crown-6. On the other hand, water may effectively form a coordination sphere around the cyanide anion and accompany the anion into the organic phase; the anion so "solvated" may be less reactive. This latter effect has also been documented.[57]

An excess of water can be additionally detrimental to our particular reaction system because of several potential side reactions. First, slow hydrolysis of diazonium ion can occur, resulting in phenols which can further react to form azo coupling products (equation 15). Secondly, the presence of water may

(15)
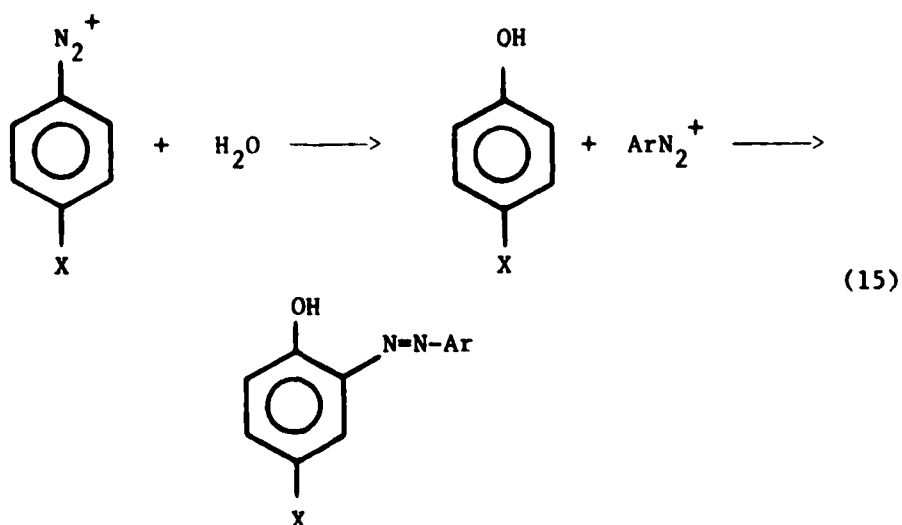
encourage either the dissociation of the cis-isomer first

formed to diazonium and cyanide ions, or its decomposition reac-

tions, both of which are known to be facile in polar media

(equation 16). Finally, the azo-bonded cyano group is extremely

$$
\begin{array}{c}
\text{N} \overset{\text{Ar}}{\underset{\text{CN}}{\overset{\|}{\text{N}}}} \quad \rightleftharpoons \quad ArN_2^+ + CN^- \\[2em]
\xrightarrow{\dfrac{\text{EtOH or}}{\text{Acetone}}} \quad Ar^\bullet + CN^\bullet + N_2
\end{array}
\tag{16}
$$
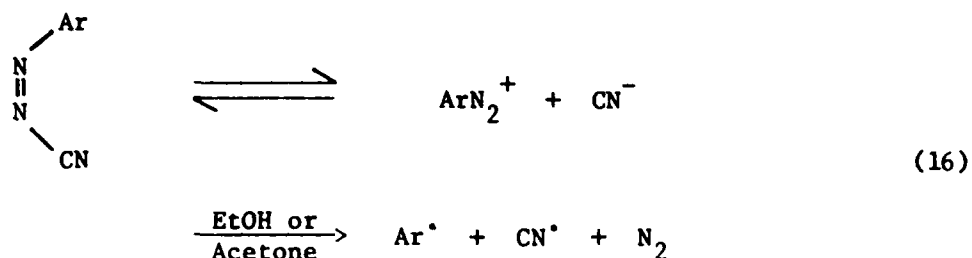
susceptible to nucleophilic addition, and can undergo hydrolysis

to form a phenylazocarbonamide (equation 17), although higher

temperatures are normally required for this reaction to take

place in neutral solution.

$$
Ar-N=N-CN + H_2O \longrightarrow Ar-N=N-\overset{\overset{\text{O}}{\|}}{C}-NH_2
\tag{17}
$$
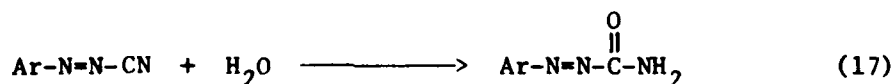
From the discussion above, it seems clear that adventitious

moisture can conceivably affect the formation of azocyanides in

this system in a variety of ways. However, the details of this

process have not been worked out, and the above suggestions con-

cerning the role of water remain speculation.

C. Synthesis of Arylazocyanides in Polar Organic Solvents

The solvation (and ultimate reaction) of both the diazonium ion substrate and the cyanide nucleophile depends upon their mutual complexation by 18-crown-6. However, crown ethers are not unique in their ability to phase-transfer cyanide ion. Quaternary ammonium salts such as tricaprylylmethylammonium chloride (Stark's catalyst), and benzyltriethylammonium chloride (BTEAC) are also known to be extremely effective in this role. For example, aliphatic nitriles can be synthesized in high yields from alkyl halides by a phase-transfer process in which cyanide ion is ion-paired with a quaternary ammonium ion in an aqueous phase, and then transferred into an organic phase containing the substrate (Figure 4).[51]

$$Q^+CN^- \ + \ R\text{-}Cl \ \longrightarrow \ R\text{-}CN \ + \ Q^+Cl^- \quad \text{(organic phase)}$$

$$\text{(phase boundary)}$$

$$Q^+CN^- \ + \ NaCl \ \rightleftharpoons \ NaCN \ + \ Q^+Cl^- \quad \text{(Aq phase)}$$

Figure 4.   Quaternary Ammonium Phase-transfer of Cyanide

We were naturally interested in knowing whether quaternary ammonium salts could be similarly used to advantage in our system. It was thought that such catalysis might circumvent the problem

of crown-complexation of ortho-substituted aryldiazonium ions,
and complement the crown-catalyzed method.

Aryldiazonium tetrafluoroborate salts can be dissolved in
more polar organic solvents such as acetone or acetonitrile
without the use of 18-crown-6. However, these solvents are them-
selves freely miscible with water, so a two-phase liquid-liquid
system (Figure 4) could not be used. Although the use of quater-
nary ammonium chloride salts for the phase-transfer of cyanide
ion has been essentially restricted to such liquid-liquid systems,[51]
we decided to first attempt the phase-transfer of solid KCN with
these catalysts, using solvents in which the aryldiazonium ion
itself was freely soluble.

Thus, when solid KCN (1 equiv) was added to a stirred acetone
solution containing 4-chlorobenzenediazonium tetrafluoroborate (7) and
Stark's catalyst (25 mol-%), the solution turned red-orange within 5
min, and was red-brown after stirring 13 h. However, although the
color of the mixture was encouraging, the reaction yielded only
uncharacterized tarry material; both ^{1}H nmr and tlc analysis
showed none of the desired azocyanide present. In a similar
reaction in acetone using BTEAC (25 mol-%), a red color again
developed within minutes. After stirring only 30 min, the reac-
tion again yielded an uncharacterized brown tar, along with some
residual diazonium salt. A trace (4%) amount of product 8 was
isolated using Stark's catalyst in acetonitrile. When 18-crown-6

was used as the catalyst in acetonitrile, a small amount (12%) of
8 was isolated, again along with tarry material.

The failure of these reactions cannot necessarily be attri-
buted to the inability of quaternary ammonium salts to phase-
transfer solid KCN, since even 18-crown-6 did not afford a
satisfactory product under these conditions. Rather, the most
likely cause is the extreme lability of the first-formed cis-
azocyanide in the polar solvents used. As stated previously,
the cis-azocyanides are known to undergo radical decomposition
reactions in polar solvents such as acetone and ethanol, even
without catalysis by copper metal. Such solutions rapidly darken
and evolve some nitrogen, affording a tarry residue, some HCN,
and only small amounts of trans-azocyanides.[29] Further, the cis-
to-trans isomerization of 4-chlorophenylazocyanide is reportedly
slowest in solvents of high dielectric, having a half-life value of
ca. 45 h in cyclohexanone (ϵ = 18.3).[36] Since acetone has a similar
dielectric (ϵ = 20.7), and acetonitrile is even more polar (ϵ =
38.8), it is not surprising that even uncatalyzed decomposition can
predominate.

D. Synthesis of Arylazocyanides from Methathesized
   Diazonium Solutions in Non-Polar Media

Quaternary ammonium salts have also been used to solubilize
diazonium ions in non-polar media through a process known as
gegenion metathesis.[58] Accordingly, when the normally insoluble

4-chlorobenzenediazonium tetrafluoroborate ($\underline{7}$) is stirred in
chloroform with tetramethylammonium chloride (TMAC, 1 equiv) for
3 h at 0°C, a gegenion exchange takes place, resulting in a chloro-
form solution of 4-chlorobenzenediazonium chloride, and leaving
behind solid tetramethylammonium tetrafluoroborate (equation 18).

$$4\text{-Cl-C}_6\text{H}_4\text{-N}_2{}^+\text{BF}_4{}^- + \text{Me}_4\text{N}^+\text{Cl}^- \xrightarrow[0°C]{\text{CHCl}_3} 4\text{-Cl-C}_6\text{H}_4\text{N}_2{}^+\text{Cl}^- \text{ (sol'n)}$$

$$\text{(solid)} \qquad \text{(sol'n)} \qquad\qquad\qquad (18)$$

$$+ \text{ Me}_4\text{N}^+\text{BF}_4{}^- \quad \text{(solid)}$$
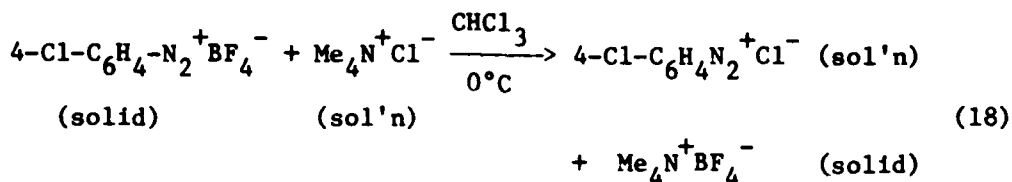
Similar non-polar solutions can be generated using BTEAC, except
in this case, the mixture becomes entirely homogeneous, with no
precipitation of the quaternary ammonium tetrafluoroborate. Thus,
appreciable concentrations ($\underline{ca}$. 0.1 M) of aryldiazonium ions can
be generated in non-polar solvents without depending upon a crown
ether for solubilization.

We fully expected, then, that the arylazocyanides could
also be prepared by stirring such a solution of aryldiazonium
chloride with solid KCN and a catalytic amount of 18-crown-6.
Further, we expected the reaction to occur more rapidly, since
the diazonium ion was already in solution.

When 4-chlorobenzenediazonium tetrafluoroborate ($\underline{7}$) (3.0
mmol) was stirred in chloroform with TMAC (1 equiv) for 3 h at
0°C, and the mixture filtered, a clear, pale-yellow solution
resulted whose ir spectrum showed a strong diazonium vibration

at $\underline{ca}$. 2275 cm^{-1}. When this solution was treated with solid KCN (2 equiv) and 18-crown-6 (5 mol-%), and stirred at ambient temperature for 24 h, it turned pale orange. Its ir spectrum still showed a prominent diazonium absorption, and an aliquot formed a dark red color when treated with N,N-dimethylaniline. The solution was then washed with water and filtered through a bed of silica gel in order to remove crown and unreacted diazonium ion. After drying over Na_2SO_4 in the dark for $\underline{ca}$. 24 h, evaporation $\underline{in\ vacuo}$ afforded a 54% yield of 4-chlorophenylazocyanide.

When a reaction identical to that described above was carried out, except that the metathesized solution of $\underline{7}$ was added dropwise over 5 h, the mixture developed an orange color more quickly, but the final result of the reaction was identical. When the reaction was conducted as above, in the $\underline{absence}$ of 18-crown-6, a slightly lower but essentially similar yield (46%) was obtained.

The rate of azocyanide formation in this reaction system appears to be appreciably slower than that observed in the phase-transfer synthesis using solid diazonium salt. Ir and ^{13}C-nmr examination of these solutions which have stirred for 5 h with crown and KCN shows no evidence of azocyanide formation, but only unreacted diazonium ion. This result is surprising, considering that the diazonium ion is already in solution, and the crown is required to solubilize only one reacting species. Further, the uncatalyzed reaction with solid KCN in the absence of crown

afforded nearly the same yield as the crown-catalyzed reaction, again suggesting an appreciable heterogeneous reactivity between the aryldiazonium ion in solution and solid KCN. As stated previously, this same heterogeneous reactivity between the two solid salts was also observed in the dichloromethane reaction system, but to a lesser extent.

The fact that metathesized solutions of aryldiazonium ions did not react rapidly with solid KCN in the presence of catalytic amounts of crown can most likely be attributed to the formation of the crown·diazonium ion complex in the bulk organic phase. This complex formation has two important consequences. First, the crown-complexed aryldiazonium ion is both less reactive and substantially less polar, which restricts its proximity to the solid KCN interface and thereby retards the heterogeneous component of the reaction. The second and major consequence is that crown which is complexed in the bulk organic phase is unavailable for use as a phase-transfer catalyst enhancing the solubility and availability of cyanide ion.

When the synthesis was conducted using a methathesized solution of 7 in conjunction with sodium cyanide and 15-crown-5, the reaction mixture turned red-brown immediately, ultimately affording 34% of crude product along with oligomeric material. The immediate formation of a brown color implies a much more efficient phase-transfer of cyanide ion when a crown too small to tie up or be tied up by aryldiazonium cation is used, thus corroborating the hypothesis set forth above.

We also attempted several reactions with metathesized solutions
of 7 in chloroform using Stark's catalyst in place of 18-crown-6.
When the solution of 7 was added dropwise to a mixture of solid
KCN (2 equiv) and Stark's catalyst (5 mol-%) and stirred for 24 h,
a 40% yield of 4-chlorophenylazocyanide was obtained. Apparently,
the quaternary ammonium catalyst is not significantly effective
in phase-transferring solid KCN in this system. When the diazonium
solution was added to a saturated aqueous reservoir of KCN and
Stark's catalyst (15 mol-%), the mixture turned black and tarry.
Obviously, the quat-catalyst is excessively efficient in this two-
phase liquid-liquid system, affording only oligomerization product.
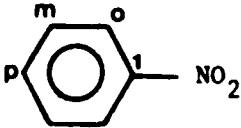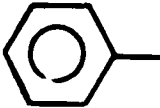
Since binding constants for aryldiazonium ions and 18-crown-6
are unavailable, and since the kinetics of solid KCN transfer
have not been determined under these conditions, this discussion
must remain speculation. The qualitative observations, however,
seem to accord with a complex role played by the crown ether
catalyst.

E. ^{13}C-nmr Spectral Properties of Arylazocyanides

We have also recorded the ^{13}C-nmr spectra of a number of
arylazocyanides. The ^{13}C-spectral properties of only three
arylazocyanides have been previously reported.[45] The spectra
indicate that the -N=N-CN functional group has approximately the
same effect upon aromatic carbon chemical shifts as does a nitro

group. Chemical shift values and coupling constants (where
applicable) are listed in Tables 3 and 4.

Table 3

Substituent Effect of the Azocyanide Functional
Group on ^{13}C-nmr Spectral Properties[a]

	C-1	ortho	meta	para
NO$_2$	+20.0	-4.8	+0.9	+5.8
N=N-CN	+24.9	-4.3	+1.2	+8.5

[a]Chemical shift values are reported relative to benzene (128.5
ppm); (+) indicates shift downfield.

The chemical shift of the cyano-group carbon, ca. 114-116
ppm, is similar to that of nitrile groups in conjungation with
carbon; (compare benzonitrile, 118.7 ppm; cyanoethylene, 117.5
ppm; and trans-1-chloro-2-cyanoethylene, 114.4 ppm). This chemical
shift value is also indicative of a strongly covalent rather than
ionic bond between the cyano group and the azo-linkage in non-
polar solvent (chloroform-d), since the carbon resonance of

Table 4

^{13}C-nmr Chemical Shifts of Representative Compounds[a]
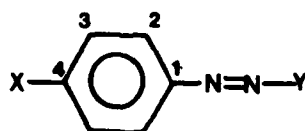
X	Y	CN	1	2	3	4	ref.
H	C_6H_5	--	152.6	122.8	128.9	130.7	60
H	CN	115.5	153.4	124.2	129.7	136.9	this work
NO_2	CN	114.7	155.1	124.9 ± .1	124.9 ± .1	151.8	this work
Br	CN	115.4	152.0	125.3	133.3	132.9	this work
Cl	CN	115.4	151.6	125.3	130.2	143.8	this work
F	CN	115.4	150.1 (d, J = 2.6)	127.0 (d, J = 10.7)	117.2 (d, J = 23.5)	168.1 (d, J = 263.7)	this work
CH_3O	CN	116.4	148.4	127.2	115.2	167.5	this work
Cl	$CONH_2$	(CO: 164.4)	149.6	124.3	129.6	137.5	this work

[a]All spectra recorded as $\underline{ca}$. 10% (w/w) in chloroform-d.

aqueous KCN is observed at 168.5 ppm downfield from TMS.[59] It
is noteworthy that the cyano carbon resonance of 4-methoxyphenyl-
azocyanide is farthest downfield (116.4) of all the arylazocyanides
surveyed. This can be rationalized in terms of the electron-
donating effect of the methoxy group, which can stabilize a
positive charge on the diazonium ion, and hence result in a
more "salt-like" compound. By the same token, the corresponding
4-nitro compound exhibits the most upfield resonance position
(114.7 ppm). Finally, although a linear cumulene-type resonance
structure can be drawn for the azocyanide group (Figure 5), the
carbon resonance position of molecules with a similar cumulene-
type structure (viz., aromatic isocyanates and dicyclohexyl-
carbodiimide, Figure 6), lies considerably further downfield
from that observed for the cyano carbon of the azocyanides.
This suggests that such a cumulene structure probably makes a
negligible contribution to the actual electron distribution.
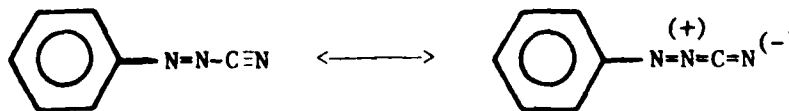
Figure 5. Cumulene-type Resonance Structure
for Phenylazocyanides.

δ = 129.5   δ = 139.0
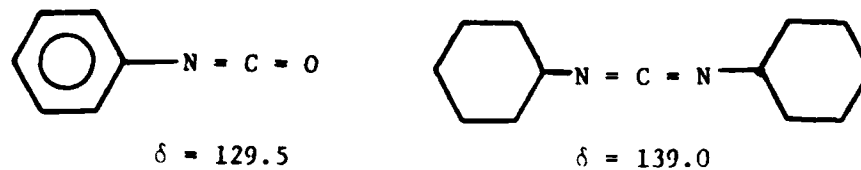
Figure 6.   Central-Carbon Resonance Positions of Phenylisocyanate[59]
and Dicyclohexylcarbodiimide.[60]

F.   Summary

We have shown that para-substituted trans-arylazocyanides
can be readily synthesized from aryldiazonium tetrafluoroborate
salts and solid KCN by a crown-mediated phase-transfer reaction
in non-polar media.   In most cases, this method affords trans-
arylazocyanides in higher yields than any method previously
reported.

III. ARYLAZOCYANIDES: ADDITION, REDUCTION, AND SUBSTITUTION REACTIONS

In an attempt to gain some immediate perspective concerning the reactivity of the arylazocyanides, we subjected them to a limited number of addition, reduction, and substitution reactions. These reactions were largely exploratory, involving no concerted effort to exhaustively vary reaction conditions, nor to isolate and characterize unwanted by-products. However, the reactions attempted were sufficient to demonstrate, in several cases, an altered reactivity for the arylazocyanides compared with other azo compounds and the corresponding aryldiazonium ions.

In addition to the previously-discussed isomerization and radical decomposition reactions, the arylazocyanides have long been known to be reactive towards nucleophiles. Specifically, the cyano group bonded to the azo-linkage is reported to display a pronounced reactivity towards nucleophilic addition of such agents as water, HCN, alcohols, ammonia, and amines. This susceptibility towards nucleophilic addition is characteristic of both the _cis_ and the _trans_ isomers.

The various nucleophilic addition products prepared from arylazocyanides have been recently reviewed;[61] the majority were first characterized by Hantzsch and his coworkers, but have been little-studied since.

The only such addition product to which we devoted even brief attention was the hydrolysis product of azocyanide (8), 4-chlorophenylazocarbonamide (16) (equation 19). This compound

$$Cl\text{-}Ar\text{-}N\text{=}N\text{-}CN \ + \ H_2O \ \xrightarrow[\text{aq THF}]{H^+} \ Cl\text{-}Ar\text{-}N\text{=}N\text{-}\overset{\overset{\displaystyle O}{\parallel}}{C}\text{-}NH_2 \qquad (19)$$
<u>8</u>   <u>16</u>
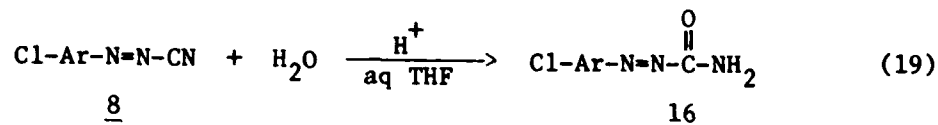
was prepared in 77% yield (using a modification of Hantzsch's original procedure)[62] by simply stirring <u>trans-8</u> in an aqueous HCl-THF solution for 24 h at ambient temperature.

Hantzsch also subjected arylazocyanides to basic hydrolysis by boiling them in aq KOH-ethanol solution (equation 20). Under these conditions, the alkali-metal salt (17) of the corresponding azo-acid can be isolated; the same product results from similar treatment of the arylazocarbonamides.[62] These salts are reported not

$$\begin{matrix} Ar\text{-}N\text{=}N\text{-}CN \text{ or} \\ \\ Ar\text{-}N\text{=}N\text{-}CONH_2 \end{matrix} \quad \xrightarrow[\text{aq EtOH}]{KOH} \quad Ar\text{-}N\text{=}N\text{-}COO^-K^+ \ + \ NH_3 \qquad (20)$$
                                                        <u>17</u>
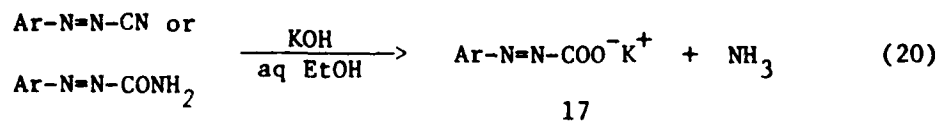
to be very stable: they occasionally undergo explosive decomposition at room temperature. In aqueous acid solution, the salts rapidly evolve carbon dioxide and nitrogen to yield the corresponding arene. This decomposition in aqueous acid is thought to proceed through the intermediate formation of an aryldiazene (18) (equation 21).[63]

43

$$Ar-N=N-COOK \xrightarrow{\text{H}_3\text{O}^+} Ar-N=N-COOH \longrightarrow [Ar-N=N-H] + CO_2$$

$$\underline{18}$$

$$\longrightarrow Ar-H + H_2 \qquad (21)$$
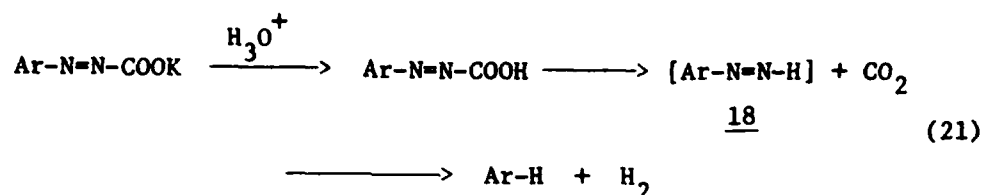
We did not attempt to isolate any of the free-acid salts, but did discover that when heterogeneous mixtures of arylazocyanides and aq KOH were refluxed for ca. 16-24 h, both decarboxylation and loss of nitrogen occurred to furnish low yields of the corresponding arenes directly. Thus, when $\underline{8}$ and $\underline{10}$ were refluxed in 10-15% (w/w) aq KOH for ca. 24 h, chlorobenzene and anisole were obtained in yields (glpc) of 25% and 30%, respectively. This direct decomposition presumably occurs through the formation of a phenyl anion, which then is protonated by solvent (equation 22).

$$Ar-N=N-CN \xrightarrow[\Delta]{\text{aq KOH}} \left[Ar-N=N-C \underset{\text{O}}{\overset{\text{O}^-}{<}} \right] \longrightarrow$$

$$N_2 + CO_2 + Ar^- \xrightarrow{\text{H}_2\text{O}} Ar-H \qquad (22)$$
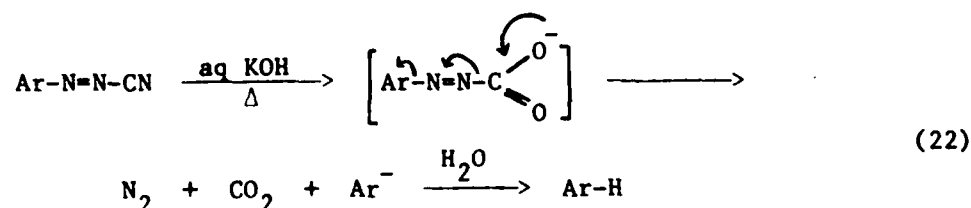
Accordingly, when $\underline{8}$ was refluxed with 15% NaOD (w/w) in D_2O, chlorobenzene was obtained in overall 28% (glpc) yield; 93% of this product was deuterated (equation 23).

$$\text{(23)}$$
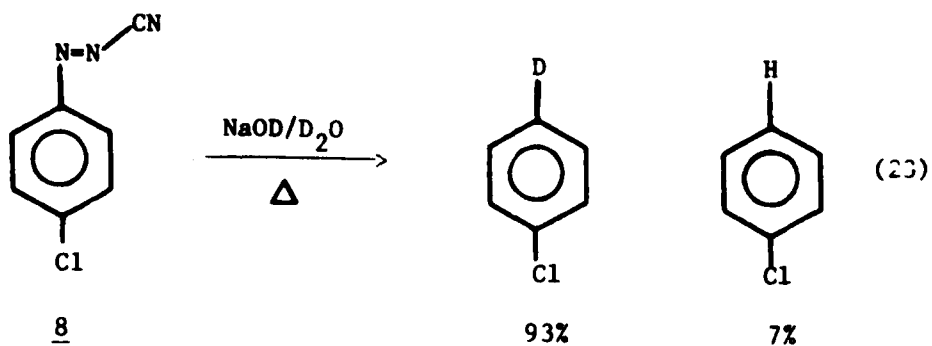
The arylazocyanides can also conceivably undergo reduction

reactions. These include hydrogenation to a cyanophenylhydrazine

(equation 24) and metal-hydride reduction to an amine (equation

25). Derivatives of phenylazocarboxylic esters and phenylazo-

carbonamides, are reported to undergo facile reduction of the

$$\text{Ar-N=N-CN} \xrightarrow{\text{H}_2} \text{Ar-NH-NH-CN} \qquad (24)$$

$$\text{Ar-N=N-CN} \xrightarrow{\text{LiAlH}_4} \text{Ar-N=N-CH}_2\text{-NH}_2 \qquad (25)$$
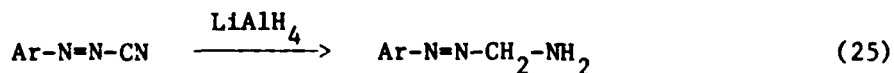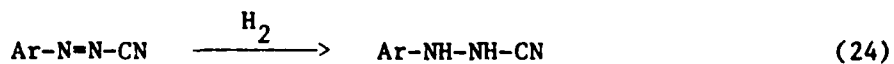
azo bond to the corresponding phenylhydrazine carboxylic acid

derivatives (equation 26).

$$\text{Ar-N=N-R} \xrightarrow{\text{[H]}} \text{Ar-NH-NH-R} \qquad (26)$$
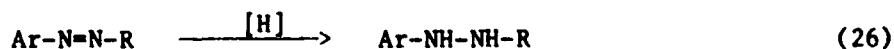
$\text{R = COOR}', \text{CONH}_2$

A wide variety of reagents, such as zinc dust in HOAc, ammonium
sulfide, and phenylhydrazine, have been employed for these reduc-
tions.[64] Hantzsch was unable to identify any product when he
attempted to reduce arylazocyanides under similar conditions;
the expected cyanophenylhydrazine was not formed, and to our
knowledge, has never been isolated.[62] Since there had been no
reports concerning the catalytic hydrogenation of arylazocyanides,
we decided to attempt this reduction method.

Low-pressure (ca. 3 atm) hydrogenation of 4-chlorophenyl-
azocyanide in benzene using 10% Pd/C catalyst resulted in a
complex mixture of products (5 spots tlc); similar results were
obtained in 95% ethanol. Both the protic and catalytic hydro-
genation of arylazocyanides may be complicated by reductive
cleavage of the azo linkage, a process which is known to occur
during the reduction of azobenzene both in protic, metal-acid
systems and during catalytic hydrogenation over platinum.[65]
Such cleavage of azobenzene results in the formation of aniline
(equation 27); a reductive cleavage of an arylazocyanide could
conceivably result in a substituted aniline and cyanamide
(equation 28).

Other catalyst-solvent systems were not examined. However,
bis-(dimethylglyoximato)cobalt (II) has been shown to catalyze
the low-pressure (1 atm) hydrogenation of azobenzene to hydra-
zobenzene in near-quantitative yield.[66] Such a catalyst might
prove useful in further investigations of azocyanide reductions.

$$\text{Ph—N=N—Ph} \xrightarrow{4[H]} 2 \; \text{C}_6\text{H}_4\text{NH}_2 \quad (27)$$

$$\text{Cl—C}_6\text{H}_4\text{—N=N—CN} \xrightarrow{4[H]} \text{Cl—C}_6\text{H}_4\text{—NH}_2 + \text{H}_2\text{N—CN} \quad (28)$$
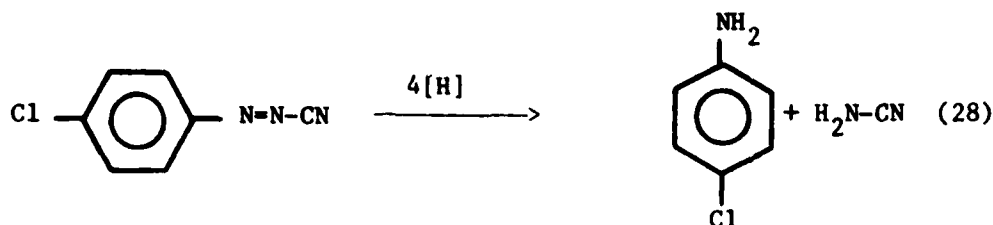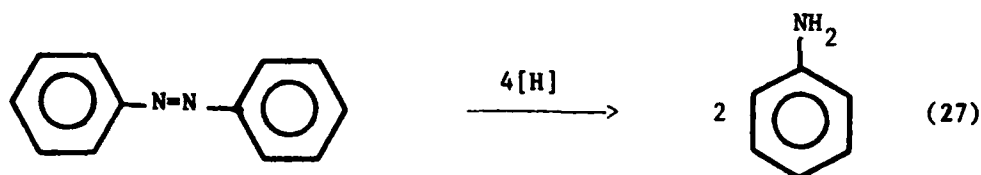
One attempt was made to reduce the cyano group of 4-chloro-phenylazocyanide with lithium aluminum hydride. Only an un-characterized red-brown tar was obtained from this reaction, rather than the desired phenylazomethylamine.

Finally, we wished to compare the reactivity of aryl-azocyanides with that of diazonium ions with respect to nucleo-philic aromatic substitution. Diazonium ions have been shown to undergo facile para-substitution by nucleophiles which are ion-paired with quaternary ammonium cations in non-polar media.[67] Although the azocyanide group could not be expected to have the same activating effect as a fully-charged diazonio group, its similarity to a nitro group in affecting the ^{13}C-nmr chemical shifts of aromatic carbons suggested that it too might be suffi-ciently electronegative to activate the aromatic ring towards nucleophilic substitution.

4-Bromobenzenediazonium tetrafluoroborate (5) undergoes
facile chlorine-for-bromine substitution, simply by stirring
in chloroform (30°C, 24 h) with 5 equiv of BTEAC. After reduc-
tion of the diazonio group (hypophosphorous acid catalyzed by
cuprous oxide), chlorobenzene was obtained in 71% yield.[67]
However, when the corresponding 4-bromophenylazocyanide (6) was
stirred in chloroform with 5 equiv of BTEAC at ambient tempera-
ture for 5 days, only a small amount of the 4-chlorophenylazo-
cyanide (8) substitution product could be discerned in the ^{1}H-nmr
spectrum of the reaction product. A similar result was obtained
when 6 was refluxed in chloroform-d with Stark's catalyst (1
equiv). After 4 days, the ^{1}H-nmr spectrum of the mixture indicated
only a negligible amount of the chloro-substitution product.

Since nitro is also known to be a particularly good leaving
group (as the nitrite ion) in aromatic substitutions,[68] similar
displacements were attempted on 4-nitrophenylazocyanide (11).
However, when 11 was reacted with 2 equiv of Stark's catalyst
under various conditions (21 h reflux in CH_2Cl_2; 21 h at 60°C
in toluene), again no reaction was observed.

A final attempt at aromatic substitution was performed
using a carbanion nucleophile. Makosza has demonstrated that
the carbanion from 2-phenylbutyronitrile (19) (generated in
situ by mixing with aq NaOH and a catalytic amount of BTEAC),
readily displaces the nitro group of 4-chloro-4'-nitrobenzophenone
(20) to form the ketonitrile (21) in 70% yield (equation 29).[69]

$$C_6H_5-\overset{\displaystyle C_6H_5}{\underset{\displaystyle C_2H_5}{CH}}-CN \;+\; Cl-\!\!\!\bigcirc\!\!\!-\overset{O}{\overset{\|}{C}}-\!\!\!\bigcirc\!\!\!-NO_2 \;\xrightarrow[\substack{\text{BTEAC}\\ \text{3 h 60°C}}]{\text{aq NaOH}}$$

$$\underline{19} \qquad\qquad\qquad \underline{20}$$

$$\text{(29)}$$

$$C_6H_5-\overset{\displaystyle CN}{\underset{\displaystyle C_2H_5}{\overset{|}{\underset{|}{C}}}}-\!\!\!\bigcirc\!\!\!-\overset{O}{\overset{\|}{C}}-\!\!\!\bigcirc\!\!\!-Cl$$

$$\underline{21}$$
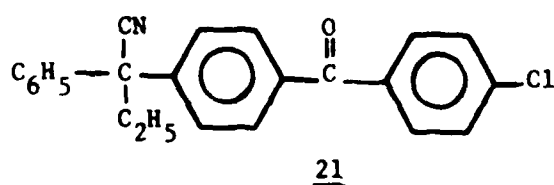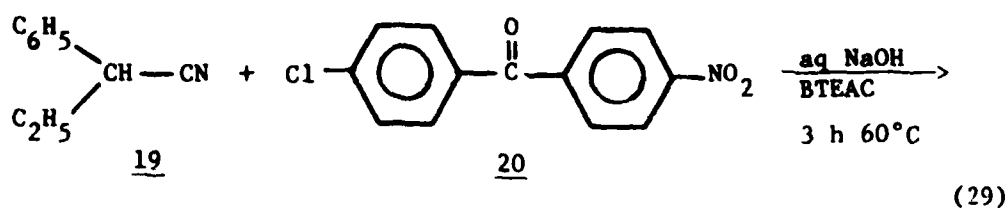
We postulated that a similar displacement might be possible using
$\underline{11}$ as the substrate (equation 30).

$$\overset{\displaystyle C_6H_5}{\underset{\displaystyle C_2H_5}{CH}}-CN \;+\; NC-N=N-\!\!\!\bigcirc\!\!\!-NO_2 \;\xrightarrow[\text{BTEAC}]{\text{aq NaOH}}$$

$$\underline{19} \qquad\qquad\qquad\qquad \underline{11}$$

$$\text{(30)}$$

$$NC-N=N-\!\!\!\bigcirc\!\!\!-\overset{\displaystyle C_6H_5}{\underset{\displaystyle CN}{\overset{|}{\underset{|}{C}}}}-C_2H_5$$
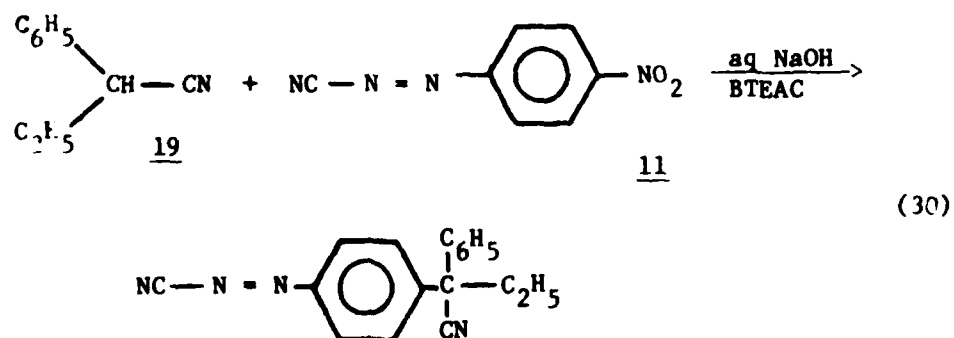
Accordingly, when 11 and nitrile 19 (1.6 equiv) were stirred with 50% aq (w/w) NaOH and a catalytic amount (3 mol-%) of BTEAC, an exothermic reaction occurred, and the mixture became brown and viscous. However, after stirring for 3 h at 60°C, the mixture had formed a dark tar, from which no product was characterized.

It seems clear from the failure of the experiments described above that although the arylazocyanides are suitably activated, nucleophilic addition to the cyano group rather than the aromatic ring invariably predominates.

IV. CYCLOADDITION REACTIONS OF ARYLAZOCYANIDES

A. Introduction

The reaction between diethyl azodicarboxylate and cyclo-
pentadiene (equation 31) was among the earliest examples of the
Diels-Alder or (2 + 4)-cycloaddition reactions to be discovered.
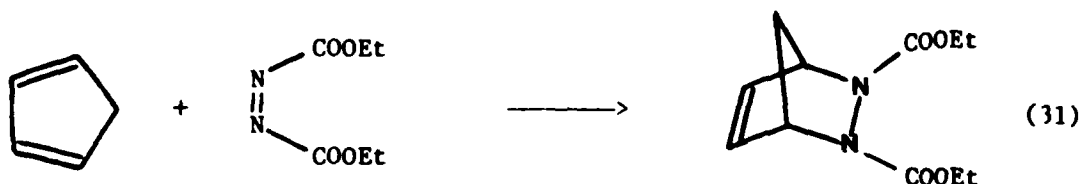
These cycloaddition adducts formed from an azo compound
and a diene are derivatives of the 1,2-diazine, or pyridazine
ring system (22, Figure 7). Thus, 23 is a reduced pyridazine,
specifically, 1,2-dicarbethoxy-1,2,3,6-tetrahydropyridazine.
Other types of reduced pyridazines include the 1,4,5,6-tetra-
hydropyridazines such as 24, and 4,5- and 1,6-dihydropyridazines
25 and 26, respectively. Finally, N-substituted but fully-
aromatic pyridazinium salts such as 27 are also known.[19,70]

Relatively few compounds containing the pyridazine ring
structure are known and of these, even fewer are biologically
active. Included among these are maleic acid hydrazide (28),
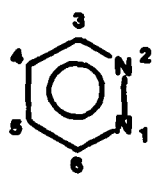
22

Pyridazine
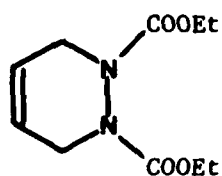
23

1,2-Dicarbethoxy-
1,2,3,6-tetrahydro-
pyridazine
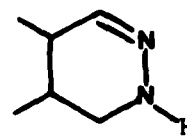
24

4,5-Dimethyl-
1,4,5,6-tetrahydro-
pyridazine
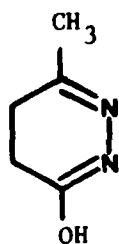
25

3-Methyl-6-hydroxy-
4,5-dihydropyridazine
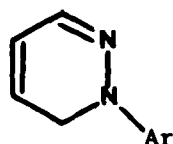
26

1-Phenyl-1,6-
dihydropyridazine
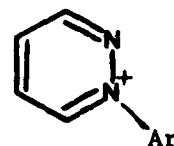
27

Pyridazinium
Salt

Figure 7. The Pyridazine Ring System and its Oxidation States.

which is a plant growth regulator,[71] and luminol (29), which is involved in the chemiluminescence mechanism of the firefly[72] (Figure 8). Other pyridazines have exhibited appreciable biological activity in such uses as herbicides, fungicides, anti-tumor, and anti-microbial agents.[73]
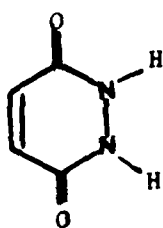
28

Maleic Acid Hydrazide
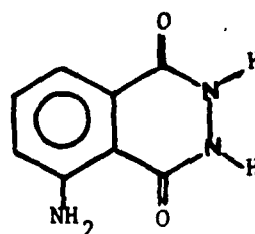
29

Luminol

Figure 8. Biologically-Active Compounds Containing the Pyridazine Ring Structure.

Although the Diels-Alder reaction is an important synthetic route for preparing various alkyl- or aryl-substituted pyridazines,[74] the types of stable azo compounds used as dienophiles have remained restricted to a disproportionately small number (Figure 9). By far the most widely used have been the stable azodicarbonyl compounds such as azodicarboxylate esters (30) and azodiaroyls (31). These form (2 + 4)-cycloaddition adducts with most conjugated dienes and some adducts with anthracene have also been reported. Several unstable azodicarbonyl compounds have
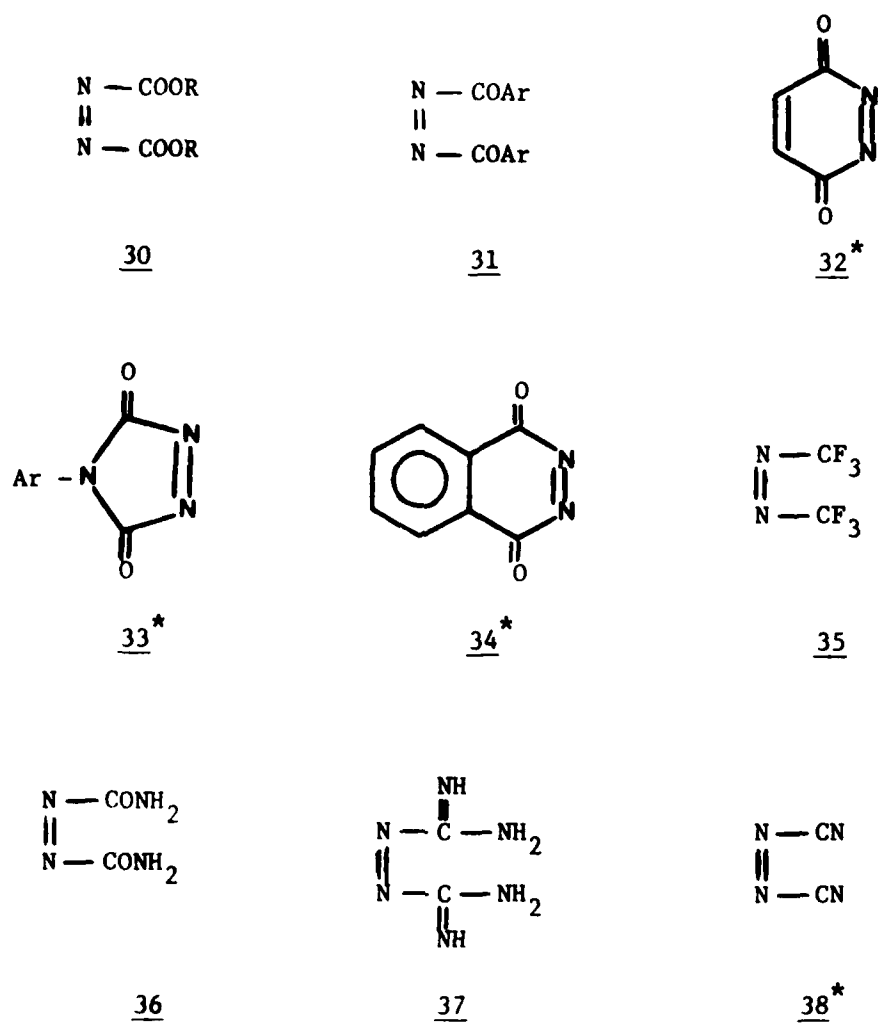
Figure 9. Azo Dienophiles (* indicates unstable compound).

been generated at low temperatures, and trapped in situ as their

cycloaddition adducts. These include pyridazine-3,6-diones (32),

triazoline-diones (33), and 1,4-phthalazinedione (34).[75] Certain

fluorinated azoalkanes (35) have been found to react with dienes

at elevated temperatures.[76] Finally, a small number of cyclo-

addition adducts have been prepared from azodicarboxamide[77] (36),

its corresponding amidine[78] (37), and the explosively unstable

azodicarbonitrile[79] (37).

There are numerous examples in the literature of (2 + 2)-

cycloaddition reactions between aromatic azo compounds and diphenyl-

ketene or diketene. Such reactions are known for azobenzene

and arylazocarboxylate esters.[47,80] Arylazocyanides have also

been shown to undergo such a (2 + 2)-cycloaddition reaction with

diphenylketene to yield a diazetidinone (39) (equation 32). This

product was later found to undergo a rather unusual thermal re-

arrangement to 40[48] (equation 33).

$$\underset{\substack{4-Cl-C_6H_4}}{\overset{CN}{\underset{N}{\overset{\|}{N}}}} \quad + \quad \underset{Ph}{\overset{O}{\underset{\|}{C}}}\underset{Ph}{\overset{\|}{C}} \quad \longrightarrow \quad \underset{4-Cl-C_6H_4}{\overset{Ph}{\underset{N}{\overset{NC}{\underset{N}{\bigtriangleup}}}}}\overset{Ph}{\underset{O}{}} \qquad (32)$$

39

$$(33)$$
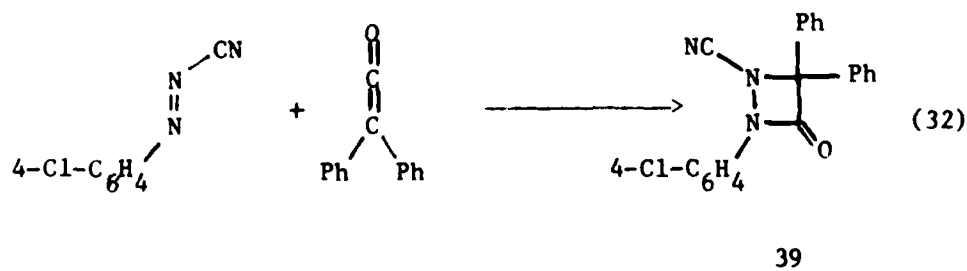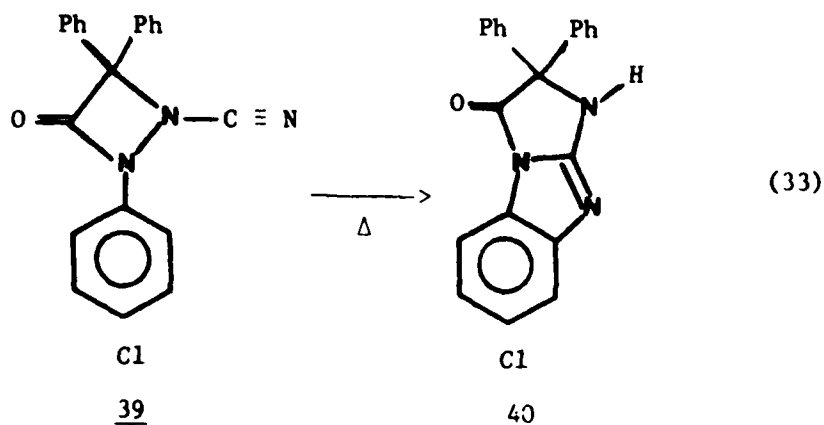
Significantly, however, an analagous <u>dienophilic</u> reactivity has not been observed for aromatic azo compounds. Both <u>cis</u>- and <u>trans</u>-azobenzene, for example, fail to react with cyclopentadiene.[81] 4,4'-Dinitroazobenzene reportedly forms a (2 + 4)-cycloaddition adduct with 2,3-dimethyl-1,3-butadiene at elevated temperatures in unspecified yield.[82]

Thus, to our knowledge, no general dienophilic reactivity has been reported for any azo compound containing an azo-bonded aromatic ring. The only such example found in the literature which resembles an aromatic azo dienophile is the unstable indazolone (<u>41</u>), formed from the <u>in situ</u> oxidation of indazolidone with lead tetraacetate (LTA) at low temperatures. The resulting azo intermediate forms a cycloaddition adduct (<u>42</u>) in unspecified yield with 1,3-butadiene[83] (equation 34).

Cycloaddition reactions of aryldiazonium ions themselves are even less general. This is surprising when one considers that facile (2 + 4)-cycloaddition reactions generally take place
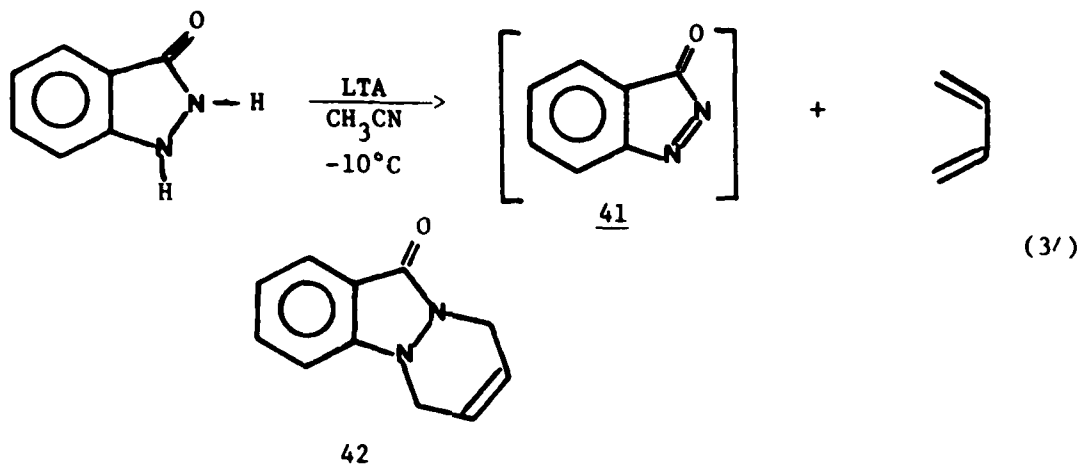
between a diene and a dienophile of differing electron density.[84,85]
Most common cycloaddition reactions involve an "electron-deficient"
dienophile and an "electron-rich" diene. Therefore aryldiazonium
ions, as fully charged species, and thus electron-deficient by
definition, might be expected to display potent dienophilic
activity in cycloaddition reactions.

This general reactivity pattern has not been realized.
Carlson, Sheppard and Webster have published the only report of
aromatic diazonium (2 + 4)-cycloaddition to date,[19] in which
various aryldiazonium hexafluorophosphate salts were reacted with
acyclic dienes. The dienophilic activity observed was far from
general: only the strongly electrophilic 4-nitrobenzenediazonium
ion afforded high yields of the 1,6-dihydropyridazine product (43).

Other substituted diazonium ions reacted satisfactorily only
with the highly activated 2,3-dimethyl-1,3-butadiene to afford
oxidation products (apparently formed in situ) of the 1,6-dihydro-
pyridazines, namely, the corresponding pyridazinium salts (44).
None of the diazonium ions surveyed reacted with the less-activated
1,3-butadiene. The results of these diazonium ion cycloaddition
reactions, as reported by Carlson, Sheppard, and Webster, are
summarized in Table 5.

B.   Cycloaddition Reactions of Arylazocyanides
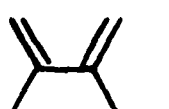
In view of the fact that aromatic azo compounds have not
been generally used as dienophiles, and considering the limited
reactivity of aryldiazonium ions themselves in this respect, we
felt that arylazocyanides might constitute a reactive and general
aryldiazonium ion equivalent.

When 4-chlorophenylazocyanide (8) was heated at ca. 100°C
with 2,3-dimethyl-1,3-butadiene (DMBD, 2 equiv) in a pressure
tube for 3 h, the (2 + 4)-cycloaddition adduct (46) was isolated
in 90% yield (equation 35). (The same reaction was carried out
with a larger excess, 5 equiv, of DMBD at ambient temperature
for 7 h, and afforded a nearly-identical yield of adduct 46).

Under similar conditions, 4-chlorophenylazocyanide afforded
analogous adducts with several other acyclic dienes (including
chloroprene), cyclopentadiene, and 1,3-cyclohexadiene. The

Table 5

Reaction of Diazonium Salts with Dienes[19]

Yield of Pyridazine, %

Diene	Product	H	p-Cl	p-F	p-NO$_2$
	(43)	--	--	--	73
	(44)	Trace	26	--	--
	(43)	--	--	--	79
	(44)	42	60	72	--

X =

$$\xrightarrow[100^\circ C]{3\ h}$$

(35)

8   **46**
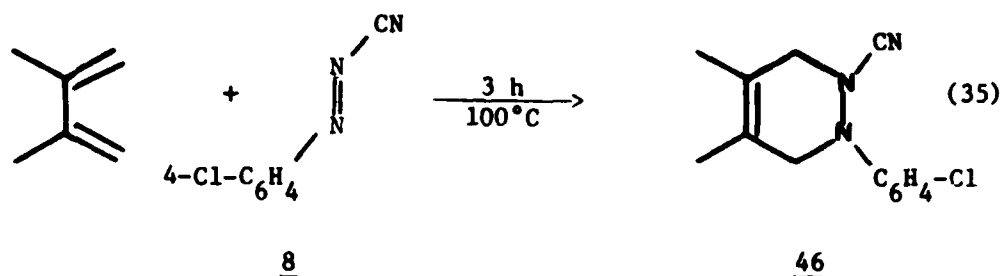
reactions of 4-methoxyphenylazocyanide (**10**) and 4-nitrophenyl-
azocyanide (**11**) were also investigated with these same dienes.
The results of these cycloaddition reactions are summarized in
Table 6.

The majority of the reactions were carried out in a 150 mm
(50-mL), thick-walled Carius tube to which had been fused a
Teflon high-vacuum valve.[86] The reactions were conducted in most
cases simply by mixing the solid azocyanide and liquid diene.
In many cases, the mixtures became dark and homogeneous as the
reactions proceeded. The products were normally isolated by
evaporation of the residual diene and chromatography of the
reaction residue on silica gel. The pyridazine products were
obtained as white to pale-yellow solids with melting points
generally in the range 50-100°C. The products were freely soluble
in most organic solvents, and insoluble in water. The ir spectra
exhibited a strong cyanide stretching vibration (2210-2216 cm^{-1}).

4-Methoxyphenylazocyanide (**10**) was, as expected, the least
reactive dienophile. Although it was clearly less reactive than

Table 6

Cycloaddition Reactions of 4-Substituted Arylazocyanides
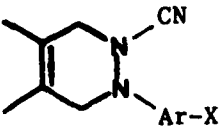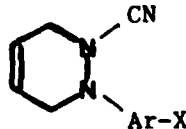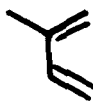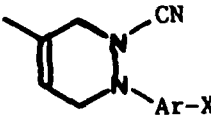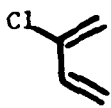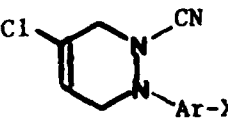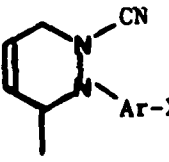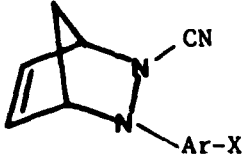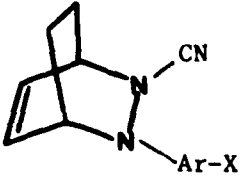
Diene	Product	% Yield[a], X =		
		OMe	Cl	NO_2
		70	90	94
		(45)	(46)	(47)
		No[b] Rxn	85	84
			(48)	(49)
		46	67[c]	55
		(50)	(51)	(52)
	(major isomer)	--	100[d]	--
			(53)	
		47[e]	100[f]	96[g]
		(8:1)	(4:1)	(2:1)
		(54)	(55)	(56)
	(major isomer)			

Table 6 (Continued)

| Diene | Product | % Yield X = | | |
		OCH$_3$	Cl	NO$_2$
		No Rxn	58 (57)	100 (58)
		No Rxn	43 (59)	26 (60)
	No Product Isolated	--	h	--

[a]Yields based upon arylazocyanide.

[b]Starting azocyanide recovered in 96% yield after 5 days.

[c]Trace amount of alternate regioisomer observed in ^{13}C-nmr.

[d]Major (10:1) regioisomer estimated by ^{13}C-nmr.

[e]Major (8:1) regioisomer. Composition estimated by ^{1}H-nmr peak heights and structure assigned by ^{13}C-nmr.

[f]Major (4:1) regioisomer, determined as in e.

[g]Major (2:1) regioisomer, determined as in e.

[h]Reaction with 4-chlorophenylazocyanide at ambient temperature resulted in a darkening of reaction mixture, with formation of black residue.

other azocyanides, it still displayed considerable reactivity
with several acyclic dienes.

4-Nitrophenylazocyanide (11) was, predictably, the most
reactive of the azocyanides surveyed. Its direct combination
with many dienes resulted in visibly exothermic reactions.
Unfortunately, this increased reactivity was sometimes manifested
not by enhanced yields of pyridazines, but by concurrent formation
of dark, tarry reaction by-products. These by-products were
generally immobile on solid chromatographic supports. This
type of behavior was observed during the reaction of 4-nitro-
phenylazocyanide with both isoprene and 1,3-cyclohexadiene.
The use of a cosolvent such as benzene, with dropwise addition
of an azocyanide solution to a stirred diene solution (rather
than direct combination) was only partially effective in reducing
this by-product formation. Temperature effects were not
investigated.

The reactions of arylazocyanides with cyclic dienes did not
proceed as readily as those with acyclic dienes in most cases,
and generally afforded reduced yields. 4-Chlorophenylazocyanide
displayed a distinctly reduced reactivity with cyclopentadiene,
a surprising result considering the favorable, cisoid conformation
of the diene. As stated previously, 4-methoxyphenylazocyanide
did not react with cyclic dienes. Of the arylazocyanides surveyed,
only 4-nitrophenylazocyanide displayed significant reactivity

toward cyclopentadiene, reacting with the latter exothermically and quantitatively at ambient temperature.

Although the yields of cycloaddition adducts obtained from 1,3-cyclohexadiene were relatively low, these yields generally exceeded those reported for the reaction of known azo dienophiles with this olefin. The reaction of diethyl azodicarboxylate and 1,3-cyclohexadiene, for example, results in high yields of a product from the competing intermolecular ene reaction (61), and only mediocre yields of the corresponding cycloaddition adduct[87] (equation 36). Similarly, diethyl azodicarboxylate affords an ene reaction product quantitatively when treated with cycloheptatriene.[88]

(36)

61
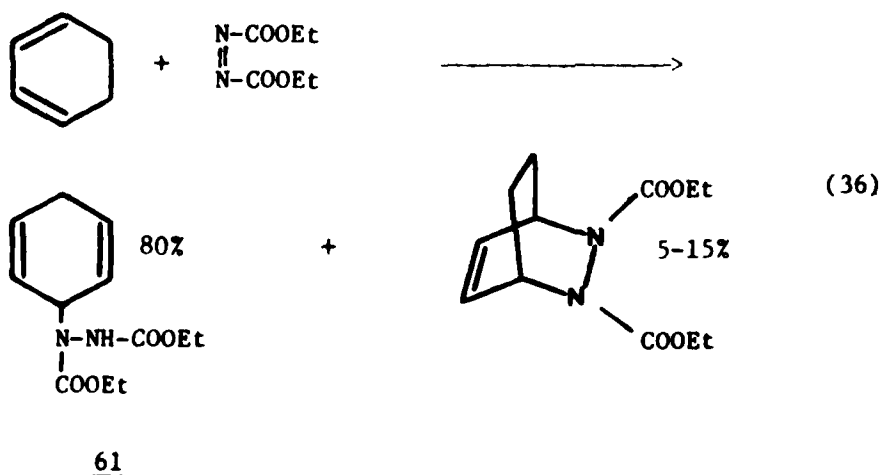
Gillis[89] has postulated that a delicate steric balance exists when using trans-azo dienophiles and dienes which are highly

substituted in the 1,4-positions. In the case of diethyl azo-
dicarboxylate, the difference of a single methylene unit between
cyclopentadiene and 1,3-cyclohexadiene is sufficient to alter
the preferred reaction from cycloaddition (97% yield) to ene
reaction (85% yield), respectively. The fact that in two cases
the arylazocyanides afforded greater cycloaddition yields than
diethylazodicarboxylate with 1,3-cyclohexadiene can probably be
attributed to smaller steric demands. In no case was any ene
reaction product isolated from the arylazocyanide reactions,
although reactions with cyclic dienes like cycloheptatriene,
which might favor such a reaction, were not attempted.

Since cis-dienophiles could be expected to encounter less
steric hindrance in a cycloaddition reaction, an enhanced reac-
tivity might be displayed by cis-arylazocyanides; however,
these reactions have not yet been carried out. Cycloaddition
reactions might conceivably be carried out by simply adding the
diene to the reaction mixture normally used for the phase-trans-
fer synthesis of the arylazocyanides. The first-formed cis-
isomer might be sufficiently reactive to undergo cycloaddition at
or near ambient temperatures, resulting in a one-step synthesis
for the pyridazine adducts. This potentially useful method is
currently under investigation by other members of the research
group.

Norbornadiene is known to react with a variety of dieno-
philes to afford cycloaddition products. Its reaction with

dimethyl azodicarboxylate in particular produces inter alia

an adduct which results from addition across the 2,6-position

of the diene.[90] The analogous reaction with an arylazocyanide

could conceivably afford either the 2,6-adduct (62), a simple

dipolar-addition product (63), or a product resulting from further

1,2-rearrangement of an intermediate carbonium ion (64)

(Scheme 2).

Accordingly, the reaction of 4-chlorophenylazocyanide with

norbornadiene (ca. 1 equiv) in chloroform-d (ca. 0.7 M in both

reagents) at ambient temperature was monitored by ^{1}H-nmr. Forma-

tion of any product in Scheme 2 would result in a decrease of the

aromatic:vinyl proton ratio, measured by integration. Over 10 h,

the initially red-orange solution darkened considerably, with

concurrent formation of insoluble, tarry, black solids on the

walls of the reaction tube. Notwithstanding this apparent

reaction, no change was observed in the ^{1}H-nmr spectrum of the

mixture over this period of time. Resonance signals due to both

starting materials remained clearly visible, with no appreciable

change in the aromatic:vinyl proton integral ratio. Moreover,

no new resonance signals were observed.

A final cycloaddition reaction was carried out between

4-chlorophenylazocarbonamide (16) and DMBD. The purpose of this

reaction was to determine whether or not the dienophilic activity

of the aromatic azo compounds is restricted to the arylazocyanides.

62

63

64
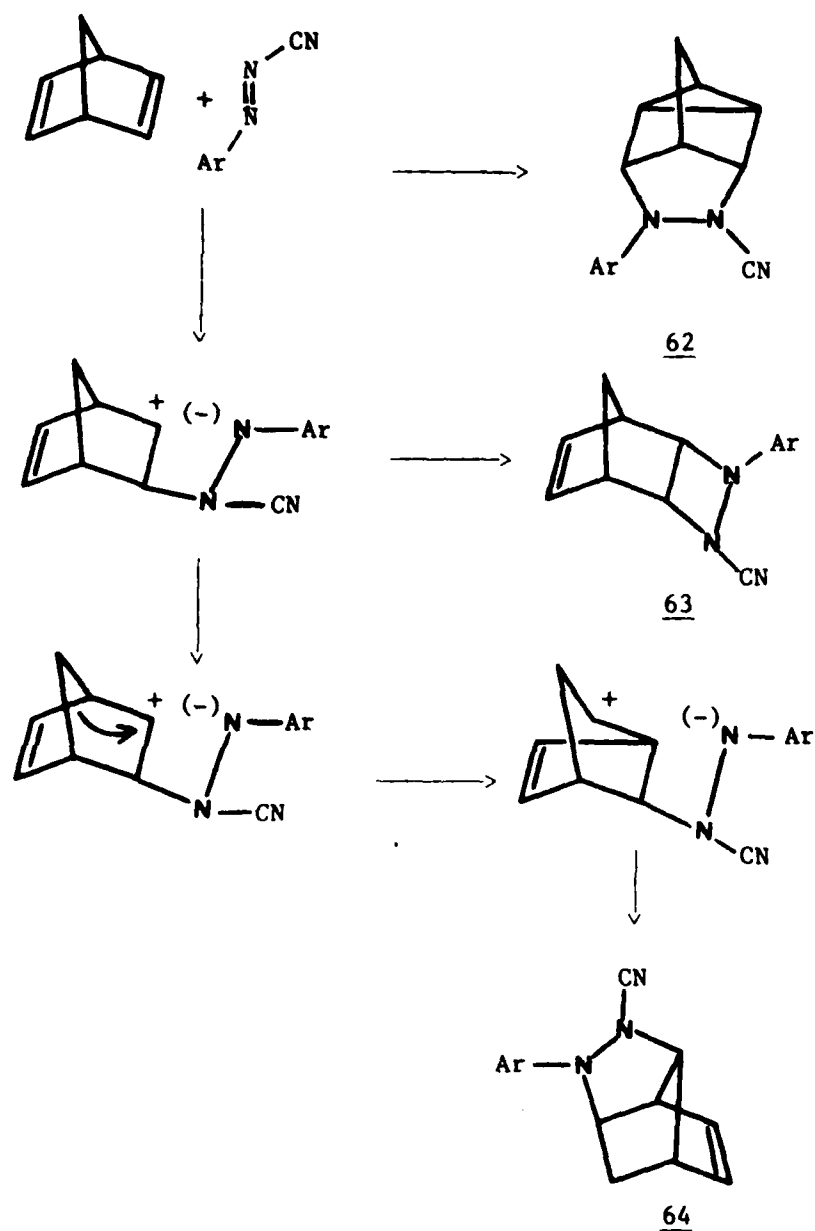
Scheme 2. Possible Reaction Pathways for the Addition of an Arylazoc   to Norbornadiene.

When 16 (obtained by aq acid-THF hydrolysis of the azo-cyanide) was heated for 6 h at 100°C with DMBD (4 equiv), the adduct (65) was obtained in 93% yield (equation 37). The fact that 16 also underwent facile cycloaddition suggests that

$$(37)$$
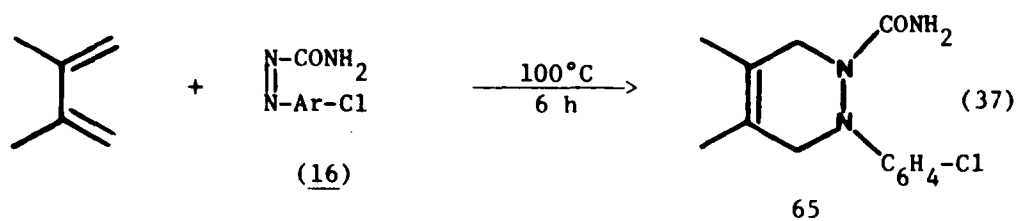
arylazosulfones ($ArN=N-SO_2Ar$) and the analogous arylazocarboxylate esters ($Ar-N=N-COOR$) would also be likely dienophiles. Since the latter can be easily prepared from arylhydrazine carboxylate esters by mild oxidation with a variety of agents,[91] the cyclo-addition reaction may eventually prove to be a very general reaction of unsymmetrical azo compounds.

C.   Structural Determination of Unsymmetrical Adducts

Obviously, the reaction between an unsymmetrical dienophile and an unsymmetrical diene can result in two possible regio-isomeric products. Such regioisomerism is possible in the reactions involving any unsymmetrical diene such as isoprene, chloroprene, and trans-piperylene (Figure 10). If more than one

A: R = Me
B: R = Cl
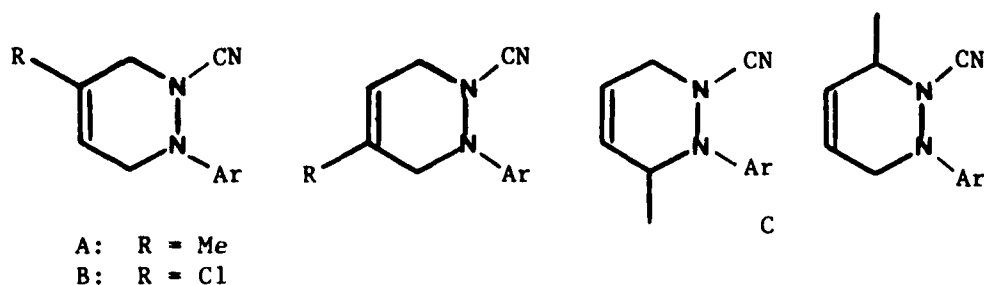
Figure 10. Possible Regioisomeric Pyridazines from Reaction with
Isoprene (A); Chloroprene (B); and trans-Piperylene (C).

product formed in any cycloaddition reaction, it would be necessary
to identify products and determine the percent composition of
mixtures.

The ^{1}H-nmr spectrum of all three isoprene adducts (50,
X = OMe; 51, X = Cl; 52, X = NO$_2$) showed only a broad pseudo-
singlet methyl group resonance near 1.85 ppm which was almost
invariant despite differences in the aromatic ring substituent,
(1.85, X = Cl; 1.86, X = OMe; 1.83, X = NO$_2$). On the other
hand, the ^{1}H-nmr spectrum of all three trans-piperylene adducts
(54, 55, 56) showed two overlapping doublets (J = 7) in the region
1.3-1.7 ppm. In each case, one doublet was greater in intensity
than the other, but overlap precluded exact integration. The
presence of these two distinct signals suggested that the trans-
piperylene adducts were actually mixtures composed of a major and

a minor regioisomer. (This conclusion was corroborated by the fact that two of these adducts failed to crystallize.)

Thus, ^{1}H-nmr spectroscopy alone did not permit conclusive structural assignment of the arylazocyanide adducts with either isoprene or trans-piperylene, although in the latter case an isomer mixture was indicated. A comprehensive ^{13}C-nmr spectral study of the cycloaddition adducts proved much more informative.

Our rationale for structural assignments based upon ^{13}C-nmr focused on the allylic carbons (carbons numbered 3 and 6, vide infra) of the 1,2,3,6-tetrahydropyridazine ring system. We had prepared adducts (45, 46, 47) from symmetrical 2,3-dimethyl-1,3-butadiene which had three different para-substituents on the ring. Several resonance forms for this ring system can be envisioned (Figure 11).
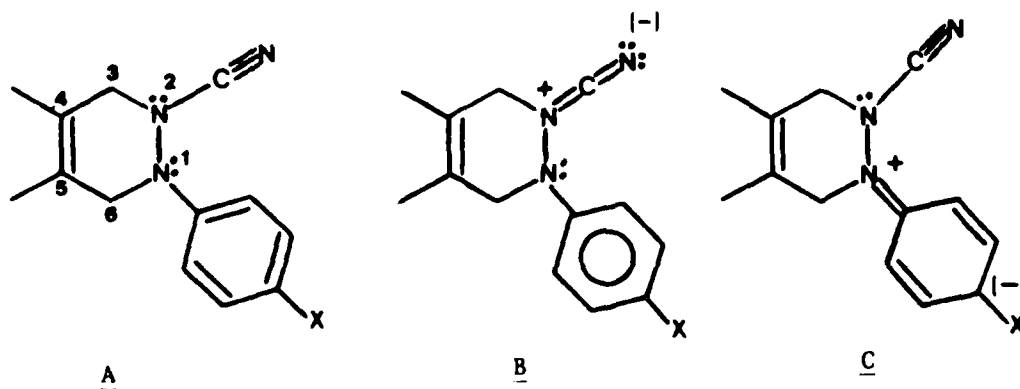
Figure 11. Resonance Forms of the 1,2,3,6-Tetrahydropyridazine Ring System.

As substituent X becomes more electron-withdrawing, resonance form $\underline{C}$ should become increasingly favored. This should cause a downfield shift of C-6 because of the increasing partial positive charge on N-1. As form $\underline{C}$ becomes more favored, form $\underline{B}$ should make less of a contribution, because of the adjacent positive charges on the nitrogens. Thus, electron-density on N-2 might be expected to increase as X becomes more electron-withdrawing, causing a corresponding upfield shift of C-3. Further, the cyanide resonance might also be expected to move upfield as form $\underline{B}$ becomes less favored, since the chemical shift of the central carbon in cumulene-type structures such as represented by $\underline{B}$ is found farther down-field than in nitriles.

Accordingly, the ^{13}C-nmr spectra were obtained; the assigned allylic, vinyl, and cyano chemical shift values are presented in Table 7 for the acyclic diene adducts. Complete ^{13}C-nmr data are listed individually with each compound in the Experimental Section.

As can be seen from a perusal of Table 7, one allylic carbon was shifted downfield and the other (along with the cyano group) upfield as X became more electronegative in the adducts $\underline{45}$, $\underline{46}$, and $\underline{47}$. In accordance with the above rationale, these resonances were assigned to positions C-6 and C-3, respectively, with C-6 (the allylic carbon adjacent to the aryl-substituted nitrogen) always appearing 4-6 ppm downfield from C-3.

Table 7

^{13}C-nmr Chemical Shifts of Pyridazines[a,b]
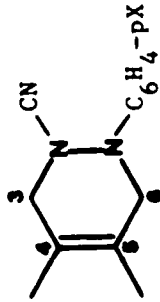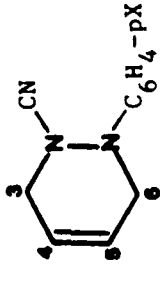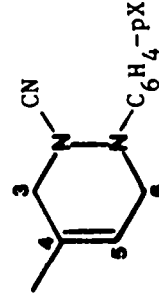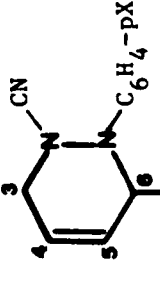
Product	Cpd No.	X	C-3	C-4	C-5	C-6	CN[c]
	45	OMe	49.7	122.2	123.3	53.9	114.6
	46	Cl	49.1	122.3	122.9	54.1	114.2
	47	NO$_2$	48.2	122.5	122.5	54.4	113.7
	--	OMe	--	--	--	--	--
	48	Cl	45.2	122.8	123.8	50.9	114.0
	49	NO$_2$	44.6	122.8	123.4	51.3	not obsd
	50	OMe	49.5	131.8	116.7	50.2	not obsd
	51	Cl	48.9	131.4	116.7	50.5	114.1
	52	NO$_2$	48.1	131.0	116.8	50.8	113.7
(major isomer)	54	OMe	45.2 (t)	123.4 (d)	128.5 (d)	56.3	not obsd
	55	Cl	44.6 (t)	122.8 (d)	128.4 (d)	56.4 (d)	not obsd
	56	NO$_2$	44.0 (t)	122.3 (d)	128.5 (d)	56.8 (d)	not obsd

72

Table 7 (Continued)

[a] Chemical shifts in ppm downfield from TMS.

[b] (m) indicates multiplicity of signal observed in off-resonance-decoupled spectrum (where applicable).

[c] See Note 92.

Next, by comparing the chemical shifts of the isoprene adducts
(50, 51, and 52) with those of the 4,5-dimethyl adducts, the
resonance position of C-3 was found to remain nearly constant,
while C-6 was shifted upfield. This observation is consistent
with methyl group substitution at C-4, a position which is pseudo-
para to the aromatic ring, as illustrated. Interestingly, the
^{13}C-nmr spectrum of the chloro-substituted isoprene adduct (50)
showed additional weak signals in the allylic and methyl regions,
indicating a trace of the other regioisomer (5-methyl)
present in this product. However, since ^{13}C-nmr signal intensi-
ties in proton-decoupled spectra cannot necessarily be quantita-
tively correlated with the number of carbons responsible for the
signal,[93] no numerical estimate of the isomer ratio can be made.
The 4-methyl isomer probably predominates since separate methyl
resonances are not seen in the ^{1}H-nmr. No minor isomer signals
are visible in the spectra of the other isoprene adducts.

The structure of the major regioisomers formed with trans-
piperylene (54, 55, and 56) was determined in an analogous manner;
methyl substitution at C-6 causes a downfield shift of 5-6 ppm
for both C-5 and C-6. ^{13}C-nmr resonance signals for nearly all
carbon atoms in the minor regioisomer can also be distinguished
in the spectra, and were also correlated with appropriate chemical
shifts. The isomer assignments for the trans-piperylene adducts
were further confirmed by their off-resonance-decoupled spectra.

In the case of the trans-piperylene adducts, the isomer ratio
could also be estimated from the ^{1}H-nmr spectra, since signals
for two distinct methyl groups were visible. The overlap of the
signals prevented any exact comparison by proton integration.
However, manual measurements of peak areas indicated the isomer
ratios to be approximately 2:1 (X = NO_2); 4:1 (X = Cl); and 8:1
(X = OMe).

The major regioisomer of the adduct (53) formed in the reac-
tion between 4-chlorophenylazocyanide and chloroprene corresponded
to that of the isoprene compounds; the ^{13}C-nmr spectrum also
indicated a small amount of the alternate regioisomer.

D.   Regiochemistry and Mechanism

It is often difficult to rationalize the regiochemical out-
come of cycloaddition reactions involving either an unsymmetrical
diene or dienophile. In many cases, cycloaddition reactions
involving unsymmetrical components proceed with a high degree of
regiospecificity, often forming a single product.[94] To account
for these results, a dipolar mechanism, or transition state, has
often been invoked, in which bond formation is "directed" by the
most probable polarities of both the diene and the dienophile.
This type of "dipolar mechanism" is illustrated in Figure 12 for
the reactions of trans-piperylene with nitrosobenzene (66),
N-sulfinyl tosylamide (67), and sulfonylimine 68, all of which
afford only a single product.[95]
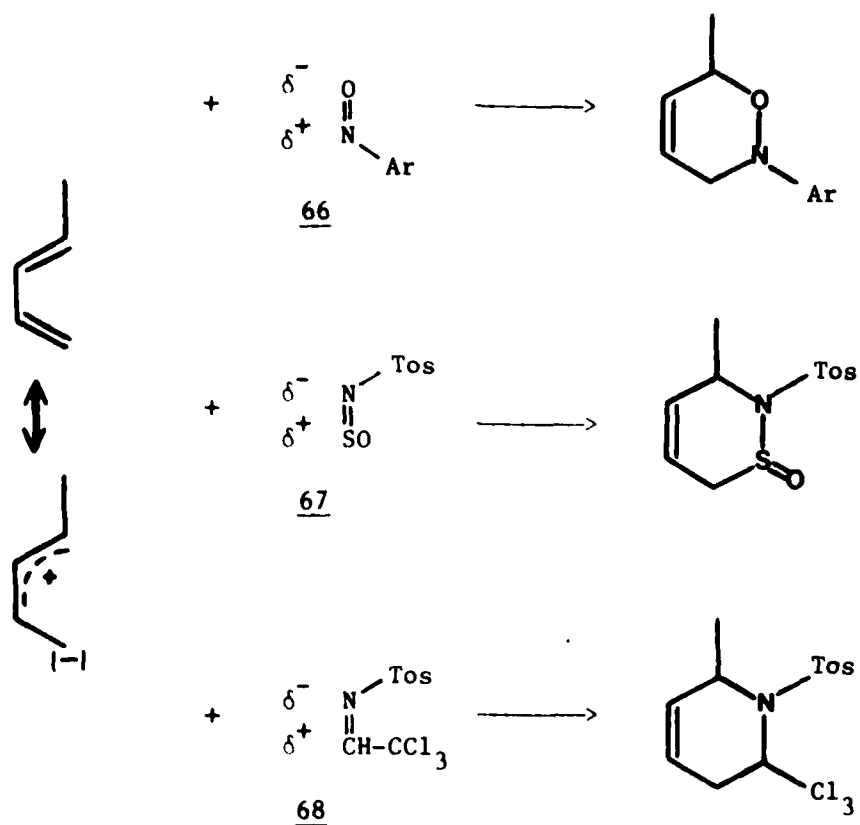
Figure 12. Dipolar Orientation Mechanism for Unsymmetrical
Cycloaddition Reactions.

The assignment of dipoles for dienophiles such as <u>66</u>, <u>67</u>,

and <u>68</u>, in which one atom is clearly more electronegative than

the other, is reasonably straightforward and unequivocal. How-

ever, the assignment of partial dipoles becomes more difficult

in the case of the arylazocyanides, in which both unsaturated

centers are nitrogen atoms. Further, the molecule is a completely conjugated system, in which resonance interactions can play a significant role in determining the preferred orientation.

We have found that Hammett-type inductive constants can be used to estimate the dipolar orientation of the arylazocyanides. These constants were determined for various substituted phenyl groups by Taft,[96] and are listed (along with that of the cyano group) in Table 8.

Table 8

Inductive Constants (σ_I) for para-Substituted Phenyl Substituents[96]

Substituent	σ_I (para)
-CN	+0.52
$-C_6H_4OMe$	-0.12
$-C_6H_4Cl$	+0.27
$-C_6H_4NO_2$	+0.82

A positive value of σ_I indicates electron-withdrawing character, and a negative σ_I-value corresponds to electron-donating character. Thus, in the case of 4-methoxyphenylazocyanide, the cyano-substituted nitrogen will possess the lesser electron density, favoring bond formation in the orientation shown (equation 38). And since

$$\text{(38)}$$
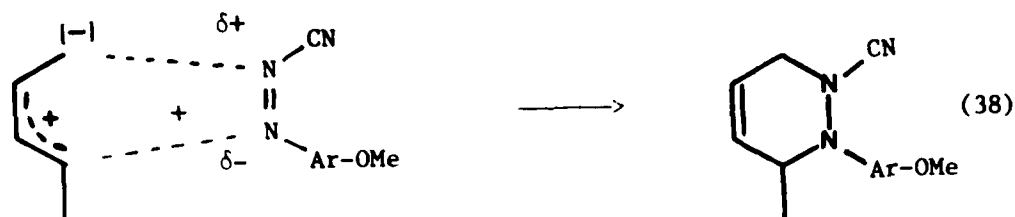
the difference between the σ_I-values for the cyano group and the
substituted phenyl group is greatest in this case (+0.52 versus
-0.12), the methoxy-substituted adduct should show the highest
degree of regiospecificity. As indicated previously, the estima-
ted ratio was 8:1 in favor of this regioisomer.

With 4-chlorophenylazocyanide, the dipolar orientation remains
the same, but the difference between σ_I-values is smaller. The
regiospecificity should therefore decrease, and this is reflected
in an isomer ratio of 4:1 in favor of the same isomer.

Finally, the σ_I-value for nitro-substituted phenyl indicates
that this group now exerts a stronger electron-withdrawing effect
than the cyano group. In strictly inductive terms, this would
result in an opposite dipolar orientation for 4-nitrophenyl-
azocyanide, presumably favoring formation of the opposite regio-
isomer (equation 39). This "crossover" is not observed; the isomer
depicted in equation 38 remains the major product. Nevertheless,
the regiospecificity is greatly diminished: the estimated isomer
ratio is 2:1.

$$(39)$$
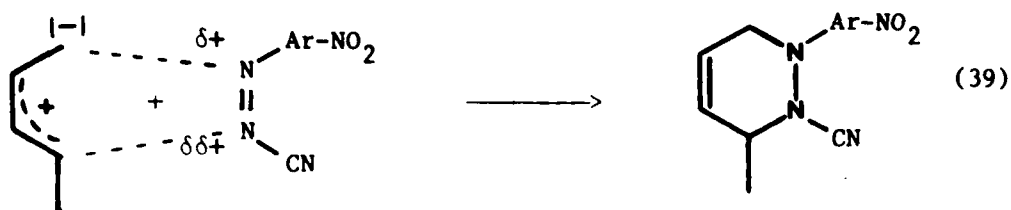
This simple model, based on Hammett-type inductive constants, seems to account for the trend in regiospecificity, and may be of broader applicability.

Cycloaddition reactions involving unsymmetrical dienophiles often display less regiospecificity with isoprene than with pipery-lene.[97] Obviously, such was not the case in the reactions between arylazocyanides and isoprene. The observed regiospecificity with isoprene thus appears anomalous, although the regioisomers obtained can again be correlated (with the exception of the nitro-substi-tuted adduct) with the preferred orientation of both the diene and the azocyanide (equation 40).

$$(40)$$
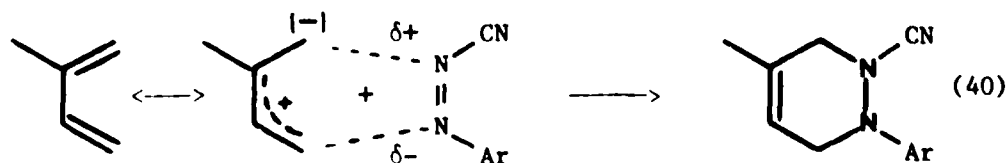
The reaction between 4-chlorophenylazocyanide and chloro-
prene also displayed a high degree of regiospecificity, although
the dipolar structure for the diene shown above (equation 40)
should be less stable for chloroprene than for isoprene.

E. Arylazocyanides and Aryldiazonium Ions: Reactivity
    Comparison

It is significant to note that the dienophilic activity of
the arylazocyanides exceeds that reported by Carlson and coworkers
for the corresponding aryldiazonium ions.[19] This result is rather
surprising, since the full positive charge on the diazonium ion
should make it a potent dienophile.

It must be noted, however, that the diazonium ion cyclo-
additions referred to above were conducted in acetonitrile sol-
ution. In such a polar system, the electron-deficiency of the
diazonio group is probably reduced by extensive solvation. Thus,
we fully expected that if similar cycloaddition reactions were
attempted in a non-polar solvent such as chloroform or dichloro-
methane, the solvation would be weaker and the dienophile more
reactive. Notwithstanding this attractive rationale, when cyclo-
addition reactions were attempted using solutions of diazonium
chlorides in chloroform or dichloromethane, only intractable red
oils were obtained.[98]

The fact that arylazocyanides are excellent dienophiles,
and that aryldiazonium ions seem to be dienophilic only in polar
solvents, suggests that the formation of a "pseudo-azo" compound

(69) via solvent interactions may be a prerequisite for diazonium
ion cycloaddition. This possibility is formulated for acetonitrile
in equation 41.

$$Ar-N{\equiv}N: \quad \longleftrightarrow \quad Ar-\ddot{N}{=}N: \quad + \quad NC-CH_3 \quad \longrightarrow$$

(41)
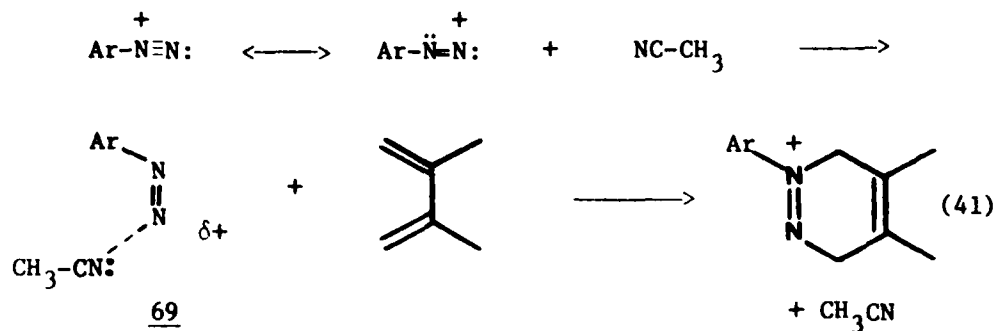
Such a reaction sequence is tantamount to "Lewis-base-catalysis"
of a cycloaddition reaction, in which the electron density of the
dienophile must be increased in order for it to react. This
intriguing concept is obviously antithetical to currently-accepted
notions concerning these reactions, and must bear the scrutiny of
further investigation.

F.   Kinetic Studies

The observation that 4-chlorophenylazocyanide also reacted
smoothly with 2,3-dimethyl-1,3-butadiene (DMBD) over 7 h at
ambient temperature prompted us to investigate the kinetics of
this particular reaction. Since the arylazocyanides represented
a new dienophilic family, we were interested in comparing the

activation parameters for cycloaddition with those of other
dienophiles.

Kinetic parameters were determined by use of variable-
temperature [1]H-nmr spectroscopy. Measurements were based on the
fact that the vinyl protons of DMBD become allylic protons in
the adduct. The large chemical shift difference between the
resonance positions of these protons in DMBD and adduct (4.95
and 3.77, respectively) permitted facile integration of their
separate resonance signals (Figure 13). And since the number of
protons responsible for each signal was the same (4) in both
diene and product, proton integration provided a direct measure-
ment of the relative concentrations of both with time. These
integral values could be converted to concentrations simply by
relating the initial integral value (at t = 0) of the diene vinylic
protons to the known initial concentration of diene in the reac-
tion mixture.

The detailed experimental procedures and calculations used
for these kinetic studies are described in the Experimental
Section. Raw data is tabulated in the Appendix.

The second-order rate constants for the reaction between
DMBD and 4-chlorophenylazocyanide in chloroform-d were determined
at 26°, 37°, and 45°C. Graphic plots of product concentration/
DMBD concentration versus time were linear at all three temperatures
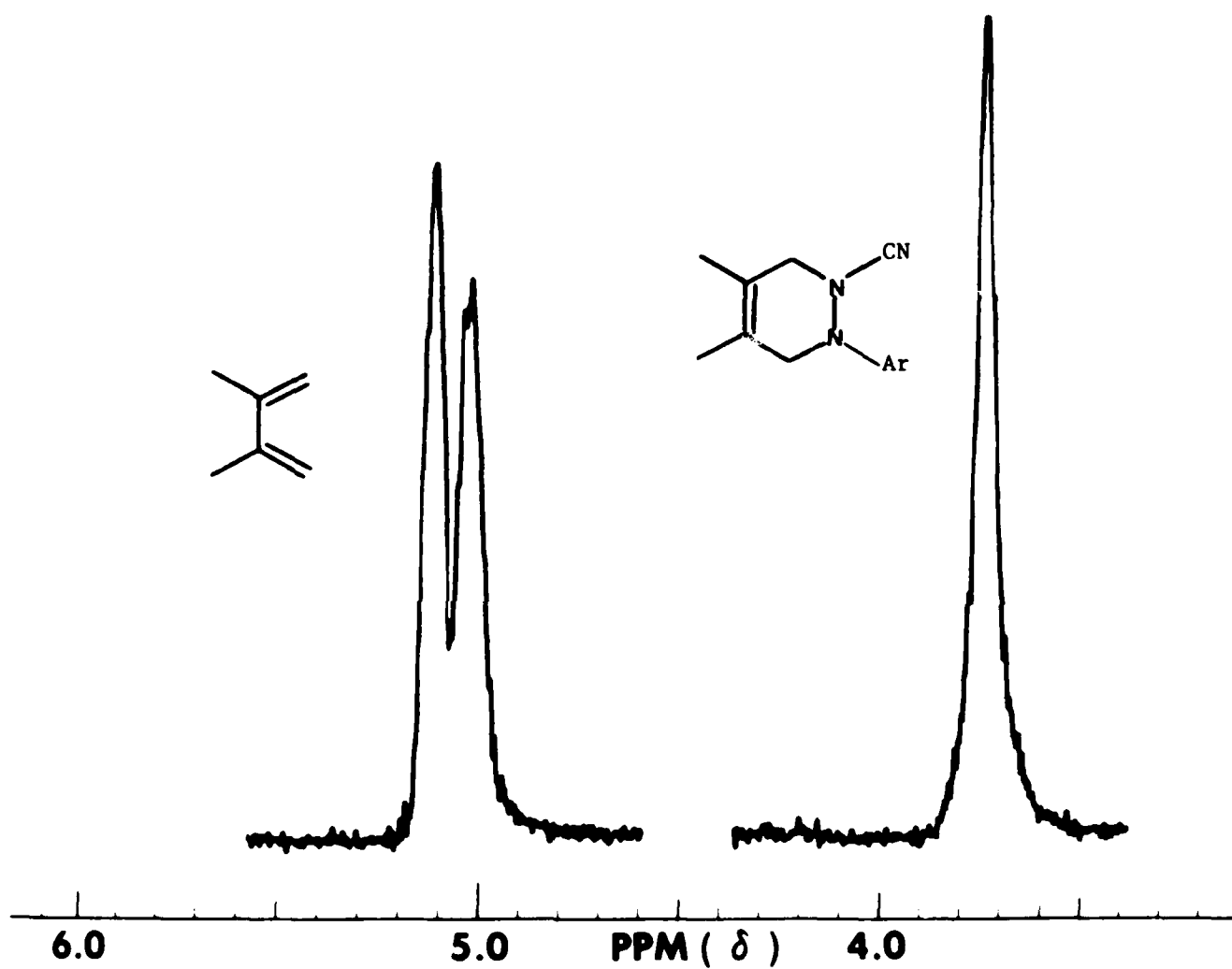
Figure 13. ^{1}H-nmr of 2,3-Dimethyl-1,3-butadiene Vinyl Protons and Adduct Allyl Protons.

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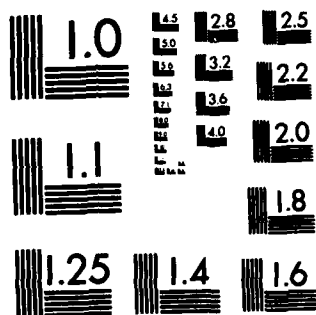
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through at least two half-lives, and linear correlation coeffi-
cients of 0.9990 or better were obtained in all cases (Figure 14).

The Arrhenius activation energy and frequency factor were
determined in the usual manner: a plot of log (rate constant)
versus 1/T yielded a straight line with a linear correlation
coefficient of -0.998. The rate constants, along with the derived
activation parameters, are listed in Table 9.

Table 9

Rate Constants and Activation Parameters

°C	$k_2 \times 10^4$ $(M^{-1}sec^{-1})$	ΔE^* (kcal/mol)	log A	ΔS^* (e.u.)
26	1.08			
37	2.92	15.5	7.36	-26.9
45	5.04			

Both the second-order kinetics and the fairly large negative
value for the entropy of activation are consistent with a con-
certed cycloaddition reaction. A comparison of the activation
parameters with those measured for other cycloaddition systems
is shown in Table 10. It is apparent that the reactivity of
4-chlorophenylazocyanide compares very favorably with that of
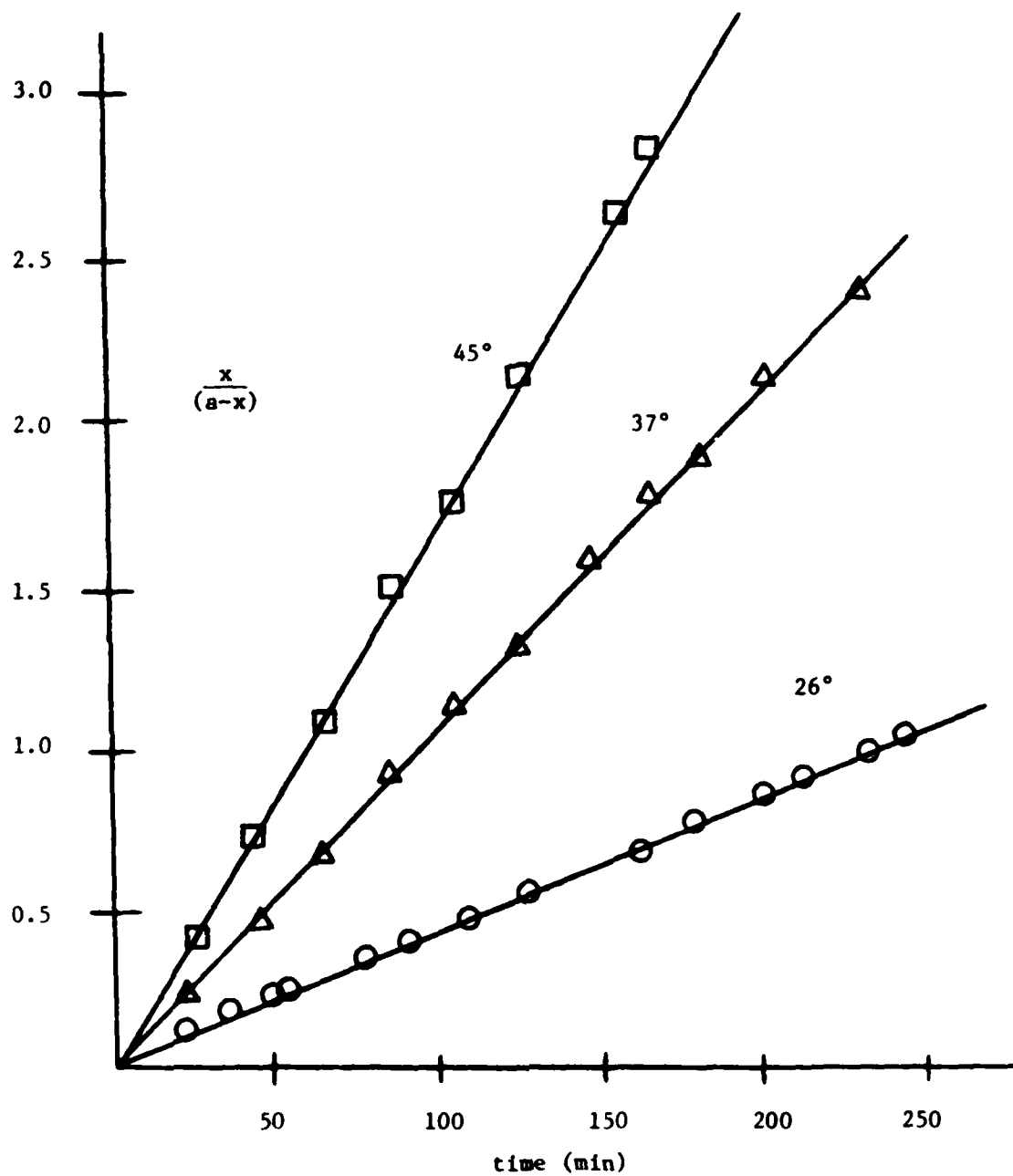
Figure 14. Second-Order Kinetics of Cycloaddition Reaction Between 4-Chlorophenylazocyanide and DMBD.

Table 10

Activation Energies and Entropies for Various Cycloaddition Reactions

Dienophile	Diene	E^* (kcal/mol)	log A	S^* (e.u.)	Ref
trans-4-Cl-Ar-N=N-CN	2,3-Dimethyl-1,3-butadiene	15.5	7.36	-26.9	this work
trans-Ph-C-CH=CH-C-Ph (O, O)	2,3-Dimethyl-1,3-butadiene	15.9	7.46	-26	99
trans-NC-CH=CH-CN	2,3-Dimethyl-1,3-butadiene	17.8	6.80	-30	99
Maleic Anhydride	1,3-butadiene	11.7	--	--	100
trans-Ph-C-N=N-C-Ph (O, O)	Cyclopentadiene	9.0	--	--	101
trans-EtOOC-N=N-COOEt	Cyclopentadiene	12.3	--	--	81

other strong dienophiles; the similarity with trans-1,2-dibenzoyl-
ethylene is particularly striking.

G. Reactions of 1-Aryl-2-Cyano-1,2,3,6-Tetrahydropyridazines

As with the arylazocyanides, we also investigated the
reactivity of the pyridazine cycloadducts toward both catalytic
and metal hydride reduction, along with hydrolysis of the cyano
group. The adduct from 4-chlorophenylazocyanide and DMBD (46)
was chosen as the model compound for these exploratory reactions.

When 46 was refluxed in 15% aq KOH for 24 h, the correspond-
ing carbonamide (65) was obtained in 93% yield (equation 42).
As stated previously, 65 was also obtained by the direct cyclo-
addition of 4-chlorophenylazocarbonamide with the same diene;
the two compounds were identical in every respect. The carbona-
mide could be prepared in similar yield by acidic hydrolysis
(10% aq HCl, reflux 24 h).

$$\text{(42)}$$
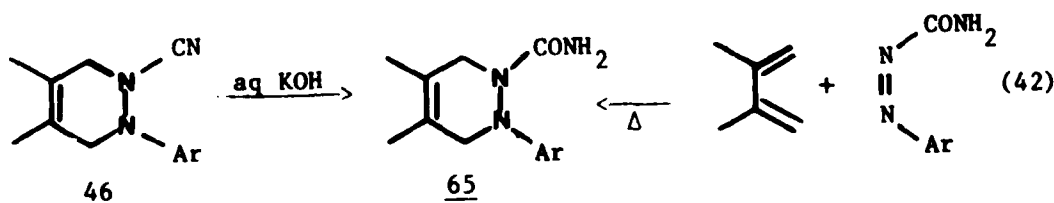
Apparently 65 is resistant to further hydrolysis. Extending
the basic hydrolysis reaction time of 46 to three days resulted
simply in a quantitative yield of 65.

Cycloaddition adducts derived from azodicarboxylate esters and various dienes generally undergo facile catalytic hydrogenation to the fully-saturated ring system. For example, when the cycloadduct of diethyl azodicarboxylate and 2,3-dimethyl-1,3-butadiene was hydrogenated at 56 psi over 10% Pd/C catalyst in ethanol, the saturated product was obtained in 84% yield.[102] However, when 46 was hydrogenated in a single reaction under similar conditions, none of the corresponding saturated cyclo-adduct was isolated. Instead, the reaction afforded a yellow oil whose ir, [1]H-nmr, and ^{13}C-nmr spectra were consistent with the formamide (70) (equation 43). Such a product presumably

(43)

46   70
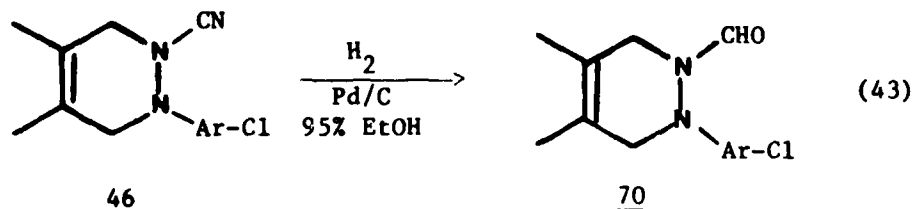
arises from partial hydrogenation of the cyano group to an imine intermediate, which then undergoes hydrolysis in situ to the formamide. Such behavior is known for the reduction of nitriles in several catalyst-solvent systems.[103] Apparently, under these relatively mild conditions, the cyano group is more easily reduced than is the tetra-substituted and sterically-hindered carbon-carbon double bond.

Although spectral results were generally in agreement with structure (70), an acceptable elemental analysis was not obtained. Thus, 70 must be regarded as only a tentative structural assignment. The product also tended to darken over a period of days.

Finally, a single attempt to reduce 46 to a primary amine with lithium aluminum hydride proved unsuccessful. The product mixture (yellow oil) obtained exhibited an ammoniacal odor, was basic to wet litmus,and contained at least three components as judged by tlc analysis. This mixture was not further characterized.

V. EXPERIMENTAL SECTION

Melting points (mp) were recorded on a Thomas Hoover capillary melting point apparatus using Kimax soft glass tubes, and are corrected. Infrared (ir) spectra were recorded on a Perkin-Elmer Model 267 Diffraction Grating Spectrophotometer, and were calibrated against both the 2851 cm^{-1} and 1601 cm^{-1} bands of polystyrene. Spectral bands are reported in reciprocal centimeters (cm^{-1}). Proton nuclear magnetic resonance (^{1}H-nmr) spectra were recorded on a Varian Associates Model A-60A Analytical NMR Spectrometer as ca. 10% solutions in chloroform-d unless otherwise noted. Variable-temperature kinetics experiments were carried out on the same instrument equipped with a Varian Model 6040 Variable Temperature Controller. Chemical shifts are reported in parts per million [ppm (δ)] downfield from internal tetramethylsilane (TMS). Coupling constants (J) are reported in Hertz (Hz). Data are reported in the following order: chemical shift, spin multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet; Ψ = pseudo), integration, coupling constant, and interpretation. Carbon-13 nuclear magnetic resonance (^{13}C-nmr) spectra were recorded on a JEOL JNM-PS-100 High Resolution NMR Spectrometer equipped with a Nicolet Instrument Corporation computer. Chloroform-d was used as solvent and provided an

internal deuterium lock. ^{13}C-nmr spectral data were obtained in the ^{1}H-fully-decoupled mode unless otherwise indicated. Carbon chemical shifts are reported in parts per million [ppm (δ)] downfield from internal TMS. In cases where off-resonance-decoupled (ord) carbon spectra were obtained, spin multiplicity is reported as in ^{1}H-nmr spectra. ^{13}C-nmr data for individual pyridazine (cycloaddition) products are reported in accordance with the carbon numbering system shown in Table 7, and the structures below:
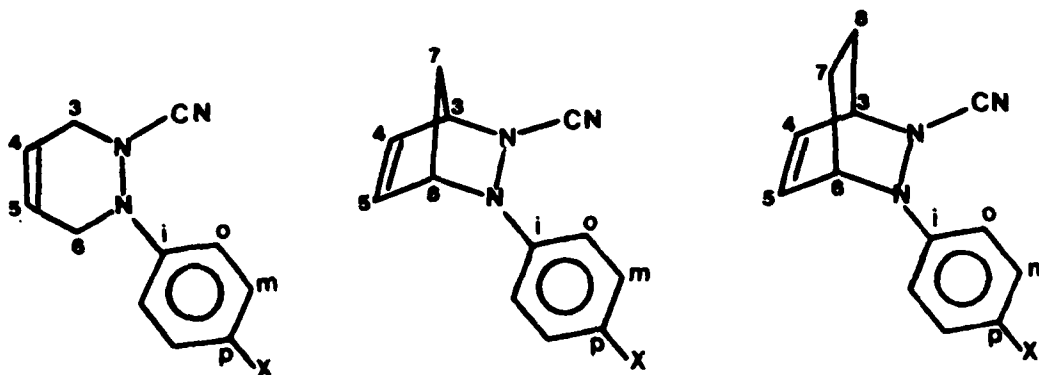
Combustion analyses were performed by Dr. Franz Kasler of The University of Maryland. Mass spectral (MS) data were obtained using a Finnegan Model 3200 Gas Chromatograph-Mass Spectrometer (GC-MS) equipped with a Finnegan Model 6000 Data Center using a 5' x 0.079" 3% OV-1 on 60-80 mesh NAW Chromosorb Q column.

Preparative chromatography columns were packed with either activated alumina (80-325 mesh, MCB) or silica gel 60 (70-230 mesh, E. Merck). Thin layer chromatography (tlc) was carried out on plates made by dipping microscope slides into a dichloromethane slurry of either tlc-grade alumina or silica gel, and then allowing the plates to air dry.

Gas chromatographic analyses (glpc) were conducted using a Varian Associates Model 920 analytical gas chromatograph equipped with a thermal conductivity detector and either a 5' or 10' x 0.25" 10% SE-30 on 60-80 mesh NAW Chromosorb P column at a flow rate of ca. 60 ml/min of helium. Yields obtained by glpc were determined by means of an internal standard, and are corrected for detector response factor.

The following reagent-grade solvents were used as obtained without further purification unless otherwise indicated: dichloromethane (Aldrich or MCB); methanol (MCW or Fisher); benzene, toluene, and chloroform (Fisher). Tetrahydrofuran (THF) was distilled from sodium-benzophenone ketyl immediately prior to use. Potassium cyanide was dried in vacuo (0.2-1.0 torr) at 90-100°C for 48 h and powdered prior to use. The aryl-diazonium tetrafluoroborate salts were reprecipitated from acetone-ether, and air-dried for ca. 2 h immediately prior to use. 18-Crown-6 was synthesized by the method of Gokel et al.[104] Tetramethylammonium chloride (TMAC, Eastman and Aldrich), and

benzyltriethylammonium chloride (BTEAC, Eastman) were dried

in vacuo (0.2-1.0 torr) at 60-90°C for at least 2 h before use.

Tricaprylylmethylammonium chloride (Stark's catalyst, General

Mills, Kankakee, MI) was used as obtained. Deuterated solvents

were obtained from Merck Ltd., Canada, and contained 99.8 atom-%

deuterium in the indicated positions. All other solvents and

reactants were of the best commercial quality available, and

were used without further purification unless otherwise

indicated. Quaternary ammonium salts, KCN, and 18-crown-6

were stored in a desiccator containing Drierite. Aryldiazonium

tetrafluoroborate salts were stored in the dark in a desiccator

containing P_2O_5.

Synthesis of cis-Arylazocyanides from Aromatic Amines in Aqueous Acid: General Procedure

A 500-mL, 3-necked flask fitted with a mechanical stirrer

and an addition funnel was charged with the appropriate aromatic

amine (0.1 mol), concentrated HCl (45 mL) and water (45 mL).

This mixture was mechanically stirred and cooled in an ice-water-

salt bath to ca. -5°C. Diazotization was accomplished by drop-

wise addition (10 min) of an ice-cold aq solution of $NaNO_2$

(6.90 g, 0.10 mol in 40 mL water). The diazotized solution

was then filtered into a 500-mL, 3-necked flask fitted with a

magnetic stirring bar which had been pre-cooled to -10°C in a

solid carbon dioxide-ethanol bath. An ice-cold solution of KCN

(13.0 g, 0.2 mol in 25 mL water) was then added dropwise over 5

min, the mixture being well-stirred. The final mixture remained

acid to litmus. The orange-colored precipitate was filtered off,

washed with ice-cold water, and spread on filter paper to air-dry.

Preparation of cis-4-Bromophenylazocyanide from 4-Bromoaniline in Aqueous Acid

A 250-mL, 3-necked flask fitted with a mechanical stirrer

and an addition funnel was charged with 4-bromoaniline (8.60 g,

0.05 mol), conc HCl (22.5 mL) and water 22.5 mL). The stirred,

heterogeneous mixture was cooled in an ice-water-salt bath to

ca. -5°C. An ice-cold aq solution of $NaNO_2$ (3.45 g, 0.05 mol

in 20 mL water) was added dropwise over a 5 min period; after

addition, the solution was pale-yellow and nearly homogeneous.

The mixture was quickly filtered into a pre-cooled (-10°C)

250-mL, 3-necked flask. An ice-cold aq solution of KCN (6.5 g,

0.10 mol in 15 mL water) was then added dropwise with stirring

over 2-3 min; a bright-orange precipitate immediately formed.

After stirring an additional 10 min, the mixture was suction-

filtered. The orange solids were washed once with ice-cold

water, and spread on filter paper to air-dry. Yield: 1.18 g,

(11%), mp 41-42° d, (Lit. mp 42-43° d).[43]

$Ir(CHCl_3)$: 1580; 1477; 1437; 1147; 1069; 1007; 830, $(CHCl_3)$.

^1H-nmr: 7.82 (s, aromatic)

Preparation of trans-4-Chlorophenylazocyanide
from 4-Chloroaniline in Aqueous Acid

4-Chloroaniline (6.4 g, 0.05 mol) was diazotized in aq HCl
and treated with aq KCN as described in the general procedure.
The orange precipitate was suction-filtered, washed with ice-
cold water, and air-dried on the filter for ca. 5 min. The
damp cis-azocyanide was then dissolved in dichloromethane (50 ml);
the red-brown solution was washed with water (2 x 25 mL), and
allowed to dry over Na_2SO_4 in the dark for 18 h. The solution
was then filtered and evaporated in vacuo. Yield: 0.94 g (11%),
mp 96-101°C, (Lit. mp 105°C).[43]

Ir(CH_2Cl_2): 2190; 1589; 1479; 1397; 1252; 1212; 1153; 1092;
1012; 842.

Preparation of Aryldiazonium Tetrafluoro-
borate Salts: General Procedure

A 250-mL Erlenmeyer flask fitted with a mechanical stirrer
was charged with the desired aromatic amine (0.15 mol) and 48%
(w/w) aq HBF_4 (Alfa, 53.0 mL, 0.375 mol). This mixture was
then stirred and cooled in an ice-water-salt bath, maintaining
the temperature at ca. -5°C throughout. Diazotization was
accomplished by dropwise addition (15 min) of an ice-cold aq
solution of $NaNO_2$ (10.35 g, 0.15 mol in 23 mL water). When
necessary, small amounts of cold water were added to improve
the fluidity during the $NaNO_2$ addition. Stirring was continued

for 30 min after the nitrite addition was completed. The mixture
was filtered through a sintered-glass funnel; the solid diazonium
salt was then washed with 50 mL of cold 5% (w/w) aq HBF_4, ice-
cold 95% ethanol (2 x 100 mL), and ice-cold ether (3 x 125 mL).
The resulting powder was air dried on filter paper. The aryl-
diazonium salts were purified by dissolving the salt in the
minimum amount of acetone, filtering if necessary, and then
slowly adding an equal volume of ether to precipitate the pure
product. The purified salts were stored in the dark at ambient
temperature in a desiccator containing P_2O_5. The aryldiazonium
salts prepared as described above are listed in Table 11.

Synthesis of Arylazocyanides from Diazonium Tetrafluoroborate Salts: General Procedure, (3-6 mmol Scale)

A 100-mL, 3-necked flask fitted for nitrogen purge and
magnetic stirring was charged with aryldiazonium tetrafluoro-
borate salt (3 mmol) and 30 mL dichloromethane. Stirring was
commenced, and 18-crown-6 (0.04 g, 5 mol-%) was added; the
resulting mixture was allowed to stir ca. 5 min. Solid KCN
(0.20 g, 1 equiv) was then added in one portion; the solution
turned yellow. The heterogeneous mixture was stirred vigorously
at ambient temperature for 5 h, during which time the reaction
mixture gradually darkened from yellow to red-orange or red-
brown. After stirring, the mixture was suction-filtered, and

Table 11

Preparation of Aryldiazonium Salts $(X-Ar-N_2^+BF_4^-)$

X	% Yield	Obsd mp (°C dec)[a]	Lit mp (°C dec)
H	87	106–107.5	104[105]
4-F	77	163–165	154.5[106]
4-Cl	83	137–138.5	136–137[107]
4-Br	90	137–138	137–138[107]
4-NO$_2$	91	149–150	141[105]
4-MeO	82	142–143	142[107]
2-Cl	86	178–179	166[105]
2,4-Cl$_2$	81	150–151	149–149.5[16]
4-Me	76	103–104.5	106[105]
4-Et	46	84–85	––
3-Cl	92	149–150	146–148[107]

[a]In a few cases, obsd mp's were appreciably higher than those reported in the literature. In these cases, the diazonium salts were examined spectroscopically; spectral properties were consistent with assigned structures in all cases.

the filtrate washed with 10% (w/w) aq KOAc (3 x 20 mL). The
organic layer was then dried over Na_2SO_4 in the dark ca. 24 h,
filtered, and evaporated in vacuo to yield the crude arylazo-
cyanide as an orange to red-brown solid. Products were identi-
fied by standard spectroscopic techniques; where applicable,
spectra were consistent with those reported in the literature
for the assigned structure. The crude products were purified
by sublimation, extraction, or distillation as appropriate.
Arylazocyanides prepared according to this procedure are
summarized in Table 1.

E-4-Bromophenylazocyanide

4-Bromobenzenediazonium tetrafluoroborate (0.81 g, 3.0 mmol)
was stirred in CH_2Cl_2 (30 mL) with KCN (0.20 g, 1 equiv) in the
presence of 18-crown-6 (0.04 g, 5 mol-%) for 5 h as described in
the general procedure. Crude E-4-bromophenylazocyanide was
obtained as a red-orange solid (0.53 g, 84%), mp 107-115°C.
The crude solid was sublimed (0.15 torr, 95-100°C, 1 h) to yield
E-4-bromophenylazocyanide as red-orange needles (0.36 g, 57%),
mp 124-128°C, (Lit. mp 132°C).[43]

$Ir(CH_2Cl_2)$: 2191; 1584; 1478; 1393; 1310; 1213; 1158; 1069; 1010; 840.

^1H-nmr: 7.84 (s, aromatic)

E-4-Chlorophenylazocyanide

4-Chlorobenzenediazonium tetrafluoroborate (0.68 g, 3.0 mmol) was stirred in CH_2Cl_2 (30 mL) with KCN (0.20 g, 1 equiv) in the presence of 18-crown-6 (0.04 g, 5 mol-%) for 5 h as described in the general procedure. Crude 4-chlorophenylazocyanide was obtained as an orange solid (0.45 g, 91%), mp 96-101°C. The crude solid was sublimed (1.0 torr, 60-65°C, 3 h) to yield E-4-chlorophenyl-azocyanide as red-orange needles (0.38 g, 77%), mp 100-104°C, (Lit. mp 105°C).[43]

Ir(CH_2Cl_2):   2198; 1586; 1478; 1392; 1308; 1212; 1155; 1092; 1010; 840.

[1]H-nmr: 7.96, 7.81, 7.61, 7.46 (AB q, J = 9).

E-4-Fluorophenylazocyanide

4-Fluorobenzenediazonium tetrafluoroborate (0.63 g, 3.0 mmol) was stirred in CH_2Cl_2 (30 mL) with KCN (0.20 g, 1 equiv) in the presence of 18-crown-6 (0.04 g, 5 mol-%) for 5 h as described in the general procedure. Crude E-4-fluorophenylazocyanide was obtained as an orange solid (0.41 g, 92%), mp 58-64°C. The crude solid was sublimed (0.1 torr, 45-45°C) to yield E-4-fluorophenyl-azocyanide as orange needles (0.32 g, 71%), mp 60-61°C.[44]

Ir(CH_2Cl_2):   2196; 1593; 1496; 1441; 1408; 1246; 1142; 849.

[1]H-nmr):   8.11, 8.02, 7.95, 7.87 ($J_{F-H\ meta}$ = 5)

7.37, 7.25, 7.22, 7.10 ($J_{F-H\ ortho}$ = 8)

E- 4-Methoxyphenylazocyanide

4-Methoxybenzenediazonium tetrafluoroborate (0.67 g, 3.0 mmol) was stirred in CH_2Cl_2 (30 mL) with KCN (0.20 g, 1 equiv) in the presence of 18-crown-6 (0.04 g, 5 mol-%) for 5 h as described in the general procedure. E-4-Methoxyphenylazocyanide was obtained as a red solid (0.42 g, 87%), mp 117-122°C, (Lit. mp 121-122°C).[43] The compound was not further purified.

Ir(CH_2Cl_2):   2196; 1598; 1503; 1426; 1378; 1326; 1257-1238; 1146; 1023; 894; 846.

[1]H-nmr: 8.09, 7.93, 7.17, 7.03 (AB q, 4H, J = 9)
            3.99 (s, 3H, OCH_3).

E-4-Nitrophenylazocyanide

4-Nitrobenzenediazonium tetrafluoroborate (0.71 g, 3.0 mmol) was stirred in CH_2Cl_2 (30 mL) with KCN (0.20 g, 1 equiv) in the presence of 18-crown-6 (0.04 g, 5 mol-%) for 5 h as described in the general procedure. Crude E-4-nitrophenylazocyanide was obtained as a red-brown semi-solid (0.42 g, 80%), mp 70-77°C. The crude product was purified by extraction with boiling hexane-THF (4:1 v/v), which afforded E-4-nitrophenylazocyanide after evaporation as bright-orange platelets (0.25 g, 48%), mp 83-85°C, (Lit. mp 86°C).[43]

Ir(CH_2Cl_2):   2196; 1615; 1540; 1407; 1330-1325; 1205; 1160; 1015; 867; 837.

[1]H-nmr: 8.62, 8.46, 8.28, 8.13 (AB q, J = 9).

E-Phenylazocyanide

Benzenediazonium tetrafluoroborate (7.68 g, 40.0 mmol) was stirred in CH_2Cl_2 (400 mL) with KCN (5.2 g, 2 equiv) in the presence of 18-crown-6 (1.06 g, 10 mol-%) for 18 h as described in the general procedure. Crude E-phenylazocyanide was obtained as a dark-brown oil (5.0 g, 95%). Vacuum-distillation (60-65°C, 0.1 torr) afforded 0.8 g (16% recovery) of red oil which solidified into prisms, mp 29°C.[45]

Ir(CH_2Cl_2): 2190; 1593; 1463; 1415; 1318; 1211; 1157.

[1]H-nmr: 8.05-7.50 (m).

E-2-Chlorophenylazocyanide

2-Chlorobenzenediazonium tetrafluoroborate (1.36 g, 6.0 mmol) was stirred in CH_2Cl_2 (60 mL) with KCN (0.40 g, 1 equiv) in the presence of 18-crown-6 (0.08 g, 5 mol-%) as described in the general procedure. Crude E-2-chlorophenylazocyanide was obtained as a dark-brown semi-solid (0.44 g, 44%). No further purification was carried out.

Ir(CH_2Cl_2): 2190; 1585; 1465; 1405; 1215; 1165; 1130; 1070.

[1]H-nmr: 7.90-7.15 (m)

E-2,4-Dichlorophenylazocyanide

2,4-Dichlorobenzenediazonium tetrafluoroborate (0.78 g, 3.0 mmol) was stirred in CH_2Cl_2 (30 mL) with KCN (0.20 g, 1 equiv)

in the presence of 18-crown-6 (0.04 g, 5 mol-%) for 5 h as des-
cribed in the general procedure. Crude $\underline{E}$-2,4-dichlorophenyl-
azocyanide was obtained as a brown semi-solid (0.09 g, 15%).
No further purification was carried out.

Ir(CH_2Cl_2): 2195; 1570; 1458; 1423; 1375; 1248; 1210; 1135;
1108; 823.

Reaction of E-4-Chlorophenylazocyanide
with KCN and 18-Crown-6

E-4-Chlorophenylazocyanide (0.25 g, 1.5 mmol, mp 101-103°C),

and 18-crown-6 (0.02 g, 5 mol-%) were dissolved in 15 mL CH_2Cl_2

and placed in a 25-mL, round-bottomed flask; the solution was

bright orange. Solid KCN (0.20 g, 1 equiv) was added in one

portion to the stirred solution, which immediately turned red-

brown. After stirring 10 h, the solution was filtered, washed

with 10% aq (w/w) KOAc (3 x 50 mL), dried over Na_2SO_4 in the

dark for 24 h, and evaporated $\underline{in\ vacuo}$ to afford a red-brown

solid, mp 98-101°C. The ir spectrum of this solid was identical

to that of the starting azocyanide.

Reaction of E-4-Chlorophenylazocyanide with
KCN and 18-Crown-6 in the Presence of KBF$_4$

The reaction was carried out as above, except that solid KBF$_4$

(0.19 g, 1 equiv) was combined with the starting azocyanide,

18-crown-6 and CH_2Cl_2. When KCN was added to the stirred solu-

tion, no color change took place; the mixture remained bright

orange. After stirring 10 h, the mixture was worked up as above to afford an orange solid, mp 101-103°C. The ir spectrum of this solid was identical to that of the starting azocyanide.

Reaction of 4-Chlorobenzenediazonium Tetrafluoroborate with KCN in the Absence of 18-Crown-6

E-4-Chlorobenzenediazonium tetrafluoroborate (1.36 g, 6.0 mmol) was stirred in CH_2Cl_2 (60 ml) with KCN (0.4 g, 1 equiv) in the absence of 18-crown-6 for 5 h according to the general procedure. During the course of reaction, the mixture turned yellow. The mixture was suction-filtered, dried over Na_2SO_4, and evaporated in vacuo to yield E-4-chlorophenylazocyanide (0.05 g, 5%). When the experiment was repeated using 5 equiv KCN, 0.84g (34%) was isolated after stirring for 5 days.

Reaction of 4-Chlorobenzenediazonium Tetrafluoroborate with NaCN in the Presence of 15-Crown-5

E-4-Chlorobenzenediazonium tetrafluoroborate (0.68 g, 3.0 mmol) was stirred in CH_2Cl_2 (30 mL) with NaCN (0.15 g, 1 equiv) in the presence of 15-crown-5 (0.04 g, 6 mol-%) as described in the general procedure. After stirring for 5 h at ambient temperature, the pale orange mixture was suction-filtered, dried over Na_2SO_4, and evaporated in vacuo to yield E-4-chlorophenyl-azocyanide (0.12 g, 24%), mp 86-95°C.

Solid-State cis-to-trans Isomerization
of Z-4-Bromophenylazocyanide

Z-4-Bromophenylazocyanide (mp 41-42° d) was placed in a
sealed vial and stored in the dark at ambient temperature.
After 6 days, the mp was 125-130°C, (Lit. mp of E-isomer 132°C).[43]

Determination of Initial Isomer Formed
During Phase-Transfer Synthesis of
4-Bromophenylazocyanide at 0°C

4-Bromobenzenediazonium tetrafluoroborate (0.81 g, 3.0 mmol)
was treated with KCN (1 equiv) and 18-crown-6 (5 mol-%) in CH_2Cl_2
according to the general procedure, except that the mixture was
cooled in an ice-water bath and stirred for only 2 h. The result-
ing pale-orange mixture was suction-filtered and the filtrate
evaporated in vacuo on a cold-water bath. No attempt was made
to remove residual crown. A red-orange solid was obtained, mp
38-39°C. A portion (0.02 g) of this product was quickly re-
dissolved in 1.0 mL CH_2Cl_2, and its infrared spectrum examined
immediately, and after 21 h had elapsed. Spectral results were
as indicated below.

time = 0 h: ν_{CN} (2191) weak; ν_{ring} (1395) weak.

time = 21 h: ν_{CN} (2191) medium; ν_{ring} (1395) strong.

After standing 48 h, the remainder of the above solution was
evaporated to yield a red-orange solid, mp 128-129°C.

Determination of Initial Isomer Formed During Phase-Transfer Synthesis of 4-Chlorophenylazocyanide at Ambient Temperature

4-Chlorobenzenediazonium tetrafluoroborate (1.36 g, 6.0 mmol) was stirred in CH_2Cl_2 with KCN (1 equiv) and 18-crown-6 (5 mol-%) at ambient temperature according to the general procedure. The pale-orange mixture was suction-filtered after stirring only 2 h. The filtrate was evaporated in vacuo on a cold-water bath; no attempt was made to remove residual crown. The orange, semi-solid residue was quickly redissolved in CH_2Cl_2 and its infrared spectrum examined as a function of time. Spectral results were as indicated below.

time = 0 h: ν_{CN} (2190) weak; ν_{ring} (1395) medium

time = 18 h: ν_{CN} (2190) medium; ν_{ring} (1395) strong

time = 27 h: ν_{CN} (2190) strong; ν_{ring} (1395) strong

Effect of Scale-Up on the Yield of E-4-Chlorophenylazocyanide (30 mmol scale)

The reaction was carried out in a 500-mL, 3-necked flask according to the general procedure, using 4-chlorobenzenedia-zonium tetrafluoroborate (6.80 g, 30 mmol), KCN (2.0 g, 1 equiv), 18-crown-6 (0.40 g, 5 mol-%) and 300 ml CH_2Cl_2. The mixture was stirred at ambient temperature for 5 h. E-4-Chlorophenylazo-cyanide (2.1 g, 42%) was isolated as a red-brown solid, mp 88-95°C, and identified by ir spectrum.

Effect of Increased Reaction Time on the Yield
of 4-Chlorophenylazocyanide (60 mmol scale)

The reaction was carried out in a 1-L, 3-necked flask, according to the general procedure, using 4-chlorobenzenediazonium tetrafluoroborate (13.6 g, 60 mmol), KCN (4.1 g, 1 equiv), 18-crown-6 (0.80 g, 5 mol-%), and 600 ml CH_2Cl_2. The mixture was magnetically stirred for 16 h. E-4-Chlorophenylazocyanide was isolated as a brown solid (6.6 g, 66%), and identified by [1]H-nmr and ir spectrum.

Effect of Increased Surface Area on the Yield
of 4-Chlorophenylazocyanide (150 mmol scale)

The reaction was carried out in a 2-L, 3-necked flask fitted with a sintered-glass nitrogen purge according to the general procedure, using 4-chlorobenzenediazonium tetrafluoroborate (33.9 g, 150 mmol), KCN (9.75 g, 1 equiv), 18-crown-6 (1.98 g, 5 mol-%), and 1500 mL CH_2Cl_2. After the addition of KCN, however, silica gel (10 g, 70-230 mesh) was also added to the mixture, which was then mechanically stirred vigorously for 20 h. Crude E-4-chloro-phenylazocyanide was isolated as a dark-brown semi-solid (5.34 g, 22%), and identified by ir spectrum.

Effect of Increased 18-Crown-6 and
Increased Reaction Time on the Yield
of 4-Chlorophenylazocyanide (83 mmol scale)

The reaction was carried out in a 2-L, 3-necked flask according to the general procedure, using 4-chlorobenzenediazonium

tetrafluoroborate (18.8 g, 83 mmol), KCN (5.4 g, 1 equiv), 18-crown-6 (4.38 g, 20 mol-%) and 830 mL CH_2Cl_2. The mixture was mechanically stirred vigorously for 20 h. 4-Chlorophenylazo-cyanide was isolated as a dark-brown semi-solid (11.37 g). This represented a yield of 83%, figuring the solid as pure product. [1]H-nmr showed this product to be contaminated by 7 mol-% 18-crown-6.

Effect of Increased KCN on the Yield of 4-Chlorophenylazocyanide (50 mmol scale)

The reaction was carried out in a 1-L, 3-necked flask according to the general procedure, using 4-chlorobenzenediazonium tetrafluoroborate (11.3 g, 50 mmol), KCN (13.0 g, 4 equiv),18-crown-6 (0.66 g, 5 mol-%), and 50 ml CH_2Cl_2. The mixture was mechanically stirred vigorously for 5 h. 4-Chlorophenylazo-cyanide was isolated as a red-brown solid (2.84 g, 34% if pure), mp 93-96°C. This product contained 1.5 mol-% 18-crown-6, ([1]H-nmr).

Effect of Increased KCN and Increased Crown on the Yield of 4-Chlorophenylazocyanide (50 mmol scale)

The reaction was carried out in a 1-L, 3-necked flask according to the general procedure, using 4-chlorobenzenediazonium tetrafluoroborate (11.3 g, 50 mm91), KCN (13 g, 4 equiv), 18-crown-6 (1.32 g, 10 mol-%), and 500 mL CH_2Cl_2. The mixture

was mechanically stirred vigorously for 5 h. 4-Chlorophenyl-
azocyanide (4.0 g, 48% if pure), was isolated as a red-brown
semi-solid, mp 84-92°C. This product contained 4 mol-% 18-crown-
6, (^{1}H-nmr).

Effect of Increased KCN and Increased Reaction Time on the Yield of 4-Chloro-phenylazocyanide (50 mmol scale)

The reaction was carried out in a 1-L, 3-necked flask
according to the general procedure, using 4-chlorobenzenedia-
zonium tetrafluoroborate (11.3 g, 50 mmol), KCN (13 g, 4 equiv),
18-crown-6 (0.66 g, 5 mol-%), and 500 mL CH_2Cl_2. The mixture
was mechanically stirred vigorously for 30 h. 4-Chlorophenyl-
azocyanide was isolated as a red-brown solid (7.1 g, 86% if pure),
mp 92-95°C. This product contained 0.5 mol-% 18-crown-6, (^{1}H-nmr).

E-4-Nitrophenylazocyanide (50 mmol scale)

The reaction was carried out in a 1-L, 3-necked flask
according to the general procedure, using 4-nitrobenzenedia-
zonium tetrafluoroborate (11.85 g, 50 mmol), KCN (13 g, 4 equiv),
18-crown-6 (0.26 g, 2 mol-%), and 50 mL CH_2Cl_2. The mixture
was mechanically stirred vigorously for 5 h. E-4-Nitrophenyl-
azocyanide (8.75 g, 99%) was isolated as a dark-brown solid,
mp 72-80°C. This product contained 0.7 mol-% 18-crown-6, (^{1}H-nmr).

Reaction of 4-Chlo~ benzenediazonium Tetra-
fluoroborate with KCN in the Presence of
Stark's Catalyst in Acetone

A 100-mL, 3-necked flask fitted for nitrogen purge and

magnetic stirring was charged with 4-chlorobenzenediazonium

tetrafluoroborate (1.36 g, 6.0 mmol) and 60 mL acetone, forming

a clear, homogeneous solution. Solid KCN (0.40 g, 1 equiv)

and Stark's catalyst (0.75 g, 25 mol-%) were added to the

stirred solution, which turned bright red within ca. 5 min.

After stirring 13 h at ambient temperature, the mixture was

red-brown. Tlc analysis on a silica plate using 1:1 ether-

hexane (v/v) as the developing solvent showed no azocyanide

present. Chromatography on silica gel using 1:4 ether-hexane

(v/v) as the solvent yielded two fractions, both of which

afforded red, tarry solids after evaporation in vacuo.

^{1}H-nmr (Fraction 1): 7.5-7.0 (m); 1.3 (Ψs, hexane).

^{1}H-nmr (Fraction 2): 7.5-7.70 (m); 2.5 (Ψd); 1.6 (s);
$\qquad\qquad\qquad$ 1.3 (Ψs, hexane).

Reaction of 4-Chlorobenzenediazonium Tetra-
fluoroborate with KCN in the Presence of
BTEAC in Acetone

A 100-mL, 3-necked flask fitted for nitrogen purge and

magnetic stirring was charged with 4-chlorobenzenediazonium

tetrafluoroborate (1.36 g, 6.0 mmol) and acetone (50 mL), forming

a clear, homogeneous solution. Solid KCN (0.40 g, 1 equiv)

and BTEAC (0.34 g, 25 mol-%) were added to the stirred solution,

which became red-orange within ca. 15 min. After stirring 30 min, the solution was filtered, and the filtrate evaporated in vacuo. The red-brown residue was extracted with 25 mL dichloromethane and refiltered. The solids which were insoluble in dichloromethane were soluble in acetone and formed a colored solution when treated with N,N-dimethylaniline. The filtrate was washed with water (2 x 150 mL), dried over Na_2SO_4, and evaporated in vacuo to yield a brown, tarry solid (0.21 g). Both tlc (silica, 1:1 ether-hexane, v/v) and [1]H-nmr analysis showed no azocyanide present in the product.

[1]H-nmr: 7.64, 7.58 (Ψd); 5.35 (s, CH_2Cl_2); 2.67 (s).

Reaction of 4-Chlorobenzenediazonium Tetrafluoroborate with KCN in the Presence of Stark's Catalyst in Acetonitrile

A 50-mL, 3-necked flask fitted for nitrogen purge and magnetic stirring was charged with 4-chlorobenzenediazonium tetrafluoroborate (0.68 g, 3.0 mmol) and acetonitrile (30 mL). Solid KCN (0.20 g, 1 equiv) and Stark's catalyst (0.37 g, 25 mol-%) were then added; the resulting solution was stirred at ambient temperature for 18 h. After stirring, the solution was dark brown with some tan solids present. The solution was filtered, and evaporated in vacuo to a brown residue. This residue was redissolved in CH_2Cl_2 (50 mL), washed with water (3 x 100 mL), dried over Na_2SO_4, and evaporated in vacuo to a

dark-brown, tarry solid. Chromatography on silica gel using ether-hexane (1:10 v/v) as the solvent yielded a trace amount (0.02 g, 4%) of 4-chlorophenylazocyanide, (identified by ir).

Reaction of 4-Chlorobenzenediazonium Tetra-fluoroborate with KCN in the Presence of 18-Crown-6 in Acetonitrile

A 100-mL, 3-necked flask fitted for nitrogen purge and magnetic stirring was charged with 4-chlorobenzenediazonium tetrafluoroborate (1.36 g, 6.0 mmol) and acetonitrile (50 mL), forming a clear, homogeneous solution. Solid KCN (0.78 g, 2 equiv) and 18-crown-6 (0.16 g, 10 mol-%) were added to the stirred solution, which immediately turned red-orange. After stirring 5 h, the solution was filtered and evaporated _in vacuo_ to a red oil. This oil was redissolved in CH_2Cl_2 (50 mL), washed with 10% (w/w) aq KOAc (3 x 25 mL), and dried over Na_2SO_4. Chromatography on silica gel using ether-hexane (1:9 v/v) as the solvent yielded E-4-chlorophenylazocyanide, 0.12 g (12%), (identified by ir).

Reaction of 4-Chlorobenzenediazonium Tetrafluoroborate with TMAC in $CHCl_3$ at 0°C; (Gegenion Metathesis)

A 100-mL, 3-necked flask fitted for nitrogen purge and magnetic stirring was charged with 4-chlorobenzenediazonium tetrafluoroborate (0.68 g, 3.0 mmol), TMAC (0.33 g, 1 equiv),

and $CHCl_3$ (30 mL). The mixture was cooled in an ice-water bath, and stirred for 3 h. After stirring, the mixture was filtered to afford a clear, pale-yellow solution.

Reactions of 4-Chlorobenzenediazonium Chloride (Metathesized $CHCl_3$ Solutions) with KCN and 18-crown-6

Solutions of 4-chlorobenzenediazonium chloride in $CHCl_3$ were prepared immediately prior to use according to the gegenion metathesis reaction described above. The resulting solutions were 0.10 M in diazonium ion (3.0 mmol in 30 mL of solution), assuming 100% efficiency of metathesis.

a. A metathesized solution of 4-chlorobenzenediazonium chloride was placed in a 100-mL, 3-necked flask fitted for nitrogen purge and magnetic stirring. 18-Crown-6 (0.04 g, 5 mol-%) and KCN (0.40 g, 2 equiv) were added together in one portion. After stirring 24 h at ambient temperature, the mixture was pale orange. A filtered aliquot was subjected to infrared analysis and exhibited a strong absorption characteristic of diazonium ions at 2275 cm^{-1}, and a red color was observed when the aliquot was treated with N,N-dimethylaniline. When the solution was washed with water (3 x 10 mL), it turned bright orange. After drying over Na_2SO_4 for 1 h, the solution was filtered through a bed of silica gel (ca. 20 g in a sintered-glass funnel). Evaporation in vacuo afforded a red-orange semi-solid. This

material was redissolved in CH_2Cl_2, and allowed to stand in the dark for an additional 24 h. Evaporation *in vacuo* afforded crude E-4-chlorophenylazocyanide as an orange solid (0.27 g, 54%), mp 85-98°C (slow softening and melt). The product was identified by ir and [1]H-nmr analysis.

b. When the reaction was repeated by adding a metathesized solution of 4-chlorobenzenediazonium chloride (*ca*. 3 mmol in 30 mL $CHCl_3$) dropwise over 5 h to a stirred mixture of 18-crown-6 (0.04 g, 5 mol-%) and KCN (0.40 g, 2 equiv) in 20 mL $CHCl_3$, the mixture turned orange. After stirring 24 h at ambient temperature, the ir spectrum of a filtered aliquot showed a strong diazonium absorption at 2275 cm^{-1}. Work-up as above afforded E-4-chloro-phenylazocyanide (0.26 g, 52%) as an orange solid, mp 97-101°C.

c. Identical dropwise addition of 4-chlorobenzenediazonium chloride (*ca*. 3 mmol in 30 mL $CHCl_3$) to a suspension of KCN (0.40 g, 2 equiv) in $CHCl_3$ (20 mL) in the *absence* of 18-crown-6, and stirring for 24 h at ambient temperature, afforded 0.23 g (46%) of crude E-4-chlorophenylazocyanide, mp 83-98°C (slow softening and melt). This product was identified by ir and [1]H-nmr.

Reaction of 4-Chlorobenzenediazonium Chloride (Metathesized $CHCl_3$ Solution) with NaCN and 15-Crown-5

A 100-mL, 3-necked flask fitted for nitrogen purge, an additional funnel, and magnetic stirring was charged with $CHCl_3$

(20 mL), NaCN (0.29 g, 2 equiv), and 15-crown-5 (0.04 g, 6 mol-%). A solution of 4-chlorobenzenediazonium chloride (<u>ca</u>. 3 mmol in 30 mL CHCl$_3$, prepared by the gegenion metathesis described above) was added dropwise to the stirred mixture, which immediately turned red-brown. When the addition was complete (5 h), the ir spectrum of a filtered aliquot showed a weak diazonium absorption at 2275 cm^{-1}, along with absorptions characteristic of 4-chlorophenylazocyanide. After stirring 24 h, the mixture remained red-brown. The mixture was washed with water (3 x 100 mL), dried over Na$_2$SO$_4$, and filtered through a bed of silica gel (<u>ca</u>. 20 g in a sintered-glass funnel). A dark-brown material was deposited on the silica gel as the solution filtered through. Evaporation <u>in</u> <u>vacuo</u> afforded 0.17 g of brown solid, mp 84-90°C. The ir spectrum of this solid was characteristic of <u>E</u>-4-chlorophenylazocyanide.

<u>Reaction of 4-Chlorobenzenediazonium</u>
<u>Chloride (Metathesized CHCl$_3$ Solution)</u>
<u>with Solid KCN and Stark's Catalyst</u>

A 100 mL, 3-necked flask fitted for nitrogen purge, an addition funnel, and magnetic stirring was charged with CHCl$_3$ (20 mL), KCN (0.40 g, 2 equiv), and Stark's catalyst (0.08 g, 5 mol-%). A solution of 4-chlorobenzenediazonium chloride (<u>ca</u>. 3 mmol in 30 mL CHCl$_3$, prepared by the gegenion metathesis described above) was added dropwise to the stirred mixture over

5 h at ambient temperature. The mixture was pale yellow after
addition, and remained yellow after stirring 24 h. When washed
with water (3 x 100 mL), the solution turned orange. The solution
was then dried over Na_2SO_4 for 1 h, filtered through a bed of
silica gel, and allowed to stand in the dark for 24 h. Evapora-
tion in vacuo afforded 0.20 g, of orange solid, mp 96-101°C.
This product was identified as E-4-chlorophenylazocyanide
(yield 40%) by ir and [1]H-nmr.

Reaction of 4-Chlorobenzenediazonium
Chloride (Metathesized $CHCl_3$ Solution)
with Aqueous KCN and Stark's Catalyst

A 100-mL, 3-necked flask fitted with a mechanical stirrer
was charged with 10 mL of a saturated aq KCN solution, 20 mL
$CHCl_3$, and Stark's catalyst (0.22 g, 15 mol-%). A solution
of 4-chlorobenzenediazonium chloride (ca. 3 mmol in 30 mL $CHCl_3$,
prepared by the gegenion metathesis described above) was added
dropwise to the stirred mixture. The mixture immediately turned
black, and remained black during addition. The reaction was
abandoned.

Reaction of 2-Chlorobenzenediazonium
Chloride (Metathesized $CHCl_3$ Solution)
with KCN and 18-Crown-6

2-Chlorobenzenediazonium tetrafluoroborate (0.68 g, 3.0
mmol) was stirred with TMAC (0.33 g, 1 equiv) in $CHCl_3$ (30 mL)
for 3 h at 0°C. The mixture was filtered, and the resulting

solution placed in a 100-mL, 3-necked flask fitted for nitrogen purge and magnetic stirring. KCN (0.40 g, 2 equiv) and 18-crown-6 (0.04 g, 5 mol-%) were added together in one portion to the stirred mixture at ambient temperature. The mixture immediately turned bright yellow, but darkened to black within 30 min. The reaction was abandoned.

Hydrolysis of 4-Chlorophenylazocyanide to 4-Chlorophenylazocarbonamide

A 50-mL round-bottomed flask fitted for magnetic stirring was charged with E-4-chlorophenylazocyanide (2.00 g, 12.0 mmol), THF (172 g), and 20% HCl (28 g). The resulting solution was 3% (w/w) HCl in 11% aq (w/w) THF. The red-orange solution was stirred at ambient temperature for 24 h. The mixture was then diluted with water (100 mL), and extracted with one portion of CH_2Cl_2 (200-mL). The organic extract was dried over Na_2SO_4, filtered, and evaporated in vacuo to a red-orange solid. The crude product was chromatographed on silica gel using ethyl acetate-ether (1:50 v/v) as the solvent to yield 4-chlorophenyl-azocarbonamide, 1.70 g (77%), mp 182-183°C, (Lit, mp 182°C).[57]

Ir($CHCl_3$): 3526; 3416; 1742; 1585; 1500; 1327; 1157; 1095; 842.

^{1}H-nmr (DMSO-d6): 8.3-7.7 (m).

Hydrolysis of E-4-Methoxyphenylazocyanide in Aqueous KOH

A 25-mL, round-bottomed flask fitted with a reflux condenser and a magnetic stirring bar was charged with E-4-methoxyphenylazo-cyanide (1.0 g, 6 mmol) and ca. 13 g of 10% aq (w/w) KOH. The heterogeneous mixture was heated to reflux; at reflux, moist litmus held to the condenser top turned blue. After heating for 16 h, the mixture was allowed to cool to ambient temperature, and extracted with CH_2Cl_2 (3 x 25 mL). Glpc analysis indicated the presence of anisole (30% glpc yield, 1-chlorooctane as internal standard).

Hydrolysis of E-4-Chlorophenylazocyanide in Aqueous NaOH

A 25-mL, round-bottomed flask fitted with a reflux condenser and a magnetic stirring bar was charged with E-4-chlorophenyl-azocyanide (0.50 g, 3 mmol), and 12 g of 15% aq (w/w) NaOH. The heterogeneous mixture was heated to reflux, at which time moist litmus paper held to the condenser top turned blue. After refluxing for 24 h, the mixture was cooled to ambient tempera-ture, and extracted with CH_2Cl_2 (3 x 25 mL). Glpc analysis in-dicated the presence of chlorobenzene (25% glpc yield, bromo-benzene as internal standard).

Hydrolysis of E-4-Chlorophenylazocyanide in NaOD/D$_2$O

A solution of 13-15% (w/w) NaOD in D$_2$O was prepared by adding 1.0 g of freshly-cut sodium metal in small pieces to 12.0 g D$_2$O under a continuous stream of dry nitrogen. The resulting solution was transferred to a 25-mL, round-bottomed flask fitted with a reflux condenser and a magnetic stirring bar. E-4-chlorophenyl-azocyanide (0.50 g, 3.0 mmol) was then added. The mixture was heated to reflux, and stirred for 24 h. After cooling to ambient temperature, the mixture was extracted with CH$_2$Cl$_2$ (2 x 25 mL). The organic extract was dried over Na$_2$SO$_4$, and analyzed by glpc and gc-ms. Glpc analysis indicated the presence of chlorobenzene (28% yield, bromobenzene as internal standard). Gc-ms indicated that this product contained chlorodeuteriobenzene (93%) and chlorobenzene (7%).

Attempted Hydrogenation of E-4-Chlorophenyl-azocyanide (10% Pd/C in Benzene)

E-4-Chlorophenylazocyanide (0.50 g, 3.0 mmol) was dissolved in benzene (35 mL) and 10% Pd/C catalyst (10% w/w) was added. The mixture was hydrogenated on a Parr apparatus for 24 h at a pressure of 38-42 psi. The mixture was then filtered through a bed of Celite to obtain a clear yellow solution which was evaporated in vacuo, leaving a brown oil (0.20 g). Analysis by tlc on a silica plate using ether-hexane (1:1 v/v) as the

developing solvent indicated the presence of at least five

products. No further attempt was made to isolate or characterize

the reaction products.

Attempted Hydrogenation of E-4-Chlorophenylazocyanide (10% Pd/C in 95% Ethanol)

E-4-Chlorophenylazocyanide (0.50 g, 3.0 mmol) was dissolved

in 100 mL 95% ethanol, and 10% Pd/C catalyst (10% w/w) was added.

The mixture was hydrogenated on a Parr apparatus for 5 h at a

pressure of 44-39 psi. The mixture was then filtered through

Celite to obtain a clear, pale-yellow solution which was evapo-

rated in vacuo, leaving a brown oil (0.55 g). Analysis by tlc

on a silica plate using ether as the developing solvent indicated

the presence of at least five products. No further attempt was

made to isolate or characterize the reaction products.

Attempted Reduction of E-4-Chlorophenylazocyanide with LiAlH₄

Lithium aluminum hydride (0.06 g, 1.6 mmol) was placed in

a dry, 50-mL, 3-necked flask and covered with 10 mL anhydrous

ether. The stirred mixture was cooled in an ice-water bath

while a solution of E-4-chlorophenylazocyanide (0.50 g, 3.0 mmol

in 25 mL anhydrous ether) was added dropwise over 15 min. As

the azocyanide solution was added, the mixture turned black,

and was stirred at ca. 0°C for 2 h after addition was complete.

The mixture was poured into a 500-mL Erlenmeyer flask to which

4 mL of aq NaOH (8% w/w) was slowly added with swirling. The

mixture was then filtered through Celite, and the red-brown

filtrate was dried over Na_2SO_4 and evaporated in vacuo, leaving

a red-brown, tarry solid (0.33 g). Tlc analysis on a silica

plate using ether-hexane (1:1 v/v) as the developing solvent

showed a trace of starting azocyanide, possibly two other products,

and a large amount of residue which did not move from the origin.

The infrared spectrum of the reaction product showed no absorp-

tion due to cyanide. However, its [1]H-nmr spectrum showed only

a broad multiplet (7.6-7.0), with no methylene protons as would

be expected from the desired product. No further attempt was

made to characterize this reaction product.

Reaction of E-4-Bromophenylazocyanide with
BTEAC in CHCl$_3$ at Ambient Temperature

A 100-mL, round-bottomed flask was charged with E-4-bromo-

phenylazocyanide (0.32 g, 1.5 mmol), BTEAC (1.72 g, 5 equiv),

and chloroform (45 mL). The homogeneous solution was stirred

at ambient temperature for five days, and then allowed to filter

through a short column of silica gel to remove BTEAC. The

solution was then evaporated in vacuo, leaving an orange solid,

which was immediately redissolved in chloroform-d. The [1]H-nmr

spectrum indicated that unreacted 4-bromophenylazocyanide (7.77, s)

predominated in the mixture, along with a weak AB-quartet (7.98, 7.84, 7.62, 7.47; J = 9) characteristic of E-4-chlorophenylazo-cyanide.

Reaction of E-4-Bromophenylazocyanide with Stark's Catalyst in Refluxing Chloroform-d

E-4-Bromophenylazocyanide (0.32 g, 1.5 mmol) and Stark's catalyst (0.75 g, 1 equiv) were combined with chloroform-d (10 mL) in a 25-mL, 3-necked flask fitted with a reflux condenser and a magnetic stirring bar. The solution was heated to reflux, and the ^{1}H-nmr spectrum of aliquots was recorded at intervals. After ca. 24 h, the spectrum showed only starting materials. After four days, the aromatic region of the spectrum showed pre-dominantly unreacted 4-bromophenylazocyanide (as above), with only a weak AB-quartet due to 4-chlorophenylazocyanide.

Attempted Reaction of E-4-Nitrophenylazocyanide with Stark's Catalyst in CH_2Cl_2

E-4-Nitrophenylazocyanide (0.53 g, 3.0 mmol), Stark's catalyst (3.0 g, 2 equiv), and CH_2Cl_2 (50 mL) were combined in a 100-mL, round-bottomed flask fitted with a reflux condenser and a magnetic stirring bar, and stirred for 18 h at ambient temperature. After this time, the ^{1}H-nmr of the solution showed only unreacted starting materials (aromatic region: AB quartet, 8.53, 8.38, 8.22, 8.07; J = 9). The solution was then refluxed

for an additional 21 h. After this time, the ^{1}H-nmr spectrum
again showed only starting materials. The reaction was abandoned.

Attempted Reaction of E-4-Nitrophenylazocyanide with Stark's Catalyst in Toluene at 60°C

E-4-Nitrophenylazocyanide (0.53 g, 3.0 mmol), Stark's
catalyst (3.0 g, 2 equiv), and toluene (50 mL) were combined in
a 100-mL, round-bottomed flask fitted with a reflux condenser
and a magnetic stirring bar. The mixture was immersed in a water
bath which was maintained at 60 ± 2°C, and stirred for 21 h.
An aliquot was then removed, evaporated in vacuo to a residual
oil, and then redissolved in chloroform-d. The aromatic region
of the ^{1}H-nmr spectrum showed only unreacted 4-nitrophenylazo-
cyanide and some residual toluene. The reaction was abandoned.

Attempted Reaction of E-4-Nitrophenylazocyanide with 2-Phenylbutyronitrile in the Presence of Aqueous NaOH and BTEAC

E-4-Nitrophenylazocyanide (0.53 g, 3.0 mmol), 2-phenyl-
butyronitrile[108] (0.73 g, 1.6 equiv), and BTEAC (0.02 g, 3 mol-%)
were combined in a 10-mL, round-bottomed flask fitted for magnetic
stirring. Aqueous NaOH (2 mL, 50% w/w) was added to the stirred
mixture. An exothermic reaction occurred; the mixture bubbled,
turned dark and viscous, and became appreciably warm. The
mixture was heated to 60° on an oil bath, stirred for 3 h, then
cooled to ambient temperature. The brown,tarry mixture was

diluted with water and extracted with CH_2Cl_2. The purple-colored extract was evaporated in vacuo to minimum volume, and analyzed by tlc on an alumina plate using ether-hexane (1:1 v/v) as the developing solvent. The tlc analysis showed starting materials, a slower-moving product, and an appreciable amount of brown residue which remained at the origin. The reaction product was chromatographed on alumina, using ether-hexane (1:4 v/v) as solvent. A yellow solid (0.2 g) was obtained which further tlc analysis indicated was not a pure compound.

$Ir(CHCl_3)$: 3515; 3420; 2915; 2260; 1625; 1605; 1590; 1505; 1337-1315; 1255; 1185; 1117; 843.

The 2260 absorption was close to the absorption of the starting 2-phenylbutyronitrile (2250), but the azocyanide cyano absorption (2195) was absent. No nitro-group absorptions (1540 and 1350) were present.

^{1}H-nmr: Possible weak AB-quartet (8.08, 7.94, 6.64, 6.50, J = 8.4). Weak singlets at 7.38 and 3.63. No signals characteristic of an ethyl group observed.

The product was not analyzed further.

Reaction of Arylazocyanides with Dienes:
General Procedure

Arylazocyanide (3.0 mmol) and the appropriate diene (2-4 equiv) were placed in a Carius pressure tube fitted with a

Teflon screw-cap and a magnetic stirring bar. The tube was capped
and the mixture was heated (100°C, oil bath) and stirred for 3 h.
After cooling to ambient temperature, the mixture was washed from
the tube with dichloromethane, and adsorbed onto silica gel.
Chromatography on silica gel using ether-hexane solvent afforded
the cycloaddition adduct as a white or off-white solid.

Reaction of E-4-Chlorophenylazocyanide with 1,3-Butadiene

E-4-Chlorophenylazocyanide (0.50 g, 3.0 mmol) was placed
in a pressure reaction tube into which was then condensed 1,3-
butadiene (2.24 g, 14 equiv,Matheson) at -45°C. The tube was
capped, and the mixture allowed to warm to ambient temperature
while stirring. After 4 h, all the azocyanide had dissolved to
form an orange, homogeneous solution. After stirring 48 h, the
color of the solution had faded to pale yellow. After 5 days,
the tube was opened, and the excess butadiene allowed to boil
off; a yellow solid remained in the tube. This solid was dissolved
in methanol and warmed with a small portion of activated charcoal.
This procedure was repeated using ether-hexane (50:50 v/v).
Evaporation of the resulting filtrate in vacuo yielded 1-(4-
chlorophenyl)-2-cyano-1,2,3,6-tetrahydropyridazine (0.56 g, 85%)
as a straw-colored solid. mp 68-70°C.

Ir(CH_2Cl_2):   2926; 2821; 2216; 1599; 1490; 1435; 1355;

1295; 1217; 1125; 1195; 1005; 905; 825.

^{1}H-nmr: 7.42, 7.27, 7.08, 6.94 (AB-quartet, 4H, J = 9,

aromatic); 6.00 (Ψs, 2H, vinyl); 3.98 (Ψs,

4H, allyl).

^{13}C-nmr:

C-3:	45.2	ipso:	127.3
C-4:	122.8	ortho:	116.5
C-5:	123.8	meta:	129.2
C-6:	50.9	para:	144.7
CN:	114.0		

Anal: Calculated for $C_{11}H_{10}ClN_3$: C, 60.14; H, 4.59;

N, 18.91. Found: C, 59.87; H, 4.54; N, 18.91.

Attempted Reaction of E-4-Methoxyphenylazo-
cyanide with 1,3-Butadiene

E-4-Methoxyphenylazocyanide (0.48 g, 3.0 mmol) was allowed to

react with 1,3-butadiene as described above for E-4-chloro-

phenylazocyanide. After stirring at ambient temperature for 5

days, the mixture remained heterogeneous. The tube was opened,

and excess butadiene allowed to boil off. The starting azocyanide

was recovered in 95% yield.

Reaction of E-4-Nitrophenylazocyanide
with 1,3-Butadiene

E-4-Nitrophenylazocyanide (0.53 g, 3.0 mmol) was allowed to react with 1,3-butadiene (2.43 g, 15 equiv) as described above for E-4-chlorophenylazocyanide. After stirring ca. 1 h, the mixture had formed a dark-brown oil which was insoluble in the butadiene; after 3 h, this oil had crystallized into a pale-yellow solid. The tube was opened, and the excess butadiene allowed to boil off. The residual solid was washed from the tube with dichloromethane, which was then evaporated in vacuo to a brown oil. The oil was dissolved in methanol and warmed with a small portion of activated charcoal; this procedure failed to decolorize the sample or improve its purity. The oil was then chromatographed on silica gel using ether-hexane (50:50 v/v) as the solvent to yield 1-(4-nitrophenyl)-2-cyano-1,2,3,6-tetra-hydropyridazine (0.65 g, 84%) as a pale-yellow solid, mp 78-83°C. The analytical sample was obtained by recrystallization from ether-hexane, mp 83-85°C.

Ir(CH_2Cl_2): 2222; 1596; 1501; 1326, 1221; 1116; 841.

^{1}H-nmr: 8.33, 8.15, 7.16, 6.98 (AB quartet, 4H, J = 11, aromatic); 6.02 (Ψs, 2H, vinyl); 4.08 (Ψs, 4H, allyl).

^{13}C-nmr: C-3: 44.6   ipso: 141.7

C-4: 122.8   ortho: 113.4

C-5: 123.4   meta: 125.8

C-6: 51.2   para: 150.9

CN: not obsd[92]

Anal: Calculated for $C_{11}H_{10}N_4O$: C, 57.39; H, 4.38;

N, 24.33. Found: C, 56.79; H, 4.27; N, 24.35.

Reaction of E-4-Chlorophenylazocyanide with Isoprene

E-4-Chlorophenylazocyanide (0.50 g, 3.0 mmol) was heated
and stirred at 95°-105°C for 3 h with isoprene (0.41 g, 2 equiv)
according to the general procedure. Chromatography on silica gel
using ether-hexane (1:3 v/v) as the solvent yielded an off-white
solid (0.47 g, 67%), mp 80-82°C. The product was found by
^{13}C-nmr to contain 1-(4-chlorophenyl)-2-cyano-4-methyl-1,2,3,6-
tetrahydropyridazine (major isomer) and the corresponding 5-methyl
regioisomer (trace). An analytical sample was obtained by
recrystallizing twice (from petroleum ether-THF and then petroleum
ether-ether) to yield a straw-colored solid, mp 88-91°C.

Ir(CCl$_4$):   3050; 2985; 2925; 2220; 1595; 1495; 1447; 1300;

1225; 1099; 1005.

^{1}H-nmr: 7.41, 7.26, 7.07, 6.92 (AB quartet, 4H, J = 9,

aromatic); 5.63 (m, 1H, vinyl); 3.85 (Ψs, 4H,

allyl); 1.85 (Ψs, 3H, methyl).

^{13}C-nmr: Major Isomer:

C-3:	48.9	4-Me:	20.2
C-4:	131.4	ipso:	127.1
C-5:	116.7	ortho:	116.5
C-6:	50.5	meta:	129.2
CN:	114.1	para:	144.7

Minor Isomer:

C-3:   45.0

C-4:   114.1

C-5:   117.5

C-6:   53.9

5-Me: 19.5

Anal: Calculated for $C_{12}H_{12}ClN_3$:   C, 61.67; H, 5.18;

N, 17.98.   Found: C, 61.77; H, 5.09; N, 18.07.

Reaction of E-4-Methoxyphenylazocyanide
with Isoprene

E-4-Methoxyphenylazocyanide (0.56 g, 3.5 mmol) was heated

with isoprene (1.19 g, 5 equiv) at 100°-115°C for ca. 3 h, accord-

ing to the general procedure.   Chromatography on silica gel using

an ether-hexane solvent gradient (1:19 → 1:3 v/v) afforded a red-orange oil. Trituration with petroleum ether afforded 1-(4-methoxyphenyl)-2-cyano-4-methyl-1,2,3,6-tetrahydropyridazine as an off-white solid (0.37 g, 46%), mp 64-66°C. An analytical sample was obtained after two recrystallizations from petroleum ether-hexane to yield long, off-white needles, mp 70-71.5°C.

Ir(CH_2Cl_2):   2926; 2850; 2218; 1506; 1441; 1221; 1182; 1036; 829.

^{1}H-nmr: 7.03, 6.98 (Ψd, 4H, aromatic); 5.64 (m, 1H, vinyl); 3.82 (m, Ψs, 7H, OMe and allyl); 1.86 (Ψs, 3H, methyl).

^{13}C-nmr:

C-3:	49.5	OMe:	55.4
C-4:	131.8	ipso:	139.8
C-5:	116.7	ortho:	117.7
C-6:	50.2	meta:	114.5
CN:	not obsd[92]	para:	155.4
4-Me:	20.3		

Anal: Calculated for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.55; N, 18.33. Found: C, 67.73; H, 6.60; N, 18.26.

Reaction of E-4-Nitrophenylazocyanide with Isoprene

A solution of E-4-nitrophenylazocyanide (0.53 g, 3.0 mmol) in ca. 2 mL benzene was added dropwise over a period of 25 min

to a stirred solution of isoprene (0.82 g, 4 equiv in 2 mL benzene)
at ambient temperature. During the addition, the mixture darkened
slowly; some dark-brown solid material also formed on the walls
of the flask. The mixture was stirred an additional 4 h after
addition was complete, and then diluted with dichloromethane,
filtered, and adsorbed onto silica gel. Chromatography on silica
gel using ether-hexane (50:50 v/v) as the solvent afforded a
yellow oil. After trituration of this oil with ether-hexane
(1:3 v/v), 1-(4-nitrophenyl)-2-cyano-4-methyl-1,2,3,6-tetrahydro-
pyridazine was obtained as a yellow solid (0.40 g, 55%) which
slowly softened and melted from 90-105°C. After recrystallization
from hexane-THF, an analytically-pure sample was obtained as
yellow platelets, mp 104-108°C.

Ir(CH_2Cl_2): 2926; 2866; 2221; 1601; 1506; 1351; 1231; 1116;
844.

^{1}H-nmr: 8.39, 8.23, 7.25, 7.08 (AB quartet, 4H, J = 10,
aromatic); 5.77 (Ψs, 1H, vinyl); 4.02 (Ψs, 4H,
allyl); 1.88 (Ψs, 3H, methyl).

^{13}C-nmr:

C-3:	48.1	4-Me:	20.1
C-4:	131.0	ipso:	141.4
C-5:	116.8	ortho:	113.2
C-6:	50.8	meta:	125.7
CN:	113.7	para:	150.8

Anal: Calculated for $C_{12}H_{12}N_4O_2$: C, 59.01; H, 4.95;

N, 22.94. Found: C, 59.65; H, 5.00; N, 23.24,

(see note 109).

Reaction of E-4-Chlorophenylazocyanide with 2,3-Dimethyl-1,3-Butadiene

E-4-Chlorophenylazocyanide (0.50 g, 3.0 mmol) was heated

at 95-105° for 3 h with 2,3-dimethyl-1,3-butadiene (0.49 g, 2

equiv) as described in the general procedure. Chromatography on

silica gel using ether-hexane (1:3 v/v) as the solvent afforded

1-(4-chlorophenyl)-2-cyano-4,5-dimethyl-1,2,3,6-tetrahydropyrida-

zine (0.67 g, 90%) as an off-white solid, mp 97-99°C. An analyti-

cal sample was recrystallized from petroleum ether-THF to yield

small, white platelets, mp 102.5-104.5°C.

Ir(CCl$_4$): 2996; 2916; 2866; 2806; 2211; 1600; 1495; 1447;

1304; 1230; 1095; 998.

^{1}H-nmr: 7.30, 7.16, 6.97, 6.82 (AB quartet, 4H, J = 9,

aromatic); 3.71 (Ψs, 4H, allyl); 1.71, 1.63

(Ψd, 6H, methyl).

^{13}C-nmr:

C-3:	49.1	5-Me:	15.9
C-4:	122.3	ipso:	126.9
C-5:	122.9	ortho:	116.3
C-6:	54.1	meta:	129.1
CN:	114.2	para:	144.6
4-Me:	15.1		

Anal: Calculated for $C_{13}H_{14}ClN_3$: C, 63.03; H, 5.70;

N, 16.96. Found: C, 62.98; H, 5.74; N, 16.94.

Reaction of E-4-Chlorophenylazocyanide with 2,3-Dimethyl-1,3-Butadiene at Ambient Temperature

E-4-Chlorophenylazocyanide (4.0 g, 24 mmol) and 2,3-dimethyl-
1,3-butadiene (8.0 g, 4 equiv) were combined in a 25 mL, round-
bottomed flask equipped with a magnetic stirring bar. The mixture
was stirred at ambient temperature, and became dark and homo-
geneous after 1 h. After stirring ca. 2 h, the mixture had
solidified into a solid mass. Additional diene (2.0 g, 1 equiv)
was then added, and the soft solid mass broken up with a spatula.
After stirring an additional 5 h, the mixture was adsorbed onto
silica gel. Chromatography on silica gel using ether-hexane
(1:9 v/v) as the solvent afforded 1-(4-chlorophenyl)-2-cyano-
4,5-dimethyl-1,2,3,6-tetrahydropyridazine (5.07 g, 85%) as a white
solid, mp 102-103°C. The product was characterized by ir and
^{1}H-nmr (vide supra).

Reaction of E-4-Methoxyphenylazocyanide with 2,3-Dimethyl-1,3-Butadiene

E-4-Methoxyphenylazocyanide (0.48 g, 3.0 mmol) was heated
for 3 h at 95-105°C with 2,3-dimethyl-1,3-butadiene (0.49 g, 2
equiv) as described in the general procedure. Chromatography
on silica gel using ether-hexane (1:3 v/v) as the solvent yielded

1-(4-methoxyphenyl)-2-cyano-4,5-dimethyl-1,2,3,6-tetrahydropyrida-
zine as a yellow oil (0.51 g, 70%) which crystallized on standing
to a solid, mp 62-65°C. An analytical sample was obtained after
two recrystallizations from petroleum ether-THF as long, pale-
yellow needles, mp 69-70°C.

Ir(CCl_4):   3053-2803; 2213; 1507; 1422; 1387; 1349; 1247;

                      1182; 1042.

^{1}H-nmr: 7.02, 6.96 (Ψd, 4H, aromatic); 3.78 (Ψs, 7H,

                      OMe and allyl); 1.76, 1.68 (Ψd, 6H, methyl).

^{13}C-nmr:

C-3:	49.7	5-Me:	16.0
C-4:	122.2	ipso:	139.7
C-5:	123.3	ortho:	117.5
C-6:	53.9	meta:	114.4
CN:	114.6	para:	155.3
4-Me:	15.0		

Anal: Calculated for $C_{14}H_{17}N_3O$: C, 69.11; H, 7.04;

            N, 17.27. Found: C, 69.23; H, 7.19; N, 17.36.

Reaction of E-4-Nitrophenylazocyanide with 2,3-Dimethyl-1,3-Butadiene

A solution of E-4-nitrophenylazocyanide (0.53 g, 3.0 mmol)
in ca. 3 mL benzene was added dropwise over 25 min to a 5-mL,
round-bottomed flask containing a stirred solution of 2,3-dimethyl-
1,3-butadiene in 1 mL benzene at ambient temperature. During the

addition, a light-colored solid formed in the mixture. The mixture
was stirred for 3 h after addition was complete, diluted with
dichloromethane, and adsorbed onto silica gel. Chromatography
on silica gel using ether-hexane (1:3 v/v) as the solvent afforded
1-(4-nitrophenyl)-2-cyano-4,5-dimethyl-1,2,3,6-tetrahydropyridazine
as a pale-yellow solid (0.73 g, 94%), mp 143-147°C. An analytical
sample was obtained after recrystallization from hexane-THF as
short, yellow needles, mp 147-149°C.

Ir(CH_2Cl_2): 2926; 2216; 1600; 1508; 1338; 1118; 846.

^{1}H-nmr: 8.36, 8.19, 7.23, 7.06 (AB quartet, 4H, J = 10,
aromatic); 3.96 (Ψd, 4H, allyl); 1.79 (Ψs,
6H, methyl).

^{13}C-nmr:

C-3:	48.2	5-Me:	15.9
C-4:	122.5	ipso:	141.3
C-5:	122.5	ortho:	113.1
C-6:	54.4	meta:	125.6
CN:	113.7	para:	150.8
4-Me:	15.2		

Anal: Calculated for $C_{13}H_{14}N_4O_2$: C, 60.46; H, 5.46;
N, 21.69. Found: C, 60.48; H, 5.53; N, 21.68.

Reaction of E-4-Chlorophenylazocyanide
with E-Piperylene

E-4-Chlorophenylazocyanide (0.50 g, 3.0 mmol) was heated
(3 h, 95-108°C) with E-piperlyene (0.41 g, 2 equiv) according
to the general procedure. Chromatography on silica gel using
ether-hexane (50:50 v/v) as the solvent afforded a yellow oil
(0.72 g, 100%). This product was identified by ^{13}C-nmr as a
mixture of 1-(4-chlorophenyl)-2-cyano-6-methyl-1,2,3,6-tetra-
hydropyridazine and the corresponding 3-methyl regioisomer.
The isomeric ratio was estimated by ^{1}H-nmr as 4:1, respectively.

Ir(neat):   3061; 2991; 2944; 2821; 2211; 1597; 1492; 1442;
             1297; 1222; 1130; 1092; 1006; 822.

^{1}H-nmr: 7.30, 7.15, 6.97, 6.82 (AB quartet, 4H, J = 9,
             aromatic); 5.82 (Ψs, 2H, vinyl); 3.84 (Ψs, 3H,
             allyl); 1.50, 1.40 (d, J = 6, methyl); 1.44,
             1.33 (d, J = 6, methyl).

^{13}C-nmr: Major Isomer:

C-3:	44.56 (t)	CN:	not obsd[92]
C-4:	122.8 (d)	ipso:	126.8
C-5:	128.4 (d)	ortho:	116.1
C-6:	56.4 (d)	meta:	129.0
6-Me:	17.5	para:	145.0

Minor Isomer:

C-3:	52.13 (d)	CN:	not obsd
C-4:	129.4	ipso:	not obsd
C-5:	120.9	ortho:	116.9
C-6:	47.0 (t)	meta:	129.2
3-Me:	18.1	para:	144.5

Anal: Calculated for $C_{12}H_{12}N_3Cl$: C, 61.67; H, 5.18;

N, 17.98. Found: C, 61.14; H, 5.07; N, 17.85,

(see note 109).

Reaction of E-4-Methoxyphenylazocyanide with E-Piperylene

E-4-Methoxyphenylazocyanide (0.48 g, 3.0 mmol) was heated

(3 h, 94-105°C) with E-piperylene (0.41 g, 2 equiv) as described

in the general procedure. Chromatography on silica gel using

ether-hexane (50:50 v/v) as the solvent afforded a yellow oil

(0.32 g, 47%). This product was identified by ^{13}C-nmr as a

mixture of 1-(4-methoxyphenyl)-2-cyano-6-methyl-1,2,3,6-tetra-

hydropyridazine and the corresponding 3-methyl regioisomer.

The isomeric ratio was estimated by ^{1}H-nmr as 8:1, respectively.

Ir(neat):   3046; 2986; 2936; 2846; 2216; 1513; 1443;

1373; 1253; 1218; 1185; 1133; 1038; 831;

763; 715.

^{1}H-nmr: 6.90, 6.85 (Ψd, 4H, aromatic); 5.81 (Ψs, 2H,

vinyl); 3.74 (Ψs, 6H, OMe and allyl); 1.45,

1.33 (d, J = 7, methyl); 1.42, 1.30 (d, J = 7,

methyl).

^{13}C-nmr: Major Isomer:

C-3:	45.2 (t)	ipso:	140.1
C-4:	123.4 (d)	ortho:	117.4
C-5:	128.5 (d)	meta:	114.4
C-6:	56.3 (d)	para:	155.3
6-Me:	17.7	OMe:	55.4
CN:	not obsd[92]		

Minor Isomer:

C-3:	52.2 (d)	CN:	not absd[92]
C-4:	130.1	ipso:	140.1
C-5:	121.1	ortho:	117.4
C-6:	46.6	meta:	114.4
3-Me:	19.1	para:	155.3
		OMe:	55.4

Anal: Calculated for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59;

N, 18.33. Found: C, 67.91; H, 6.62; N, 18.19.

Reaction of E-4-Nitrophenylazocyanide
with E-Piperylene

A 5-mL, round-bottomed flask fitted with a magnetic stirring
bar was charged with E-4-nitrophenylazocyanide (0.53 g, 3.0 mmol).
E-Piperlyene was poured in, and stirring commenced. An exothermic
reaction occurred: all of the solid azocyanide dissolved to form
a dark-red mixture, and the flask became appreciably warm. This
exotherm lasted ca. 2-3 min; a dark-orange oil remained suspended
in the excess diene. The mixture was stirred an additional 10
min, and the excess diene allowed to evaporate, leaving a tan
solid. The reaction mixture was washed out of the flask with
dichloromethane; evaporation of this solution in vacuo left a
brown oil, which resolidified upon trituration with ether-hexane.
This solid was filtered off, washed with cold hexane, and air-dried
to afford a pale-yellow solid (0.70 g, 96%), mp 63-75°C. This
product was identified by ^{13}C-nmr as a mixture of 1-(4-nitro-
phenyl)-2-cyano-6-methyl-1,2,3,6-tetrahydropyridazine and the
corresponding 3-methyl regioisomer. The isomeric ratio was
estimated by [1]H-nmr to be 2:1, respectively. An analytical sample
was obtained after recrystallization from ether-hexane as a
pale-yellow solid, mp 64-70°C.

$Ir(CH_2Cl_2)$: 2932; 2832; 2212; 1600; 1495; 1345-1245;

1220; 1115; 840.

^{1}H-nmr: 8.36, 8.21, 7.23, 7.09 (AB quartet, 4H, J = 9,

aromatic); 6.03 (Ψs, 2H, vinyl); 4.16 (Ψs, 3H,

allyl); 1.66, 1.54 (d, J = 7, methyl); 1.50,

1.40 (d, J = 6, methyl).

^{13}C-nmr: Major Isomer:

C-3:	44.0 (t)	CN:	not obsd[92]
C-4:	122.3	ipso:	141.4
C-5:	128.5	ortho:	113.0
C-6:	56.8 (d)	meta:	125.6
6-Me:	17.6	para:	151.2

Minor Isomer:

C-3:	52.3	CN:	not obsd[92]
C-4:	129.0	ipso:	141.4
C-5:	121.1	ortho:	112.1
C-6:	49.0	meta:	126.0
3-Me:	17.3	para:	151.2

Anal: Calculated for $C_{12}H_{12}N_4O_2$: C, 59.01; H, 4.95

N, 22.94. Found: C, 57.97; H, 5.00; N, 22.53,

(see note 109).

Reaction of E-4-Chlorophenylazocyanide
with Cyclopentadiene

E-4-Chlorophenylazocyanide (0.50 g, 3.0 mmol) was heated

(i h, 50–56°C) with cyclopentadiene (0.40 g, 2 equiv, freshly-

distilled from dimer at bp 39°C) according to the general procedure.

Chromatography on silica gel using ether-hexane (1:3 v/v) as the
solvent afforded 1-(4-chlorophenyl)-2-cyano-1,2-diazabicyclo[2.2.1]-
4-heptene (0.40 g, 58%) as an off-white solid, mp 92-95°C. An
analytical sample was further purified by preparative-tlc on
silica gel, using ether-hexane (3:1 v/v) as the solvent to yield
small platelets, mp 95-96°C.

Ir(CH$_2$Cl$_2$):   2215; 1591; 1551; 1486; 1331; 1181; 1091;

1029; 1008; 901; 826.

^{1}H-nmr: 7.38, 7.22, 7.10, 6.94 (AB quartet, 4H, J = 9,

aromatic; 6.47 (m, 2H, vinyl); 4.85 (m, 2H,

allyl); 2.25, 2.10, 1.94, 1.79 (AB quartet,

J = 9, 2H, methylene bridge).

^{13}C-nmr:

C-3:	69.3	CN:	not obsd[92]
C-4:	134.3	ipso:	127.9
C-5:	137.6	ortho:	119.2
C-6:	69.9	meta:	128.9
C-7:	47.1	para:	147.9

Anal: Calculated for C$_{12}$H$_{10}$N$_3$Cl: C, 62.21; H, 4.35;

N, 18.14. Found: C, 62.52; H, 4.43; N, 18.18.

Attempted Reaction of E-4-Methoxy-
phenylazocyanide with Cyclopentadiene

E-4-Methoxyphenylazocyanide (0.48 g, 3.0 mmol) was heated
(4 h, 50-52°C) with cyclopentadiene (0.40 g, 2 equiv, freshly-
distilled from dimer at bp 39°C) as described in the general
procedure. After stirring, the mixture was heterogeneous; the
solid azocyanide did not appear to have dissolved or reacted.
Tlc analysis on a silica plate using ether-hexane (50:50 v/v)
as the solvent indicated only starting materials. The reaction
was abandoned.

Reaction of E-4-Nitrophenylazocyanide
with Cyclopentadiene

E-4-Nitrophenylazocyanide (0.53 g, 3.0 mmol) was placed in
a 10-mL, round-bottomed flask. Cyclopentadiene (2.5 g, 13 equiv,
freshly-distilled from dimer at bp 39°C) was poured in, and the
mixture stirred with a spatula. A red-orange homogeneous solution
formed immediately; after 5 min, its color had faded to light
orange, with precipitation of a yellow solid. Evaporation of
the excess cyclopentadiene yielded 1-(4-nitrophenyl)-2-cyano-
1,2-diazabicyclo[2.2.1]-4-heptene as a yellow solid (0.73 g, 100%),
mp 100-108°C. An analytical sample was obtained after recrystalli-
zation from ether-hexane as short, yellow needles, mp 110-112°C.

$Ir(CH_2Cl_2)$: 2212; 1592; 1512; 1492; 1342-1252; 1182;

1112; 1030; 902; 862; 844.

^{1}H-nmr:	8.26, 8.12, 7.23, 7.10 (AB quartet, 4H, J = 8, aromatic); 6.57 (Ψs, 2H, vinyl); 5.27 (Ψs, 1H, allyl); 5.00 (Ψs, 1H, allyl); 2.37, 2.20, 2.10, 1.95 (AB quartet, 2H, J = 10, methylene bridge).

^{13}C-nmr:

C-3:	68.4	CN:	115.8
C-4:	134.4	ipso:	142.5
C-5:	137.7	ortho:	117.0
C-6:	70.5	meta:	125.1
C-7:	47.8	para:	154.6

Anal: Calculated for $C_{12}H_{10}N_4O_2$: C, 59.50; H, 4.16; N, 23.13. Found: C, 59.31; H, 4.10; N, 23.37.

Reaction of E-4-Chlorophenylazocyanide with 1,3-Cyclohexadiene

E-4-Chlorophenylazocyanide (0.50 g, 3.0 mmol) was heated (3 h, 95-105°C) with 1,3-cyclohexadiene (0.48 g, 2 equiv) as described in the general procedure. Chromatography on silica gel using ether-hexane (1:9 v/v) as the solvent yielded 1-(4-chlorophenyl)-2-cyano-1,2-diazabicyclo[2.2.2]-4-octene as a yellow oil which slowly crystallized under vacuum (0.32 g, 43%), mp 93-99°C. An analytical sample was obtained after two recrystallizations from hexane as off-white needles, mp 99-99.5°C.

Ir(CH$_2$Cl$_2$): 2946; 2216; 1486; 1387; 1211; 1091; 1056; 1006; 951; 846.

^{1}H-nmr: 7.38, 7.23, 7.12, 6.97 (AB quartet, 4H, J = 9,

aromatic); 6.51 (m, 2H, vinyl); 4.41 (m, 2H,

allyl); 2.42, 2.28 (Ψd, 2H methylene bridge);

1.58, 1.39 (Ψd, 2H, methylene bridge).

^{13}C-nmr:

C-3:	53.61	CN:	116.0
C-4:	130.7	ipso:	127.5
C-5:	133.1	ortho:	119.1
C-6:	54.7	meta:	128.7
C-7:	21.7	para:	142.2
C-8:	20.2		

Anal: Calculated for $C_{13}H_{12}ClN_3$: C, 63.55; H, 4.92;

N, 17.10. Found: C, 63.58; H, 4.90; N, 17.23.

Attempted Reaction of E-4-Methoxyphenylazocyanide with 1,3-Cyclohexadiene

E-4-Methoxyphenylazocyanide (0.48 g, 3.0 mmol) was heated

(17 h, 95-97°C) with 1,3-cyclohexadiene (1.2 g, 5 equiv) according

to the general procedure. Tlc analysis using a silica plate and

ether-hexane (50:50 v/v) as the solvent showed a trace of starting

azocyanide, a mixture of very slow-moving products, and a large

amount of immobile residue. Chromatography on silica gel using

the same solvent afforded two fractions (0.12 g of red, tarry

material; 0.09 g of red solid, respectively). ^{1}H-nmr spectra of

these products were completely devoid of signals except for a weak multiplet (3.80) in each case. The reaction was abandoned.

Reaction of E-4-Nitrophenylazocyanide with 1,3-Cyclohexadiene

A 10-mL, round-bottomed flask fitted with a magnetic stirring bar was charged with a solution of 1,3-cyclohexadiene (0.96 g, 4 equiv) in ca. 1 mL of benzene. A solution of E-4-nitrophenyl-azocyanide (0.53 g, 3.0 mmol) in ca. 3 mL of benzene was added dropwise with stirring over 60 min. As the azocyanide solution was added, an orange-brown solid formed in the reaction mixture. After addition was complete, ca. 3 mL of dichloromethane was added to the mixture, which was then stirred an additional 2 h. After stirring, the filtered mixture was adsorbed onto silica gel. Chromatography on silica gel using ether-hexane (50:50 v/v) as the solvent afforded 1-(4-nitrophenyl)-2-cyano-1,2-diazabicyclo-[2.2.2]-4-octene as a pale-yellow solid (0.20 g, 26%), mp 138–140°C.

$Ir(CH_2Cl_2)$:   2950; 2220; 1593; 1513; 1496; 1338; 1113; 843.

^{1}H-nmr: 8.33, 8.16, 7.30, 7.15 (AB quartet, 4H, J = 10, aromatic); 6.66 (m, 2H, vinyl); 4.81, 4.48 (Ψd, 2H, allyl); 2.44, 2.27 (Ψd, 2H, methylene bridge); 1.64, 1.47 (Ψd, 2H, methylene bridge).

^{13}C-nmr:

C-3:	53.8	CN:	115.3
C-4:	131.7	ipso:	142.4
C-5:	133.3	ortho:	116.6
C-6:	54.4	meta:	125.2
C-7:	21.7	para:	154.8
C-8:	20.6		

Anal: Calculated for $C_{13}H_{12}N_4O_2$: C, 60.93; H, 4.72;

N, 21.86. Found: C, 61.55; H, 4.82; N, 21.82,

(see note 109).

Reaction of E-4-Chlorophenylazocyanide with Chloroprene

E-4-Chlorophenylazocyanide (0.50 g, 3.0 mmol) was heated

(3 h, 100-105°C) with chloroprene (1.06 g, 4 equiv) according to

the general procedure. Chromatography on silica gel using ether-

hexane (1:3 v/v) as the solvent afforded 0.78 g (100%) of off-

white solid, mp 94-96°C. ^{13}C-nmr indicated this product to be

a mixture of the major isomer 1-(4-chlorophenyl)-2-cyano-4-

chloro-1,2,3,6-tetrahydropyridazine, and the corresponding

5-chloro regioisomer as the minor product.

Ir(CH_2Cl_2): 2229; 1669; 1601; 1498; 1220; 1102; 1014; 830.

^{1}H-nmr: 7.35, 7.20, 6.99, 6.84 (AB quartet, 4H, J = 9,

aromatic); 5.94 (Ψs, 1H, vinyl); 3.96 (Ψs, 4H,

allyl).

^{13}C-nmr: Major Isomer:

C-3:	50.0	ipso:	128.1
C-4:	127.9	ortho:	116.9
C-5:	119.7	meta:	129.4
C-6:	50.0	para:	143.7
CN;	113.3		

Minor Isomer:

C-3:	45.9	ipso:	not obsd
C-4:	120.6	ortho:	116.8
C-5:	128.0	meta:	129.4
C-6:	54.5	para:	143.7
CN:	113.3		

Anal: Calculated for $C_{11}H_9Cl_2N_3$: C, 51.99; H, 3.57; N, 16.54. Found: C, 50.89; H, 3.41; N, 16.20, (see note 109).

¹H-nmr Investigation of the Reaction of
E-4-Chlorophenylazocyanide with Norbornadiene

E-4-Chlorophenylazocyanide (ca. 0.10 g, 0.7 mmol) was mixed
with norbornadiene (ca. 1 equiv) in mL of chloroform-d, and
filtered into 5 mm nmr-sample tube, which was then sealed with
a rubber septum cap. The initial solution was red-orange and
homogeneous. The ¹H-nmr spectrum of the mixture was then
determined at intervals.

t = 0:   The spectrum showed only starting materials;

            resonances observed at 8.12, 7.94, 7.78, 7.60

            (AB quartet, azocyanide); 6.82 (m, vinyl); 3.60

            (m, allyl); 2.00 (m, methylene); norbornadiene.

            Ratio of integral values, aromatic/vinyl: 1.27.

t = 1.5 h: The solution had darkened slightly. The nmr

            signals were unchanged. Aromatic/vinyl ratio:

            1.22.

t = 5 h: The solution had become dark-brown, depositing

            solid material on the walls. The nmr signals

            remained unchanged. Aromatic/vinyl ratio: 1.17.

t = 10 h: Solution had become nearly black and opaque;

            black solids were present. The nmr signals

            remained unchanged. Aromatic/vinyl ratio: 1.18.

The reaction was abandoned after 10 h; no attempt was made either
to isolate or further characterize reaction products.

Hydrolysis Reactions of 1-(4-Chlorophenyl)-
2-cyano-4,5-dimethyl-1,2,3,6-tetrahydropyridazine

A 15 mL, round-bottomed flask fitted with a magnetic stirring
bar and a reflux condenser was charged with 1-(4-chlorophenyl)-
2-cyano-4,5-dimethyl-1,2,3,6-tetrahydropyridazine (0.74 g, 3.0
mmol) and 5 mL 15% aq (w/w) KOH. The stirred, heterogeneous
mixture was refluxed for 24 h. After cooling to ambient tempera-
ture, the mixture consisted of a heavy, pale-yellow oil which had
settled below the aqueous phase. The aqueous layer was decanted
and this oil was dissolved in dichloromethane. The resulting
solution was washed with 2% aq (w/w) HCl (1 x 25 mL) and water
(2 x 25 mL), then dried over Na_2SO_4. Evaporation _in vacuo_ yielded
1-(4-chlorophenyl)-2-carboxamido-4,5-dimethyl-1,2,3,6-tetrahydro-
pyridazine as a pale yellow oil which foamed into a solid, color-
less glass under vacuum (0.74 g, 93%). This product did not
display a sharp melting point, but instead softened and liquefied
over a broad temperature range, 55-75°C.

Increasing the reflux time to 3 days increased the yield
of this product to 100%.

Similar hydrolysis in 10% aq (w/w) HCl (reflux 24 h) furnished
a 90% yield of the same product.

The products obtained by the above procedures tended to
darken from colorless to grey or purple over a few days. An
analytical sample was chromatographed on silica gel using

ether-hexane (3:1 v/v) as the solvent. The product was obtained as a colorless, solid glass, mp 62-70°C.

Ir(CH_2Cl_2): 3530; 3415; 2920; 2870; 1677; 1660; 1554; 1492; 1437; 1206; 1096; 825.

^{1}H-nmr: 7.27, 7.11, 6.87, 6.72 (AB quartet, 4H, J = 9, aromatic); 5.80 (Ψs, 2H, amide); 4.52, 4.22, 3.46, 3.17 (Ψ-AB quartet, 2H, J = 18, allyl); 3.81 (Ψs, 2H, allyl); 1.67, 1.54 (d, 6H, methyl).

^{13}C-nmr:

C-3:	40.5	CO:	158.5
C-4:	121.4	ipso:	126.4
C-5:	123.5	ortho:	116.6
C-6:	50.2	meta:	129.3
4-Me:	15.4	para:	146.1
5-Me:	15.9		

Anal: Calculated for $C_{13}H_{16}ClN_3O$: C, 58.76; H, 6.07; N, 15.81. Found: C, 58.44; H, 6.07; N, 15.30.

The analysis for nitrogen is slightly outside normal combustion analytical error limits. However, the fact that the identical compound could be prepared by direct cycloaddition of the arylazocarbonamide and the same diene (see below) is considered conclusive proof of structure.

Reaction of E-4-Chlorophenylazocarbonamide
with 2,3-dimethyl-1,3-butadiene

E-4-Chlorophenylazocarbonamide (0.55 g, 3.0 mmol) was heated
(6 h, 100°C) with 2,3-dimethyl-1,3-butadiene (0.98 g, 4 equiv)
as described in the general procedure for arylazocyanides.
Chromatography on silica gel using ether-hexane (3:1 v/v) as the
solvent afforded 1-(4-chlorophenyl)-2-carboxamido-4,5-dimethyl-
1,2,3,6-tetrahydropyridazine as a pale-yellow oil which foamed
into a colorless glass under vacuum (0.74 g, 93%). The infrared
spectrum of this compound was identical with that of the compound
obtained from either acid or base hydrolysis of the corresponding
2-cyano-pyridazine (vide supra).

Catalytic Hydrogenation of 1-(4-Chlorophenyl)-
2-cyano-4,5-dimethyl-1,2,3,6-tetrahydropyridazine

1-(4-Chlorophenyl)-2-cyano-4,5-dimethyl-1,2,3,6-tetrahydro-
pyridazine (0.74 g, 3.0 mmol) was suspended in 50 mL of 95%
ethanol. 10% Pd/C catalyst (0.07 g, 10% w/w) was added, and
the mixture was hydrogenated on a Parr apparatus at 33 psi for
ca. 4 h. (At this time, the pressure had remained constant
at 28 psi for 1 h.) The mixture was filtered through a bed of
Celite, producing a clear, straw-colored solution. After stand-
ing ca. 48 h, the solution had become dark purple; evaporation
in vacuo afforded a purple, tarry residue. The major portion of
this residue was soluble in dichloromethane. However, a small

amount (0.07 g) of dichloromethane-insoluble solid was filtered

off. This solid did not melt when heated to 220°C, and was not

further examined. The filtrate was adsorbed onto silica gel,

and chromatographed using ether-hexane (50:50 v/v) as the solvent.

A yellow-orange oil was obtained whose ir, [1]H-nmr, and ^{13}C-nmr

spectra were consistent with the structure 1-(4-chlorophenyl)-

2-carboxaldehyde-4,5-dimethyl-1,2,3,6-tetrahydropyridazine (31%).

However, its elemental analysis was not in agreement with cal-

culated values. The yellow-orange oil tended to darken to brown

over a period of days.

| Ir(neat): | 2920; 2868; 1695; 1680; 1598; 1495; 1445; |
| | 1400; 1360; 1350; 1230; 1205; 825; 755; 690. |

[1]H-nmr: 8.36 (s, 1H, formamide); 7.27, 7.13, 6.91,

6.78 (AB quartet, 4H, J = 8, aromatic); 3.87

(Ψs, 4H, allyl); 1.67, 1.57 (Ψd, 6H, methyl).

[13]C-nmr:

C-3:	39.6	CO:	164.4 ± 0.1
C-4:	121.5	ipso:	122.3 or 121.7
C-5:	116.5	ortho:	115.0
C-6:	52.9	meta:	129.3
4-Me:	15.6 ± 0.2	para:	148.1
5-Me:	15.6 ± 0.2		

Anal: Calculated for $C_{13}H_{15}ClN_2O$: C, 62.28; H, 6.03;

N, 11.17. Found: C, 69.77; H, 7.11; N, 12.27.

Attempted Reduction of 1-(4-Chlorophenyl)-2-cyano-4,5-dimethyl-1,2,3,6-tetrahydro-pyridazine with Lithium Aluminum Hydride

Lithium aluminum hydride (0.12 g, 3.3 mmol) was placed in

a dry, 3-necked, 40-mL flask fitted with a nitrogen inlet, reflux

condenser, additional funnel, and magnetic stirrer. Anhydrous

ether (10 mL) was poured in, and the stirred mixture cooled on an

ice-water bath. A solution of 1-(4-chlorophenyl)-2-cyano-4,5-

dimethyl-1,2,3,6-tetrahydropyridazine (0.74 g, 3.0 mmol in 20 mL

anhydrous ether) was then added dropwise to the stirred mixture

over a period of 10 min. The mixture was stirred 30 min at 0°C

after addition was complete, and an additional 30 min at ambient

temperature. The mixture was then transferred to a 500-mL

erlenmeyer flask, and chilled in an ice bath with swirling while

10% aw (w/w) NaOH was slowly added. The ether solution was

decanted from the coagulated salts, which were in turn washed

with two more portions of ether. The combined ether solution

was filtered through Celite and dried over Na_2SO_4. Evaporation

in vacuo afforded a yellow oil (0.61 g). This oil had an ammonia-

cal odor and was basic to wet litmus. Tlc analysis on a silica

plate using ether-hexane (50:50 v/v) as the solvent indicated

a mixture of at least three moving products, none of which

corresponded to starting material. A solution of this oil in

chloroform-$\underline{d}$ rapidly darkened from yellow to brown over 15 min.

The ir spectrum (neat) of this oil showed the total absence of

cyano absorption, and a strong band at 1625 cm^{-1} which lies in

the correct region for the N-H bending vibration of a primary

amine (1650-1590). However, no N-H stretching bands were

observed (expected at 3460-3280 cm^{-1}). The ^{1}H-nmr spectrum was

uninterpretable, and this product was not further analyzed.

Determination of Reaction Kinetics for the
Cycloaddition of 4-Chlorophenylazocyanide
with 2,3-Dimethyl-1,3-butadiene

A.   Experimental Procedure

Equimolar solutions of 4-chlorophenylazocyanide and 2,3-

dimethyl-1,3-butadiene were prepared by weighing ($\pm$ 0.1 mg) $\underline{ca}$.

1.2 mmol of each reagent into separate, 1.00-mL volumetric flasks,

and diluting to the mark with chloroform-$\underline{d}$. The reaction solu-

tion was prepared by injecting 250-μL of each reagent solution

into a standard ^{1}H-nmr sample tube which had been sealed with a

rubber septum cap and immersed in an ice-water bath until its

insertion into the nmr-probe. In no case did the time between

reagent mixing and tube insertion exceed 20 min.

The probe temperature was determined by measuring the chemical

shift difference (Hz) between the proton resonances (hydroxylic

and methylene) of an ethylene glycol standard sample. The probe

was equilibrated prior to each run such that the observed ethylene glycol chemical shift difference remained constant ($\pm$ 0.5 Hz) for at least 1 h prior to sample tube insertion, indicating constant temperature. After each run was completed, the probe temperature was rechecked using the same procedure. We estimate that probe temperatures measured in this way are accurate to $\pm$ 1°C.

After thermal equilibration of the probe, the spectrometer was tuned using a sample which contained a chloroform-d solution of 2,3-dimethyl-1,3-butadiene in approximately the same concentration as that of the reaction mixture. After tuning the instrument, the reaction tube was removed from the ice-water bath, dried, placed in the probe, and a timer started.

Each data point was determined from five integral scans over the region 5.5-3.5 ppm; these scans were performed in succession as quickly as possible. The integral values thus obtained compared diene and product concentrations almost simultaneously; these five values were then averaged. The time at which the five scans was started and completed was noted; the data point time was taken to be the midpoint of this scanning time period. In this manner, data points were obtained ca. every five min during the first half-life, and ca. every 10-20 min thereafter until at least two half-lives had elapsed.

B.   Calculations

The rate law of the second order reaction
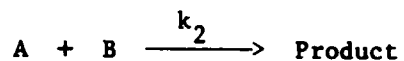
$$A \; + \; B \; \xrightarrow{\; k_2 \;} \; Product$$

in which the initial concentrations of A and B are equal is expressed in integrated form[110] as

$$\frac{x}{a-x} \; = \; k_2 at \; ,$$

where x = concentration of product formed at time t;

　　a = initial concentration of A = B;

　　k_2 = second-order rate constant

In the above equation,

　　x = integral value of allylic protons in product at time t;

　　(a − x) = integral value of vinyl protons in unreacted

　　　　　diene at time t;

　　a = initial concentration of diene (moles/liter).

A plot of x/(a − x) versus time (t) should be linear, with slope $k_2 a$. Since the initial concentration is known in moles/liter for diene, the second-order rate constant k_2 is obtained in units of $M^{-1} \, sec^{-1}$.

From the Arrhenius expression

$$k_2 = A \exp (-E_a^*/RT) \quad \text{and}$$

$$\log k_2 = \log A - \frac{E_a^*}{2.303 \ R} \cdot \frac{1}{T}$$

a plot of $\log k_2$ versus $1/T$ yields a straight line with slope $= -E_a^*/2.303 \ R$, and intercept $= \log A$.

The entropy of activation ΔS^* is calculated from the equation[111]

$$\Delta S^* = R(\ln A - \ln \frac{kT}{h} - 1)$$

where A = frequency factor

      k = Boltzmann constant

      h = Planck's constant

      T = average temperature

The accuracy of the experimental parameters is estimated to be:

    a. Temperature: $\pm$ 1°C

    b. ^{1}H-nmr Integral Values: $\pm$ 5%

    c. Reactant Concentrations: $\pm$ 5%

An overall accuracy of $\pm$ 10% is assigned to the measured rate constants, and to the derived activation parameters.

APPENDIX

Kinetic Data: Reaction Between 4-Chlorophenylazocyanide and 2,3-Dimethyl-1,3-butadiene

I. Temperature: 26°C

A. Initial Azocyanide Concentration: 0.658 M

B. Initial Diene Concentration: 0.658 M

C. Data:

Data Point	Time (Min.)	Average Integral Value Diene (a-x)	Product (x)	$\frac{x}{a-x}$
1	1.6	194.0	2.0	0.010
2	7.5	190.2	6.0	0.032
3	11.7	185.4	10.5	0.057
4	16.9	180.5	14.0	0.078
5	22.9	182.8	18.2	0.100
6	34.0	175.2	26.0	0.148
7	42.8	169.4	31.0	0.183
8	50.9	163.6	34.8	0.213
9	59.4	159.5	39.0	0.245
10	67.6	155.0	44.0	0.284
11	75.9	151.8	47.6	0.314
12	88.2	147.2	52.6	0.357
13	97.1	142.8	56.5	0.396
14	107.1	138.8	61.4	0.442
15	124.7	131.4	67.6	0.514
16	134.2	127.8	71.0	0.556
17	146.6	124.3	75.5	0.607
18	159.5	121.0	79.0	0.653
19	175.9	113.7	83.8	0.737
20	184.6	111.8	87.0	0.778
21	198.3	108.8	90.2	0.829
22	213.1	105.0	95.2	0.907
23	229.7	100.8	97.4	0.966
24	241.1	98.4	100.6	1.02
25	257.6	96.0	104.4	1.09

Kinetic Data: Reaction Between 4-Chlorophenylazocyanide
and 2,3-Dimethyl-1,3-butadiene (Continued)

Data Point	Time (Min.)	Average Integral Value Diene (a-x)	Product (x)	$\frac{x}{a-x}$
26	273.2	93.8	108.0	1.15
27	292.8	90.0	112.4	1.25
28	313.3	86.2	115.2	1.34
29	335.2	83.4	118.2	1.42
30	354.8	80.6	120.8	1.50
31	377.6	77.8	123.6	1.59
32	414.4	72.2	127.8	1.77

D.   Plot x/a-x vs time (t):

Slope $= 4.246 \times 10^{-3}$ min^{-1} $= k_2 a$

$K_2 = 1.08 \times 10^{-4}$ M^{-1} sec^{-1}

Linear Correlation Coefficient $= 0.9996$

Kinetic Data: Reaction Between 4-Chlorophenylazocyanide
and 2,3-Dimethyl-1,3-butadiene (Continued)

II. Temperature: 37°C

A. Initial Azocyanide Concentration: 0.624 M

B. Initial Diene Concentration: 0.613 M

C. Data:

Data Point	Time (Min.)	Average Integral Value Diene (a-x)	Product (x)	$\frac{x}{a-x}$
1	1.0	164.0	5.0	0.031
2	6.0	161.5	6.5	0.040
3	9.0	157.0	11.0	0.070
4	10.5	153.5	12.5	0.081
5	12.0	147.0	16.0	0.109
6	14.5	141.0	18.0	0.128
7	16.5	139.0	20.0	0.144
8	18.0	132.0	22.5	0.170
9	20.0	131.0	26.0	0.199
10	23.0	128.2	27.0	0.211
11	31.0	122.6	38.2	0.312
12	36.0	117.6	43.4	0.369
13	41.0	111.8	46.8	0.419
14	46.0	108.4	51.0	0.471
15	51.0	105.8	54.6	0.516
16	56.0	101.8	61.2	0.601
17	61.0	98.2	61.6	0.627
18	66.0	95.6	65.0	0.680
19	71.0	91.4	68.6	0.751
20	76.0	89.2	69.8	0.783
21	81.0	85.2	75.4	0.885
22	86.0	82.6	76.2	0.923
23	91.0	81.8	79.0	0.966
24	96.0	78.4	82.4	1.05
25	101.0	77.0	85.0	1.10
26	106.0	77.2	86.0	1.11
27	112.0	75.2	89.3	1.19
28	116.0	74.4	90.2	1.21
29	121.0	70.6	90.4	1.28

Kinetic Data: Reaction Between 4-Chlorophenylazocyanide
and 2,3-Dimethyl-1,3-butadiene (Continued)

Data Point	Time (Min.)	Average Integral Value Diene $(a-x)$	Average Integral Value Product (x)	$\dfrac{x}{a-x}$
30	126.0	71.4	95.6	1.34
31	131.0	69.8	94.8	1.36
32	136.0	68.4	99.4	1.45
33	141.0	65.4	100.6	1.54
34	151.0	64.3	104.8	1.63
35	156.0	63.6	105.8	1.66
36	161.0	61.4	107.8	1.76
37	177.0	60.0	112.4	1.87
38	196.0	54.4	116.2	2.14
39	226.0	49.4	119.2	2.41
40	271.0	44.0	126.4	2.87
41	331.0	38.7	134.5	3.48
42	367.0	36.0	140.3	3.90

D.   Plot $x/a-x$ vs time (t):

Slope $= 1.07 \times 10^{-2}$ min^{-1} $= k_2 a$

$K_2 = 2.92 \times 10^{-4}$ M^{-1} sec^{-1}

Linear Correlation Coefficient $= 0.9996$

Kinetic Data: Reaction Between 4-Chlorophenylazocyanide
and 2,3-Dimethyl-1,3-butadiene (Continued)

III. Temperature: 45°C

    A. Initial Azocyanide Concentration: 0.610 M

    B. Initial Diene Concentration: 0.610 M

    C. Data:

Data Point	Time (Min.)	Average Integral Value Diene (a-x)	Average Integral Value Product (x)	$\frac{x}{a-x}$
1	0.5	168.0	0	0
2	4.0	155.8	10.0	0.064
3	6.4	149.8	16.2	0.108
4	11.2	137.3	24.8	0.181
5	16.3	129.2	34.0	0.263
6	21.1	121.8	43.6	0.358
7	26.0	113.8	48.8	0.429
8	31.0	108.0	55.6	0.515
9	36.0	103.0	60.6	0.588
10	41.0	97.8	66.4	0.679
11	46.0	92.0	72.6	0.789
12	51.3	89.7	76.0	0.847
13	56.0	85.4	80.8	0.946
14	61.0	81.0	82.8	1.02
15	66.0	78.4	86.0	1.10
16	71.2	76.2	89.8	1.18
17	81.0	67.6	97.4	1.44
18	86.0	67.8	97.8	1.44
19	91.0	65.0	101.4	1.56
20	96.0	64.2	102.8	1.60
21	101.0	61.0	104.8	1.72
22	106.0	57.6	107.2	1.86
23	111.2	57.0	109.0	1.91
24	116.2	54.7	109.7	2.01
25	121.0	53.0	111.8	2.11
26	126.0	51.2	114.2	2.23
27	133.0	50.0	116.0	2.32
28	147.0	46.8	119.4	2.55
29	151.0	45.6	120.6	2.64

Kinetic Data: Reaction Between 4-Chlorophenylazocyanide
and 2,3-Dimethyl-1,3-butadiene (Continued)

Data Point	Time (Min.)	Average Integral Value Diene (a-x)	Average Integral Value Product (x)	$\frac{x}{a-x}$
30	161.0	43.4	122.6	2.82
31	174.0	40.4	126.6	3.13
32	184.0	38.8	128.8	3.32
33	201.0	36.0	132.2	3.67
34	211.2	34.8	135.4	3.89
35	226.0	32.6	136.8	4.20
36	246.0	30.6	139.6	4.56

D. Plot x/a-x vs time (t):

Slope $= 1.85 \times 10^{-2}$ min^{-1} $= k_2 a$

$K_2 = 5.04 \times 10^{-4}$ M^{-1} sec^{-1}

Linear Correlation Coefficient $= 0.9990$

Kinetic Data: Reaction Between 4-Chlorophenylazocyanide
and 2,3-Dimethyl-1,3-butadiene (Concluded)

IV.   Activation Parameters

A. $\log k_2 = \log A - \dfrac{\Delta E*}{2.303R} \cdot \dfrac{1}{T}$

B.   Plot $\log k_2$ vs. $1/T$ ($^{\circ}$k)

Slope $= -\Delta E*/2.303R = -3.375 \times 10^3$

Intercept $= \log A = 7.36$

Linear Correlation Coefficient $= -0.9980$

$\Delta E* = 15.5$ kcal/mole

C. $\Delta S* = R \left(\ln A - \ln \dfrac{kT}{h} - 1 \right)$

Let T = average temperature = 309°k

$\Delta S* = -26.9$ e.u.

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