Thermal Rearrangements of 2-Azido- and 2,3-Diazido-1,4-quinol Diacetates[1,2]

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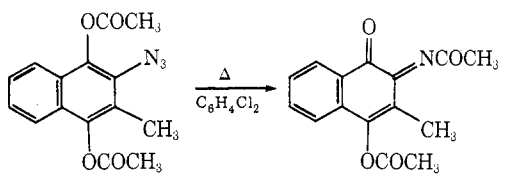
The thermal rearrangements of various 1,4-diacetoxy-2-azidobenzenes (**3a–c**) to *N*-acyl-*o*-quinoneimines (**4**) and of 1,4-diacetoxy-2,3-diazidobenzenes (**3f–h**) to *trans,trans*-1,4-diacetoxy-*cis,cis*-1,4-dicyano-1,3-butadienes (**21**) are reported. The scopes and mechanisms of these transformations are discussed. In addition, further synthetic utility of the pyrolytic cleavage of 1,4-diacetoxy-2,3-diazidoaryls is illustrated by the conversion of 1,4-diacetoxy-2,3-diazidonaphthalene (**3e**) to a mixture of *cis*- and *trans*-1,2-diacetoxy-1,2-dicyanobenzocylobutene (**22, 23**) and 1,4-diacetoxy-3-cyanoisoquinoline (**24**).

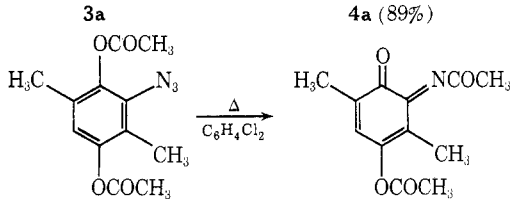
The general availability of azidoquinones[3] and their ease of conversion to reduced hydroquinone derivatives provide a convenient and facile route to a large variety of highly substituted aryl azides. Reported here is the synthesis and an investigation of the thermal chemistry of two such series of compounds. Specifically, the pyrolytic rearrangement of the 1,4-diacetoxy-2-azidobenzenes (**3a–c**) to the corresponding *N*-acyl quinoneimines (**4a–c**) and the thermally induced cleavage of 1,4-diacetoxy-2,3-diazidobenzenes (**3f–h**) to 1,4-diacetoxy-1,4-dicyano-1,3-butadienes (**21a–c**) are reported. The former transformation is without precedent in aryl azide chemistry, while the latter finds direct analogy in the previously reported thermal cleavage of *o*-diazidobenzenes to *cis,cis*-1,4-dicyano-1,3-butadienes.[4] To our knowledge, the only other report in the literature concerning the chemistry of 1,4-dioxygenated aryl azides is the observation that azidohydroquinones thermally disproportionate to the corresponding aminoquinones.[5]

Synthesis of Azidohydroquinone Diacetates. All of the azidohydroquinone diacetates (**3a–h**) reported here were conveniently prepared in reasonable yield by the simple sodium dithionite reduction of the corresponding azidoquinones (**1a–h**) followed by their acylation with acetic anhydride–pyridine. The hydroquinones (**2a–h**) were not isolated, but were converted *in situ* to the diacetates (**3a–h**) (Scheme I). The syntheses of all of the starting azidoquinones, with the exception of **1f** and **1g** (Experimental Section) have been previously reported.[3,6]

Thermolysis of 1,4-Diacetoxy-2-azidobenzenes. Thermal decomposition of the monoazidohydroquinone diacetates (**3a–c**) in refluxing *o*-dichlorobenzene (180°) or chlorobenzene (132°) resulted in their facile transformation to the corresponding *N*-acyl-1,2-quinoneimines (**4a–c**). The reactions were most conveniently accomplished by slowly adding a solution of the azide to the refluxing solvent. In most cases this resulted in an instantaneous reaction upon contact. The yields of the products were appreciably enhanced when the reactions were run in this manner as compared to simply refluxing a preformed solution of the azide.

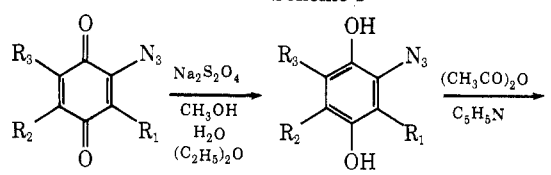


3a **4a** (89%)



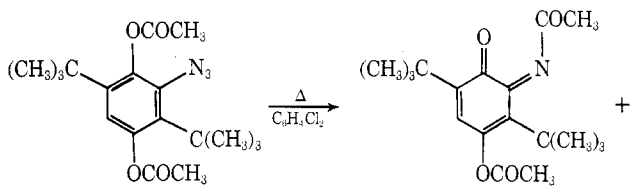
3b **4b** (45%)

Scheme I

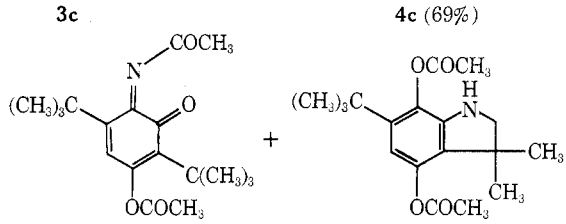


1 **2** **3**

	R_1	R_2	R_3	Yield, %
3a	CH_3	$-CH{=}CHCH{=}CH-$		66
b	CH_3	H	CH_3	92
c	$C(CH_3)_3$	H	$C(CH_3)_3$	44
d	C_6H_5	H	C_6H_5	84
e	N_3	$-CH{=}CHCH{=}CH-$		69
f	N_3	$-CH_2CH_2CH_2CH_2-$		64
g	N_3	C_6H_5	H	63
h	N_3	CH_3	CH_3	72



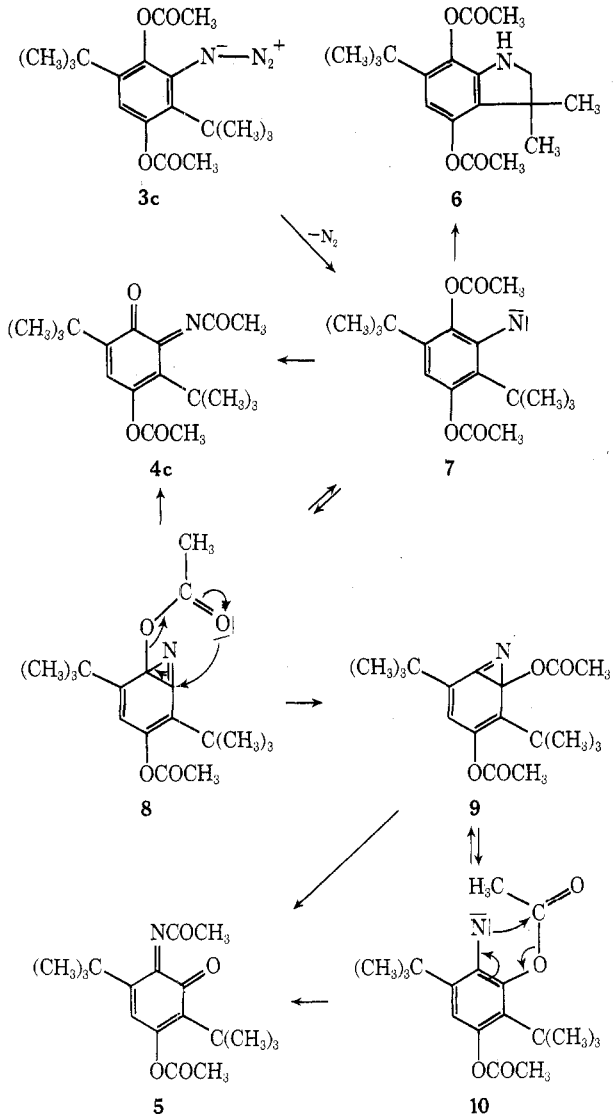
3c **4c** (69%)



5 (17%) **6** (1.5%)

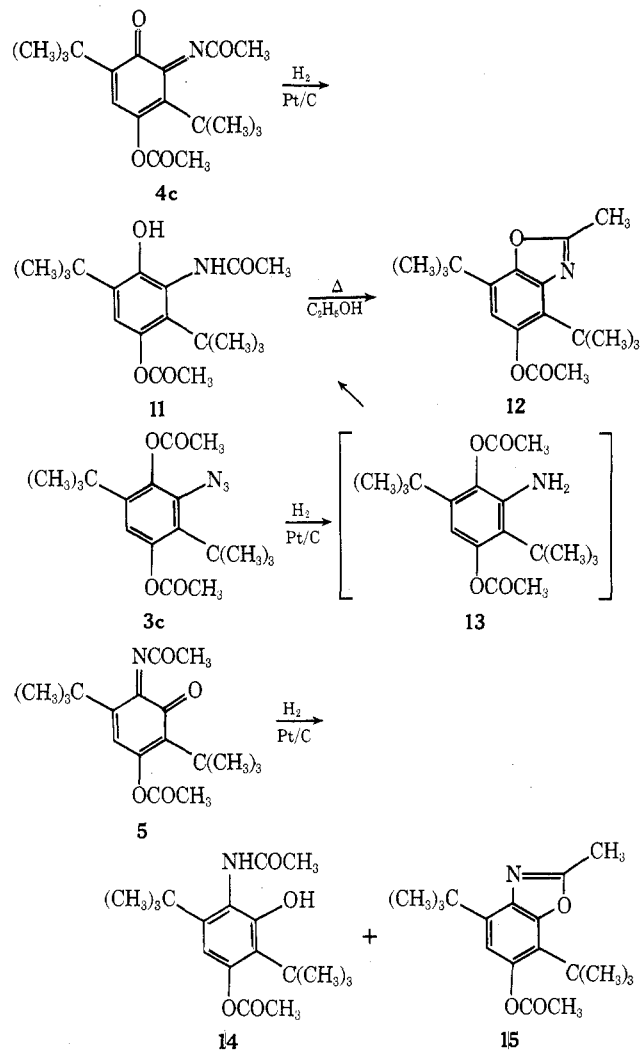
N-Acyl-1,2-quinoneimines of the type presented here constitute a previously unreported class of compounds and would be most difficult to prepare by other known methods. Their potential utility as *o*-quinone precursors is under investigation.

Scheme II



It should be noted that two additional products were isolated from the decomposition reaction of the azide **3c**. In addition to the major and anticipated product, **4c**, a minor isomeric quinoneimine, tentatively identified as **5**, and the ring-closed dihydroindole **6** were obtained. The quinoneimine **5** could arise *via* the azirine **8** while **6** most certainly is generated from an insertion reaction of a nitrene precursor (**7**). Whether the penultimate precursors of the isomeric quinoneimines, **4c** and **5**, are the respective azirines or nitrenes is not known. However, the fact that both isomers are formed suggests the conversion of **8** to **9** *via* the interesting indicated sigmatropic shift represented in Scheme II. These azirines could collapse directly to the quinoneimines or equilibrate with the respective nitrenes, which could then give the products *via* acyl migration.

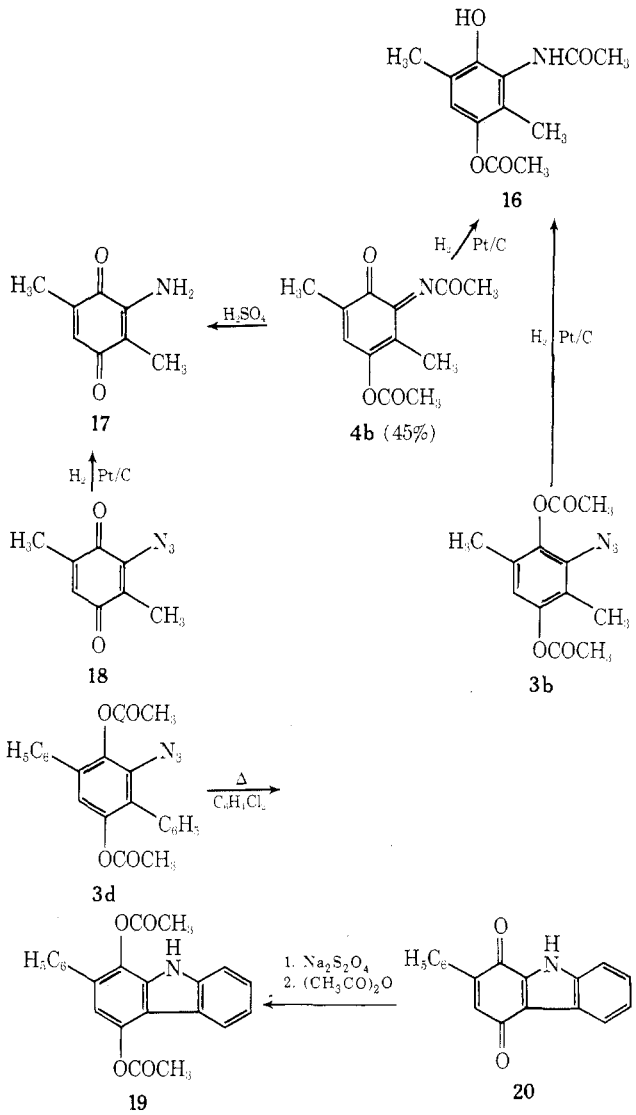
The structures of the products reported above are based upon both spectral and chemical properties. The quinoneimines all show characteristic ir absorptions for both carbonyl and imine double bonds. Their nmr spectra (Experimental Section) are also in strict agreement with their indicated formulations. Compound **4a** was chemically identified by its acid hydrolysis to the known aminoquinone, 2-amino-3-methyl-1,4-naphthoquinone.[5] Catalytic reduction of **4c** gave the phenol **11**, which was readily converted to the benzoxazole **12** in refluxing ethanol or in acetic anhydride–pyridine at 0–5°. The structural relationship of the various substituents of **4c** was established by the independent synthesis of **11** and **12** starting with 1,4-diacetoxy-2-azido-3,6-di-*tert*-butylbenzene (**3c**). Reduction of this azide with molecular hydrogen (Pt/C) gave **11** *via* the precursor **13**. The phenol **11**, in turn, was converted to the benzoxazole **12** as described above. The quinoneimine **5** was converted to **14** and **15** upon catalytic reduction. However, since these same compounds were not prepared by an independent route and since the spectral properties of **5**, **14**, and **15** do not unambiguously establish the orientation of the various substituents, the exact isomeric relationship of **4c** to **5** remains somewhat clouded.



Like **4a** and **4c**, the structure of **4b** was also well documented. The phenol, 2-acetamido-4-acetoxy-3,6-dimethylphenol (**16**), was obtained from both the quinoneimine **4b** and the azide **3b** by catalytic reduction. In addition, hydrolysis of **4b** in concentrated sulfuric acid gave 2-amino-3,6-dimethyl-1,4 benzoquinone (**17**), which was identical in all respects with the aminoquinone obtained by catalytic reduction of 2-azido-3,6-dimethyl-1,4-benzoquinone[3] (**18**).

Thermal decomposition of 1,4-diacetoxy-2-azido-3,6-diphenylbenzene (**3d**) in refluxing *o*-dichlorobenzene took a different course from that described above in that no quinoneimine was isolated. The only product identified was the carbazole **19**, obtained in 61% yield. The same heterocyclic compound was prepared in an independent manner by reductive acylation of the known indolequinone **20**,[7] thus firmly documenting its constitution.

The formation of **19** from the azide **3d** is suggestive of a nitrenoid intermediate.[8] This, along with the fact that the



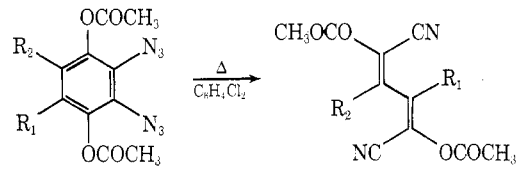
dihydroindole **6** is also generated from the azide **3c**, implies that monovalent nitrogen intermediates may be precursors to the quinoneimines **4a-c**. See, for example, Scheme II. However, the detailed mechanistic pathways for these transformations await further study. It is worthy of note that the formation of the quinoneimines does involve an acyl migration, a process rarely observed in the pyrolytic decomposition of organic azides.[9]

Thermolysis of 1,4-Diacetoxy-2,3-diazidobenzenes. Unlike the monoazides, 1,4-diacetoxy-2,3-diazidobenzenes (**3f-h**) (Scheme III) smoothly undergo a thermally induced ring cleavage in refluxing *o*-dichlorobenzene to give the 1,4-diacetoxy-1,4-dicyano-1,3-butadienes, respectively (**21a-c**). The stereochemistry of these dienes was not determined. However, based upon the unique report of Hall and Patterson[4] that simpler *o*-diazidobenzenes thermally cleave to *cis,cis*-1,4-dicyano-1,3-butadienes, it is assumed that a completely analogous transformation occurs here.

The fact that a large variety of substituted quinones are commercially and synthetically available and that they are easily converted to the corresponding *o*-diazidobenzenes provides a convenient source of highly substituted *trans,trans*-1,4-diacetoxy-*cis,cis*-1,4-dicyano-1,3-butadienes *via* the route described here. The highly functionalized dienes **21a-c**, which can be regarded as the acylated cyanohydrins of bis(ketenes), are masked 1,4-dicarbonyl moieties and may find corresponding synthetic utility.

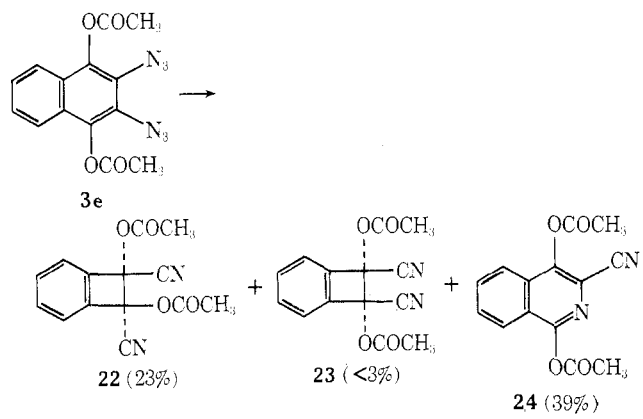
The spectral properties of the dienes **21a-c** are in agreement with their proposed structures (Experimental Section).

Scheme III

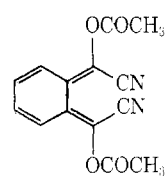


	R_1	R_2	Yield, %
21a	$-CH_2CH_2CH_2-$		77
b	C_6H_5	H	72
c	CH_3	CH_3	94

As yet, nothing is known of their chemical properties except that they are very poor Diels-Alder dienes, as one might expect since they are 1,4 tetrasubstituted. Molecular models, in fact, show a serious steric interaction between the linear cyano substituents when the dienes are in the s-cis conformation. Synthetic advantage was taken of the propensity of these dienes to avoid the planar s-cis conformation. Thermal decomposition of 1,4-diacetoxy-2,3-diazidonaphthalene (**3e**) would give a quinodimethane (**25**) in which the exocyclic diene system is obliged to reside in a planar s-cis conformation. Electronically as well as sterically, such a compound is favored to undergo electrocyclic ring closure and thus provide a direct route to the benzocyclobutene ring system. Indeed, such a transformation was observed. Decomposition of the diazidonaphthalene **3e** gave a mixture of the isomeric benzocyclobutenes **22** and **23** along with the unexpected isoquinoline **24**.



The stereochemical constitutions of **22** and **23** were not unambiguously established. However, from orbital symmetry considerations one would predict the major, if not the exclusive, isomer to be the trans, *i.e.*, **22**, which would arise *via* a conrotatory ring closure of the intermediate quinodimethane **25**.[10] Also, the ultraviolet absorption



spectra of **22** and **23** are in good agreement with their respectively assigned structures and stereochemistry. That is, an acetonitrile solution of **22** showed absorptions at 257 (2.74), 263 (2.89), and 270 nm (2.85) as compared to a solution of the cis isomer **23**, which absorbed at 257 (2.81), 263 (2.97), and 270 nm (2.90). Note that the extinction coefficients for the cis isomer are slightly larger than those for the trans. This observation, along with the characteris-

tic position of the three absorptions, are in strict accord with other 1,2-dioxygenated benzocyclobutenes.[11] For example, *trans*-1,2-dimethyl-1,2-dihydroxybenzocyclobutene absorbs at 258 (2.96), 265 (3.15), and 270.5 nm (3.09) while the cis isomer absorbs at 258 (3.02), 264 (3.18), and 270.5 nm (3.14).

In addition to its spectral characteristics (Experimental Section), the constitution of the isoquinoline **24** has its foundation on the fact that it undergoes hydrolytic (HI) conversion to the known 4-hydroxy-1-2*H*-isoquinolone.[12]

The formation of 1,4-diacetoxy-3-cyanoisoquinoline (**24**) from **3e** is most intriguing and must result from a very deep-seated rearrangement. An attractive possibility for such a mechanism is based upon the well-documented and fascinating gas-phase equilibration of phenylnitrenes and α-pyridylcarbenes.[13] In the case at hand, the nitrene **26** would rearrange to the azidocarbene **30** which, upon nitrogen loss, would give **24** (Scheme IV).

The rearrangements and cleavage reactions described in this paper illustrate further the synthetic utility of azidoquinones and related compounds. These compounds are readily available and constitute a synthetically versatile class of reagents. Depending upon their substitution pattern and, as illustrated here, their oxidation state, they can be converted to γ-cyanoalkylidene-$\Delta^{\alpha,\beta}$-butenolides,[3] 2-cyano-4-cyclopentene-1,3-diones,[7] cyanoketenes,[14] azepine-2,5-diones,[15] diacyl cyanides,[6,16] 3-cyano-2-azaquinones,[16] aminoquinones,[5] indolequinones,[17] 2-alkenyl-2,3-dihydroindole-4,7-diones,[1] and, now, 4-acetoxy-1,2-quinone-2-(*N*-acetyl)imines (**4**) and *trans,trans*-1,4-diacetoxy-*cis,cis*-1,4-dicyano-1,3-butadienes (**21**).

Experimental Section

General Procedure for the Preparation of 1,4-Diacetoxy-2-azido- (or 2,3-diazido-) benzenes (3). A suspension or solution of the corresponding azidoquinone **1** (0.5 mmol) in approximately 50–100 ml of diethyl ether and 10–20 ml of methanol was stirred at ambient temperature under an atmosphere of nitrogen. Excess aqueous sodium dithionite solution was then added and the two-phase mixture was vigorously stirred until the color stopped fading (10–30 min). The organic layer was separated and the aqueous layer was washed several times with ether. The combined organic layers were then dried and the solvent was removed *in vacuo* at temperatures below 30°. The resulting residue was dissolved in acetic anhydride–pyridine (4:1) and allowed to stand at room temperature or below for 5–20 hr. The reaction solution was then poured into ice and water and the resulting diacetates **3** were collected by filtration. Recrystallization from ethanol gave the pure samples.

1,4-Diacetoxy-2-azido-3-methylnaphthalene (3a). The title compound was prepared in 66% yield by the general procedure. Characteristic properties of **3a** follow: mp 145–146 dec; ir (Nujol) 2120, 1760 cm^{-1}; nmr ($CDCl_3$) δ 2.20 (s, 3), 2.49 (s, 6), 7.5 (m, 4).

Anal. Calcd for $C_{15}H_{13}N_3O_4$: C, 60.20; H, 4.38; N, 14.04. Found: C, 60.20; H, 4.50; N, 13.90.

1,4-Diacetoxy-2-azido-3,6-dimethylbenzene (3b). The title compound was prepared in 92% isolated yield as described above and showed the following characteristic properties: mp 81–83°; ir (Nujol) 2114, 1764 cm^{-1}; nmr ($CDCl_3$) δ 2.03 (s, 3), 2.09 (s, 3), 2.26 (s, 3), 2.34 (s, 3), 6.75 (s, 1).

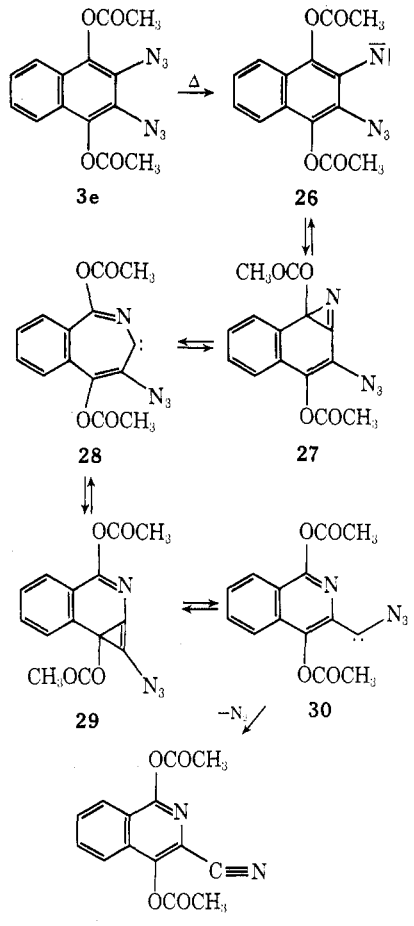
Anal. Calcd for $C_{12}H_{13}N_3O_4$: C, 54.74; H, 4.94; N, 15.96. Found: C, 54.56; H, 4.94; N, 15.93.

1,4-Diacetoxy-2-azido-3,6-di-*tert*-butylbenzene (3c). The title compound was prepared in 44% isolated yield as described above and showed the following characteristic properties: mp 134–136°; ir (Nujol) 2105, 1773, 1754 cm^{-1}; nmr ($CDCl_3$) δ 1.31 (s, 9), 1.47 (s, 9), 2.24 (s, 3), 2.40 (s, 3), 6.78 (s, 1).

Anal. Calcd for $C_{18}H_{25}N_3O_4$: C, 62.24; H, 7.20; N, 12.10. Found: C, 62.18; H, 7.15; N, 12.14.

1,4-Diacetoxy-2-azido-3,6-diphenylbenzene (3d). The title compound was prepared in 84% isolated yield as described above and showed the following characteristic properties: mp 149–151°; ir (Nujol) 2123, 1783, 1767 cm^{-1}; nmr ($CDCl_3$) δ 1.87 (s, 3), 2.04 (s, 3), 7.0 (s, 1), 7.55–7.18 (m, 10).

Scheme IV



Anal. Calcd for $C_{22}H_{17}N_3O_4$: C, 68.21; H, 4.39; N, 10.85. Found: C, 67.95; H, 4.56; N, 10.56.

1,4-Diacetoxy-2,3-diazidonaphthalene (3e). The title compound was prepared in 69% isolated yield as described above and showed the following characteristic properties: mp 134–135° dec; ir (Nujol) 2120, 1770 cm^{-1}; nmr ($CDCl_3$) δ 2.48 (s, 6), 7.4–7.8 (m, 4).

Anal. Calcd for $C_{14}H_{10}N_6O_4$: C, 51.53; H, 3.09; N, 25.76. Found: C, 51.47; H, 3.11; N, 25.76.

1,4-Diacetoxy-2,3-diazido-5,6,7,8-tetrahydronaphthalene (3f). The title compound was prepared in 64% isolated yield as described above and showed the following characteristic properties: mp 107–109 dec; nmr ($CDCl_3$) δ 1.5–1.7 (m, 4), 2.3–2.6 (m, 4), 2.32 (s, 6).

Anal. Calcd for $C_{14}H_{14}N_6O_4$: C, 50.91; H, 4.27; N, 25.45. Found: C, 50.99; H, 4.22; N, 25.38.

1,4-Diacetoxy-2,3-diazido-5-phenylbenzene (3g). The title compound was prepared in 63% isolated yield as described above and showed the following characteristic properties: mp 79–81°; ir (Nujol) 2120, 1760, 1560 cm^{-1}; nmr ($CDCl_3$) δ 2.05 (s, 3), 2.31 (s, 3), 6.96 (s, 1), 7.37 (s, 5).

Anal. Calcd for $C_{16}H_{12}N_6O_4$: C, 54.54; H, 3.43; N, 23.85. Found: C, 54.58; H, 3.41; N, 23.88.

1,4-Diacetoxy-2,3-diazido-5,6-dimethylbenzene (3h). The title compound was prepared in 72% isolated yield as described above and showed the following characteristic properties: mp 101–101.5° dec; ir (Nujol) 2120, 1760 cm^{-1}; nmr ($CDCl_3$) δ 2.01 (s, 6), 2.33 (s, 6).

Anal. Calcd for $C_{12}H_{12}N_6O_4$: C, 47.37; H, 3.96; N, 27.63. Found: C, 47.40; H, 3.91; N, 27.61.

2,3-Diazido-5,6,7,8-tetrahydro-1,4-naphthoquinone (1f). A solution of 4 g of sodium azide in 10 ml of water was added to a well-stirred solution of 3.0 g (13 mmol) of 2,3-dichloro-5,6,7,8-tetrahydro-1,4-naphthoquinone[18] in 50 ml of dichloromethane–methanol (1:1). The two-phase mixture was stirred at room temperature for 12 hr and then diluted with water. The organic layer was collected and dried ($MgSO_4$), and the solvent was removed *in vacuo*. The resultant deep red semisolid was recrystallized (methanol) to give the diazide as deep maroon crystals, mp 75–77° dec.

This diazide showed the following characteristic spectral properties: ir (Nujol) 2120, 1650, 1560 cm^{-1}; nmr ($CDCl_3$) δ 1.77 (m, 4), 2.44 (m, 4).

Anal. Calcd for $C_{10}H_8N_6O_2$: C, 49.18; H, 3.30; N, 34.42. Found: C, 49.26; H, 3.42; N, 34.50.

2,3-Diazido-5-phenyl-1,4-benzoquinone (1g). A solution of 5 g of sodium azide in 25 ml of water was added to a well-stirred solution of 5.0 g (20 mmol) of 2,3-dichloro-5-phenyl-1,4-benzoquinone in 200 ml of ethanol–dichloromethane (1:1). The two-phase mixture was stirred at room temperature for 2 hr, at which time it had become a deep purple color. Water was added and the organic layer was collected. It was dried and the solvent was removed *in vacuo*. The residue was recrystallized from ethanol–dichloromethane to give the diazide as lustrous purple crystals, mp 115–117° dec. This diazide showed the following characteristic spectral properties: ir (Nujol) 2100, 1640, 1575 cm^{-1}; nmr ($CDCl_3$) δ 6.65 (s, 1), 7.31 (s, 5).

Anal. Calcd for $C_{12}H_6N_6O_2$: C, 54.05; H, 2.43; N, 31.51. Found: C, 54.28; H, 2.34; N, 31.51.

4-Acetoxy-3-methyl-1,2-naphthoquinone-2-(*N*-acetyl)imine (4a). A solution of 0.50 g (1.7 mmol) of 1,4-diacetoxy-2-azido-3-methylnaphthalene (**3a**) in 5 ml of warm *o*-dichlorobenzene was slowly added to 10 ml of gently refluxing *o*-dichlorobenzene. Nitrogen gas was immediately evolved and the solution became a honey-yellow color. The solvent was removed *in vacuo* and the resulting yellow solid was recrystallized (dichloromethane–cyclohexane) to give, in two crops, 0.41 g (89%) of the imine **4a** as deep yellow needles, mp 175–178° dec.

Characteristic spectral properties of **4a** follow: ir (Nujol) 1760, 1690, 1670, 1630, 1590 cm^{-1}; nmr ($CDCl_3$) δ 1.98 (s, 3), 2.31 (s, 3), 2.43 (s, 3), 7.2–8.2 (m, 4).

Anal. Calcd for $C_{15}H_{13}NO_4$: C, 66.46; H, 4.76; N, 5.20. Found: C, 66.41; H, 4.83; N, 5.16.

2-Amino-3-methyl-1,4-naphthoquinone. The imine **4a** (0.10 g) was slowly added to 5 ml of cold concentrated sulfuric acid, resulting in a pale red solution. The solution was warmed to room temperature, stirred for 1 hr further, and then poured over ice. Recrystallization of the resulting precipitate (ethanol) gave 50 mg of 2-amino-3-methyl-1,4-naphthoquinone, mp 165–167°, which was identical with that prepared independently by catalytic reduction of 2-azido-3-methyl-1,4-naphthoquinone.

4-Acetoxy-3,6-dimethyl-1,2-benzoquinone-2-(*N*-acetyl)imine (4b). A suspension of 2.2 g (8.2 mmol) of 1,4-diacetoxy-2-azido-3,6-dimethylbenzene (**3b**) in 5 ml of chlorobenzene was slowly (1 min) dropped into 10 ml of refluxing *o*-dichlorobenzene and the solution was refluxed for an additional 40 min. The solvent was then removed *in vacuo* and the residue was chromatographed on 70 g of silica gel. Elution with chloroform gave 1.2 g of recovered starting material (**3b**) and 410 mg (45% yield based upon reacted azide) of the quinoneimine **4b**, mp 112–113°. Characteristic spectral properties for **4b** follow: ir (Nujol) 1751, 1681, 1653, 1613 cm^{-1}; nmr ($CDCl_3$) δ 1.91 (br, 6), 2.30 (s, 3), 2.26 (s, 3), 6.73 (q, 1, J = 1.2 Hz).

Anal. Calcd for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.53; N, 5.95. Found: C, 61.18; H, 5.53, N, 5.95.

2-Amino-3,6-dimethyl-1,4-benzoquinone. A sample of 118 mg (0.5 mmol) of **4b** was slowly added to 3 ml of cold concentrated sulfuric acid. The color immediately changed from orange to purple and after 5 min of continued stirring the solution was poured into ice–water. The resulting mixture was extracted with dichloromethane, and the solvent was removed *in vacuo*. The residue was chromatographed on 15 g of silica gel using chloroform as the eluent, giving 25 mg (33%) of 2-amino-3,6-dimethyl-1,4-benzoquinone and 30 mg (31%) of 2-(*N*-acyl)-2-amino-3,6-dimethyl-1,4-benzoquinone.

The purple crystalline aminoquinone, mp 183° (sublimed), was identical with the product obtained upon catalytic reduction of 2-azido-3,6-dimethyl-1,4-benzoquinone. The *N*-acyl derivative, mp 157–159°, showed the following characteristic spectral and analytical properties: ir (Nujol) 3279, 1681, 1656, 1631 cm^{-1}; nmr ($CDCl_3$) δ 1.91 (s, 3), 2.03 (d, 3, J = 1.2 Hz), 2.20 (s, 3), 6.60 (q, 1, J = 1.2 Hz), 7.67 (br, 1).

Anal. Calcd for $C_{10}H_{11}NO_3$: C, 62.17; H, 5.69; N, 7.25. Found: C, 62.07; H, 5.68; N, 7.22.

Thermolysis of 1,4-Diacetoxy-2-azido-3,6-di-*tert*-butylbenzene. Formation of 4-Acetoxy-3,6-di-*tert*-butyl-1,2-benzoquinone-2-(*N*-acetyl)imine (4c), 5-Acetoxy-3,6-di-*tert*-butyl-1,2-benzoquinone-2-(*N*-acetyl)imine (5), and 4,7-Diacetoxy-6-*tert*-butyl-3,3-dimethyl-2,3*H*-indole (6). A suspension of 2.3 g (6.62 mmol) of the azide **3c** in 5 ml of *o*-dichlorobenzene was slowly added (1 min) to 10 ml of refluxing *o*-dichlorobenzene. The solution was refluxed for 10 min, at which time all starting material had been consumed (tlc, silica gel, CH_2Cl_2). Nmr analysis of the reaction mixture showed only absorptions corresponding to **4c** and **5** in a ratio of 4.1:1.0, respectively.

The solvent was then removed with a stream of nitrogen and the orange residue was recrystallized from chloroform–ether to give 280 mg of the quinoneimine **5**. From the mother liquor, a total of 1.54 g of **4c** (contaminated with some **5**) and 30 mg of the dihydroindole **6** were isolated by fractional crystallization. Characteristic properties of these compounds follow. Quinoneimine **4c**: mp 102–104° (4% contamination of isomer **5** present); ir (Nujol) 1757, 1681, 1664, 1610 cm^{-1}; nmr ($CDCl_3$) δ 1.19 (s, 9), 1.37 (s, 9), 2.27 (s, 6), 6.50 (s, 1). *Anal.* Calcd for $C_{18}H_{25}NO_4$: C, 67.71; H, 7.83; N, 4.38. Found: C, 67.70; H, 7.90; N, 4.44. Quinoneimine **5**: mp 148–153°; ir (Nujol) 1761, 1686, 1661, 1613 cm^{-1}; nmr ($CDCl_3$) δ 1.26 (s, 9), 1.28 (s, 9), 2.27 (s, 6), 6.24 (s, 1). *Anal.* Found: C, 67.49; H, 7.80; N, 4.32. Dihydroindole **6**: mp 200–201°; ir (Nujol) 2597, 1764 cm^{-1}; nmr ($CDCl_3$) δ 1.31 (s, 6), 1.36 (s, 9), 2.25 (s, 6), 3.70 (s, 2), 6.75 (s, 1), 10.85 (s, 1, disappears completely with D_2O added in 3.5 days). *Anal.* Found: C, 67.64; H, 7.85; N, 4.33.

Catalytic Reduction of 4-Acetoxy-3,6-di-*tert*-butyl-1,2-benzoquinone-2-(*N*-acetyl)imine (4c). A solution of 957 mg (3 mmol) of **4c** in 100 ml of diethyl ether was hydrogenated in the presence of 200 mg of 5% Pt/C at ambient temperature under 37 psi for 4 min. The catalyst and solvent were removed, leaving a slightly colored oily residue. This residue was dissolved in low-boiling petroleum ether and cooled to give 400 mg of 4-acetoxy-2-(*N*-acetyl)-3,6-di-*tert*-butylphenol (**11**), mp 145–148°. Five careful recrystallizations from dichloromethane–petroleum ether gave the analytical sample, mp 157–158°. Characteristic spectral properties follow: ir (Nujol) 3333, 3247, 1742, 1669 cm^{-1}; nmr ($CDCl_3$) δ 1.43 (s, 9), 1.52 (s, 9), 2.17 (s, 3), 2.25 (s, 3), 2.72 (s, 1), 6.85 (s, 1), 7.47 (s, 1).

Anal. Calcd for $C_{18}H_{27}NO_4$: C, 67.28; H, 8.41; N, 4.36. Found: C, 67.26; H, 8.28; N, 4.35.

From the above mother liquor 410 mg of the oxazole derivative **12** was isolated, mp 92–95°. Five recrystallizations (ether–petroleum ether) gave the analytical sample, mp 93–95°. Characteristic spectral properties of **12** follow: ir (Nujol) 1757, 1608 cm^{-1}; nmr ($CDCl_3$) δ 1.52 (s, 9), 1.68 (s, 9), 2.28 (s, 3), 2.59 (s, 3), 6.70 (s, 1).

Anal. Calcd for $C_{18}H_{25}NO_3$: C, 71.28; H, 8.25; N, 4.62. Found: C, 71.36; H, 8.22; N, 4.48.

Conversion of the Phenol 11 to the Benzoxazole 12. A solution of 40 mg of **11** in 5 ml of 95% ethanol was refluxed for 3 hr. Evaporation of the solvent gave 35 mg of **12**, which was identical in all respects with the compound described above. The same transformation was accomplished in 84% yield when **11** was treated with acetic anhydride–pyridine at 0–5° for 2 days.

Catalytic Reduction of 1,4-Diacetoxy-2-azido-3,6-di-*tert*-butylbenzene (3c). A solution of 347 mg of **3c** in 100 ml of diethyl ether was hydrogenated in the presence of 100 mg of 5% Pt/C at ambient temperature at 36 psi for 20 min. From the reaction solution, 80 mg of the phenol **11** was isolated. If the hydrogenation was allowed to go for 4.75 hr, a 12% yield of **11** and a 69.3% yield of **12** were obtained; after 40 hr only the oxazole was isolated (89%).

Catalytic Reduction of 5-Acetoxy-3,6-di-*tert*-butyl-1,2-benzoquinone-2-(*N*-acetyl)imine (5). A suspension of 200 mg of **5** in 50 ml of 95% ethanol was hydrogenated in the presence of 100 mg of 5% Pt/C at ambient temperature under 36 psi for 15 min. Filtration and removal of the solvent at room temperature gave a residue which upon recrystallization from dichloromethane–petroleum ether gave 100 mg of 5-acetoxy-2-(*N*-acetyl)-3,6-di-*tert*-butylphenol (**14**). Recrystallization again gave the pure sample, mp 148–151°. Characteristic spectral properties of **14** follow: ir (Nujol) 3571, 3236, 1742, 1656 cm^{-1}; nmr ($CDCl_3$) δ 1.46 (s, 9), 1.56 (s, 9), 1.62 (s, 1, exchangeable), 2.25 (s, 3), 2.27 (s, 3), 6.50 (s, 1), 7.63 (s, 1, exchangable).

The mother liquor from the above yielded 50 mg of the benzoaxazole **15**. Recrystallization from diethyl ether gave the analytical sample: mp 100–101°; ir (Nujol) 1757, 1608 cm^{-1}; nmr ($CDCl_3$) δ 1.58 (s, 9), 1.60 (s, 9), 2.30 (s, 3), 2.59 (s, 3), 6.47 (s, 1).

Anal. Calcd for $C_{18}H_{25}NO_3$: C, 71.28; H, 8.25; N, 4.62. Found: C, 71.39; H, 8.26; N, 4.71.

Catalytic Reduction of 4-Acetoxy-3,6-dimethyl-1,2-benzoquinone-2-(*N*-acetyl)imine (4b). Formation of 4-Acetoxy-2-(*N*-acetyl)-3,6-dimethylphenol (16). A solution of 100 mg (0.425 mmol) of **4b** in 50 ml of diethyl ether was hydrogenated at ambient temperature in the presence of 100 mg of 5% Pt/C at 36 psi.

After approximately 5 min the reaction mixture was filtered and the solvent was removed *in vacuo*. Recrystallization of the residue gave 80 mg (79%) of the phenol **16**: mp 185–186°; ir (Nujol) 3413, 3226, 1742, 1667 cm^{-1}; nmr ($CDCl_3$) δ 1.87 (s, 3), 2.12 (s, 3), 2.20 (s, 3), 2.27 (s, 3), 6.75 (s, 1), 7.62 (s, 1, exchangeable), 7.73 (s, 1, exchangable).

Anal. Calcd for $C_{12}H_{15}NO_4$: C, 60.76; H, 6.32; N, 5.90. Found: C, 60.81; H, 6.32; N, 5.82.

Catalytic Reduction of 1,4-Diacetoxy-2-azido-3,6-dimethylbenzene (3b). Formation of 4-Acetoxy-2-(*N*-acetyl)-3,6-dimethylphenol (16). The phenol **16** was obtained in 93% yield by catalytic reduction of **3b** under the same above-described conditions.

1,4-Diacetoxy-2-phenylcarbazole (19). A suspension of 3.87 g (10 mmol) of 1,4-diacetoxy-2-azido-3,6-diphenylbenzene (**3d**) in 10 ml of *o*-dichlorobenzene was slowly dropped (2 min) into 10 ml of refluxing *o*-dichlorobenzene. Refluxing was continued for an additional 40 min. Most of the solvent was removed by passing a stream of nitrogen over the surface of the reaction solution. Then chloroform–ether (1:1) was added which caused precipitation of 1.76 g of nearly pure carbazole **19**. The solvent from the mother liquor was removed *in vacuo* and the residue was chromatographed on 200 g of silica gel using methylene chloride as the solvent. This yielded 620 mg more of **19**, bringing the total yield to 61%. Recrystallization from methylene chloride–petroleum ether gave the analytical sample: mp 219–220°; ir (Nujol) 3401, 1757 cm^{-1}; nmr ($CDCl_3$) δ 2.08 (s, 3), 2.48 (s, 3), 7.07–8.09 (m, 10), 8.26 (s, 1, exchangeable).

Anal. Calcd for $C_{22}H_{17}NO_4$: C, 73.53; H, 4.73; N, 3.89. Found: C, 73.42; H, 4.73; N, 3.81.

The same carbazole (**19**) was prepared by dithionite reduction of the quinone **20** followed by acetic anhydride–pyridine acylation of the resulting hydroquinone; all operations were done under known standard conditions.

A red crystalline compound was also isolated from the above chromatography. Recrystallization twice from ethyl acetate–ether–petroleum ether gave a sample melting at 203–205°. Spectral properties follow: ir (Nujol) 1767, 1751, 1724, 1645 cm^{-1}; nmr ($CDCl_3$) δ 1.83 (s, 3), 1.95 (s, 3), 2.61 (s, 3), 6.85 (s, 1), 7.50 (m, 17), 8.30 (m, 2).

Anal. Found: C, 76.11; H, 4.89; N, 4.01.

***trans,trans*-1,4-Diacetoxy-*cis,cis*-1,4-dicyano-2,3-tetramethylene-1,3-butadiene (21a).** A solution of 0.416 g (1.26 mmol) of 1,4-diacetoxy-2,3-diazido-5,6,7,8-tetrahydronaphthalene (**3f**) in 3 ml of warm *o*-dichlorobenzene was added dropwise in 3 ml of gently refluxing *o*-dichlorobenzene. A pink color formed which faded to a yellow orange. After 10 min of further refluxing, the solution was cooled and the solvent was removed *in vacuo*. Recrystallization of the resulting residue from benzene–carbon tetrachloride gave 0.26 g (77%) of the diene **21a**, mp 153–155°. Characteristic spectral properties of **21a** follow: ir (Nujol) 2220, 1775, 1640 cm^{-1}; nmr ($CDCl_3$) δ 1.5–3.0 (m, 8), 2.26 (s, 6); mass spectrum *m/e* (rel intensity) 232 (2), 190 (16), 43 (100); uv (acetonitrile) 208 (4.81), 246 nm (3.88).

Anal. Calcd for $C_{14}H_{14}N_2O_4$: C, 61.30; H, 5.14; N, 10.22. Found: C, 61.25; H, 5.05; N, 10.24.

***trans,trans*-1,4-Diacetoxy-*cis,cis*-1,4-dicyano-2-phenyl-1,3-butadiene (21b).** A solution of 1.5 g (4.25 mmol) of 1,4-diacetoxy-2,3-diazido-5-phenylbenzene in 3 ml of warm *o*-dichlorobenzene was added dropwise to 25 ml of gently refluxing decalin. The solution turned a deep red and then lightened to an orange color. The solution was then refluxed for an additional 5 min and cooled. The resulting precipitate was washed with hexane to give 0.9 g (72%) of the diene **21b**, mp 82–86°. Recrystallization from carbon tetrachloride gave the analytical sample, which showed the following characteristic properties: mp 89–90°; ir (Nujol) 2220, 1770, 1630, 1590 cm^{-1}; nmr ($CDCl_3$) δ 2.00 (s, 3), 2.23 (s, 3), 7.4 (m, 6); mass spectrum *m/e* (rel intensity) 254 (1), 212 (5), 43 (100); uv (acetonitrile) λ_{max} 270 nm (4.24).

Anal. Calcd for $C_{16}H_{12}N_2O_4$: C, 64.86; H, 4.08; N, 9.46. Found: 64.91; H, 4.14; N, 9.51.

***trans,trans*-1,4-Diacetoxy-*cis,cis*-1,4-dicyano-2,3-dimethyl-1,3-butadiene (21c).** A solution of 2.0 g (6.6 mmol) of 1,4-diacetoxy-2,3-diazido-5,6-dimethylbenzene in 10 ml of *o*-dichlorobenzene was added dropwise to 10 ml of gently refluxing *o*-dichlorobenzene. A red color developed which faded to a pale yellow. The solution was diluted with 20 ml of hexane and cooled to −10° to give 1.47 g (94%) of diene **21c** as a white, crystalline solid, mp 125–127°. Characteristic spectral properties for **21c** follow: ir (Nujol) 2240, 1770, 1645 cm^{-1}; nmr ($CDCl_3$) δ 1.97 (s, 6), 2.25 (s, 6); uv (acetonitrile) λ_{max} 206 nm (4.25).

Anal. Calcd for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.17. Found: C, 58.12; H, 4.79; N, 11.29.

Thermolysis of 1,4-Diacetoxy-2,3-diazidonaphthalene (3e). Formation of the 1,2-Diacetoxy-1,2-dicyanobenzocyclobutenes (22 and 23) and 1,4-Diacetoxy-3-cyanoisoquinoline (24). A solution of 2.0 g (6.1 mmol) of the diazide **3e** in 10 ml of warm *o*-dichlorobenzene was added over a 2-min period to 10 ml of gently refluxing *o*-dichlorobenzene. The solution became deep red and then litened to amber. The solvent was removed *in vacuo* and the yellow solid was dissolved in 20 ml of hot benzene. Upon cooling a precipitate formed and was collected by filtration to give 0.64 g (39%) of the 1,4-diacetoxy-3-cyanoisoquinoline (**24**) as a yellow solid. This sample was chromatographed (silica gel) and then recrystallized from benzene to give the analytical sample, mp 183–186°. Characteristic spectral properties of **24** follow: ir (Nujol) 1780, 1670, 1640, 1600, 1580 cm^{-1}; nmr ($CDCl_3$) δ 2.61 (s, 3), 2.65 (s, 3), 7.6–8.2 (m, 4); uv (acetonitrile) 231 (4.43), 253 (4.18), 262 (4.20), 304 nm (4.03).

Anal. Calcd for $C_{14}H_{10}N_2O_4$: C, 62.22; H, 3.73; N, 10.37. Found: C, 62.33; H, 3.76; N, 10.38.

The above benzene mother liquor was chromatographed over 150 g of silica gel. Elution with dichloromethane–pentane (1:1) gave 0.38 g (23%) of the *trans*-1,2-diacetoxy-1,2-dicyanobenzocyclobutene (**22**), mp 144–147°. Recrystallization from benzene–carbon tetrachloride gave the analytical sample, mp 147–148°, as a white, crystalline compound. Characteristic spectral properties of **22** follow: ir (Nujol)[19] 1770, 1760 cm^{-1}; nmr ($CDCl_3$) δ 2.29 (s, 6), 7.76 (s, 4); uv (acetonitrile) 257 (2.74), 2.63 (2.89), 270 nm (2.85); mass spectrum *m/e* (rel intensity) 186 (1.7), 114 (0.5), 102 (0.5), 44 (1.7), 43 (100), 42 (1.5).

Anal. Calcd for $C_{14}H_{10}N_2O_4$: C, 62.22; H, 3.73; N, 10.37. Found: C, 62.14; H, 3.74; N, 10.37.

From the above chromatography another fraction was collected upon elution with dichloromethane. The tan solid obtained was recrystallized from benzene–carbon tetrachloride to give 50 mg (3%) of *cis*-1,2-diacetoxy-1,2-dicyanobenzocyclobutene (**23**), mp 160–161° dec. Characteristic spectral properties of **23** follow: ir (Nujol)[19] 1755 cm^{-1}; nmr ($CDCl_3$) δ 2.20 (s, 6), 7.6–7.7 (m, 4); uv (acetonitrile) 257 (2.81), 263 (2.97), 270 nm (2.93); mass spectrum *m/e* (rel intensity) 186 (4.3), 114 (0.8), 102 (1.2), 44 (6), 43 (100), 42 (3).

Anal. Calcd for $C_{14}H_{10}N_2O_4$: C, 62.22; H, 3.73; N, 10.37. Found: C, 62.19; H, 3.84; N, 10.36.

4-Hydroxy-1(2*H*)-isoquinolone. A solution of 0.4 g (1.5 mmol) of 1,4-diacetoxy-3-cyanoisoquinoline (**24**) in 3 ml of 47% HI was refluxed for 5 hr, and 10 ml of distilled water containing 0.1 g of sodium thiosulfate was added. Cooling gave a brown solid which, when recrystallized from dilute sodium thiosulfate, gave 0.15 g (62%) of 1,4-dioxo-1,2,3,4-tetrahydroisoquinoline as a yellow, crystalline solid which was identical with an authentic sample prepared by an alternate route.[12]

Registry No.—**1f**, 51021-93-3; **1g**, 51021-94-4; **3a**, 51021-95-5; **3b**, 51021-96-6; **3c**, 51021-97-7; **3d**, 51021-98-8; **3e**, 51021-99-9; **3f**, 51022-00-5; **3g**, 51022-01-6; **3h**, 51022-02-7; **4a**, 51022-03-8; **4b**, 51022-04-9; **4c**, 51022-05-0; **5**, 51022-06-1; **6**, 51022-07-2; **11**, 51022-08-3; **12**, 51022-09-4; **14**, 51022-10-7; **15**, 51022-11-8; **16**, 51022-12-9; **19**, 51022-13-0; **21a**, 51021-74-0; **21b**, 51021-75-1; **21c**, 51021-76-2; **22**, 51021-77-3; **23**, 51021-78-4; **24**, 51022-14-1; *N*-acetyl-2-amino-3,6-dimethyl-1,4-benzoquinone, 51022-15-2.

References and Notes

(1) This is paper XIV in a series concerning the chemistry of azidoquinones and related compounds. For paper XIII see P. Germeraad, W. Weyler, Jr., and H. W. Moore, *J. Org. Chem.*, **39**, 781 (1974).

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A Synthetic Approach to Aporphine Alkaloids. A New Tetracyclic Benzodiazepine Derivative from the Benzyne Cyclization of a Bromophenolic 1-Benzyltetrahydroisoquinoline

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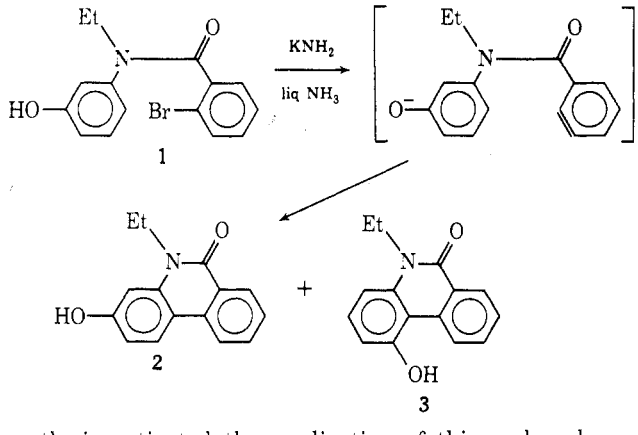
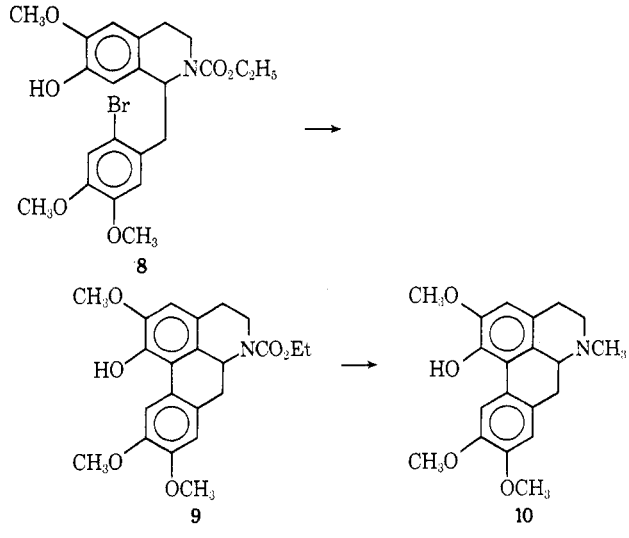
The synthesis of aporphine alkaloids by the benzyne reaction of bromophenolic 1-benzyltetrahydroisoquinolines containing a carbethoxy protecting group on the isoquinoline nitrogen was examined. The benzyne reaction of 1-(2′-bromo-4′,5′-dimethoxybenzyl)-2-carbethoxy-1,2,3,4-tetrahydro-7-hydroxy-6-methoxyisoquinoline (8) gave a new tetracyclic benzylisoquinoline derivative, 17, in good yield. Aryl-aryl coupling *via* intramolecular attack of phenoxide on the intermediate aryne to give the *N*-carbethoxynoraporphine 9 was not observed. This process provides a useful new synthesis of certain benzodiazepines.

It is well established that a variety of nucleophiles readily add to benzyne. When the nucleophile is part of a side chain attached to the benzyne, the intramolecular nucleophilic addition results in ring closure; numerous demonstrations of this process have been described.[1] For example, Hey, Leonard, and Rees have shown that, when the nucleophile is the ambident phenoxide ion, its intramolecular nucleophilic addition results in an aryl-aryl coupling reaction (1 → 2 + 3).[2] Several groups[3-8] have recently investigated the application of this aryl-aryl coupling process to the synthesis of aporphine alkaloids[9] (*e.g.*, 5) from 1-benzyltetrahydroisoquinoline precursors (*e.g.*, 4) as shown in Scheme I, path a. In every case except one in which the yield of aporphine 5 is reported as "about 30% as estimated by tlc,"[6] only minor amounts of aporphine are obtained.[10] Competing with aporphine formation is the formation of morphinandienones (*e.g.*, 6) *via* para attack of the phenoxide on the aryne (Scheme I, path b), the formation of indolizine derivatives (*e.g.*, 7) by the attack of the nucleophilic isoquinoline nitrogen on the aryne (Scheme I, path c), and the formation of primary aromatic amines by the addition of ammonia to the aryne. In most cases the major cyclized products are the indolizine derivatives 7; in fact this general method provides a useful synthesis of indolizine derivatives.[11,12] Thus, if this process is to be a useful synthesis of aporphine alkaloids, the isoquinoline nitrogen must be protected during the cyclization reaction. In this paper we wish to describe the results of the reaction of urethane 8 with potassium amide–liquid ammonia; in 8 the isoquinoline nitrogen is no longer nucleophilic, indolizine formation is thus prevented, and we anticipated that synthetically useful yields of aporphine alkaloid precursors such as 9 might be obtained. After cyclization the *N*-carbethoxy noraporphines (*e.g.*, 9) can be readily converted to the desired aporphine alkaloids (*e.g.*, 10); this last step has also been used in other recent aporphine syntheses.[9b,f]





Results and Discussion

The required precursor 8 was synthesized as outlined in Scheme II. Thus heating the β-phenethylamine 11[13] with the phenylacetic ester 12[14] at 140–150° gave the amide 13 (70% yield), which was then readily converted to the hy-