in EtOH solution of **6a** at 20 °C over 10% Pd/C catalyst provided a product crystallizing from absolute EtOH as colorless needles, mp 206–207 °C.

Anal. Calcd for $C_{10}H_{12}N_2O_2$: C, 62.5; H, 6.3; N, 14.6. Found: C, 62.8; H, 6.4; N, 14.8.

Phosphorazo coupling[6,7] of 2-methylbenzoic acid and glycinamide, as in earlier examples, provided a product which was identical by melting point, mixture melting point, and TLC criteria with that obtained from the hydrogenation.

In similar fashion hydrogenation of **6b** provided 2-methyl-*N*-(4-methylphenyl)benzamide, mp 143.5–144 °C, identical in melting point, mixture melting point, and TLC behavior with a synthesized sample.

Registry No.—**5**, 58249-83-5; **6a**, 58249-84-6; **6b**, 58249-85-7; phthalide, 87-41-2; benzoyl chloride, 98-88-4; potassium 2-hydroxymethylbenzoate, 58249-86-8; benzoyl cyanide, 613-90-1; 2-benzoyloxymethylbenzoyl chloride, 58249-87-9; 2-benzoyloxymethylbenzoic acid 4-nitrophenyl ester, 58249-88-0; 4-nitrophenol, 100-02-7; tri(4-nitrophenyl) phosphite, 23485-35-0; glycinamide, 598-41-4; *p*-toluidine, 106-49-0; acetyl cyanide, 631-57-2; 2-(2-methylbenzamide)acetamide, 6754-94-5; 2-methyl-*N*-(4-methylphenyl)-benzamide, 58249-89-1.

References and Notes

(1) This work was supported by the Auckland Division of the New Zealand Cancer Society Inc., and in part by the Medical Research Council of New Zealand.
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Synthesis of 2-Benzyl-4-phenyl-2,4-dihydropyrrolo[3,4-*b*]indole

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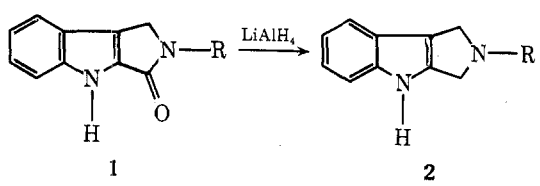
The preparation of a limited number of 1,2,3,4-tetrahydropyrrolo[3,4-*b*]indoles has been reported in the literature, but no compounds of the corresponding 2,4-dihydropyrrolo[3,4-*b*]indole series have been described. We report here the preparation of the first example of this series via lithium aluminum hydride reduction of the corresponding 2-benzyl-1,4-dihydropyrrolo[3,4-*b*]indol-3(2*H*)-one.

The preparation of 2-substituted 1,2,3,4-tetrahydropyrrolo[3,4-*b*]indoles (**2**) through $LiAlH_4$ reduction of the corresponding pyrrolo[3,4-*b*]indol-3(2*H*)-ones (**1**) at elevated temperatures has been reported by Southwick and Owellen.[1] In conjunction with investigations of the chemistry of 2-substituted pyrrolo[3,4-*b*]indoles bearing a phenyl substituent in the 4 position it was decided to adapt this procedure to our series. Thus, 2-benzyl-4-phenylpyrrolo[3,4-*b*]indol-3(2*H*)-one (**3**), prepared in excellent yield from 1-benzyl-2,3-pyrrolidinedione[2] and diphenylhydrazine, when reduced by the procedure of Southwick and Owellen afforded two major products which were readily separated by silica gel chromatography.



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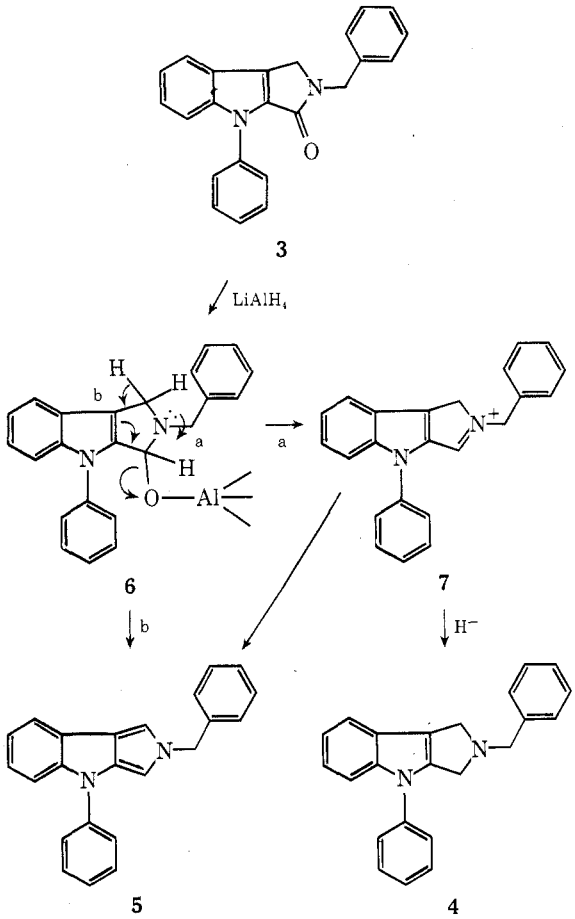


3 6 7 5 4

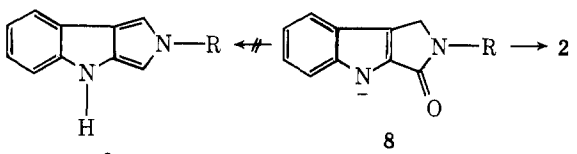
The more polar of these was identified as the expected 2-benzyl-4-phenyl-1,2,3,4-tetrahydropyrrolo[3,4-*b*]indole (**4**) through spectral and analytical data. Spectral and analytical data obtained on the less polar, relatively stable (>4 weeks at 0 °C) product as the free base or picrate salt confirmed its structure as 2-benzyl-4-phenyl-2,4-dihydropyrrolo[3,4-*b*]indole (**5**). The relatively simple mass spectrum of **5** consisted of the parent ion (*m/e* 322, base peak) and an ion at *m/e* 231 representing loss of the tropylium ion, indicating a highly stable nucleus. In the NMR spectrum of **5**, only the benzyl methylene protons at δ 4.91 lie outside the aromatic region, although both the C(1) and C(3) methine protons can be observed. Proton decoupling experiments demonstrate that these protons are coupled to each other with a coupling constant of 1.8 Hz, consistent with values established for 2,5-proton coupling in pyrrole and its derivatives.

The formation of a dihydropyrrolo[3,4-*b*]indole under these conditions represents a novel and unprecedented action of $LiAlH_4$ which may be rationalized through the following mechanistic considerations. Formation of **7**, the immonium precursor of **4** (path a), by elimination of an oxyaluminum species from the initially formed **6** generates considerable ring strain in the 6-5-5 ring nucleus and is probably not favored energetically. The relative stability of **6** thus allows a second mechanism (path b) to become operative, that is, the abstraction of a relatively acidic (due to polarization of the C(3)–N bond) C(1) proton generating **5** via the 1,4 elimination illustrated. Alternatively, proton abstraction from C(1) in **7** could yield **5**. This pathway is deemed less likely, owing to the known rapid addition of hydride ion to such immonium species.

Further evidence in support of either of these mechanisms was obtained through the reduction of **3** in the presence of the soluble tertiary amine base *N*-ethylpiperidine (bp 130 °C). The yield of **5** under these conditions was increased from 27% to 42% (the yield of **4** remaining the same) reflecting a more

efficient abstraction of the C(1) proton by soluble base. It is of interest to note that energetic requirements for operation of either mechanism appear to be high, since our attempted reductions at lower temperatures were unsuccessful. The reduction of α,β-unsaturated γ-lactones to the corresponding furans with dialkylaluminum hydrides has been reported[3] to proceed at low (−20 to −25 °C) temperatures in good yield. This difference most likely reflects the energy differences between formation of the pseudoaromatic furan ring and disruption of the indole nucleus to form **5**.

It is of interest to note that Southwick did not report formation of dihydropyrrolo[3,4-*b*]indoles **9** from N(4) unsubstituted pyrrolo[3,4-*b*]indolones **1**, although yields of the tetrahydro species and conditions of reduction were comparable. Owing to the relative acidity of indole nitrogen protons, it is quite likely that generation of the N(4) anion (i.e., **8**) in Southwick's series would prevent abstraction of a proton from C(1) and hence the elimination sequence envisioned in path b above. Also of interest is the stability of these compounds by comparison with that of isoindoles.[4] Clearly the subject compounds resemble disubstituted pyrroles rather than the isoindole type of molecule. This stability and the extended chromophore apparent from our uv data imply (but do not confirm) electronic interaction between the rings of this interesting molecule.



9 8

Experimental Section[5]

2-Benzyl-4-phenylpyrrolo[3,4-*b*]indol-3(2*H*)-one (3). A solution of 11.90 g (63.0 mmol) of 1-benzyl-2,3-pyrrolidinedione in 200 ml of glacial acetic acid was added to a suspension of diphenylhydrazine hydrochloride (13.88 g, 63.0 mmol) in 200 ml of glacial acetic acid and the resulting suspension was heated briefly on a steam bath to effect hydrazone formation. Then 100 ml of concentrated hydrochloric acid was added to the warm solution and heated for a further 20 min. The reaction mixture was diluted slowly with water giving 17.8 g (84%) of crystalline **3**. Recrystallization from ethyl acetate gave colorless crystals, mp 145.5–146.5 °C: ir (KBr) 3.35, 3.52, 5.97, 6.91, 7.25, 8.15, 13.17, 13.40 μ; NMR ($CDCl_3$) δ 4.30 (2 H, s), 4.75 (2 H, s), 7.12–7.76 (9 H, m), 7.30 (5 H, s); uv (MeOH) λ_{max} 246 nm (log ϵ 4.265), 299 nm (4.141); mass spectrum *m/e* 338 (parent ion). Anal. Calcd for $C_{23}H_{18}N_2O$: C, 81.66; H, 5.33; N, 8.28. Found: C, 81.35; H, 5.51; N, 8.24.

2-Benzyl-4-phenyl-1,2,3,4-tetrahydropyrrolo[3,4-*b*]indole (4) and 2-Benzyl-4-phenyl-2,4-dihydropyrrolo[3,4-*b*]indole (5). To a solution of 13.0 g (38.5 mmol) of **3** dissolved in 350 ml of dry toluene (4A molecular sieves) at reflux was added 2.92 g (76.9 mmol) of $LiAlH_4$. The resulting suspension was heated at reflux for 16 h and then cooled to room temperature. After the slow addition of 150 ml of ethyl acetate, 150 ml of water was added and the resulting suspension was filtered. The separated aluminum salts were washed thoroughly with ethyl acetate and the washings combined with the filtrate. The aqueous phase was extracted thoroughly with ethyl acetate, the combined organic extracts were then dried ($MgSO_4$), and the solvent was evaporated to give 17 g of an orange oil. This material was chromatographed on 340 g of Brinkmann silica gel. The benzene eluent consisted of 3.39 g of an oil (R_f 0.75, benzene) and the 1:1 benzene–ethyl acetate fraction was 5.16 g of an oil (R_f 0.11, benzene). Neither product could be induced to crystallize; however, the less polar product, identified below as **5**, yielded a crystalline picrate salt from ethanol whereas the more polar product **4** formed a crystalline hydrochloride salt from ether with dry HCl gas.

2-Benzyl-4-phenyl-1,2,3,4-tetrahydropyrrolo[3,4-*b*]indole Hydrochloride (4): mp 198.0–199.5 °C; mass spectrum *m/e* 324 (parent ion), 323 (M − 1, 100%), 232, 218, 204, 91; NMR ($CDCl_3$) δ 4.47 (4 H, d),[6] 4.69 (2 H, d),[6] 6.94–7.50 (12 H, m), 7.50–7.74 (2 H, m); uv (MeOH) λ_{max} 254 nm (log ϵ 4.159), 287 (3.963).

Anal. Calcd for $C_{23}H_{20}N_2$·HCl: C, 67.54; H, 5.87; N, 7.76. Found: C, 67.23; H, 5.95; N, 7.71.

2-Benzyl-4-phenyl-2,4-dihydropyrrolo[3,4-*b*]indole Picrate (5): mp 134–135 °C; mass spectrum *m/e* 323 (parent ion, 100%); NMR (free base, $CDCl_3$) δ 4.91 (2 H, s), 6.37 (1 H, d, J = 1.5 Hz), 6.73 (1 H, d, J = 1.5 Hz), 6.80–7.67 (14 H, m); uv (MeOH) λ_{max} 250 nm (log ϵ 4.065), 270 (3.807), 282 (3.817), 303 (3.678).

Anal. Calcd for $C_{23}H_{18}N_2$·$C_6H_3N_3O_7$: C, 63.16, H, 3.84; N, 12.70. Found: C, 63.19; H, 3.93; N, 12.85.

Reduction of 3 with $LiAlH_4$ in the Presence of *N*-Ethylpiperidine. A solution of 0.50 g (4.4 mmol) of distilled *N*-ethylpiperidine and 0.50 g (1.48 mmol) of compound **3** in 15 ml of dry toluene was heated to reflux at which time 0.11 g (2.89 mmol) of $LiAlH_4$ was added. Reflux was continued for 16 h. Then the reaction mixture was cooled, worked up, and subjected to column chromatography as outlined above. The benzene eluent yielded 200 mg (42%) of compound **5** and the 1:1 benzene–ethyl acetate fractions contained 218 mg (45%) of compound **4** identical in all respects with the compounds described above.

Acknowledgment. We are grateful to Dr. E. B. Whipple and associates for the proton decoupling experiments and to Mr. R. L. Taylor and Mr. F. C. Kohansky for valuable technical assistance.

Registry No.—**3**, 58485-96-4; **4** HCl, 58485-97-5; **5** picrate, 58485-99-7; 1-benzyl-2,3-pyrrolidinedione, 58485-00-3; diphenylhydrazine HCl, 29666-92-0; *N*-ethylpiperidine, 766-09-6; $LiAlH_4$, 16853-85-3.

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(4) For example, see J. D. White and M. E. Mannin, *Adv. Heterocycl. Chem.*, **10**, 113 (1969).
(5) Melting points (uncorrected) were taken with a Thomas-Hoover capillary apparatus. NMR spectra were recorded on Varian A-60 and T-60 spectrometers with Me_4Si as internal standard. Proton decoupling experiments were conducted on a Varian XL-100 spectrometer. Ir spectra were determined with a Perkin-Elmer Model 21 spectrophotometer. Uv spectra were recorded on a Cary Model 14 spectrophotometer. Mass spectra were obtained with a Perkin-Elmer RMU-6E mass spectrometer. Microanalyses were performed by the Pfizer Analytical Department. All evaporations were conducted in vacuo using either a water aspirator or a vacuum pump.
(6) It is apparent that, in the hydrochloride salt, the α and β C(1) and C(3) methylene protons are nonequivalent owing to the quaternary nature of N(2). In NMR spectra of the free base of **4**, this region collapses to a 6 H singlet at δ 4.10.

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s-Triazines. 1. Reaction of Cyanuric Chloride with Unsaturated Nitrogen Compounds

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Since 1940 applications of *s*-triazine derivatives, especially melamine and its derivatives, have been extended into nearly every industrial field.[1] In addition, many melamine derivatives have been found to exhibit[1,2,3] antineoplastic, antibiotic, antibacterial, and/or insecticidal activity. We believe, therefore, that other hitherto unknown *s*-triazines, especially melamine derivatives, will probably have potential antineoplastic and antibiotic action.

Although several synthetic methods for the preparation of *s*-triazine derivatives from cyanuric halides have been developed,[1] few studies have been reported of the reaction of cyanuric halides with unsaturated nitrogen compounds other than pyridine.[4] In the course of work on potential anticarcinogens we have found that cyanuric chloride (CC) reacts at room temperature with dicyclohexylcarbodiimide (DCC, **1**),