Hydrolysis of 2-Ditolylmethylene-3-oxazolin-5-ones (IV).—A sample (1.16 g) of IV was dissolved in 10 ml of dioxane. To this solution, 2.5 ml of concentrated HCl was added, and the mixture was kept at 80–90° for 9 hr. After evaporation of the reaction mixture, 100 ml of ether and 50 ml of 7% HCl were added. The layer of ether was collected. After evaporation of the ether the resulting solid was recrystallized from cyclohexane, yield 71% (0.68 g). This compound is *p,p*-ditolylacetic acid (VII), mp 137–138° (lit.[5] mp 144°).

Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.73; H, 6.73.

Hydrolysis of 2-ditolylmethylene-4-isopropyl-3-oxazolin-5-one gave the same compound.

Reaction of IVa with Benzylamine.—A mixture of IVa (1.49 g, 0.005 mol) and benzylamine (2.68 g, 0.025 mol) in benzene (10 ml) was kept at 80° for 5 hr. The resulting solid was collected by filtration and recrystallized from cyclohexane to give 2.1 g of crystals (VIII), yield 83%, mp 111.5–112.0°.

Anal. Calcd for $C_{33}H_{35}N_3O_2$: C, 78.33; H, 6.98; N, 8.31. Found: C, 78.30; H, 7.15; N, 8.43.

Registry No.—IVa, 30318-25-3; IVb, 30318-26-4; IVc, 30318-27-5; Va, 30318-28-6; Vb, 30318-29-7; VIa, 30318-30-0; VIb, 30318-31-1; VII, 20809-78-3; VIII, 30318-33-3; toluene, 108-88-3.

(5) P. Fritsch and F. Feldmann, *Justus Liebigs Ann. Chem.*, **306**, 72 (1899).

The Preparation and Some Reactions of 9-(Disubstituted amino)-9*H*-pyrrolo[1,2-*a*]indoles

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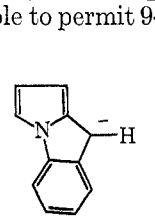
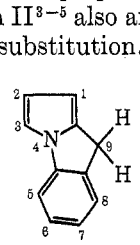
We wish to report a convenient method for the direct synthesis of 9-(*N,N*-disubstituted amino)-9*H*-pyrrolo-[1,2-*a*]indoles. At present, the only general procedure[2] for introducing substituents at the 9 position utilizes the anion I. Previous methods for preparing the 9*H*-pyrrolo[1,2-*a*]indole ring system II[3–5] also are not readily adaptable to permit 9-amino substitution.



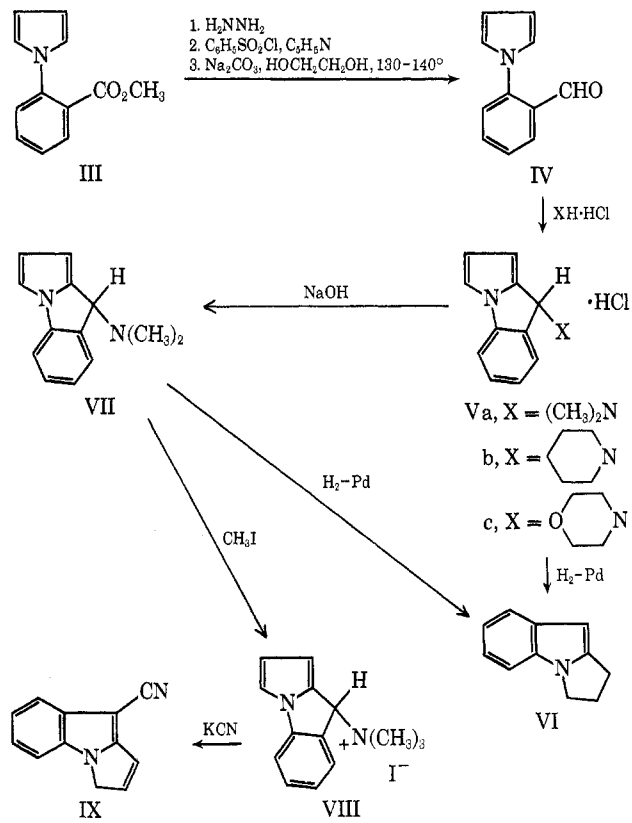
I



II

N-(*o*-Formylphenyl)pyrrole (IV) is prepared from *N*-(*o*-carbomethoxyphenyl) pyrrole (III) by a McFadden–Stevens reaction (Scheme I). Compound IV is converted directly to compounds Va–c by a Mannich reaction. The trimethylammonium iodide VIII also was prepared from Va. With two exceptions where acetaldehyde was successfully utilized as the carbonyl component,[6,7] Mannich reactions on pyrrole compounds have been limited to the use of formaldehyde.

SCHEME I



Catalytic reduction of the dimethylamino compound either as the free base VII or the hydrochloride salt Va is accompanied by prototropic tautomerism to give the known indole VI.[5] This is consistent with the work of Laschtuvka and Huisgen.[5]

Treatment of the quaternary ammonium compound VIII with potassium cyanide gave 9-cyano-3*H*-pyrrolo-[1,2-*a*]indole (IX). It was reported by Franck and Bernady[2] that treatment of the anion I with ethyl chloroformate or carbon dioxide also gives a 9-substituted 3-H derivative. As prototropic tautomerism took place in the former case where the pyrroloindole VIII is the electrophile as well as in the latter case where the pyrroloindole system (I) is the nucleophile and as the amino substituted compounds Va–e occur as 9-H derivatives, it appears that the 3-H compounds are the thermodynamically more stable products when the 9 position has an electron-withdrawing substituent and that 9-H compounds are favored when there is an electron-donating substituent at the 9 position.

Experimental Section

A Varian A-60A, Perkin-Elmer 137, and Cary recording spectrophotometer Model 14 were employed for obtaining spectral data. Uv. and ir spectra appear in Table I.

***o*-(Pyrrol-1-yl)benzohydrazide.**—Methyl *o*-(pyrrol-1-yl)benzoate[8] (III) (60.4 g, 0.3 mol), anhydrous hydrazine (200 ml), and ethanol (200 ml) were combined and stirred at reflux for 3 hr. The reaction mixture was next concentrated to a thick residue by rotary evaporation with the aid of heat. The residue crystallized to give a quantitative yield of product which was recrystallized

(1) Merrell National Laboratories, Division of Richardson-Merrell, Inc., Cincinnati, Ohio 45215.

(2) R. W. Franck and K. F. Bernady, *J. Org. Chem.*, **33**, 3050 (1968).

(3) E. E. Schweizer and K. K. Light, *ibid.*, **31**, 2913 (1966).

(4) G. R. Allen, Jr., and M. J. Weiss, *ibid.*, **30**, 2904 (1965). The 7-benzyloxy derivative was prepared in this paper.

(5) E. Laschtuvka and R. Huisgen, *Chem. Ber.*, **93**, 81 (1960).

(6) U. Eisner, *J. Chem. Soc.*, 854 (1957).

(7) W. Herz and U. Toggweiler, *J. Org. Chem.*, **29**, 213 (1964).

(8) A. D. Josey and E. L. Jenner, *ibid.*, **27**, 2466 (1962).

from chloroform: mp 123–125°; ir (Nujol) 3.10 (NH) and 6.11 μ (CO).

Anal. Calcd for $C_{11}H_{11}N_3O$: C, 65.67; H, 5.51; N, 20.88. Found: C, 65.66; H, 5.38; N, 20.73.

***N*-(*o*-Pyrrol-1-ylbenzoyl)-*N'*-benzenesulfonyl Hydrazine.**—To a stirred solution of *o*-(pyrrol-1-yl)benzohydrazide (4.0 g, 0.02 mol) dissolved in pyridine (25 ml) and cooled in an ice bath, benzenesulfonyl chloride (5.2 g, 0.03 mol) was added in a dropwise manner. After addition was complete, the stirring of the cooled reaction mixture was continued for 1 hr, and then the reaction mixture was poured onto an ice–hydrochloric acid mixture (100 g of ice and 100 ml of concentrated hydrochloric acid). A yellow solid formed which was removed by filtration and washed with dilute hydrochloric acid. After drying, the yellow product (4.3 g, 63%) was recrystallized from benzene: mp 151.5–153.5°; ir (Nujol) 3.10 (NH), 3.20 (NH), 6.08 (CO), 8.52 (SO_2), and 8.60 μ (SO_2).

Anal. Calcd for $C_{17}H_{15}N_3O_3S$: C, 59.81; H, 4.43; N, 12.31. Found: C, 59.96; H, 4.62; N, 12.63.

***o*-(Pyrrol-1-yl)benzaldehyde (IV).**—*N*-(*o*-Pyrrol-1-ylbenzoyl)-*N'*-benzenesulfonyl hydrazine (68.2 g, 0.2 mol) and ethylene glycol (800 ml) were stirred together while the temperature was slowly raised to 135°, at which time powdered anhydrous potassium carbonate (150 g) was added all at once. The reaction was stirred for 1.5 min and then cooled by the addition of warm water (500 ml). After cooling, the reaction mixture was extracted with ether which in turn was washed with water. The ether extracts were dried and filtered, and the solvent was removed, leaving a dark brown oil. Upon distillation of the oil, 16 g (47% yield) of product was collected at 70–72° (0.05 mm): ir (film) 3.60 (CH aldehyde), 3.70 (CH aldehyde), and 6.00 μ (CO).

Anal. Calcd for $C_{11}H_9NO$: C, 77.17; H, 5.30; N, 8.18. Found: C, 76.95; H, 5.10; N, 8.41.

General Procedure for the Preparation of 9-(*N*,*N*-Disubstituted amino)-9*H*-pyrrolo[1,2-*a*]indole Compounds (Va–c).—To a solution of disubstituted amine hydrochloride (0.05 mol) dissolved in a mixture of ethanol (30 ml) and methanol (20 ml) [for Va, only ethanol (50 ml) was used], compound IV (0.05 mol) was added rapidly and stirred for 3 hr at 25°. The products were precipitated by the addition of ether and separated by filtration: Va, nmr ($CDCl_3$) δ 2.72 (s, 6, CH_3), 5.57 (s, 1, HC-9), 6.44–6.70 (m, 2, HC-1, HC-2), 7.18–7.62 (m, 5, HC-3, HC-5–8), 8.52 (d, 1, HC-1).

9-*N*,*N*-Dimethylamino-9*H*-pyrrolo[1,2-*a*]indole (VII).—Va (1.0 g) was dissolved in water, made basic with a 10% aqueous sodium hydroxide solution, and extracted with ether. The dried ether extracts were concentrated, giving an oil which solidified on standing. The solid was sublimed at 62–68° (0.05 mm): nmr ($CDCl_3$) δ 2.17 (s, 6, CH_3), 4.85 (s, 1, HC-9), 6.12–6.43 (m, 2, HC-1, HC-2).

9-*N*,*N*-Dimethylamino-9*H*-pyrrolo[1,2-*a*]indole Methiodide (VIII).—To a solution of compound VII (3.9 g, 0.02 mol) dissolved in methanol (5 ml), methyl iodide (5 ml) was added. On standing in the cold, crystals were deposited which were separated by filtration: nmr ($CDCl_3$) δ 3.45 (s, 9, CH_3), 6.28–6.70 (m, 3, HC-1, HC-2, HC-9), 7.00–7.92 (m, 5, HC-3, HC-5–8).

9-Cyano-3*H*-pyrrolo[1,2-*a*]indole (IX).—To a stirred mixture of compound VIII (17.0 g, 0.05 mol) and water (100 ml), potassium cyanide (13.0 g, 0.2 mol) dissolved in water (100 ml) was rapidly added, followed by refluxing for 2 hr. A dark solid, filtered from the cooled reaction mixture, was extracted using hot ethanol which was next passed through a charcoal column. The ethanol (3.0 l.) was removed on a rotary evaporator and the residue was recrystallized: nmr ($CDCl_3$) δ 3.82 (s, 2, H_2C-3), 6.10–6.30 (m, 1, HC-2), 6.95 (d, 1, HC-1), 7.08–7.90 (m, 4, HC-5–8).

Reduction of 9-Dimethylamino-9*H*-pyrrolo[1,2-*a*]indole Hydrochloride (Va) and 9-Dimethylamino-9*H*-pyrrolo[1,2-*a*]indole (VII).—Compounds Va (0.01 mol) and VII (0.01 mol) were reduced in a Parr hydrogenator at 50 lb/in.[2] over a 2-hr period utilizing ethanol (150 ml) as solvent and Pd–C (10%) as catalyst. The reduction of compound Va resulted in the uptake of 2 equiv of hydrogen while that of VII was slightly over 1 equiv. Prior to evaporation of the solvent in the case of compound Va, the catalyst was removed by filtration and dimethylamine hydrochloride (0.5 g) was precipitated by the addition of ether. With compound VII, after removal of catalyst, the solvent and dimethylamine, whose presence was shown by the strong amine odor, were removed on a rotary evaporator. The solid residues were recrystallized from ethanol. The reduction of hydrochloride salt Va gave a 65% yield while the free base, VII, gave 30% yield of product: mp 77–80° (lit.[5] 79–80°); uv max (ethanol) 281.9 mμ (lit.[5] 280 mμ).

Anal. Calcd for $C_{11}H_{11}N$: C, 84.04; H, 7.05; N, 8.91. Found: C, 84.21; H, 7.02; N, 8.77.

TABLE I

EXPERIMENTAL DATA[a]

No.	Yield, %	Mp, °C[b]	Recrystn solvent[c]	Uv spectra,[d] λ_{max}, mu (ε)	Ir spectra,[e] μ
Va	53	185	A–C	253 (12,000)	4.02 (NH^+)
				265 (10,000)	4.32 (NH^+)
Vb	44	210	A–C	252 (11,500)	3.92 (NH^+)
				266 (10,100)	4.13 (NH^+)
Vc	56	180	A–C	253 (11,300)	4.00 (NH^+)
				265 (10,000)	4.21 (NH^+)
VII		54–56		263 (10,900)	
VIII	98	130	B–C	255 (12,900)	
				270 (7,200)	
IX	50	106–108.5	A	260 (14,200)	4.58 (CN)
				271 (14,200)	
				275 (14,200)	
				282 (13,600)	
				292 (12,100)	
				95% EtOH	

[a] Satisfactory analytical data (±0.3% for C, H, N, and, when present, Cl) were reported for all compounds in table: Ed. [b] Decomposes. [c] A = ethanol, B = methanol, C = ether. [d] Va–c (methanol), VII–IX (95% ethanol). [e] Nujol.

Registry No.—IV, 31739-56-7; Va, 31739-57-8; Vb, 31739-58-9; Vc, 31739-59-0; VII, 31739-60-3; VIII, 31739-61-4; IX, 31739-62-5; *o*-(pyrrol-1-yl)-benzohydrazide, 31739-63-6; *N*-(*o*-pyrrol-1-ylbenzoyl)-*N'*-benzenesulfonyl hydrazine, 31739-64-7.

Pyrrole Studies. XVII.[1] Alkylation of Pyrrylthallium(I)

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Whereas alkylation of pyrrylmagnesium bromide with alkyl halides yields the isomeric 2- and 3-alkylpyrroles as the major products, alkylation of alkali metal salts of pyrrole gives, with few exceptions, the 1-substituted compounds as the predominant products with only small amounts of the C-alkylated compounds. The position of electrophilic attack on the pyrryl anion appears, however, to be determined largely by the ionic radius of the alkali metal ion and the polarity of the solvent and significant variations in the isomer ratios have also been observed with different alkyl halides.[2]

The similarity in the ionic radius of K^+ and Tl^+ (1.33 and 1.47 Å, respectively) prompted a study of pyrrylthallium(I) and its reaction with alkyl halides. More-

(1) Part XVI: C. F. Candy and R. A. Jones, *J. Chem. Soc. C*, 1405 (1971).

(2) For a summary of references, see K. Schofield, "Heteroaromatic Nitrogen Compounds: Pyrroles and Pyridines," Butterworth, London, 1967; R. A. Jones, *Advan. Heterocycl. Chem.*, **11**, 383 (1970).