Fragmentation of 2-(2-Azidophenyl)pyridine and Isomerisation of 5λ⁵σ³-Pyrido[1,2-*b*]indazole

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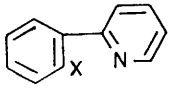
The action of heat on 2-(2-azidophenyl)pyridine (1) quantitatively produced 5λ⁵σ³-pyrido[1,2-*b*]indazole (7) in tetralin, mesitylene, or acetophenone, and gave a nearly 1 : 1 mixture of (7) and 2-(2-aminophenyl)pyridine (3) in di-n-butylamine. The photoreaction of the azide (1) in cyclohexane was complete after 3 h, and gave quantitatively a 1 : 2 mixture of pyrido[3,2-*b*]indole (4) and the pyridoindazole (7) from irradiation at 254 or 300 nm and a 1 : 5 mixture from irradiation at 350 nm. Irradiation of a mixture of the azide and acetophenone (1 : 85) in cyclohexane gave the amine (3) (39%) and lesser amounts of the heterocycles (4) and (7), and irradiation in diethyl or di-n-butylamine transformed the azide into the corresponding 2-dialkylamino-3-(2-pyridyl)-3*H*-azepine (5) (51 and 65%). 5λ⁵σ³-Pyrido[1,2-*b*]indazole (7) in tetrahydrofuran was converted (40%) into the pyridoindole (4) (100%) by irradiation at 254 nm for 136 h. Solvent and sensitisation effects on the photolysis of the azide (1) and the indazole (7) are presented. Mechanisms for the thermal and photochemical reactions are discussed.

THE efficient pyrrole ring closure observed in the photoconversion of 2-azidobiphenyl into carbazole has been ascribed to a reaction of a singlet nitrene, and this explanation has been extended to the corresponding thermal conversion.[1,2] On the other hand pyrrole ring closure was reported to be noncompetitive (except in one example) with an alternative pyrazole ring closure in the thermolysis of derivatives of 2-(2-azidophenyl)-pyridine (1) substituted at position 3 or 5 of the phenyl ring.[3,4,†] A reinvestigation of the consequences of fragmentation of the azido group in compound (1) was undertaken in order (*a*) to determine the photolability of the azide,[‡] (*b*) to establish the formation of 2-(2-aminophenyl)pyridine (3),[§,5] and (*c*) to bring about ring



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(2) X = N:
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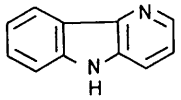

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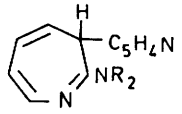

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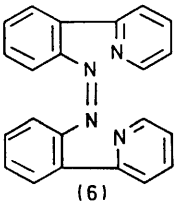

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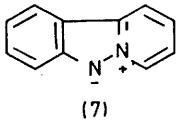

(7)

closure to pyrido[3,2-*b*]indole (4), ring expansion to a 2-dialkylamino-3-(2-pyridyl)-3*H*-azepine (5), and formation of 2,2′-di-(2-pyridyl)azobenzene (6) [the formal dimer of 2-(2-nitrenophenyl)pyridine (2)].

† The formation of 6-trifluoromethylpyrido[3,2-*b*]indole (29%) by thermolysis of 2-(2-azido-3-trifluoromethylphenyl)pyridine was unique. This and four other substituted phenyl derivatives of 2-(2-azidophenyl)pyridine on thermolysis gave the corresponding derivatives of 5λ⁵σ³-pyrido[1,2-*b*]indazole (7) (44—95%).[3,4]

‡ The azide (1) was erroneously described as photostable.[3]

§ A thermolysis product from the azide (1) was isolated as a dipicrate of an amine which was assigned the structure (3).[5] 5λ⁵σ³-Pyrido[1,2-*b*]indazole (7) (60%) was subsequently obtained as the major thermolysis product with traces of diazotisable material.[3] Current attempts to prepare dipicrates of the amines (3) and (7) have been unsuccessful.

RESULTS

Nitrogen evolution was complete in 20 to 30 min when the azide (1) was heated above 150 °C in tetralin, mesitylene, or acetophenone, resulting in quantitative conversion into 5λ⁵σ³-pyrido[1,2-*b*]indazole (7). A similar reaction in di-n-butylamine gave (7) (50%) and the amine (3) (40%). Continued heating above 200 °C for 24 h brought no further change in any case.

Irradiation at 254 nm converted 98% of the azide (1) in tetrahydrofuran or cyclohexane after 1.5—3 h into a 2 : 1 mixture of the indazole (7) and the indole (4). Irradiation at 300 nm produced a similar result, but at 350 nm a product ratio of 5 : 1 was obtained. The presence of oxygen during irradiation at 254, 300, or 350 nm lowered the conversion and gave a product ratio approaching 1 : 1. Indazole (7) formation was most efficient (93%) from irradiation at 350 nm for 3 h of the azide in acetophenone, and indole (4) formation was most efficient (49%) from irradiation at 350 nm for 6 h of an equimolar mixture of the azide and pyrene in cyclohexane [the indazole (7) (49%) was also obtained]. Sensitisation was less effective from (*E*)-stilbene, anthracene, naphthalene, or benzophenone. Irradiation at 350 nm transformed the azide in tetralin into (7) (24%) and unidentified material.

Irradiation at 350 nm for 3 h gave a mixture of 2-(2-aminophenyl)pyridine (3) (39%), the indole (4) (29%), and the indazole (7) (23%) from the azide and acetophenone (1 : 85) in cyclohexane, and the corresponding 2-dialkylamino-3-(2-pyridyl)-3*H*-azepine (5) (51 and 65%) and minor amounts (3—16%) of (4) and (7) from the azide in diethyl- or di-n-butyl-amine.

Irradiation at 254 nm for 136 h caused consumption of 40% of the indazole (7) in tetrahydrofuran, and gave the indole (4) (100%). The photoisomerisation was less effective in methanol and was not detected in cyclohexane. The indazole in either methylene chloride or a dialkylamine was not effected by irradiation at 350 nm, but at 254 nm an unidentified 1 : 1 adduct with diethylamine was obtained.

[1] R. J. Sundberg, D. W. Gillespie, and B. A. DeGraff, *J. Amer. Chem. Soc.*, 1975, **97**, 6193, and references therein.
[2] P. A. S. Smith and B. B. Brown, *J. Amer. Chem. Soc.*, 1951, **73**, 2435.
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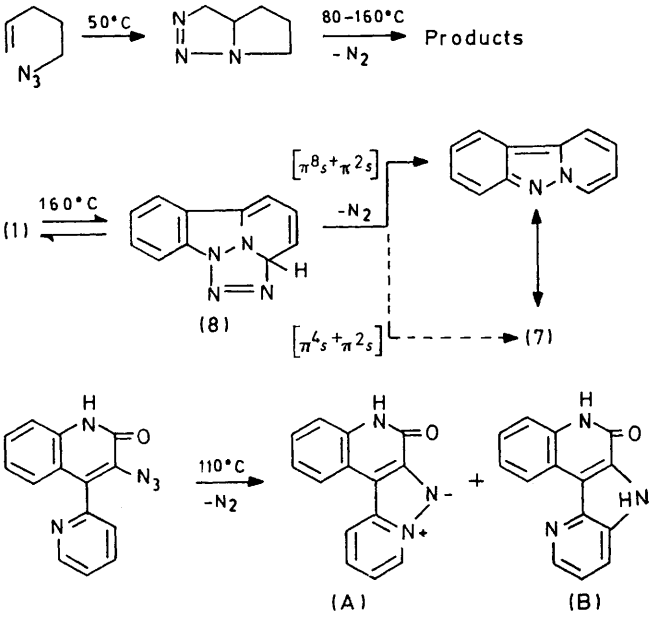
[5] P. A. S. Smith and J. H. Boyer, *J. Amer. Chem. Soc.*, 1951, **73**, 2626.

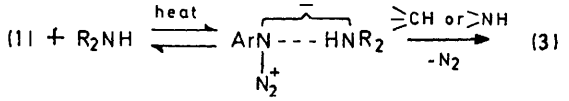
DISCUSSION

Quantitative thermal conversion of the azide (1) into the indazole (7) would not be expected of a discrete and indiscriminate nitrene intermediate. It is compatible with a sequence of two proposed thermally allowed reactions. An initial $[_{\pi}4_s + _{\pi}2_s]$ reversible isomerisation of the azide into a tetrazoloindazole (8) resembles the thermal isomerisation of γ-azido-olefins into triazolines [6] and γ-azido-cyanides into tetrazoles.[7,8] The addition of an azido-group to a carbon–nitrogen multiple bond, *e.g.* the last-named reaction and the transformation (1) ⟶ (8), generally requires more forcing conditions than those needed for triazoline formation.[9,10] Although a reversible association [4] between azide and pyridine

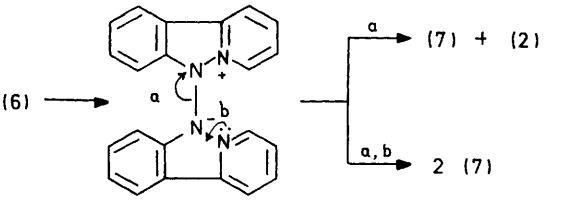


nitrogen atoms might perhaps initiate a non-concerted transformation (1) ⟶ (8), it is seen to be otherwise ineffective (an inverse temperature dependence is expected) in controlling product predominance since 3-azido-4-(2-pyridyl)-2(1*H*)-quinolone was converted in refluxing toluene (110 °C; 6 h) into the pyrazole (A) (35%), the pyrrole (B) (>25%), and unidentified material.[11] The evolution of molecular nitrogen from (8) is thermally allowed by either a $[_{\pi}8_s + _{\pi}2_s]$ or a $[_{\pi}4_s + _{\pi}2_s]$ cycloreversion and produces the indazole (7).

When the azide (1) in di-n-butylamine was nearly quantitatively converted thermally into a mixture of the indazole (7) (50%) and the amine (3) (40%), the lack of a detectable amount of the azepine (5; R = Bu^n) was considered to be additional evidence for the absence of a discrete intermediate nitrene and its isomeric azirine.[12-14] Solvent participation with the azide (1) can bring about the formation of the amine (3) without the intermediacy of a nitrene; [13,14] however, the exact timing of nitrogen evolution and hydrogen abstraction was not determined.



That singlet sensitisation from pyrene (E_S 77, E_T 48 kcal mol^{-1}) enhanced pyrrole ring closure from a nitrene was established in the photoconversion of 2-azidobiphenyl into carbazole.[15] An increase in the yield of pyridoindole (4) by photolysis of the azide (1) in the presence of pyrene can be attributed to similar singlet sensitisation [no more than a trace of (4) can result from the photoisomerisation of the indazole (7); see below]. On the other hand nearly quantitative conversion into the indazole (7) was brought about by triplet sensitisation from acetophenone (E_S 79, E_T 74 kcal mol^{-1}). Since the formation of azobiphenyl [15] and other azobiaryls [16] was enhanced by similar triplet sensitisation in the photolysis of the corresponding 2-azidobiaryls, the formation of 2,2′-di-2-pyridylazobenzene (6) from the photolysis of the azide (1) in the presence of acetophenone was expected. The absence of detectable amounts of (6) does not preclude its intermediacy in formation of the indazole (7) by fragmentation either with or without simultaneous formation of the nitrene (2).



Neither the extent of conversion of the azide (1) nor the product ratio was altered by the presence of an equimolar amount of acetophenone during irradiation in cyclohexane, but the presence of 85 mol. equiv. of the ketone brought about formation of 2-(2-aminophenyl)-pyridine (3) (39%), the indazole (7) (23%), and the indole (4) (29%), presumably by partitioning the triplet nitrene between the primary amine (3) (hydrogen

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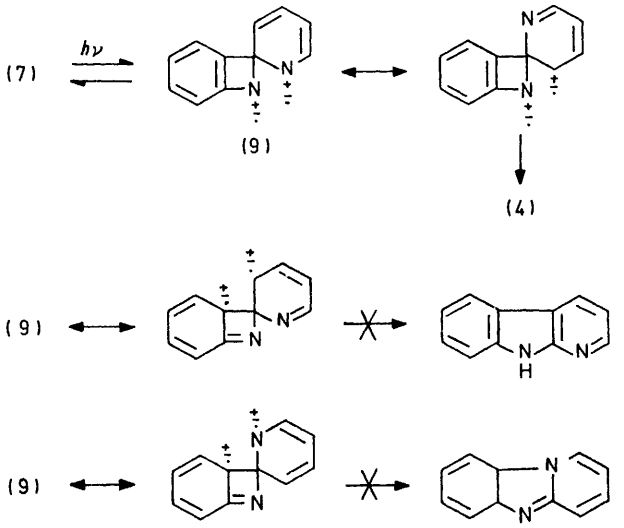
abstraction) and the indazole (7) (ring closure). Catalysis for the reduction (2) → (3) was provided by acetophenone, apparently by transferring a hydrogen atom to the nitrene after first abstracting it from cyclohexane. The expected glycol was also obtained.

$$\text{PhCOMe} \xrightarrow[-C_6H_{11}]{C_6H_{12},h\nu} [\text{PhC(OH)Me}]_x \xrightarrow[-(3)]{(2),h\nu} \text{PhCOMe}$$

$x = 1$ or 2

Anthracene (E_S 76, E_T 43 kcal mol^{-1}) was as effective as pyrene in decreasing the yield of the indazole (7), but was ineffective as a singlet sensitiser. Neither naphthalene (E_S 92, E_T 61 kcal mol^{-1}) nor (*E*)-stilbene (E_S 94, E_T <50 kcal mol^{-1}) produced a significant effect on the photolysis of the azide, and the presence of oxygen tended to retard conversion of the azide, to inhibit formation of the indazole (7) from irradiation at 254, 300, or 350 nm, and to enhance the formation of the indole (4) from irradiation at 300 or 350 nm.

A common product-determining intermediate for the phototransformation of the azide (1) and of the indazole (7) into the indole (4) is unlikely, since both a nitrene and (an) intermediate(s) interchangeable with it require the formation of the amine (3) and/or an azepine (5), which were produced from the azide (1) but not from the indazole (7).*,† The photoisomerisation (7) → (4)



can be accounted for by the intermediacy of a spirocompound (9).‡,[18] Apparently the sacrifice of benzene ring resonance, which would be required for the formation of pyrido[2,3-*b*]indole and pyridobenzimidazole from the intermediate, was prohibitive; neither product was detected.

* Snieckus and Kan [17] reported the formation of 2-diethylamino-3*H*-azepine and aniline from the intermediate phenylnitrene produced from a 1-phenyliminopyridinium ylide in diethylamine by irradiation at 350 nm. The expected substituted pyridine derivative was also obtained.

† Azepine formation may proceed from a singlet nitrene.[1,13,14]

‡ Similar [4.5]spirotrienyl intermediates have been proposed as precursors of fused ring heterocycles.[18]

EXPERIMENTAL

Instruments included Perkin-Elmer 237B and 521 grating i.r. spectrophotometers, a Varian A60 n.m.r. spectrometer, a Perkin-Elmer 270 mass spectrometer, and an A.E.I. MS30 double-beam mass spectrometer. Irradiations were carried out in a Rayonet RPR 100 photo-

TABLE 1

Photolysis of 2-(2-azidophenyl)pyridine (1) [a]

Solvent (ml) [a]	Catalyst or reagent	(mmol)	λ/ nm	t/ h	Products (%) (4)	(7)
Cyclohexane			254	4	36	61
Cyclohexane			300	2	32	64
Cyclohexane			350	3	15	80
Cyclohexane	Oxygen [b]		254	5	29	44
Cyclohexane	Oxygen [b]		300	4	44	48
Cyclohexane	Oxygen [b]		350	5	38	45
Cyclohexane	Anthracene [c]	(1.0)	254	8	35	54
Cyclohexane	Acetophenone [d]	(1.0)	300	3	29	61
Cyclohexane	Acetophenone [e]	(85.0)	350	3	29	23 [f]
Acetophenone [e] (75)			350	3	0	93
Benzene	Benzophenone [d]	(4.0)	350	3	12	87
Benzene (75)	Pyrene [g]	(10.3)	350	6	49	49
Benzene (75)	Naphthalene [g]	(9.9)	350	4	23	75
Tetrahydrofuran (200)			254	3	29	69
Tetrahydrofuran	(*E*)-Stilbene [g]	(1.0)	254	1.5	27	70
Tetralin [e] (200)			350	3		24 [h]
Diethylamine (50)			350	3	13	16 [i]
Di-n-butylamine [e] (40)			350	3	6	3 [j]

[a] Irradiation in 500 ml of solvent, unless otherwise specified, was continued until the azide (1) was no longer detected by i.r. The azide showed $\lambda_{max.}$ (95% EtOH) 234, (ε 15 400), 254 (10 914), 258 (11 500), 300 (2 451), and 350 nm (78). [b] A continuous stream of oxygen flowed through the reaction mixture. [c] Quantitatively recovered during chromatography as the monomer (11%) (eluted by hexane) and the dimer (88%) (eluted by 1 : 1 hexane–benzene). [d] Quantitatively recovered during chromatography by elution with 9 : 1 hexane–benzene. [e] Recovered by distillation. [f] A third product was 2-(2-aminophenyl)pyridine (3) (39%). In a separate experiment acetophenone was recovered (80%) and transformed into 2,3-diphenylbutane-2,3-diol (95%) when irradiated under nitrogen at 350 nm for 3 h in cyclohexane. [g] Quantitatively recovered during chromatography by elution with hexane. [h] The azide (1) was recovered (7%) by elution with 4 : 1 hexane–benzene. 1 : 1 Hexane–benzene eluted a mixture (100 mg) and chloroform eluted a mixture (120 mg). [i] The azepine (5; R = Et) (51%) was eluted with benzene and a mixture (55 mg) was eluted with 95% ethanol. 2-*Diethylamino*-3-(2-*pyridyl*)-3H-*azepine* had b.p. 135° at 0.3 mmHg; M^+ 241; $\nu_{max.}$ (CH_2Cl_2) 1 560 (C=N) and 1 508 cm^{-1} (C=C); δ($CDCl_3$) 1.13 (6 H, t, *J* 7 Hz), 3.55 (4 H, q. *J* 7 Hz), 5.37—5.57 (3 H, m), 6.43—7.57 (5 H, m), and 8.47 (1 H, d, *J* 4 Hz); $\lambda_{max.}$ (95% EtOH) 262 (ε 7 414) and 302 nm (6 912) (Found: C, 74.7; H, 8.05; N, 17.2. $C_{15}H_{19}N_3$ requires C, 74.65; H, 7.95; N, 17.4%). [j] The azepine (5; R = Bu^n) (65%) was eluted with benzene and a gummy mixture (80 mg) was eluted with 95% ethanol. 2-*Di-n-butylamino*-3-(2-*pyridyl*)-3H-*azepine* had b.p. 155° at 0.3 mmHg); M^+ 297; $\nu_{max.}$ (CH_2Cl_2) 1 561 (C=N) and 1 507 cm^{-1} (C=C); δ($CDCl_3$) 0.78—1.7 (14 H, m), 3.05—3.78 (4 H, m), 5.35—5.57 (3 H, m), 6.44—7.55 (5 H, m), and 8.47 (1 H, d); $\lambda_{max.}$ (95% EtOH) 267 (ε 8 407) and 305 nm (6 580) (Found: C, 76.55; H, 9.25; N, 13.95. $C_{19}H_{27}N_3$ requires C, 76.7; H, 9.15; N, 14.15%).

[17] V. Snieckus and O. Kan, *Chem. Comm.*, 1970, 172.
[18] J. I. G. Cadogan, *Accounts Chem. Res.*, 1972, **5**, 303.

chemical chamber reactor (Southern New England Ultraviolet Co.) equipped with 16 low-pressure lamps having principal emission at 254, 300, or 350 nm. Before irradiation under nitrogen, solutions were flushed with nitrogen (prepurified grade) for 30 min. Tetrahydrofuran, furan, and spectroscopic grade cyclohexane were distilled from lithium aluminium hydride directly into the quartz reactor tube. Benzene, acetophenone, tetralin, and the dialkylamines were distilled prior to use. Benzene was first treated with sodium wire for 12 h and each dialkylamine was first treated with sodium or potassium hydroxide. Spectroscopic grade methanol and methylene chloride were each distilled from molecular sieves. Each known product was identical with an authentic sample. Yields were based on starting materials consumed. Elemental analyses were provided by Micro-Tech Laboratories, Chicago.

Thermolysis of 2-(2-*Azidophenyl*)*pyridine* (1).—A solution of the azide (200 mg, 1.02 mmol) in tetralin (9 ml) was heated at reflux (207 °C) under nitrogen for 20 min or until the evolution of nitrogen had ceased. The residue obtained after removal of the solvent was chromatographed on an alumina column. 1 : 1 Hexane–benzene eluted 5$\lambda^5\sigma^3$-pyrido[1,2-*b*]indazole (7) (170 mg, 99%), m.p. 83—84° (lit.,[3] 84.5—85.5°). The indazole was also obtained (99 and 94%) from similar thermolyses in acetophenone at 202 °C and in mesitylene at 163 °C, respectively.

A solution of the azide (200 mg, 1.02 mmol) in di-n-butylamine (40 ml) was similarly heated at reflux (160 °C) for 20 min. The indazole (7) (50%) was eluted from an alumina column by hexane–benzene (1 : 1) and 2-(2-aminophenyl)pyridine (3), b.p. 108—109° at 0.01 mmHg (lit.,[19] 119—120° at 0.3 mmHg) (40%), was eluted with benzene; δ ($CDCl_3$) 5.67 (2 H, s), 6.6—8.0 (7 H, m), 8.57 (1 H, d, pyridyl α-proton); $\nu_{max.}$ ($CHCl_3$) 3 500, 3 300 (NH_2), 1 630, and 1 592 cm^{-1}; *m/e* (70 eV) 170 (M^+); picrate, m.p. 170—171° (decomp. 197—198°) (Found: C, 51.1; H, 3.3; N, 17.8. Calc. for $C_{17}H_{13}N_5O_7$: C, 51.1; H, 3.3; N, 17.5%) [lit.,[20] m.p. 185—186° (decomp.); Found: N, 16.4, 16.3%].

The indazole (7) was recovered unchanged after heating above 150 °C in tetralin, acetophenone, mesitylene, or di-n-butylamine for up to 24 h; a small amount (4%) of gummy material was formed on heating in toluene at 112 °C for 24 h.

Irradiation of 2-(2-*Azidophenyl*)*pyridine* (1) *and of* 5$\lambda^5\sigma^3$-*Pyrido*[1,2-b]*indazole* (7).—With and without an added reagent or catalyst, 2-(2-azidophenyl)pyridine (1) (200 mg, 1.02 mmol) or the pyridoindazole (7) (200 mg, 1.19 mmol) in a solvent was irradiated under nitrogen. The residue left after removal of most of the solvent was chromatographed on an alumina column. The indazole (7) was eluted by hexane–benzene(1 : 1), 2-(2-aminophenyl)pyridine (3) or a 2-dialkylamino-3-(2-pyridyl)-3*H*-azepine (5) by benzene, and pyrido[3,2-*b*]indole (4) by chloroform. Several experiments gave a gummy mixture (4—50 mg) eluted by ethyl acetate when the indazole (7) was irradiated in methanol, methylene chloride, cyclohexane, furan, or di-n-butylamine. The reaction details are in Tables 1 and 2.

TABLE 2

Photoisomerisation of the indazole (7) [a] to pyrido[3,2-*b*]-indole (4)

Solvent (ml)	λ/nm	*t*/h	(4) [b] Yield (%)	(7) Recovery (%)
Tetrahydrofuran (400)	254	136	100	60
Tetrahydrofuran (500)	254	24	78 [c]	78 [c]
Furan (300)	254	48	80	90
Methanol (300)	254	90	37	60
Methylene chloride (300)	350	32		92
Cyclohexane (300) [c]	254	24	*d*	90 [d]
Dialkylamine (50)	350	3		98
Diethylamine (250)	254	24		21 [e]

[a] The indazole showed $\lambda_{max.}$ (95% EtOH) 229 (ε 35 000), 254 (10 247), 269 (21 800), 300 (4 774), 327 (15 200), and 350 nm (4 774). [b] M.p. 206—207° (lit.,[21] 207—208°; lit.,[22] 216°); $\nu_{max.}$ (CH_2Cl_2) 3 455 cm^{-1} (NH); δ [$(CD_3)_2SO$] 7.61—8.82 (7 H, m) and 10.40 (1 H, s, NH); *m/e* (70 eV) 168 (M^+); monopicrate, m.p. 277—278° (lit., [22] 277—279°); methiodide, m.p. 248—249° (lit.,[21] 249—250°; lit.,[22] 250—252°). [c] A repeat experiment with an equimolar mixture of (7) and (*E*)-stilbene in tetrahydrofuran (250 ml) gave a quantitative recovery of (*E*)-stilbene, a 95% recovery of (7) and the indole (4) (17%). [d] After flushing a solution of (7) in cyclohexane (500 ml) with oxygen for 1 h, a repeat experiment with a steady stream of oxygen through the mixture gave an 88% recovery of (7) and the indole (4) (40%). [e] Benzene eluted an unidentified liquid, b.p. 145° at 0.3 mmHg (130 mg), which appears to be a 1 : 1 adduct between (7) and diethylamine. An unidentified mixture (170 mg) was eluted with benzene–chloroform.

[6/1310 *Received*, 6*th July*, 1976]

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