(C=O, amide); ^{1}H NMR (CF_3COOH) δ 2.19 (s, 3, Me), 6.76 (s, 1), 7.03–7.63 (m, 6), 7.88–8.02 (m, 1), 8.70 (m, 1). Anal. ($C_{19}H_{12}N_2O$) C, H, N.

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Registry No.—**4,** 3759-28-2; **10,** 66749-74-4; **12,** 66749-75-5; **13,** 66749-76-6; **14,** 66749-77-7; **15,** 66749-78-8; **16,** 66749-80-2; **17,** 66749-81-3; **18,** 66749-82-4; **19,** 63702-24-9; **20,** 63702-25-0; **21,** 66749-83-5; **22,** 66749-84-6; 2-bromopyridine, 109-04-6; 2-bromo-4-methylpyridine, 4926-28-7; 2-chloro-3-methylpyrazine, 95-58-9; 2-chloroquinoline, 612-62-4; 2-chloro-4-methylquinoline, 634-47-9.

References and Notes

(1) C. K. Bradsher and J. P. Sherer, *J. Org. Chem.*, **32,** 733 (1967).
(2) M. Hartmann and L. Pannizon, U.S. Patent 2 507 631 (May 16, 1950); *Chem. Abstr.*, **44,** 8379d (1950).
(3) M. Hartmann and L. Pannizon, U.S. Patent 2 508 332 (May 16, 1950); *Chem. Abstr.*, **44,** 7352g (1950).
(4) C.f., J. Klosa, *Arch. Pharm.*, **286,** 433 (1953); *Chem. Abstr.*, **49,** 8273g (1955).
(5) F. Johnson and W. A. Nasutavicus, *J. Org. Chem.*, **27,** 3953 (1962).
(6) N. Kawabata, C. K. Chen, and S. Yamashita, *Bull. Chem. Soc. Jpn.*, **45,** 1491 (1972).
(7) J. B. Lambert, W. L. Oliver, and J. D. Roberts, *J. Am. Chem. Soc.*, **87,** 5085 (1965).
(8) J. E. Douglass and D. A. Hunt, *J. Org. Chem.*, **42,** 3974 (1977).
(9) E. Ochiai and S. Suzuki, *Pharm. Bull.*, **5,** 405 (1957); *Chem. Abstr.*, **52,** 9121f (1958).

A Convenient Synthesis of Azidothiophenes and Some of Their Reactions

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Several azidothiophenes have been prepared by treatment of lithium thiophene derivatives with *p*-toluenesulfonyl azide and subsequent fragmentation of the intermediate triazene–lithium salts. High yields have been obtained for all 3-azido compounds; conversely, yields are low in the case of 2-azido derivatives. 2-Azido- and 3-azidothiophene have been converted to the corresponding 1-(thienyl)-1,2,3-triazoles by reaction with acetylene or dimethyl acetylenedicarboxylate. Thermal decomposition of 3-azidothiophene and 3-azidobenzo[*b*]thiophene in acetic anhydride or in a mixture of acetic and polyphosphoric acids has been investigated as a possible route to thienooxazoles.

The azido group represents a very attractive starting group in organic synthesis.[1] Heteroaromatic azides derived from five- and six-membered rings containing nitrogen can be obtained by nucleophilic displacement of a suitable leaving group by azide ion.[1,2] Heteroaromatic azides derived from five-membered rings containing sulfur and oxygen have received only scant attention. For example, Gronowitz and coworkers[3] reported the preparation of 3-azido-2-formylfurano and -thiophen by nucleophilic displacement of the corresponding 3-bromo derivatives with azide ion. However, no azides could be obtained from 2- and 4-bromo-3-formylthiophene, 5-bromo-2-formylthiophene, and bromothiophenes carrying electron withdrawing groups thus limiting the scope of this reaction. Moreover this method is unsuited for the preparation of the parent azides or those carrying electron releasing groups.

We wish to report a convenient synthesis of azidothiophenes and some of their reactions. We have found that azidothiophenes can be obtained by treatment of the corresponding lithium derivatives with *p*-toluenesulfonyl azide and subsequent fragmentation of the resulting triazene salts.[4] Thus, treatment of an ethereal solution of 3-lithium thiophene with tosylazide at −70 °C for 4–5 h and decomposition of the resulting triazene salt with an aqueous solution of tetrasodium pyrophosphate at room temperature afforded 3-azidothiophene (**1**) in 85% yield.

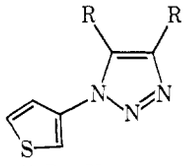
The azides **2–6, 9,** and **10** reported in Table I were prepared analogously; 3-azido-2-formylthiophene (**7**) and 4-azido-3-formylthiophene (**8**) were obtained by hydrolysis with 2 N HCl of the corresponding acetals (**3** and **4**).

All 3-azidothiophenes (**1** and **3–8**) and 3-azidobenzo[*b*]-thiophene (**10**) are stable compounds which showed no sign of decomposition on standing in the dark at room temperature for several days; 2-azidothiophene (**2**) and 2-azidobenzo[*b*]-thiophene (**9**) are somewhat unstable at room temperature but can be stored in the dark at low temperature for some days. The low yields obtained in the preparation of these two latter azides are attributed in part to some decomposition taking place during the fragmentation of the intermediate triazene salt and workup of the reaction mixture.[6]

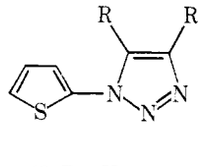
All azido compounds prepared in this work were characterized by spectra (IR, NMR, MS) and, when possible, elemental analysis.

The IR spectra showed the expected N_3 asymmetric stretching absorption in the region 2080–2100 cm^{-1}. The mass spectra showed, in addition to the parent ion, the expected peaks corresponding to loss of a nitrogen molecule [M − 28] and peaks due to subsequent loss of HCN. In particular, in the mass spectra of 2-azidothiophene (**2**) and 2-azidobenzo[*b*]-thiophene (**9**), the molecular ion peaks were noticeably less intense than the corresponding peaks of the 3-azido derivatives; this trend is in line with the reduced stability observed with 2-azido compounds.

Azides **1** and **2** were allowed to react with acetylene and dimethyl acetylenedicarboxylate at room temperature for 48–56 h affording the 1-(3-thienyl)-1,2,3-triazoles, **11** and **12,**



11, R = H
12, R = $COOCH_3$



13, R = H
14, R = $COOCH_3$

and 1-(2-thienyl)-1,2,3-triazoles, **13** and **14,** respectively, in almost quantitative yield.

On the other hand reaction of 3-azidothiophene (**1**) with acetic anhydride under reflux gave 3-diacetylamino-2-acetoxythiophene (**16**) in 52% yield as the only identifiable product. The formation of compound **16** is not unexpected

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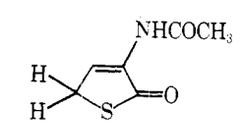
Table I. Yields and Physical, IR, and Analytical Data of Azidothiophenes (1–10)

compd	registry no.	yield, %	mp or bp (mm), °C	N_3, cm^{-1}
3-azidothiophene (1)	66768-57-8	85	55–56 (15)	2080
2-azidothiophene[d] (2)	66768-58-9	10	*a*	2100
3-azido-2-formylthiophene ethylene acetal (3)	66768-59-0	65	36–37	2085
4-azido-3-formylthiophene ethylene acetal (4)	66768-60-3	70	100–102 (15)	2095
3-azido-2-methylthiothiophene (5)	66768-61-4	68	103–107 (15)	2090
3-azido-4-methylthiothiophene (6)	66768-62-5	70	33–34	2100
3-azido-2-formylthiophene (7)	56473-97-3	88[b]	57–58[c]	2095
4-azido-3-formylthiophene (8)	66768-63-6	85[b]	50–52	2090
2-azidobenzo[*b*]thiophene[d] (9)	66768-64-7	7	38–40	2085
3-azidobenzo[*b*]thiophene (10)	66768-65-8	83	54–55	2090

[a] It was obtained as an oil whose bp could not be determined due to its decomposition on heating. [b] Obtained by hydrolysis from the corresponding acetal. [c] Lit.[3] mp 56.6–57.2 °C. [d] Satisfactory analytical data (±0.4% for C, H, N, S) were reported for all compounds except those noted.

since thermolysis of aryl azides under similar reaction conditions is known to lead to the formation of *o*-acetamidoaryl and *o*-diacetylaminoaryl acetates presumably via rearrangement of the intermediate *O,N*-diacylarylhydroxylamines.[7]

Under the same conditions 2-azidothiophene (2) did not give any identifiable products and 3-azidobenzo[*b*]thiophene (10) gave small amounts (18%) of 3-diacetylamino-2-acetoxybenzo[*b*]thiophene (17) together with a solid which has been tentatively assigned the 3-acetamido-2-acetoxybenzo[*b*]-thiophene (18) structure.



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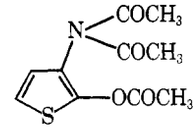

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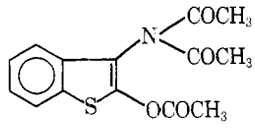

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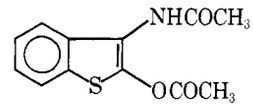

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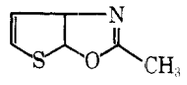

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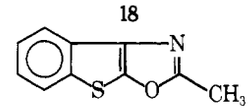

20

Attempts to obtain 2-methylthieno[3,2,*d*]oxazole (19) and 2-methyl[1]benzothieno[3,2-*d*]oxazole (20) by heating compounds 16 and 17, respectively, at 250–350 °C, in the absence or presence of phosphorus pentoxide,[8] were unsuccessful. Thermolysis of 3-azidothiophene (1) and 3-azidobenzo[*b*]-thiophene (10) in a mixture of polyphosphoric and acetic acids[9] was likewise unsuccessful; in these instances 3-acetamidothiophen-2(5*H*)-one (15) (64%) was formed from azide 1 and compound 18 (34%) from azide 10 (cf. a previous report[10c] of the failure of this method for the synthesis of the 8,8-dioxide of 2-methyl[1]benzothieno[3,2-*d*]oxazole from 3-azidobenzo[*b*]thiophen 1,1-dioxide).

In summary, azidothiophenes are obtained in fair to good yields by treatment of lithium thiophene derivatives with *p*-toluenesulfonyl azide and subsequent fragmentation of the intermediate triazene–lithium salts. This procedure offers a convenient general route to the synthesis of azidothiophenes, thus allowing an extensive investigation of their chemical reactivity.

Experimental Section

All melting points are uncorrected. 2-Bromothiophene,[11] 3-bromothiophene,[12] 2-formyl-3-bromothiophene ethylene acetal,[13] 3-formyl-4-iodothiophene ethylene acetal,[14] 3-bromo-4-methylthiothiophene,[14] 3-bromo-2-methylthiothiophene,[15] and 3-bromobenzo[*b*]thiophene[16] were prepared as described in the literature. IR spectra are for solutions in carbon disulfide unless otherwise stated; NMR spectra were recorded in carbon disulfide at 60 MHz on a JEOL C 60 HL using Me_4Si as internal standard; mass spectra were recorded on a JEOL DMS 100 instrument.

Preparation of Azidothiophenes (1–6) and Azidobenzo[*b*]-thiophenes (9 and 10). General Procedure. A solution of the appropriate bromothiophene derivative or 3-bromobenzo[*b*]thiophene (0.05 mol) in 20 mL of dry ether was added dropwise with stirring at −70 °C to *n*-butyllithium, 35 mL, 1.6 N in ether. The reaction mixture was stirred for 45 min at −70 °C, after which an ethereal solution of tosylazide[17] (0.055 mol) was added dropwise. After the addition was complete the resulting mixture was stirred for 5 h at −70 °C and the yellow triazene salt which had formed was rapidly filtered off and washed several times with dry ether. This material was then suspended in 150 mL of dry ether and treated at 0 °C with a solution of 22.5 g (0.05 mol) of tetrasodium pyrophosphate decahydrate in 250 mL of water. After stirring overnight at room temperature the ether layer was separated and the aqueous solution was extracted twice with pentane. The combined organic layers were washed with water and dried. The solvent was evaporated and the residue was chromatographed on a Florisil column using petroleum ether (bp 30–60 °C) as eluant.

2-Azidobenzo[*b*]thiophene was prepared by the same procedure except that direct metalation of benzo[*b*]thiophene was effected with a refluxing ether solution of *n*-butyllithium.

3-Azido-2-formylthiophene (7) and 4-azido-3-formylthiophene (8) were obtained from the corresponding ethylene acetals (3 and 4) by hydrolysis with 2 N HCl solution at room temperature.

Yields and physical, IR, and analytical data are collected in Table I.

1-(2-Thienyl)- and 1-(3-Thienyl)-1,2,3-triazoles (11–14). General Procedure. About 2 molar equiv of acetylene or dimethyl acetylenedicarboxylate were added to 20 mL of an acetone or benzene solution respectively of azides 1 and 2 (500 mg). The reaction mixture was allowed to stand at room temperature for 24–56 h until TLC showed the absence of azide. The excess solvent was removed and the residue was chromatographed on a silica gel column using 10% ether–pentane as eluant.

1-(2-Thienyl)-1,2,3-triazole (13) was obtained in 95% yield as white plates: mp 58–60 °C; NMR δ 7.04 (3 H, m), 7.59, and 7.78 (AB q, J = 1.2 Hz); mass spectrum, *m/e* 151 [M^+], 123, 122, 96, 70. Anal. Calcd for $C_6H_5N_3S$: C, 47.66; H, 3.33; N, 27.78; S, 21.20. Found: C, 47.68; H, 3.32; N, 27.85; S, 21.35.

1-(3-Thienyl)-1,2,3-triazole (11) was obtained in 96% yield as white needles: mp 70–72 °C; NMR δ 7.50 (3 H, m), 7.70 and 7.92 (AB q, J = 1.2 Hz); mass spectrum, *m/e* 151 [M^+], 123, 122, 96, 83. Anal. Found: C, 47.75; H, 3.37; N, 27.85; S, 21.15.

4,5-Dimethoxycarbonyl-1-(2-thienyl)-1,2,3-triazole (14). This product was obtained in 95% yield as white needles: mp 56–57 °C; NMR δ 3.80 (6 H, s), 7.20 (3 H, m); mass spectrum, *m/e* 267 [M^+], 239, 208, 207, 149. Anal. Calcd for $C_{10}H_9N_3O_4S$: C, 44.94; H, 3.39; H, 15.72; S, 11.99. Found: C, 45.05; H, 3.38; N, 15.65; S, 12.03.

4,5-Dimethoxycarbonyl-1-(3-thienyl)-1,2,3-triazole (12). This product was obtained in 92% yield: mp 91–92 °C; NMR δ 3.98 (6 H, s), 7.40 (3 H, m); mass spectrum, *m/e* 267 [M^+], 239, 208, 207, 149, 83. Anal. Found: C, 44.98; H, 3.35; N, 15.81; S, 11.86.

Thermal Decomposition of 3-Azidothiophene (1) in Acetic Acid–Polyphosphoric Acid. A mixture of the 3-azidothiophene (0.5

g), polyphosphoric acid (4 g), and acetic acid (10 mL) was stirred and heated at 100 °C for 1 h and then poured on ice. Extraction with chloroform gave a solid which was chromatographed on silica gel. Elution with 20% ether–pentane furnished 3-acetamidothiophen-2(5*H*)-one (**15**) (0.4 g, 64%): mp 153–155 °C; IR ν_{max} 3380 (NH), 1705 (amide C=O), and 1675 cm^{-1} (C=O); NMR ($CDCl_3$) δ 2.21 (3 H, s), 4.03 (2 H, d, J = 3.1 Hz), and 7.87 (1 H, t, J = 3.1 Hz); mass spectrum, *m/e* 157 [M^+], 115, 86. Anal. Calcd for $C_6H_7NO_2S$: C, 45.85; H, 4.49; N, 8.92; S, 20.39. Found: C, 45.90; H, 4.50; N, 8.89; S, 20.30.

Thermal Decomposition of 3-Azidothiophene (1) in Acetic Anhydride. A solution of 3-azidothiophenone (0.4 g) in 6 mL of acetic anhydride was refluxed for 6 h (until TLC showed that no starting material was left). The reaction mixture was poured into water and extracted with chloroform. The combined extracts were washed with water, dried, and evaporated to give an oily residue which was chromatographed on silica gel. Elution with pentane afforded 3-diacetylamino-2-acetoxythiophene (**16**) (0.4 g, 52%) as a yellow oil: bp 118–120 °C (1 mm); IR ν_{max} 1780 (ester C=O) and 1720 cm^{-1} (amide C=O); NMR δ 2.20 (6 H, s), 2.24 (3 H, s), 6.47 and 6.77 (AB q, J = 5.6 Hz); mass spectrum, *m/e* 241 [M^+], 199, 157, 139. Anal. Calcd for $C_{10}H_{11}NO_4S$: C, 49.80; H, 4.56; N, 5.80; S, 13.27. Found: C, 49.85; H, 4.54; N, 5.86; S, 13.21.

The same compound (**16**) was obtained in quantitative yield from 3-acetamidothiophene-2(5*H*)-one (**15**) in refluxing acetic anhydride.

Thermal Decomposition of 3-Azidobenzo[*b*]thiophene in Acetic Anhydride and in an Acetic Acid–Polyphosphoric Acid Mixture. Decomposition of 3-azidobenzo[*b*]thiophene (**10**) (0.5 g) in boiling acetic anhydride (10 mL) as described above for 3-azidothiophene led, after column chromatography, to (i) trace amounts of an unidentified yellow oil, (ii) 3-diacetylamino-2-acetoxybenzo[*b*]thiophene (**17**) (0.15 g, 18%) as white plates, and (iii) a solid material (**18**) (0.25 g). **17** had: mp 117–118 °C; IR ($CHCl_3$) ν_{max} 1775 (ester C=O) and 1720 cm^{-1} (amide C=O); NMR δ 2.4 (9 H, s), 7.4 (4 H, m); mass spectrum, *m/e* 291 [M^+], 249, 207, 189, 165. Anal. Calcd for $C_{14}H_{13}NO_4S$: C, 57.72; H, 4.50; N, 4.81; S, 11.00. Found: C, 57.78; H, 4.48; N, 4.89; S, 10.93. **18** had: mp 148–152 °C; IR ($CHCl_3$) ν_{max} 3410 (NH), 1775 (ester C=O), and 1690 cm^{-1} (amide C=O); NMR 2.1 (3 H, s), 2.28 (3 H, s), 7.3 (4 H, m); mass spectrum, *m/e* 249 [M^+], 207, 165, 164, 136, 86, 84.

A satisfactory elemental analysis could not be obtained for **18**.

Thermolysis of azide **10** (0.5 g) in a mixture of polyphosphoric acid (4 g) and acetic acid (10 mL) at 100 °C gave, after chromatography: (a) a solid material (0.1 g), mp 140–150 °C, whose spectral analysis showed it to be a mixture of products, the major component being compound (**18**); and (b) a complex mixture of unidentifiable products (0.3 g).

Acknowledgment. The authors thank C.N.R. for a research grant.

Registry No.—**11,** 66768-66-9; **12,** 66768-67-0; **13,** 66768-68-1; **14,** 66768-69-2; **15,** 66768-70-5; **16,** 66768-71-6; **17,** 66768-72-7; **18,** 66768-73-8; 2-bromothiophene, 1003-09-4; 3-bromothiophene, 872-31-1; 2-formyl-3-bromothiophene ethylene acetal, 56857-02-4; 3-formyl-4-iodothiophene ethylene acetal, 66768-74-9; 3-bromo-4-methylthiothiophene, 58414-59-8; 3-bromo-2-methylthiothiophene, 66768-75-0; 3-bromobenzo[*b*]thiophene, 7342-82-7; 2-bromobenzo[*b*]thiophene, 5394-13-8; tosylazide, 941-55-9; acetylene, 74-86-2; dimethyl acetylenedicarboxylate, 762-42-5.

Supplementary Material Available: Full NMR and mass spectral data for compounds 1–10 (2 pages). Ordering information is given on any current masthead page.

References and Notes

(1) S. Patai, Ed., "The Chemistry of the Azido Group", Interscience, New York, N.Y. 1971.
(2) P. A. S. Smith in "Nitrenes", W. Lwowski, Ed., Interscience, New York, N.Y., pp 142–158.
(3) S. Gronowitz, C. Westerlund, and A. B. Hornfeldt, *Acta Chem. Scand., Ser B,* **29,** 224 (1975).
(4) Fragmentation of the magnesium salts to 1-aryl-3-*p*-toluenesulfonyltriazenes with sodium pyrophosphate to give aryl azides has been reported.[5]
(5) P. A. S. Smith, C. D. Rowe, and L. B. Bruner, *J. Org. Chem.,* **34,** 3430 (1969); S. Ito, *Bull. Chem. Soc. Jpn.,* **39,** 635 (1966).
(6) An attempt to prepare 2-azido-3-formylthiophene ethylene acetal by the same general procedure was unsuccessful, a mixture of colored products being obtained after fragmentation of the corresponding triazene salt. The failure in isolating any azide in this case and the low yields obtained with 2-azidothiophene (**2**) and 2-azidobenzo[*b*]thiophene (**9**) might be attributed to unfavorable fragmentation of the triazene–lithium salts; the observed instability of the 2-azido derivatives most probably plays an important role in affecting the nature of the reaction products. This point is being under investigation.
(7) R. K. Smalley and H. Suschitzky, *J. Chem. Soc.,* 5571 (1963).
(8) R. C. Elderfield, Ed. "Heterocyclic Compounds", Vol. 5, Wiley, New York, N.Y., 1957, pp 420–424.
(9) Thermolysis of aryl azides in a mixture of polyphosphoric acid and alyphatic carboxylic acid can represent a convenient route to benzooxazoles;[10a,b] this procedure has been recently extended to the preparation of some thienobenzoxazoles.[10c]
(10) (a) R. Gardner, E. B. Mullock, and H. Suschitzky, *J. Chem. Soc. C,* 1980 (1966); (b) E. B. Mullock and H. Suschitzky, *ibid.,* 1937 (1968); (c) B. Iddon, H. Suschitzky, D. S. Taylor, and M. W. Pickering, *J. Chem. Soc., Perkin Trans. 1,* 575 (1974).
(11) S. O. Lawesson, *Ark. Kemi,* **11,** 373 (1957).
(12) R. D. Schuetz, F. M. Gruen, D. R. Byrne, and R. L. Brennan, *J. Heterocycl. Chem.,* **3,** 184 (1966).
(13) S. Gronowitz, *Ark. Kemi,* **21,** 265 (1963).
(14) L. Lunazzi, A. Mangini, G. Placucci, M. Tiecco, and P. Spagnolo, *J. Chem. Soc., Perkin Trans. 2,* 192 (1972).
(15) R. A. Hoffman and S. Gronowitz, *Ark. Kemi,* **16,** 501 (1960).
(16) W. H. Cherry, W. Davies, B. C. Ennis, and Q. Porter, *Aust. J. Chem.,* **20,** 313 (1967).
(17) W. Von E. Doering and C. H. De Puy, *J. Am. Chem. Soc.,* **75,** 5955 (1953).

Syntheses of Indoles and Carbolines via Aminoacetaldehyde Acetals[1]

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Aminoacetaldehyde dimethyl acetal has been condensed with 1,3-cyclohexanediones and cyclized with acid to 4-oxo-4,5,6,7-tetrahydroindoles. These oxoindoles have, in turn, been condensed with formaldehyde and methylaminoacetaldehyde dimethyl acetal and cyclized with acid to octahydro-β-carboline derivatives. Indole has been condensed with formaldehyde and methylaminoacetaldehyde dimethyl acetal and cyclized with acid to a tetrahydro-γ-carboline derivative.

For several years, we have used aminoacetaldehyde acetals in the synthesis of isoquinoline derivatives.[2] In this paper, we would like to present a modified experimental procedure for the use of these versatile acetals for the synthesis of 4-oxo-4,5,6,7-tetrahydroindoles[3] and to extend the work to β- and γ-carboline systems.

4-Oxo-4,5,6,7-tetrahydroindoles, prepared by an alternate route,[4] have been developed[5,6] as synthetic intermediates. In a preliminary communication,[3] we described the preparation of these compounds (**1** → **3,** Scheme I) by an extremely simple process. The synthesis involves a remarkably stable enamine **2,** which undergoes an intramolecular condensation to yield

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