The o-Styrylnitrene Route to 2-Substituted Indoles. Pyrolysis of o-Azidostyrenes[1]

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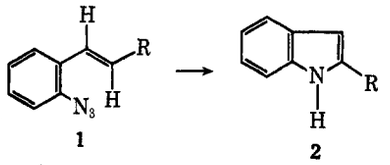
Received August 12, 1971

The utility of o-azidostyrene derivatives as indole precursors *via* o-styrylnitrenes has been examined. The cyclization proceeds efficiently for β-alkyl- and β-aryl-o-azidostyrenes and is also satisfactory for β-acyl-o-azidostyrenes. A synthesis of 2-acylindoles involving two steps, base-catalyzed condensation of a methyl ketone with o-azidobenzaldehyde and pyrolysis to the indole, was carried out successfully in five cases with yields from 21 to 73%. These yields are generally superior to yields of 2-acylindoles prepared by the deoxygenation method.

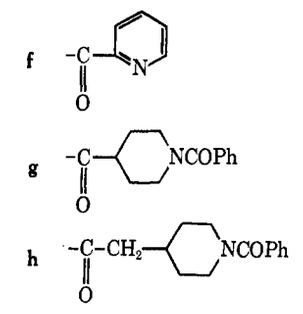
An o-styrylnitrene would be expected to cyclize to an indole on the basis of analogy with other cyclizations of aryl azides having adjacent unsaturated substituents.[2] The deoxygenation of o-nitrostyrenes to indoles may, indeed, be an example of such a cyclization.[3] In view of the efficiency with which azides serve as precursors of nitrenes on thermal or photolytic decomposition,[4] a study of the synthesis and decomposition of the requisite o-azidostyrenes was undertaken.[5] Particular attention was focused on β-acyl-o-azidostyrenes because of the desirability of developing improved methods of synthesis of 2-acylindoles. Some additional studies of the deoxygenation method are also reported for purposes of comparison.

The azides **1a** and **1b** were prepared from the corresponding o-nitrostyrenes in two steps. The nitro group was reduced with iron and acetic acid to the aniline. The azido group was introduced *via* diazotization. A mixture of azides **1c** and **1d** was obtained by condensation of o-azidobenzaldehyde with pyruvic acid followed by acid-catalyzed esterification. The azides **1e–h** were prepared by condensation of the appropriate methyl ketone with o-azidobenzaldehyde. The noncrystalline azides **1g** and **1h** were partially purified and pyrolyzed but not characterized by elemental analysis. Several attempts to condense o-azidobenzaldehyde with 4-acetylpyridine failed. Attempted condensations of o-azidobenzaldehyde with 4-acetonyl-1-benzoyl-1,2,3,6-tetrahydropyridine and 4-acetonyl-1-benzoyl-3-hydroxypiperidine also gave ill-defined products apparently containing azido groups, but no indoles could be isolated after pyrolysis of these materials. The stereochemistry about the carbon–carbon double bond is assumed to be trans in compounds **1c–h** on the basis of the known preference for formation of trans product in base-catalyzed Claissen condensations.[6]



1 2

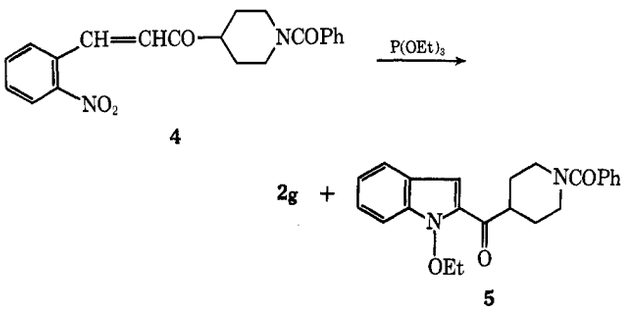
Compd	R
a	$-CH_2CH_2CH_3$
b	$-C_6H_5$
c	$-COCO_2Me$
d	$-C(OMe)_2CO_2Me$
e	$-COPh$



Pyrolysis of the azides was effected either in refluxing decalin or ethylene glycol. In the case of decalin, the solvent was removed by vacuum distillation and the indole isolated from the residue. When ethylene glycol was used, the indole could be obtained by dilution of the solution with water followed by solvent extraction.

The yields obtained in the various pyrolyses are reported in the Experimental Section. Although deoxygenation gives yields comparable to those from azidostyrene pyrolysis for alkyl- and arylindoles,[3a] the pyrolysis is usually markedly more efficient for the synthesis of 2-acylindoles.[3a,7]

The preparation of 4-acetyl-1-benzoylpiperidine (**3**) and its condensation with nitrobenzaldehyde to give **4** followed by deoxygenation to give **2g** was carried out in the course of this work. As noted previously in similar deoxygenations,[3a,7] the corresponding 1-ethoxyindole is a by-product.



4

2g + 5

Deoxygenation provided an efficient synthesis of 2-indolyl 4-pyridyl ketone[8] **2i**, although, as mentioned above, we were unable to prepare the intermediate required for synthesis of this ketone by the o-azidostyrene route. 4-Acetylpyridine was condensed with

(1) Supported by NSF Grants GP-7951 and 19374. A preliminary account of some of these results has appeared: R. J. Sundberg, L.-S. Lin, and D. E. Blackburn, *J. Heterocycl. Chem.*, **6**, 441 (1969).

(2) P. A. S. Smith and B. B. Brown, *J. Amer. Chem. Soc.*, **73**, 2435 (1951); L. Krbechek and H. Takimoto, *J. Org. Chem.*, **29**, 1150, 3630 (1964).

(3) (a) R. J. Sundberg, *J. Org. Chem.*, **30**, 3604 (1965); (b) J. I. G. Cadogan, M. Cameron-Wood, R. K. Mackie, and R. J. G. Searle, *J. Chem. Soc.*, 4831 (1965).

(4) G. L'abbe, *Chem. Rev.*, **69**, 345 (1969).

(5) Smith and coworkers have independently studied synthesis and thermal decomposition of several o-azidostyrene derivatives: unpublished work referred to in "Nitrenes," W. Lwowski, Ed., Interscience Publishers, New York, N. Y., 1970, pp 135–139.

(6) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, pp 216–224.

(7) R. J. Sundberg, *J. Org. Chem.*, **33**, 487 (1968).

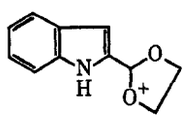
(8) Previously prepared from methyl isonicotinate by Claissen condensation with methyl propionate followed by Japp–Klingemann conversion to the phenylhydrazone and Fischer cyclization: A. Jackson, N. D. V. Wilson, A. J. Gaskell, and J. A. Joule, *J. Chem. Soc., C*, 2738 (1969).

o-nitrobenzaldehyde. The ketol was dehydrated and the resulting unsaturated ketone **6** was converted to the ethylene glycol ketal **7**. Deoxygenation of this compound proceeded efficiently to give the indole **2i**, after hydrolysis.

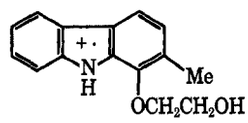
Ir, nmr, and mass spectral data were in accord with expectation for each of the new indoles **2c**,[9] **2d**, **2f**, and **2g**. Spectral data and physical constants for the known indoles **2a**,[15] **2b**,[16] **2h**,[7] and **2i**[8] were in agreement with literature values. The structure of indole **2i** was further corroborated by N-methylation to the ketone **9** which was independently prepared from 2-lithio-1-methylindole and 4-cyanopyridine.

Interrelation of **2i** and the piperidine derivative **2g** was also carried out. The ketal **8** was quaternized with ethyl bromoacetate and reduced over palladium on charcoal. The piperidine **10** was the major product along with a by-product **11** which is discussed below. These interrelations, which are summarized in Scheme I serve to establish that no substituent migration occurred in either the pyrolysis of **1g** or the deoxygenation of **7**. It was of interest to establish this, particularly in the latter case, since substituent migration is observed in deoxygenation of the phenyl analog of **7**.[7]

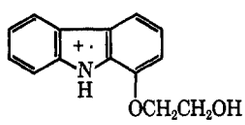
The tetracyclic skeleton assigned to the by-product **11** is that found in the uleine[17] and dasycarpidone[18] type of alkaloid. The formation of **11** under the conditions of the reduction can be rationalized by alkylation of the indole 3 position by an iminium intermediate[19] present at the dihydro or tetrahydro reduction stage. Such a cyclization might be expected to be favored by acidic hydrogenation conditions but **10** was also found to be the major product in 5% acetic acid in ethanol as well as in ethanol. Ring closures of this type have been noted using isolated tetrahydropyridine intermediates,[8] but this is the first example of the cyclization proceeding directly from the pyridine oxidation level. In addition to the molecular formula established by elemental analysis and mass spectrometry, the evidence for the structure includes a typical indole uv spectrum. The nmr shows no indole 3 H and the methylene group of the nitrogen substituent appears as an AB quartet, J_{gem} = 16 Hz, because the protons are anisochronous as a result of the introduction of the indolyl substituent at C-2 of the piperidine ring. Mass spectral comparison of **10** and **11** reveal the absence in **11** of a peak at 188 attributable to the monosubstituted indole fragment **a**. In addition peaks at 227, 210, 196, 181, and 167 can be assigned to the carbazole ring fragments of type **b**, **c**, **d**, and **e**. The mass spectrum of uleine is also dominated by fragments containing the carbazole ring system.[17]



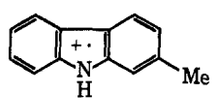
a, 188



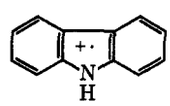
b, 241
b′, -OH (224)
b″, $-CH_2OH$ (210)
b‴, $-CH_2CH_2OH$ (196)



c, 227
c′, -OH (210)
c″, $-CH_2OH$ (196)
c‴, $-CH_2CH_2OH$ (182)



d, 181



e, 167

Experimental Section

trans-1-(*o*-Azidophenyl)-1-pentene (1a).—*trans*-*o*-(1-Pentenyl)aniline[20] (0.81 g, 5 mmol) was dissolved in a solution of glacial acetic acid (40 ml), sulfuric acid (8 ml), and water (25 ml) and cooled with an ice–salt bath. A solution of sodium nitrite (0.38 g, 5.5 mmol) in water (5 ml) was added slowly. The solution was stirred for 1 hr. The reaction mixture was diluted with ice water (50 ml) and treated with urea to destroy excess nitrous acid. A solution of sodium azide (0.67 g, 10.3 mmol) in water was added slowly. After standing 45 min at 0° and 5 hr at room temperature, the reaction mixture was extracted with petroleum ether. The extract was washed with aqueous sodium carbonate and water, dried, and concentrated on a rotary evaporator. Chromatography of the residue on alumina using petroleum ether as the eluent gave **1a** as a light yellow liquid, ν_{N_3} 2125 cm^{-1}.

Anal. Calcd for $C_{11}H_{13}N_3$: C, 70.56; H, 7.00. Found: C, 70.79; H, 7.23.

2-Propylindole (2a). A. In Decalin.—A solution of **1a** (1.1 g, 5.8 mmol) in decalin (100 ml) was reluxed for 4 hr. The decalin was distilled at reduced pressure and the residue chromatographed on silicic acid. Hexane–benzene (2:1) eluted **2a** (0.75 g, 81%), mp 32–34° after recrystallization from benzene–hexane (lit.[15] 34°), having an infrared spectrum identical with that of an authentic sample.

B. In Ethylene Glycol.—A solution of **1a** (1.0 g, 5.3 mmol) was refluxed in ethylene glycol (100 ml) for 4 hr. The cooled solution was poured into water. Ether extraction followed by purification as in A gave **2a** (0.65 g, 76%).

trans-**2-Azidostilbene** (1b).—*trans*-2-Aminostilbene[21] (1.3 g, 5.5 mmol) was converted to **1b** essentially as for **1a**. Extraction of the reaction mixture with benzene and evaporation gave **1b** (1.05 g, 4.8 mmol, 87%), mp 94–95.5° after recrystallization from benzene–hexane, ν_{N_3} 2150 cm^{-1}.

Anal. Calcd for $C_{14}H_{11}N_3$: C, 75.99; H, 5.01; N, 18.99. Found: C, 75.78; H, 4.90; N, 18.78.

2-Phenylindole (2b).—The pyrolysis of **2a** (1 g, 4.5 mmol) was carried out in ethylene glycol as described for 2-propylindole.

(9) A report[10] that esters of indole-2-glyoxylic acid can be prepared from indolylmagnesium bromide and dialkyl glyoxalates can be discounted on the basis of (1) the known[11] selectivity of this reaction for formation of 3-substituted indoles; (2) the agreement of the reported[10] melting points of the esters with literature value is for 3 derivatives [methyl ester mp 220° (lit.[12,13] mp 224°, 231°), ethyl ester mp 184° (lit.[13,14] mp 186°, 187°)]; (3) the agreement of the melting point reported[10] for the acid, 224–225°, with that of indole-3-glyoxylic acid, lit.[13] mp 218° dec.

(10) I. I. Lapkin and Yu. P. Dormidontov, *Chem. Heterocycl. Compounds*, **3**, 678 (1967); *Chem. Abstr.*, **68**, 87092 (1968).

(11) R. J. Sundberg, "The Chemistry of Indoles," Academic Press, New York, N. Y., 1970, pp 33–35, 412–414; R. A. Heacock and S. Kašpárek, *Advan. Heterocycl. Chem.*, **10**, 43 (1969).

(12) J. W. Baker, *J. Chem. Soc.*, 458 (1940).

(13) K. N. F. Shaw, A. McMillan, A. G. Gudmundson, and M. D. Armstrong, *J. Org. Chem.*, **23**, 1171 (1958).

(14) F. Millich and E. I. Becker, *ibid.*, **23**, 1096 (1958).

(15) A. Verley and J. Beduwe, *Bull. Soc. Chim. Fr.*, **37** 189 (1925).

(16) E. Fischer and T. Schmitt, *Chem. Ber.*, **21**, 1071 (1888).

(17) J. A. Joule and C. Djerassi, *J. Chem. Soc.*, 2777 (1964).

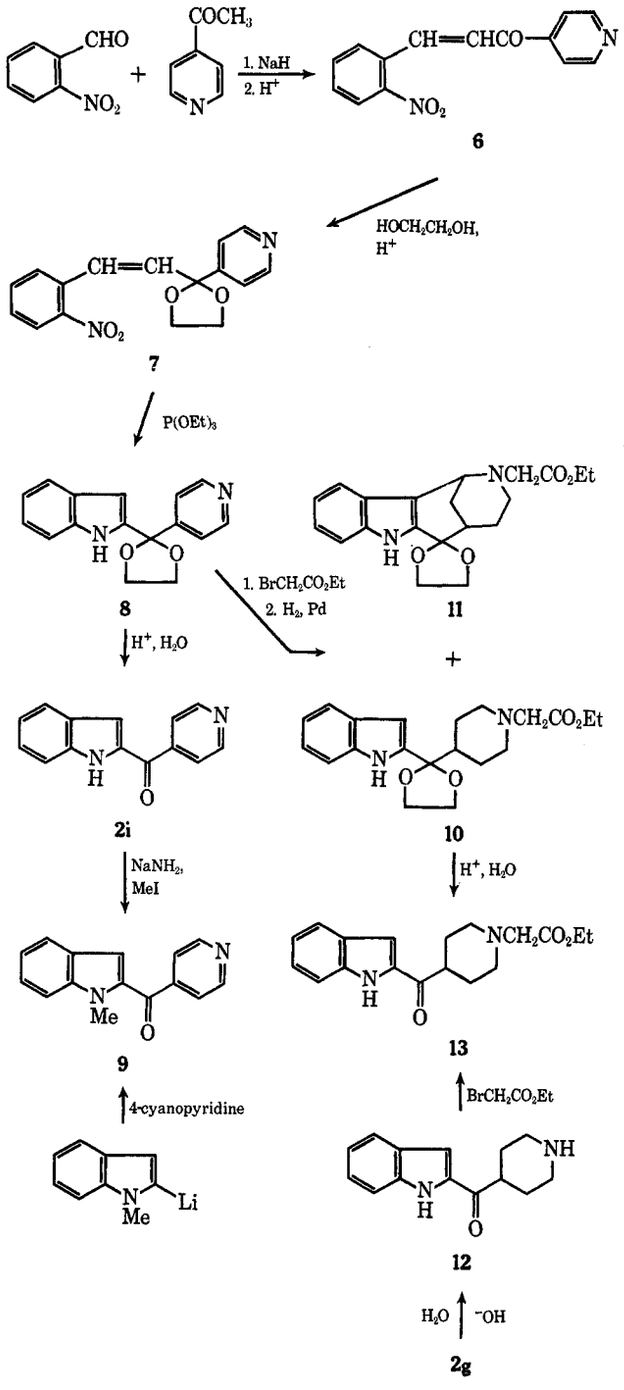
(18) J. A. Joule, M. Ohashi, B. Gilbert, and C. Djerassi, *Tetrahedron*, **21**, 1717 (1965).

(19) For a summary of electrophilic substitution of indoles by iminium intermediates, see R. J. Sundberg, "The Chemistry of Indoles," Academic Press, New York, N. Y., 1970, pp 56–67, 236–251.

(20) R. J. Sundberg, *J. Amer. Chem. Soc.*, **88**, 3781 (1966).

(21) Prepared by iron–acetic acid reduction of *trans*-2-nitrostilbene.

SCHEME I



After extraction and evaporation, there was obtained **2b** (0.75 g, 85%), mp 187–188° after recrystallization from ethanol.

Methyl Indole-2-glyoxalate (2c) and Methyl 2′,2′-Dimethoxyindole-2-acetate (2d).—o-Azidobenzaldehyde[22] (3.7 g, 25 mmol) and pyruvic acid (3.52 g, 25 mmol) were dissolved in 20 ml of anhydrous methanol cooled in an ice bath. To the vigorously stirred solution, there was added dropwise a solution of potassium hydroxide (2.1 g, 37.5 mmol) in methanol (20 ml). After about two-thirds of the potassium hydroxide solution had been added, the remainder was run in rapidly to minimize precipitation of potassium pyruvate prior to condensation. A voluminous yellow precipitate formed. The solution was stirred at room temperature and then refrigerated overnight. The precipitated sodium salt (~80% yield) was dissolved in warm (40°) water and added to vigorously stirred 1.6 *N* hydrochloric acid cooled in an ice bath. After 1 hr, the solution was extracted with ether giving the acid hydrate as a yellow-orange semisolid after concentration. The crude acid was dissolved in anhydrous methanol and a small amount of sulfuric acid was added. The solution was refluxed for 12 hr. The methanol solution was concentrated to 50 ml using a rotary evaporator and poured into a large excess of anhydrous ether. The ether solution was washed with $NaHCO_3$ solution, dried, and evaporated to give 3.8 g of a mixture of the ester **1c** and the corresponding ketal **1d**. Pyrolysis of this mixture in refluxing decalin (4 hr) gave a mixture of **2c** (1.2 g, 21%) and **2d** (0.5 g, 8%) after separation by chromatography on silicic acid. The keto ester **2c** was eluted by benzene and the ketal **2d** by 1:20 ether–benzene. After decolorization with charcoal and recrystallization from chloroform–hexane **2c** was obtained as a yellow solid: mp 138–139°; ν_{NH} 3370, ν_{CO} 1730, 1650 cm^{-1}; nmr peaks ($CDCl_3$) at δ 3.88 (3 H, s), 7.0–7.9 (6 H, m); uv $\lambda_{max}^{95\%\ EtOH}$ 240 (3.8), 331 nm (4.2).

Anal. Calcd for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.89. Found: C, 65.08; H, 4.44; N, 6.81.

Recrystallization of **2d** from chloroform–hexane gave white crystals: mp 161–162.5°; ν_{NH} 3350, ν_{CO} 1750 cm^{-1}; nmr peaks ($CDCl_3$) at δ 3.28 (6 H, s), 3.70 (3 H, s), 6.58 (1 H, d, J = 3 Hz), 7.0–7.25 (3 H, m), 7.4–7.7 (2 H, m); uv $\lambda_{max}^{95\%\ EtOH}$ 215.5 (4.53), 277.5 (4.01), 284 (4.02), 292 nm (3.89).

Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.24; H, 6.29; N, 5.74.

***trans*-1-(*o*-Azidophenyl)-3-phenylpropen-3-one (1e).**—Acetophenone (0.83 g, 6.8 mmol) was added dropwise to a solution of sodium hydroxide (0.3 g) in water (10 ml) and ethanol (5 ml) cooled in an ice bath. A solution of *o*-azidobenzaldehyde (1.0 g, 6.8 mmol) in ethanol (1 ml) was added. After 10 min the reaction solution was removed from the ice bath and stirred at room temperature for 16 hr. Filtration gave the crude product. Recrystallization from ethanol gave **1e** (1.1 g, 65%). The analytical sample was prepared by repeated recrystallization: mp 70.5–71.5°; ν_{N_3} 2145, ν_{CO} 1670 cm^{-1}; nmr peaks ($CDCl_3$) at δ 8.2–7.8 (m, 3 H), and 7.8–6.9 (m, 8 H).

Anal. Calcd for $C_{15}H_{11}N_3O$: C, 72.27; H, 4.45; N, 16.86. Found: C, 72.13; H, 4.56; N, 16.82.

2-Benzoylindole (2e).—A mixture of **1e** (0.53 g, 2.1 mmol) and decalin (80 ml) was refluxed under nitrogen for 4 hr. After removal of decalin, the residue was recrystallized from chloroform–benzene giving **2e** (0.36 g, 72%), mp 147–148.5° (lit.[23] mp 146–148°), having an ir spectrum identical with that of an authentic sample.

1-(*o*-Azidophenyl)-3-(2-pyridyl)propen-3-one (1f).—Condensation of 2-acetylpyridine (0.85 g, 7.0 mmol) and *o*-azidobenzaldehyde (1.0 g, 6.8 mmol) was carried out as for **1e**. Recrystallization of the crude product from ethanol gave **1f** (1.0 g, 59%). The analytical sample was prepared by repeated recrystallization: mp 111–112°; ν_{N_3} 2150, ν_{CO} 1680 cm^{-1}; nmr peaks ($CDCl_3$) at δ 8.7 (m, 1 H), and 8.3–7.0 (m, 9 H).

Anal. Calcd for $C_{14}H_{10}N_4O$: C, 67.19; H, 4.03; N, 22.39. Found: C, 67.37; H, 3.93; N, 22.55.

2-Indolyl 2-Pyridyl Ketone (2f).—A solution of **1f** (0.55 g, 2.2 mmol) in decalin (80 ml) was reluxed for 4 hr. The cooled reaction mixture was extracted with dilute hydrochloric acid. The aqueous extract was made alkaline and extracted with chloroform. Evaporation of the dried extract gave a residue which soon crystallized. Recrystallization from benzene gave **2f** (0.25 g, 51%). An additional recrystallization gave the analytical sample: mp 134.5–136°; ν_{NH} 3350, ν_{CO} 1630 cm^{-1}; nmr peaks ($CDCl_3$) at δ 8.7 (m, 1 H), 8.4–6.9 (m, 9 H).

Anal. Calcd for $C_{14}H_{10}N_2O$: C, 75.65; H, 4.54; N, 12.61. Found: C, 75.42; H, 4.63; N, 12.41.

4-Acetyl-1-benzoylpiperidine (3).—2-Methyl-2-(4-pyridyl)-1,3-dioxolane[24] (8.3 g, 50 mmol) in water (40 ml) was hydrogenated (50 psi) over 5% rhodium–carbon catalyst until hydrogen uptake ceased. The catalyst was removed by filtration and the filtrate was stirred vigorously for 24 hr with a mixture of potassium carbonate (32 g), water (65 ml), chloroform (70 ml), ethanol (5 ml), and benzoyl chloride (11.2 g, 80 mmol). The chloroform layer was separated and the aqueous layer was extracted again with chloroform. The crude ketal obtained by evaporation was stirred at room temperature for 1 hr with 50% aqueous ethanol containing 1% hydrochloric acid. The product was extracted with chloroform and then chromatographed on silicic acid. The major component was eluted with 1:1

(22) T. J. Schwan and C. S. Davis, *J. Pharm. Sci.*, **57**, 877 (1968).

(23) R. V. Jardine and R. K. Brown, *Can. J. Chem.*, **41**, 2067 (1963).

(24) A. T. Nielsen, D. W. Moore, J. H. Mazur, and K. H. Berry, *J. Org. Chem.*, **29**, 2898 (1964).

ether–benzene and distilled giving **3** (6.5 g, 28 mmol, 56%), bp 175–177° (0.4 mm), which readily crystallized. The analytical sample, mp 68–70°, was prepared by recrystallization from hexane: ν_{CO} 1710, 1630; nmr peaks ($CDCl_3$) at δ 1.0–3.3 (10 H, m with prominent s at 2.17), 3.5–4.7 (2 H, very broad), 7.38 (5 H, s).

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.45; H, 7.32; N, 5.87.

Smaller amounts of material having ir, nmr, and mass spectral data in accord with expectation for 1-benzoyl-4-(1-benzoyloxyethyl)piperidine and 2-(1-benzoyl-4-piperidyl)-2-methyl-1,3-dioxolane were eluted prior to **3**.

2-Indolyl 4-(1-Benzoylpiperidyl) Ketone (2g). A. *Via* 1-(1-Benzoyl-4-piperidyl)-3-(2-azidophenyl)-2-propen-1-one (1g).—The methyl ketone **3** (2.31 g, 10.0 mmol) was added to a solution of sodium hydroxide (0.8 g) in 50% aqueous ethanol (100 ml). When the ketone had completely dissolved, *o*-azidobenzaldehyde (1.5 g, 10 mmol) in ethanol (10 ml) was added slowly. After 2 hr the reaction mixture was extracted with chloroform and the chloroform was washed with brine, dried, and concentrated to an orange foam. Half of the crude product chromatographed on silicic acid with 1:4 ether–benzene gave **1g** as a tan oil (0.80 g, 2.2 mmol, 44%). The compound was not obtained in crystalline form.

A sample of chromatographed **1g** (0.60 g, 1.7 mmol) was suspended in decalin and refluxed (195°) for 4 hr. After the decalin was removed, the residual solid was chromatographed on silicic acid. Elution with 1:2 ether–benzene gave an oil which crystallized from carbon tetrachloride giving **2g** (0.20 g, 0.6 mmol, 35%): mp 166–167.5 after recrystallization from carbon tetrachloride; ν_{NH} 3350, ν_{CO} 1645 cm^{-1}; $\lambda_{max}^{95\%\ EtOH}$ 226 (log ϵ 4.30), 310 (4.37); nmr peaks ($CDCl_3$) at δ 1.6–2.2 (4 H, m), 2.8–3.7 (3 H, m), 3.8–4.2 (2 H, very broad), 7.0–7.8 (10 H, m), 9.8 (1 H, s).

Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.07; N, 8.43. Found: C, 75.83; H, 6.19; N, 8.34.

The unchromatographed portion of **1g** gave a comparable yield of **2g** (0.24 g, 43%) when subjected to an identical pyrolysis.

B. By Deoxygenation. 1-(1-Benzoyl-4-piperidyl)-3-(*o*-nitrophenyl)-2-propen-1-one (4).—A solution of the ketone **3** (2.31 g, 1.00 mmol) and *o*-nitrobenzaldehyde (3.8 g, 2.5 mmol) in ether (50 ml) was treated with 3 ml of a solution prepared by dissolving 3 ml of 10% NaOH in ethanol (25 ml). The solution was stirred at 0° for 2 hr and then refrigerated overnight. The crude product was extracted into benzene and washed with sodium bicarbonate solution and dilute hydrochloric acid. The dried solution was concentrated and redissolved in benzene (100 ml) containing *p*-toluenesulfonic acid (0.5 g). This solution was refluxed for 2 hr to complete dehydration of any intermediate ketol. The cooled solution was washed with dilute sodium bicarbonate, dried, and evaporated. Chromatography of the residue on silicic acid gave **4** (1.0 g, 2.8 mmol, 28%): mp 116–117° after recrystallization from carbon tetrachloride; ν_{CO} 1695, 1640, ν_{NO_2} 1540, 1350 cm^{-1}; nmr peaks ($CDCl_3$) at δ 0.8–2.2 (4 H, m), 2.8–3.4 (3 H, m), 3.6–4.7 (2 H, very broad), 6.7 (1 H, d, J = 16 Hz), 7.45 (5 H, s), 7.68 (3 H, broad s), 8.1 (2 H, m with prominent d, J = 16 Hz).

Anal. Calcd for $C_{21}H_{20}N_2O_4$: C, 69.21; H, 5.53; N, 7.69. Found: C, 69.02; H, 5.65; N, 7.49.

2-Indolyl 4-(1-Benzoylpiperidyl) Ketone (2g) and 2-(1-Ethoxyindolyl) 4-(1-Benzoylpiperidyl) Ketone (5).—A suspension of **4** (1.05 g, 2.9 mmol) in triethyl phosphite (100 ml) was slowly heated to 145° over a 1.5-hr period using an oil bath. The nitrostyrene dissolved during this period. The solution was kept at 145° for an additional 0.5 hr. After the mixture was cooled, the triethyl phosphite was removed by distillation at 0.1 mm. The residue was dissolved in benzene and washed with sodium bicarbonate, dilute hydrochloric acid, and water. Evaporation of the dried benzene extract gave a brown oil which was chromatographed on silicic acid. Elution with 1:4 ether–benzene gave first **5** and then **2g**. The latter product (0.20 g, 0.6 mmol 21%), was identified as **2g** by mixture melting point and ir comparison with **2g** prepared by azide pyrolysis.

The by-product **5** was crystallized from benzene–hexane (0.12 g, 0.3 mmol, 11%): mp 131–132.5°; ν_{NH} none, ν_{CO} 1660, 1625 cm^{-1}; nmr peaks ($CDCl_3$) at δ 1.43 (3 H, t), 1.6–2.2 (4 H, m), 2.75–3.6 (3 H, m), 3.8–4.8 (4 H, m superimposed on q), 7.0–7.9 (10 H); $\lambda_{max}^{95\%\ EtOH}$ 232 (log ϵ 4.35), 306 (4.37).

Anal. Calcd for $C_{23}H_{24}N_2O_3$: C, 73.38; H, 6.43; N, 7.44. Found: C, 73.16; H, 6.59; N, 7.48.

1-Benzoyl-4-acetonyl-1,2,3,6-tetrahydropyridine (14) and 1-Benzoyl-$\Delta^{4,\alpha}$-piperidine-4-acetone (15).—Sodium hydride (4.2 g of 50% mineral oil dispersion) was rinsed with hexane and covered with anhydrous ether (250 ml). A solution of diethyl acetonylphosphonate[25] (21.4 g, 0.11 mol) in ether (50 ml) was added slowly. When hydrogen evolution had ceased, a solution of 1-benzoyl-4-piperidone (20.3 g, 0.10 mol) in dry benzene (100 ml) and ether (200 ml) was added in one portion. The resulting reaction mixture was refluxed under nitrogen for 20 hr. The organic solution was decanted and the gummy precipitate was washed with additional ether. The combined organic layers were filtered, washed with water, dried ($MgSO_4$), and evaporated. The residue was chromatographed on silicic acid using 30% ether in benzene to elute a mixture of the products (12.9 g of **14**, 53%; 4.3 g of **15**, 18%). Separation of the isomers could be effected by chromatography on silicic acid using 5% ether in benzene as eluant. The exocyclic ketone **15** was eluted most rapidly and was obtained as crystals: mp 70.5–72° on recrystallization from ether–hexane; ν_{CO} 1690, 1640 cm^{-1}; nmr peaks ($CDCl_3$) at δ 7.4 (s, 5 H), 6.15 (broad s, 1 H), 3.9–3.4 (broad, 4 H), 3.1–2.8 (broad t, 2 H), 2.5–2.1 (broad t, 2 H), and 2.1 (s, 3 H).

Anal. Calcd for $C_{15}H_{17}O_2N$: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.84; H, 7.12; N, 5.54.

The endocyclic isomer **14** was an oil: ν_{CO} 1720, 1640 cm^{-1}; nmr peaks ($CDCl_3$) at δ 7.4 (s, 5 H), 5.5 (broad, 1 H), 4.3–3.3 (broad, 4 H), 3.1 (s, 2 H), 2.3–1.9 (broad, 2 H), and 2.1 (s, 3 H).

Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.89; H, 7.06; N, 5.62.

1-Benzoyl-4-piperidylmethyl Methyl Ketone (16).—A mixture of **14** and **15** (2.3 g, 9.4 mmol) was hydrogenated (40 psi) over platinum oxide (0.3 g) in ethanol for 30 min. The reaction solution was filtered and evaporated. The residue gave crystalline **16** (1.8 g, 78%) on trituration with ether, mp 62–64° (lit.[7] mp 63–65°). The ir spectrum was identical with that of an authentic sample.

1-Benzoyl-4-piperidylmethyl 2-Indolyl Ketone (2h).—Condensation of **16** (0.25 g, 10.0 mmol) and *o*-azidobenzaldehyde (0.15 g, 1.0 mmol) was carried out in basic aqueous ethanol as described for **2g**. After the reaction mixture was stirred overnight, it was diluted with water and extracted with chloroform. The residue was purified by chromatography on silicic acid giving **1h** (0.2 g, 0.5 mmol, 50%) as a gum: ν_N 2150, ν_{CO} 1680, 1650; nmr peaks ($CDCl_3$) at δ 8.0–6.9 (m, 10 H), 6.65 (d, 1 H) and 3.2–0.6 (braod, 11 H).

The azide (0.18 g, 0.48 mmol) was pyrolyzed in decalin in the usual way and the residue obtained after evaporation of the decalin was chromatographed on silicic acid (12 g). Elution with 1:10 ether–benzene gave **2h** (0.10 g, 60%), mp 154–155° after recrystallization from carbon tetrachloride (lit.[7] mp 154–156°). The ir and nmr spectra were identical with those of an authentic sample.

3-(*o*-Nitrophenyl)-1-(4-pyridyl)prop-2-en-1-one (6).—4-Acetylpyridine (10.0 g, 83 mmol), *o*-nitrobenzaldehyde (11.1 g, 83 mmol), and sodium hydride (1.00 g, 59% dispersion in mineral oil, 25 mmol) were added in that order to dry ether (150 ml). Within 2 min, dark yellow crystals separated and additional ether (50 ml) was added. The solution was stirred for an additional 30 sec and then poured as rapidly as possible into a stirred 4% hydrochloric acid solution. The two-phase system was neutralized with aqueous sodium bicarbonate. During this process most of the ether evaporated as carbon dioxide was evolved. The product was obtained by filtration, washed several times with water, and dried to give **6** (18.9 g, 90%). Recrystallization from ethanol–water gave the analytical sample, mp 147°, ν_{CO} 1680 cm^{-1}.

Anal. Calcd for $C_{14}H_{10}N_2O_3$: C, 66.14; H, 3.96; N, 11.02. Found: C, 66.14; H, 4.06; N, 10.96.

2-[2-(*o*-Nitrophenyl)vinyl]-2-(4-pyridyl)-1,3-dioxolane (7.)—The ketone **6** (18.9 g, 75 mmol), ethylene glycol (13.5 ml), and *p*-toluenesulfonic acid (12.9 g, 83 mmol) were refluxed together in benzene (340 ml) in a flask equipped with a Dean-Stark trap. After 2 hr, more ethylene glycol (20 ml) and *p*-toluenesulfonic acid (0.36 g) were added and reflux was continued for 22 hr. The reaction solution was cooled and washed with 10% potassium carbonate solution (450 ml). The aqueous wash was reextracted with chloroform and the benzene and chloroform solutions were combined, dried over potassium carbonate, and concentrated. The residue was passed through a short Florisil

(25) N. Kreutzkamp and H. Kayser, *Chem. Ber.*, **89**, 1614 (1956).

column to give pure **7** (11.7 g, 54%) after removal of the solvent. Recrystallization from chloroform–hexane gave pale yellow needles: mp 93–94°; nmr peaks ($CDCl_3$) at δ 8.9–8.6 (broad d, 2 H), 8.2–7.8 (m, 1 H), 7.7–7.2 (m, 6 H), 6.3 (d, 1 H, J = 18 Hz) and 4.2 (m, 4 H).

Anal. Calcd for $C_{16}H_{14}N_2O_4$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.21; H, 4.71; N, 9.31.

2-(2-Indolyl)-2-(4-pyridyl)-1,3-dioxolane (8).—The dioxolane **7** (5.40 g, 2.03 mmol) was dissolved in triethyl phoshite (170 ml) and this solution was added dropwise during 2 hr to refluxing triethyl phosphite (130 ml) under a nitrogen atmosphere. Reflux was continued for 4 hr after the addition was complete. The reaction mixture was then cooled and unreacted triethyl phosphite was removed by distillation at reduced pressure. The residue was dissolved in ether (300 ml). The hydrochloride of the product was precipitated as a glass by passing hydrogen chloride gas through the solution. The ether was decanted when precipitation was complete. The residue was washed with ether and stirred with a mixture of chloroform and dilute sodium hydroxide until it was completely dissolved. The chloroform layer was dried and concentrated. After elution through a Florisil column, **8** was obtained as colorless plates (2.43 g, 45%): mp 166–168° from chloroform–hexane; nmr peaks ($CDCl_3$) at δ 9.30 (1 H, broad s), 8.64 (2 H, d), 7.8–7.0 (6 H, m), 6.4 (1 H, d, J = 3 Hz) and 4.0 (4 H, m).

Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.32; H, 5.11; N, 10.53.

2-Indolyl 4-Pyridyl Ketone (2i).—The ketal (1.00 g, 3.8 mmol) was heated with 10% hydrochloric acid (100 ml) on a steam bath for 5 min. The crude product precipitated when the solution was made basic with sodium hydorxide solution. Recrystallization from aqueous ethanol gave **2i** (0.80 g, 95%), mp 172–174° (lit.[8] mp 172–174°).

Imine of 2-(1-Methylindolyl) 4-Pyridyl Ketone (17).—*N*-Methylindole (1.31 g, 10.0 mmol) in anhydrous ether (20 ml) was added at 0° to 5 ml of a 2 *M* hexane solution of butyllithium.[26] The mixture was refluxed for 7 hr, cooled to 0°, and treated with a solution of 4-cyanopyridine (1.04 g, 10.0 mmol) in ether (50 ml). The mixture was stirred overnight during which time a reddish brown solid appeared. The reaction mixture was then cooled and hydrolyzed with a mixture of crushed ice and ammonium chloride resulting in the precipitation of the imine **17**. Additional amounts of **17** were obtained by ether extraction giving a total yield of 1.85 g (7.9 mmol, 79%): mp 165–166.5° after recrystallization from benzene–hexane; ν_{NH} 3245, ν_{CN} 1605 cm^{-1}; nmr peaks ($CDCl_3$) at δ 4.03 (3 H, broad s), 6.58 (1 H, s), 7.0–7.7 (7 H, m), 8.75 (2 H, d); λ_{max}^{EtOH} 222 (log ε 4.42), 277 (3.84), 3.13 (4.03).

Anal. Calcd for $C_{15}H_{13}N_3$: C, 76.57; H, 5.57; N, 17.87. Found: C, 76.55; H, 5.62; N, 17.78.

2-(1-Methylindolyl) 4-Pyridyl Ketone (9). A. By Hydrolysis of 17.—The imine **17** (1.2 g, 5 mmol) was suspended in 60 ml of 50% ether–water and 1 *N* hydrochloric acid was added at 0° until the mixture was acidic. The mixture was then refluxed for 2 hr, cooled, made alkaline, and extracted with ether. The solvent was dried, and concentrated and the residue was triturated with hexane to give **9** as a yellow solid. Recrystallization from hexane afforded **9** (0.95 g, 4.0 mmol, 80%): mp 91–92.5°; ν_{CO} 1640 cm^{-1}; nmr peaks ($CDCl_3$) at δ 4.14 (3 H, s), 7.0–7.8 (7 H, m including a d, J = 6 Hz, at 7.7), 8.83 (2 H, d, J = 6 Hz); λ_{max}^{EtOH} 224 (log ε 4.37), 268 (3.64), 325 (4.23).

Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.11; H, 5.18; N, 11.72.

B. By Methylation of 2i. A solution of sodium amide in ammonia was prepared by addition of ferric nitrate nonahydrate (1 mg) and then sodium (0.20 g) in small pieces to liquid ammonia. The solution was stirred for 1 hr and then **2i** (1.11 g, 5.0 mmol) in anhydrous tetrahydrofuran (30 ml) was added dropwise. After the mixture was stirred for 15 min, a solution of methyl iodide (1.5 g, 10 mmol) in anhydous ether (10 ml) was added. Stirring was continued for 0.5 hr and then the ammonia was allowed to evaporate. Water (10 ml) was added cautiously and the resulting mixture was extracted with ether. Drying and evaporation gave a residue which was crystallized from chloroform–hexane to give recovered **2i** (0.55 g, 50% recovery). The mother liquors contained **9** (0.45 g, 1.9 mmol, 38%), mp 89–92° after recrystallization from hexane. The ir spectrum of this material was identical with that of the product prepared as described in part A.

1-Carbethoxymethyl-4-[1-(2-indolyl)-1-dioxolanyl]pyridinium Bromide (18).—A solution of **8** (0.45 g, 1.7 mmol) in anhydrous tetrahydrofuran (40 ml) was treated with ethyl bromoacetate (5 ml) and refluxed for 2 hr. The product **18** precipitated as a bright yellow solid (0.72 g, 98%). Recrystallization from ethanol–ether gave the analytical sample: mp 150–152° dec; ν_{CO} 1750 cm^{-1}; nmr peaks (DMSO-d_6) at δ 9.3 (d, 2 H), 8.4 (d, 2 H), 6.8–7.7 (m, 4 H), 6.3 (s, 1 H), 5.38 (s, 2 H), 3.9–4.5 (6 H, m), 3.38 (s, 1 H) and 1.25 (t, 3 H).

Anal. Calcd for $C_{20}H_{21}BrN_2O_4$: C, 55.43; H, 4.85; N, 6.47. Found: C, 55.20; H, 4.95; N, 6.47.

Reduction of 18. 1-(2-Indolyl)-1-(*N*-carbethoxymethyl-4-piperidyl)dioxolane (10) and By-Product 11.—A solution of **18** (4.1 g, 95 mmol) in absolute ethanol (150 ml) was hydrogenated at 30 psi over 10% Pd/C for 12 hr. The solution was filtered and evaporated. The residue was dissolved in chloroform and washed with 10% sodium carbonate solution. Evaporation yielded an oil which was chromatographed on silicic acid using 1:1 ether–benzene for elution. The major product **10** was eluted first and crystallized from benzene–hexane (3.4 g, 79%): mp 152–153°; ν_{NH} 3200, ν_{CO} 1750 cm^{-1}; nmr peaks ($CDCl_3$) at δ 8.4 (broad s, 1 H), 6.9–7.7 (m, 4 H), 6.45 (broad s, 1 H), 3.6–4.4 (m, 6 H including q at 4.15), 2.7–3.3 (m, 4 H including s at 3.15), 1.45–2.40 (broad, 7 H), 1.21 (t, 3 H).

Anal. Calcd for $C_{20}H_{26}N_2O_4$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.13; H, 7.38; N, 7.72.

Compound **11** was eluted immediately after **10** and was crystallized from ether–hexane (0.25 g, 7%): mp 149–150.5°; ν_{NH} 3310 cm^{-1}, ν_{CO} 1730 cm^{-1}; nmr peaks at 8.55 (broad s, 1 H), 7.0–7.75 (m, 4 H), 3.95–4.50 (m, 7 H), 3.40 (d, 1 H, J = 16 Hz), 2.83 (d, 1 H, 16 Hz), 1.7–2.8 (broad, 7 H), 1.25 (t, 3 H).

Anal. Calcd for $C_{20}H_{24}N_2O_4$: C, 67.39; H, 6.79; N, 7.86. Found: C, 67.44; H, 6.89; N, 7.93.

The yields of **10** and **11** were 66 and 12%, respectively, when the reduction was carried out in ethanol containing 5% acetic acid.

2-Indolyl 4-(1-Carbethoxymethyl)piperidyl Ketone (13).—A solution of **10** (0.20 g, 0.56 mmol) in 85% ethanol containing 3 drops of concentrated HCl was refluxed for 0.5 hr and then made alkaline with 10% sodium hydroxide solution. Most of the ethanol was removed using a rotary evaporator and the resulting suspension was extracted with chloroform. The chloroform was dried and evaporated to give an oil. Trituration with ether gave **13** (0.14 g, 80%): mp 129.5–131° after two recrystallizations from benzene–hexane; ν_{NH} 3360, ν_{CO} 1740, 1645 cm^{-1} in KBr; $\lambda_{max}^{95\% EtOH}$ 227 (log ε 4.1), 234 (sh, 4.08), 311.5 (4.34); nmr peaks ($CDCl_3$) at δ 1.25 (3 H, t, J = 7 Hz), 1.75–2.7 (7 H, m), 2.85–3.35 (m with prominent s at 2.25, 4 H), 4.15 (q, 2 H), 7.0–7.8 (m, 6 H).

Anal. Calcd for $C_{18}H_{22}N_2O_3$: C, 68.77; H, 7.05; N, 8.91. Found: C, 68.58; H, 7.08; N, 9.11.

2-Indolyl 4-(1-Carbethoxymethyl)piperidyl Ketone (13) from 2g *via* 12.—A solution of **2g** (200 mg, 0.6 mmol) and KOH (3.5 g) in 50 ml of methanol and 15 ml of water was heated under reflux for 48 hr. The solution was cooled, diluted with water, and thoroughly extracted with $CHCl_3$. The solvent was evaporated from the combined, dried extracts to give 0.16 g of yellowish oil. Trituration with anhydrous ether gave 0.13 g (95%) of cream colored solid which thin layer chromatograph and melting point showed to be slightly impure. Four recrystallizations from benzene eventually gave 2-indolyl 4-piperidyl ketone (**12**) as a pale tan solid of constant melting point (163–164°): ν_{NH} 3345, ν_{CO} 1640 cm^{-1} in KBr; nmr peaks ($CDCl_3$) at δ 7.0–7.8 (m, 6 H), 2.5–3.6 (broad m, 6 H).

A solution of **12** (20 mg, 0.88 mmol) in anhydrous benzene (5 ml) was treated with ethyl bromoacetate (10 μl) and stirred at room temperature for 4 hr. Aqueous sodium carbonate was added and the mixture was extracted with chloroform. The extract was dried and evaporated. The residual oil (22 mg, 80%) was identified as **13** by tlc. Isolation by preparative layer chromatography (250 μ, silica gel) and crystallization from benzene–hexane gave **13** (20 mg) identified by melting point and ir spectrum.

***N*-Carbethoxymethyl-4-(indol-2-ylcarbonyl)pyridinium Bromide (19).**—A solution of **2i** (3.0 g, 0.0135 mol) and ethyl bromoacetate (20 ml) in tetrahydrofuran (50 ml) was refluxed for 1 hr. The product partially separated as a heavy oil. The mother liquor was diluted with ether to precipitate the re-

(26) D. A. Shirley and P. A. Roussel, *J. Amer. Chem. Soc.*, **75**, 375 (1953).

mainder of the product. Crystallization from ethanol–ether gave **19** (4.0 g, 76%): mp 195° dec; ν_{CO} 1750, 1640 cm^{-1}; nmr peaks (DMSO-d_6) at δ 12.3 (s, 1 H), 9.5 (d, 2 H), 8.6 (d, 2 H), 7.9–7.0 (m, 4 H), 6.0 (s, 1 H), 4.31 (q, 2 H), 3.4 (s, 2 H), and 1.32 (t, 3 H).

Anal. Calcd for $C_{18}H_{17}BrN_2O_3$: C, 55.52; H, 4.37; N, 7.19. Found: C, 55.68; H, 4.31; N, 7.10.

***N*-Carbethoxymethyl-4-(1-methylindol-2-ylcarbonyl)pyridinium Bromide (20).**—A solution of **9** (2.4 g, 0.010 mmol) in anhydrous tetrahydrofuran (50 ml) was treated with 10 ml of ethyl bromoacetate with stirring. The solution was refluxed for 2 hr, cooled, and diluted with ether. The orange precipitate was recrystallized several times from ethanol–ether giving **20** (3.6 g, 89%): mp 166.5–167.5° dec; ν_{CO} 1750, 1640 cm^{-1}; nmr peaks (DMSO-d_6) at δ 9.48 (d, 2 H), 8.6 (d, 2 H), 7.0–7.9 (m, 5 H), 6.0 (s, 2 H), 4.0–4.5 (overlapping q and s, 5 H), 1.30 (t, 3 H).

Anal. Calcd for $C_{19}H_{19}BrN_2O_3$: C, 56.58; H, 4.71; N, 6.95. Found: C, 56.33; H, 4.77; N, 6.92.

Mass Spectral Data.—The principal ions in the mass spectra of compounds **2c, 2d, 2g, 2i, 9, 10, 11, 12, 13,** and **17** have been submitted in tabular form as supplementary data in the microfilm edition of this jouranl.[27]

Registry No.—**1a,** 33037-72-8; **1b,** 33037-73-9; **1e,** 33037-74-0; **1f,** 33037-75-1; **1h,** 33037-76-2; **2b,** 948-65-2; **2e,** 18132-19-9; **2d,** 33037-79-5; **2f,** 24512-42-3; **2g,** 33037-81-9; **3,** 33037-82-0; **4,** 33037-83-1; **5,** 33037-84-2; **6,** 33037-85-3; **7,** 33037-86-4; **8,** 33037-87-5; **9,** 25387-27-3; **10,** 33037-89-7; **11,** 33080-10-3; **12,** 33037-90-0; **13,** 33037-91-1; **14,** 33037-92-2; **15,** 33037-93-3; **17,** 33037-94-4; **18,** 33037-95-5; **19,** 33037-96-6; **20,** 33037-97-7.

(27) Mass spectral data will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to author, title of article, volume, and page number. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

Isocarbostyrils from Monomeric and Dimeric β-Styryl Isocyanates[1,2]

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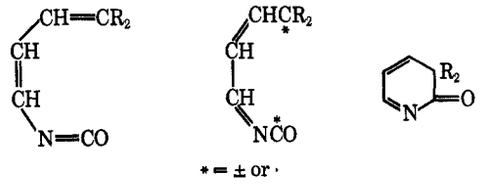
Received August 27, 1971

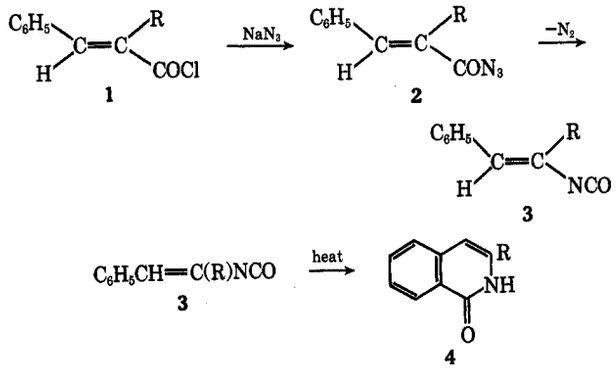
In an inert solvent at 250°, *trans*-β-styryl isocyanate (**3a**) and its β-methyl (**3b**) and β-phenyl (**3c**) derivatives were efficiently isomerized into the corresponding isocarbostyril **4a, 4b,** and **4c**. In the presence of iodine the reaction proceeded conveniently at the reduced temperature of 140°. Two dimers of β-styryl isocyanate were obtained; one was converted into **4a** on heating in refluxing pyridine.

A formal, but unestablished, interconversion by valence isomerization may be recognized for an *s-cis*-isocyanatobutadiene-1,3 and a 2-oxo-2,3-dihydropyridine. Should ring closure proceed instead from either a zwitterionic or diradical structure, then the geometrical restriction on the isocyanate disappears. Styryl



isocyanates were selected for investigation since ring closure from closely related systems was known[3] and they are more readily available than structurally simpler isocyanatodienes.

By the thermal Curtius reaction each *trans*-cinnamoyl azide (**2**), obtained by treating *trans*-cinnamoyl chloride (**1**) with sodium azide, gave the corresponding *trans*-β-styryl isocyanate (**3**) in overall yield ranging from moderate to good. The azide could, however, be converted into the isocarbostyril without isolation of **3**.



a, R = H; **b**, R = CH_3; **c**, R = C_6H_5

Each isocyanate was efficiently isomerized in mineral oil or diphenyl ether at 250°. The isomerization **3a** → **4a** in the presence of iodine occurred in dichlorobenzene at 180° or in *m*-xylene at 140°, but there was no reaction in carbon tetrachloride at 77° and *trans*-isocyanate was quantitatively recovered.[4] Reaction progress in *o*-dichlorobenzene was monitored not only by disappearance of ir absorption at 2260 cm^{-1} (NCO), but also by development, followed by disappearance, of ir absorption (*o*-dichlorobenzene solution) at 1740 cm^{-1} and by development of permanent bands at 1665 and 1650 cm^{-1}. This indicated that the forma-

(1) Financial assistance was received from NASA Grant No. NGR-012-114.

(2) G. J. Mikol and J. H. Boyer, Abstracts, 160th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1970, ORGN 51.

(3) The present investigations were completed when F. Eloy and A. Deryckere [*J. Heterocycl. Chem.*, 1191 (1970); *Chim. Ther.*, 48 (1971)] reported the preparation pf pyridine, isoquinoline, and other heterocyclic derivatives by the thermal cyclization of vinyl isocyanates substituted in the β position by a vinyl radical. H. M. Blatter and H. Lukaszewski [*Tetrahedron Lett.*, 855 (1964)] report a similar thermal cyclization for $C_6H_5N{=}C(C_6H_5)NCS$ and discuss similar cyclizations for $C_6H_5N{=}C(C_6H_5)NCO$ and for $C_6H_5C(C_6H_5){=}C(C_6H_5)CH{=}C{=}O$.

(4) L. Crombie, *Quart. Rev., Chem. Soc.*, **6**, 101 (1952), reviews methods for geometrical isomerization.