filtered through a column of 30 g of Alcoa F-20 alumina to give 1.1 g (34%) of **7**: mp 85.2–86.2° after recrystallization from ether–hexane; ir no NH or C=O; nmr ($CCl_4$) $\tau$ 2.7–3.5 (m, 3, ArH), 3.53 (s, 1, C=CH), 6.03 (s, 3, $OCH_3$), 6.06 (s, 3, $OCH_3$), and 6.66 (s, 4, $SCH_2$);[6,7] uv max (95% EtOH) 308 m$\mu$ ($\epsilon$ 11,000) and 245 (sh, 8400).[17]

*Anal.* Calcd for $C_{12}H_{14}O_2S_2$: C, 56.66; H, 5.54; S, 25.21. Found: C, 56.69; H, 5.78; S, 25.49.

Another reaction was carried out in essentially the same way as above, except that after separation of the sand and pyridine by decantation, the pyridine was distilled at atmospheric pressure and the distillates were analyzed by gas chromatography and infrared spectroscopy. A compound with a retention time corresponding with that of authentic acetonitrile on three different gas chromatography columns (15 ft × 0.125 in., 7% Apiezon L; 6 ft × 0.125 in., 1% JXR methyl silicone; and 6 ft × 0.125 in., 2% Epon 1001) was detected. The infrared spectrum of the first pyridine distillate, with a pyridine reference, contained absorptions at 2260 (C≡N) and 920 $cm^{-1}$, present in the spectrum of authentic acetonitrile.

**2,3-Dihydro-5-(3′,4′-dimethoxyphenyl)-*p*-dithiin-1,1,4,4-tetroxide (8).**—A mixture of 1 g of **7**, 2 ml of 30% $H_2O_2$, and 5 ml of glacial acetic acid was heated at 30° for 48 hr. The crystals of **8** which formed melted at 253–254° after recrystallization from glacial acetic acid.

*Anal.* Calcd for $C_{12}H_{14}O_6S_2$: C, 45.3; H, 4.41. Found: C, 45.23; H, 4.42.

**3-Acetamido-2-butanone Ethylene Thioketal (13).**—With the procedure previously described for the preparation of **5**, compound **13** was obtained from 1,2-ethanedithiol and 3-acetamido-2-butanone[18] as crystals: mp 106–107° from ether–hexane; ir ($CHCl_3$) 3400 (NH) and 1640 $cm^{-1}$ (amide C=O); nmr ($CDCl_3$) $\tau$ 3.8–4.2 (br, 1, NH), 5.55 (d of q, 1, $J_d$ = 9.5 Hz, $J_q$ = 6.3 Hz, CH), 6.65 (s, 4, $CH_2S$),[6] 7.98 (s, 3, $CH_3C$=O), 8.20 [s, 3, $CH_3C(S)S$], 8.70 (d, 3, $J$ = 6.3 Hz, $CH_3C$).

*Anal.* Calcd for $C_8H_{15}NOS_2$: C, 46.79; H, 7.36; N, 6.83; S, 31.2. Found: C, 46.7; H, 7.5; N, 6.6; S, 31.5.

**2,3-Dihydro-5,6-dimethyl-*p*-dithiin (12).**—With the procedure described for the preparation of **7**, compound **12** was obtained in 42% yield as a clear liquid: bp 113–114° (25 mm); ir (film) no NH or carbonyl; nmr ($CDCl_3$) $\tau$ 6.85 (s, 4, $CH_2S$)[6] and 8.12 (s, 6, $CH_3$).

*Anal.* Calcd for $C_6H_{10}S_2$: C, 49.3; H, 6.9; S, 43.9. Found: C, 49.1; H, 7.2; S, 43.6.

**2-Acetamido-3′,4′-dimethoxyacetophenone Propylene Thioketal (14).**—With the procedure described for the preparation of **5**, compound **14** was obtained in *ca.* 65% yield from **2** and 1,3-propanedithiol as crystals: mp 109–111° from ether–hexane; ir ($CHCl_3$) 3350 (NH) and 1675 $cm^{-1}$ (amide C=O); nmr ($CDCl_3$) $\tau$ 2.55–3.20 (m, 3, ArH), 4.1 (br, 1, NH), *ca.* 6.0 (partially obscured d, 2, $CH_2N$), 6.10 (s, 6, $OCH_3$), 6.5–7.8 (m, 4, $SCH_2$), 8.0 (m, 2, $CCH_2C$), and 8.06 (s, 3, $CH_3C$=O).

*Anal.* Calcd for $C_{15}H_{21}NO_3S_2$: C, 55.1; H, 6.46; S, 19.58. Found: C, 55.25; H, 6.41; S, 19.67.

**2-(3′,4′-Dimethoxyphenyl)-6,7-dihydro-5H-1,4-dithiepin (15).**—From 4 g of **14** treated as described for the preparation of **7** was obtained, after chromatography through alumina, 2.07 g of recovered **14** and 0.54 g (34%) of compound **15**: mp 101–103°; ir no NH or carbonyl; nmr ($CDCl_3$) $\tau$ 2.8–3.3 (m, 3, ArH), 3.91 (s, 1, C=CH), 6.10 (s, $OCH_3$), 6.38 (t, 4, $J$ = 6 Hz, $CH_2S$), and 7.81 (quintuplet, 2, $J$ = 6 Hz, $CCH_2C$).

*Anal.* Calcd for $C_{13}H_{16}O_2S_2$: C, 58.17; H, 6.01; S, 23.89. Found: C, 58.28; H, 6.07; S, 23.90.

**6-(3′,4′-Dimethoxyphenyl)-2,3-dimethoxynaphthalene (17).**—A solution of 6 g of **2**, 6 ml of 1,4-butanedithiol, and 1 g of *p*-toluenesulfonic acid in 250 ml of dry benzene was heated under reflux for 10 hr while water was removed with a Dean–Stark tube. The reaction mixture was washed with successive 100-ml portions of 1 *M* NaOH, $H_2O$, and saturated NaCl solutions and dried over anhydrous $Na_2SO_4$, and the solvent was removed at reduced pressure. The residue was chromatographed through 60 g of Alcoa F-20 alumina to give 4 g (96%) of **17** as white flakes: mp 179–180° (lit.[19] mp 179–180°); ir no NH or carbonyl; nmr ($CDCl_3$) $\tau$ 2.1–3.3 (m, 8, ArH), 6.08 (s, 3, $OCH_3$), and 6.18 (s, 9, $OCH_3$); mass spectrum parent peak 324 (calcd mol wt, 324).

(17) For 2,5-diphenyl-*p*-dithiin, uv max 309 m$\mu$ ($\epsilon$ 8900) and 259 (22,100): W. E. Parham and V. J. Traynelis, *J. Amer. Chem. Soc.*, **76**, 4960 (1954).

(18) R. H. Wiley and O. H. Borum, "Organic Syntheses," Coll. Vol. IV, John Wiley & Sons, Inc., New York, N. Y., 1963, p 5.

**Registry No.**—**2**, 5190-84-1; **3**, 22796-22-1; **4**, 22796-21-0; **5**, 22796-23-2; **7**, 22796-24-3; **8**, 22796-25-4; **12**, 22796-26-5; **13**, 22796-27-6; **14**, 22796-28-7; **15**, 22796-29-8.

**Acknowledgment.**—This investigation was supported by the Texas Christian University Research Foundation. The authors wish to thank George Grins for helpful discussions.

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## Synthesis of Substituted 1-Styryl-3,4-dihydroisoquinolines

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The conventional methods for the synthesis of 1-styrylisoquinoline or its derivatives center around two main approaches, the cyclization of the Schiff bases derived from cinnamaldehyde[1] or the condensation of 1-methylisoquinoline with aromatic aldehydes.[2] However, both of these syntheses leave the isoquinoline nucleus either completely saturated or unsaturated in the heterocyclic ring. Because of the possible usefulness of substituted 1-styryl-3,4-dihydroisoquinolines as intermediates in organic syntheses, we have developed a rather convenient method for the preparation of these compounds. The procedure involves the cyclodehydration of substituted $\beta$-phenethylamides to 3,4-dihydroisoquinolines through the Bischler–Napieralski reaction.[3]

The substituted $\beta,\beta$-diarylacryl chlorides **1a–1e** were prepared by the reaction of 1,1-diarylethylenes and oxalyl chloride.[4] The acid chlorides **1f–h** were prepared by treating the corresponding carboxylic acids (the *trans* acid **1f** was prepared by the procedure of Lipkin and Stewart,[5] whereas the acids **1g** and **1h** were commercially available) with thionyl chloride. The acid chloride **1b** was a mixture of *cis* and *trans* isomers, whereas **1g** and **1f** were *trans* isomers. Treatment of **1** with $\beta$-(3,4-dimethoxyphenyl)ethylamine (**2**) in the presence of sodium hydroxide afforded the amides **3**. The cyclodehydration of **3** to the corresponding substituted 1-styryl-3,4-dihydroisoquinolines **4** was achieved by using phosphorus oxychloride. It was possible to isolate the compounds **4** as such, but for the sake of identification they were converted into crystal-

(1) E. C. Weinbach and W. H. Hartung, *J. Org. Chem.*, **15**, 676 (1950); W. M. Whaley and T. R. Govindachari, *Org. Reactions*, **6**, 151 (1962).

(2) W. H. Mills and J. L. B. Smith, *J. Chem. Soc.*, **121**, 2724 (1922).

(3) T. Kametani, T. Terui, T. Ogino, and K. Fukumoto, *J. Chem. Soc., C*, 874 (1969).

(4) F. Bergmann, M. Weizmann, E. Dimant, J. Patai, and J. Szmuskowicz, *J. Amer. Chem. Soc.*, **70**, 1612 (1948).

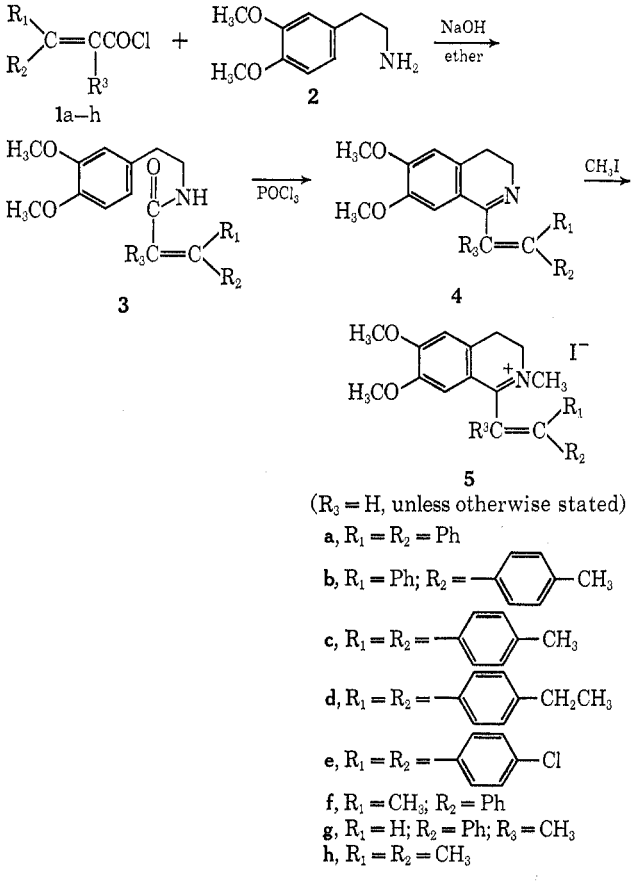
(5) D. Lipkin and T. D. Stewart, *ibid.*, **61**, 3295 (1939).

TABLE I

SPECTRAL DATA FOR COMPOUNDS 7 AND 8

| | Compd 7 ($CHCl_3$-$d$) | Compd 8 (DMSO-$d_6$) |
|---|---|---|
| Nmr, $\tau$ | 6.98 (d, 2, $J$ = 10 cps, $H_b$), 6.68 (m, 4, $CH_2$), 6.30 (s, 3, $OCH_3$), 6.20 (s, 3, $OCH_3$), 5.38 (t, 1, $J$ = 10 cps, $H_a$), 3.80 (m, 1, NH), 3.38 (s, 2, aromatic), 2.80 (m, 5, aromatic) | 7.26 (d, 2, $J$ = 6 cps, $H_{b1}$), 5.74 (t, $J$ = 6 cps, $H_{a1}$), 3.00 (m, 9, aromatic), −0.18 (s, 1, NH) |
| Ir, $\nu_{max}^{Nujol}$, $cm^{-1}$ | 3245 (NH) 1665 (C=O) | 3190 (NH) 1660 (C=O) |
| Uv, max (95% EtOH), m$\mu$ ($\epsilon$) | 284, (3620) | 254 (10,430) |

line methiodide salts **5**, which were isolated in 50–90% yields for the two steps.




($R_3$ = H, unless otherwise stated)

**a**, $R_1 = R_2$ = Ph

**b**, $R_1$ = Ph; $R_2$ = 

**c**, $R_1 = R_2$ = 

**d**, $R_1 = R_2$ = 

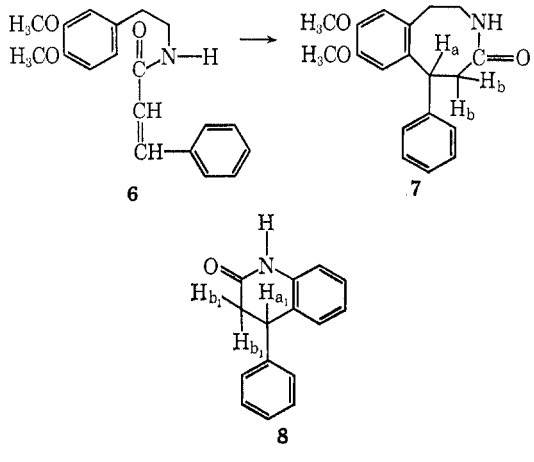
**e**, $R_1 = R_2$ = 

**f**, $R_1 = CH_3$; $R_2$ = Ph

**g**, $R_1$ = H; $R_2$ = Ph; $R_3 = CH_3$

**h**, $R_1 = R_2 = CH_3$

The reaction of cinnamoyl chloride with **2** afforded the amide **6**, which failed to undergo the expected cyclodehydration in the presence of phosphorus oxychloride. However, when **6** was heated in the presence of polyphosphoric acid, it gave an anomalous compound, which was subsequently characterized as 8,9-dimethoxy-6-phenyl-3-benzazocin-4-one (**7**). The characterization of **7** was based on elemental analysis, spectroscopic data (ir, nmr, and uv), and analogy with the reported cyclization of N-phenylcinnamides to 3,4-dihydro-4-phenylcarbostyril (**8**) with polyphosphoric acid.[6] The spectral data for compounds **7** and **8** are listed in Table I.




To test the generality of cyclization to seven-, eight-, and nine-membered rings, substituted benzyl-, phenylethyl-, and phenylpropylacrylamides were prepared and treated with polyphosphoric acid. However, all these attempts were unsuccessful, as only tars and/or starting materials could be isolated from these reactions.

### Experimental Section

The melting points were taken on a Thomas–Hoover melting point apparatus and are corrected. A Beckman IR-8 spectrophotometer was used to determine the infrared spectra. The nuclear magnetic resonance spectra were obtained with a Varian A-60 spectrometer.

**General Procedures for the Preparation of the Amides (3).**—$\beta,\beta$-Diarylacrylyl chlorides **1a–e** were prepared by the reaction of 1,1-diarylethylenes with oxalyl chloride according to the method by Bergmann, *et al.*[4] For the preparation of the acrylamides **3**, a solution of **1** (1 mol) in ether at 0° was added dropwise and with stirring to an ethereal solution containing $\beta$-(3,4-dimethoxyphenyl)ethylamine (**2**, 1 mol) in 10% sodium hydroxide solution at 0°. The reaction mixture was stirred at 5° until the precipitation of the acrylamide **3** had been completed. The compounds **3** were obtained by filtration of the precipitate and crystallization of the solid from ethanol–water. In the cases where the acids were commercially available, the acid chlorides were prepared by treating them with an excess of thionyl chloride. Evaporation of the solvent left an oil, which dissolved in ether and reacted with the amine as described above.

**General Procedure for the Preparation of 1-Styryldihydroisoquinoline Methiodide Salts (5).**—A solution of the amide **3** (3.0 g) in dry benzene (50 ml) was heated under reflux for 1 hr in the presence of phosphorus oxychloride (10 ml). The benzene was evaporated and the residual yellow oil was dissolved in chloroform (200 ml). The chloroform solution was washed with a solution of ammonium hydroxide (10%, 100 ml) and then with water (100 ml). The chloroform layer was dried ($Na_2SO_4$) and evaporated. The resulting yellow syrup **4** was dissolved in benzene (50 ml) and heated on a steam bath for 5 min in the presence of methyl iodide (10 ml). The solution turned red instantly and was allowed to stand at room temperature for 24 hr. The yellow crystals **5** which separated out were collected, washed with benzene, and recrystallized from methanol or methanol–ether. Melting points and yields are given in Table II.

**Preparation of 8,9-Dimethoxy-6-phenyl-3-benzazocin-4-one (7).**—The amide **6** (2.0 g) obtained from the reaction of **2** and cinnamoyl chloride was heated at 120–130° for 15 min in the presence of polyphosphoric acid (40 g). The reaction mixture was cooled and poured over crushed ice. The yellow solid thus obtained was recrystallized from ethanol–water and finally from benzene to yield 0.5 g (25%) colorless needles of **7**, mp 191–192°, ir $\nu_{max}^{Nujol}$ ($cm^{-1}$) 3245 (NH) and 1665 (C=O).

(6) R. T. Conley and W. N. Knopka, *J. Org. Chem.*, **29**, 496 (1964).

TABLE II

1-STYRYLDIHYDROISOQUINOLINE METHIODIDES[a]

| Compd | Mp, °C[b] | Yield, %[c] |
|---|---|---|
| 5a | 168–170 | 78 |
| 5b | 202–204 | 92 |
| 5c | 236–238 | 97 |
| 5d | 194–197 | 86 |
| 5e | 232–235 | 54 |
| 5f | 195–198 | 43 |
| 5g | 205–208 | 58 |
| 5h | 205–207 | 58 |

[a] Satisfactory analytical values (C, H, N) were reported for all compounds (Ed.). [b] All the compounds melted with decomposition. [c] Yields are based on the starting amides.

*Anal.* Calcd for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.52; H, 7.06; N, 4.46.

**Registry No.**—**5a**, 22796-30-1; **5b**, 22796-31-2; **5c**, 22796-32-3; **5d**, 22796-33-4; **5e**, 22796-34-5; **5f**, 22796-35-6; **5g**, 22796-36-7; **5h**, 22796-37-8; **7**, 22796-38-9.

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## Structural Rearrangements of Arylnitrenes and Related Intermediates[1]

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A number of skeletal rearrangements are believed to involve the conversion of arylnitrenes into isomeric reactive intermediates. These include the formation of derivatives of 2-amino-3H-azepine when phenylnitrene is formed in the presence of amines by thermal or photolytic decomposition of phenyl azide[2a,b] or photolysis of N-phenyloxaziridines.[2c,d] It has been proposed that the skeletal rearrangement involves conversion of singlet phenylnitrene[2c] into the azirine intermediate **1**, which subsequently reacts with amines to give azepines.[2a] Azepine formation is also observed during thermal deoxygenation of nitrosobenzene[3] or nitrobenzene[4] by trivalent phosphorus compounds and in photochemical deoxygenations[5] of aromatic nitro compounds in triethyl phosphite. Phenylnitrene is considered to be an intermediate in the pyrolytic conversion of phenyl azide into cyanocyclopentadiene.[6] We have also attributed the formation of pyridine derivatives during photochemical deoxygenation of *o*-alkylnitrobenzenes[5] or thermal deoxygenation of *o*-alkylnitrosobenzenes[7] to skeletal rearrangements of aryl nitrenes. The formation of azobenzene by pyrolysis of triazolo[1,5-*a*]pyridine is considered to involve the rearrangement of 2-pyridylcarbene to phenylnitrene.[8] As a step toward providing insight into the nature of the intermediates in these rearrangements, we have investigated further the structural relationships between the starting material and product in the conversion of *o*-nitrotoluene into N-(*o*-tolyl)-2-acetimidylpyridine (**4**).

*o*-Nitrotoluene labeled with $^{14}C$ at C-1 was prepared and subjected to photochemical deoxygenation in triethyl phosphite.[5] 2-Acetylpyridine was isolated by hydrolysis of **4** and subjected to the degradation shown in Scheme I. The data in Table I prove that C-1 in *o*-nitrotoluene becomes the exocyclic carbon atom in **5**.

SCHEME I

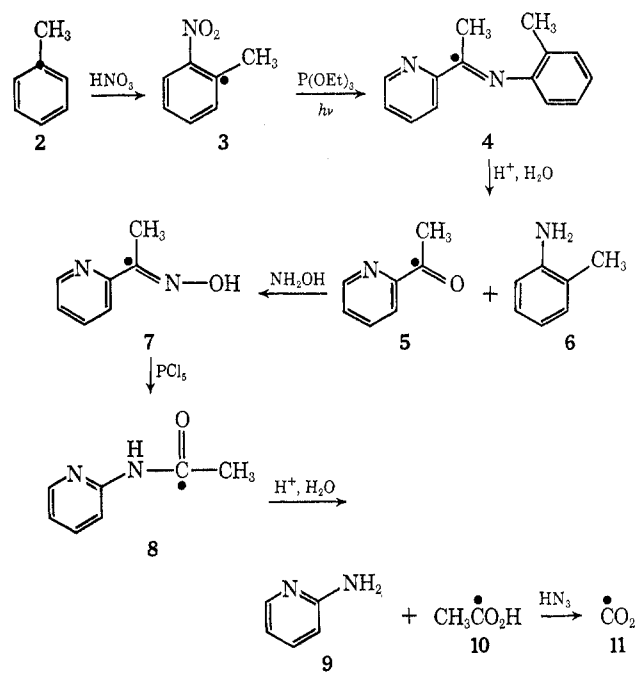


TABLE I

SPECIFIC ACTIVITY DATA

| Compd | Specific activity, dpm/mmol | Dilution factor |
|---|---|---|
| 2 | $1.07 \times 10^6$ | 1 |
| 3 | $0.51 \times 10^6$ | 2 |
| 7 | $0.51 \times 10^6$ | 2 |
| 8 | $0.26 \times 10^6$ | 4 |
| 9 | $0.64 \times 10^4$ [a] | 4 |
| 11[b] | $0.17 \times 10^6$ | 4 |

[a] Activity prior to the final recrystallization was $1.1 \times 10^4$. Further purification by preparative tlc led to no reduction in activity. [b] As $BaCO_3$.

(1) Supported by National Institutes of Health, Grant GM-14344-02.

(2) (a) R. Huisgen and M. Appl, *Chem. Ber.*, **91**, 12 (1958); (b) W. von E. Doering and R. A. Odum, *Tetrahedron*, **22**, 81 (1966); (c) J. S. Splitter and M. Calvin, *Tetrahedron Lett.*, 1445 (1968); (d) E. Meyer and G. W. Griffin, *Angew. Chem. Intern. Ed. Engl.*, **6**, 634 (1967).

(3) R. A. Odum and M. Brenner, *J. Amer. Chem. Soc.*, **88**, 2074 (1966).

(4) J. I. G. Cadogan and M. J. Todd, *Chem. Commun.*, 178 (1967).

(5) R. J. Sundberg, B. P. Das, and R. H. Smith, Jr., *J. Amer. Chem. Soc.*, **91**, 658 (1969).

(6) (a) W. D. Crow and C. Wentrup, *Tetrahedron Lett.*, 4379 (1967); (b) E. Hedaya, M. E. Kent, D. W. McNeil, R. P. Lossing, and T. McAllister, *ibid.*, 3415 (1968); (c) W. D. Crow and C. Wentrup, *ibid.*, 5569 (1968).

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(8) W. D. Crow and C. Wentrup, *Tetrahedron Lett.*, 6149 (1968).