The mixture was refluxed for 4 hr, treated with 2 ml of saturated Na_2CO_3, filtered, and finally extracted with 30 ml of 5% aqueous HCl. The acidic extract was extracted with ether and then basified with excess 50% NaOH. The organic layer which formed was taken up in ether and the dried (Na_2SO_4) ether solution was evaporated to dryness. Distillation of the residue under reduced pressure gave 0.72 g (55%) of **16** as a colorless oil [bp 119–120° (0.2 mm), $n^{24}D$ 1.5467] which solidified on standing, mp 48.5–49.5°. The nmr spectrum was consistent with the structure assigned.

Anal. Calcd for $C_{19}H_{23}N$: C, 85.99; H, 8.73; N, 5.28. Found: C, 86.14; H, 8.84; N, 5.36.

The picrate melted at 125–127° after recrystallization from ethanol.

Reaction of 1,1-Dibenzyl-3,3-dimethylazetidinium Bromide (13) with Sodium Ethoxide.—Compound **13** (5 mmol, 1.73 g) was added to 50 ml of ethanol containing 20 mmol (1.36 g) of sodium ethoxide and the homogeneous solution was refluxed for 10 hr. Water (25 ml) was then added and the ethanol was removed by distillation. An ethereal extract of the residue was dried over Na_2SO_4 and the solvent was then evaporated. The yellow oil (1.5 g, 96%) which remained, $n^{25}D$ 1.5268, was indicated to be 3-dibenzylamino-2,2-dimethyl-1-ethoxypropane by its relatively long (10.5 min) retention time on vapor phase chromatography at 195°, by its infrared spectrum, and by its nmr spectrum (CCl_4): δ 0.75 (s, 6), 2.42 (s, 2), 3.02 (s, 2), 3.54 (s, 4), 1.05 (t, 3, J = 3.5 Hz), 3.26 (q, 2, J = 3.5 Hz), and 7.20 (m, 10).

Registry No.—**4**, 16911-20-9; **4** methiodide, 16959-96-9; **9**, 16911-21-0; **9** picrate, 16911-22-1; **9** methiodide, 16957-22-5; **10**, 16911-23-2; **10** methiodide, 16911-24-3; **14**, 16911-25-4; **14** methiodide, 16911-26-5; **14** picrate, 16911-27-6; **16**, 16911-28-7; **16** picrate, 16911-29-8; 3-dibenzylamino-2,2-dimethyl-1-ethoxypropane, 16911-30-1; ammonia, 7664-41-7.

Pyrrolo[1,2-*a*]indole Chemistry. Reactions of a Tridentate Carbanion[1]

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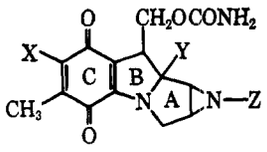
The pyrrolo[1,2-*a*]indole anion **8** has been acylated by a group of electrophiles, including ethyl carbonate, ethyl chloroformate, dimethyl oxalate, phenyl isocyanate, and carbon dioxide. Its tridentate character has been demonstrated by the isolation of products arising from attack at the 1, 3, and 9 positions. One product, the ester **11**, is the first simple example of the 3H-pyrrolo[1,2-*a*]indole system. The chemistry of ester **11** was studied, to no avail, as a possible route to the mitomycin structural array **1** or **2**.

The tetracyclic array of the mitomycins **1** and the stereochemically simpler aziridinomitosenes **2** is a



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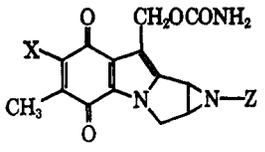

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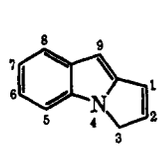
unique heterocyclic system with potent biological activity.[2] Substantial progress has been made by a Lederle group[3] in the elaboration of synthetic pathways to various tricyclic derivatives in the pyrrolo[1,2-*a*]indole series. However, the final attainment of a tetracyclic product by attaching an aziridine moiety to the tricyclics using a variety of cyclization methods was not achieved.

Our paper approach to the synthetic problem of aziridine annelation was to obtain a tricyclic compound **3** with unsaturation in the position appropriate for ring addition *via* the elegant method of dipolar addition of azide[4] followed by subsequent photochemical decomposition of the resultant triazoline.[5] The major drawback to our scheme was that the simple 3H-pyrrolo-[1,2-*a*]indole structure **3** was not known. The early report of a dehydrative acetylation of N-phenacylanthranilic acid to afford 9-hydroxy-3-keto-1-phenyl-3H-pyrrolo[1,2-*a*]indole (**4**) is not correct.[6,7] The enamine **5**, not completely characterized, may be an example of the desired system.[3b] An authentic, but more complex, 3 H derivative, the 3-methylenecarboxylate **6**, has



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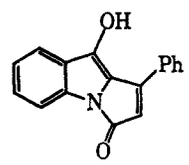

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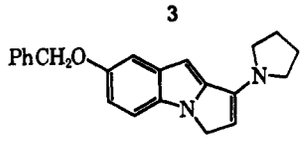

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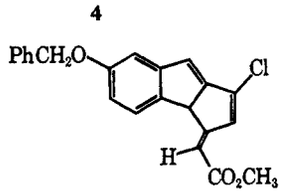

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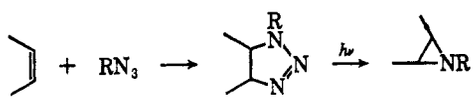
been characterized as well.[8] Two independent syntheses directed toward the preparation of the simple heterocycle **3** both afforded the isomeric 9H-pyrrolo-[1,2-*a*]indole (**7**). The Hofmann elimination route (Scheme I, path 1)[3b] and the elegant and general heterocyclic synthesis *via* a vinylphosphonium salt (Scheme I, path 2)[9] are usually unambiguous, position-specific



(1) (a) Presented at the Third Middle Atlantic Meeting of the American Chemical Society, Philadelphia, Pa., Feb 2, 1968, Abstracts, p H74. (b) Taken from the Ph.D. Thesis of K. F. B., Fordham University, 1968. (c) This research was supported by a grant from the Public Health Service, NIH GM 12758, for which we are most grateful.

(2) (a) J. S. Webb, D. B. Cosulich, J. H. Mowat, J. B. Patrick, R. W. Broschard, W. E. Meyer, R. P. Williams, C. F. Wolf, W. Fulmor, C. Pidacks, and J. E. Lancaster, *J. Amer. Chem. Soc.*, **84**, 3187 (1962); (b) J. B. Patrick, R. P. Williams, W. E. Meyer, W. Fulmor, D. B. Cosulich, R. W. Broschard, and J. S. Webb, *ibid.*, **86**, 1889 (1964).

(3) (a) G. R. Allen, Jr., J. F. Poletto, and M. J. Weiss, *J. Org. Chem.*, **30**, 3897 (1965); (b) G. R. Allen, Jr., and M. J. Weiss, *ibid.*, **30**, 2904 (1965); (c) W. A. Remers, R. H. Roth, and M. J. Weiss, *ibid.*, **30**, 2910 (1965).

(4) R. Huisgen, G. Szeimies, and L. Mobius, *Chem. Ber.*, **100**, 2494 (1967).

(5) P. Scheiner, *J. Org. Chem.*, **30**, 7 (1965).

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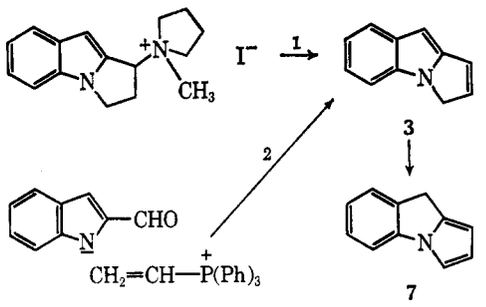
(7) R. W. Franck and J. Usilton, Fordham University, unpublished results, 1966.

(8) W. A. Remers, *J. Amer. Chem. Soc.*, **86**, 4608 (1964).

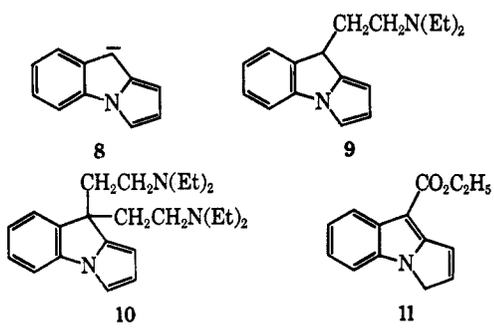
(9) E. E. Schweizer and K. K. Light, *J. Org. Chem.*, **31**, 2912 (1966).

SCHEME I

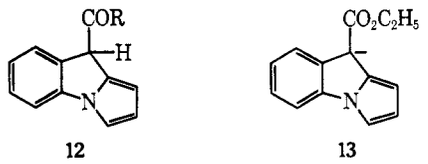


methods. Thus, it must be concluded that the 3 H product is less stable than the 9 H isomer, a fact which is supported by Hückel molecular orbital calculations.[3b,8,10] Our attention was directed toward obtaining a 3 H isomer that was stabilized relative to the 9 H compound. We proposed to accomplish this goal *via* utilization of the anion **8** of heterocycle **7**, previously described by Huisgen.[11] The reported alkylation of the anion with diethylaminoethyl chloride apparently gave exclusively the 9-alkyl product **9**. It was our plan to study the introduction of acyl groups in a similar manner.

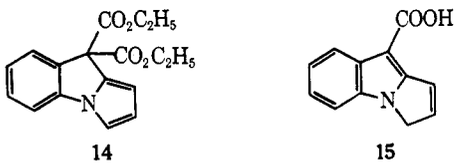
The anion **8** is prepared by treating the heterocycle **7** with butyllithium. When the reaction with diethylaminoethyl chloride was repeated, the discharge of the green anion (estimated visually) took 20 hr. Three products were detected by vapor phase chromatography (vpc) of the reaction mixture. The major product (85%) was the 9-alkyl compound **9**, its structural assignment based on an nmr spectrum with 3 pyrrole protons. Also, the 9,9-dialkyl product **10** (12%) was isolated, its characterization based on its nmr with 3 pyrrole and 28 diethylaminoethyl protons. The third product (3%) was not characterized. The formation of bisalkyl product can be explained by invoking equilibration of anion **8** with monoalkyl **9** to afford neutral **7** and the anion of **9**. When the anion **8** was added to excess diethyl carbonate, instantaneous reaction was observed. Immediate work-up of the mixture afforded material which could be purified by silica gel chromatography to yield recovered **7** (33%) and 9-carbethoxy-3H-pyrrolo[1,2-*a*]indole (**11**) (18%). Strong evidence



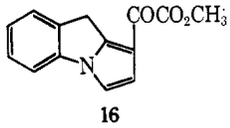
for the proposed structure is the appearance of 2 vinyl protons in the nmr spectrum of **11**; the lines appeared as doubled triplets at δ 6.32 and 6.77 (J_{12} = 6.0 and J_{13} = J_{23} = 2.0 Hz, the J_{12} being far outside the limit for vicinal coupling in pyrroles).[12] The grouping of uv maxima in the 240-and 320-mμ region with a minimum at 280 mμ (compare pyrrole **7**, uv max 265 mμ) is in agreement with every 2-vinylindole that we know of.[13] That the 3 H isomer in this system could be more stable than the 9 H isomer is supported by molecular orbital calculations.[10] The recovery of starting heterocycle **7** can be explained by considering that the intermediate acylation product **12**, more acidic than **7**, reacts with anion **8** to form anion **13** and neutral **7**. This



proton transfer must occur more rapidly than condensation of **8** with diethyl carbonate. Eventual work-up by protonation of **13** affords the product **11**. A more reactive acylating agent, ethyl chloroformate, was used so that the acylation of **8** would be a faster process. The products isolated were the 9,9-bis acylated product **14** (13%) (3 pyrrole and 10 ethyl protons in the nmr) and recovered starting material **7** (35%). This course must come from further acylation of anion **13**, with ethyl chloroformate being more reactive than diethyl carbonate which does not give bis acylation with short reaction time. When carbon dioxide was employed as the electrophile with anion **8**, 9-carboxy-3H-pyrrolo-[1,2-*a*]indole (**15**) was isolated in 7% yield and starting



7 was recovered in 74% yield. The acid **15** lost CO_2 on melting and also upon column chromatography. When dimethyl oxalate was the electrophile in the condensation, the major product isolated by chromatography was the 1-substituted 9 H compound **16** (13%). Its struc-



(12) A. R. Katritzky in "Physical Methods in Heterocyclic Chemistry," Vol. II, A. R. Katritzky, Ed., Academic Press Inc., New York, N. Y., 1963, p 128.

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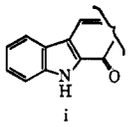
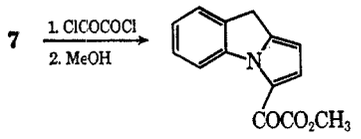


(10) C. Sherr, R. Cloney, K. Bernady, E. Leser, and R. W. Franck, Fordham University, unpublished results, 1967.

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

tural assignment is based on the nmr showing two pyrrole protons and no deshielded aromatic proton (at C_8) characteristic of the anisotropic effect of a carbonyl at the 9 position. Also a 1% yield of the 3-oxalylated compound **17** was obtained. A sample of **17** was independently prepared *via* oxalylation of **7**. In addition,



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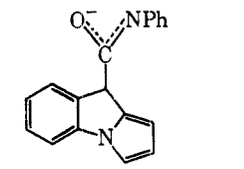
34% recovery of **7** was obtained. The anion **8** was condensed with phenyl isocyanate, since the initial condensation product **18**, being anionic, would not participate in a proton transfer with **8** since the result would be a dianion. In the event, the products isolated were the 9,9-diacylated compound **19** (3%), the 1-acyl product **20** (1%), the 3-acyl isomer **21** (14%), and recovered **7** (13%). All the products had nmr spectra consistent with the 9H-pyrrolo system. The products isolated are an example of the trapping of all three positions of the tridentate anion **8** in a single reaction.



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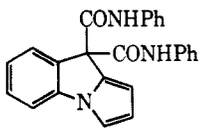

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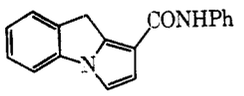

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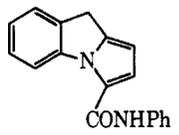

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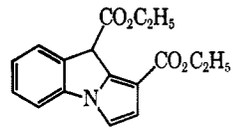
All the acylations appeared to be instantaneous reactions whereas the alkylation first described was slow. Since the alkylating agent contained a tertiary amine grouping, it was hypothesized that this amine function was forming a stable coordination complex with anion **8**, a well-known phenomenon of tertiary amines and organolithiums.[14] Further, we felt that the complex was unreactive and only its dissociation to free organolithium would provide a species that would alkylate or acylate. Thus the acylation with diethyl carbonate was repeated with prior addition of triethylamine to preformed anion **8**. The reaction was slowed markedly with incomplete discharge of the color of anion **8** after 4 hr. Work-up of the mixture at this point afforded the previously obtained 3 H ester **11** (9%), the 1,9 diester **22** (3%), and recovered **7** (76%). The diester **22** was clearly in the 9 H, or pyrrole, series, with its longest wavelength uv maximum at 272 mμ and with two typical pyrrole protons at δ 6.89 and 7.15 (J = 3 Hz). In a similar experiment where the reaction mixture was allowed to



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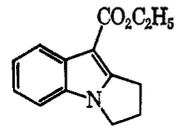
stand for 24 hr prior to work-up, the yield of diester **22** increased to 6% and monoester **11** was present in less than isolable quantity (detected only by tlc). The difference in structure of the bis acyl product obtained under these conditions compared with the rapid reaction with ethyl chloroformate suggests that the latter case is one of kinetic control of product formation, while the former is a case where thermodynamic factors determine the product formed. The conclusions that we can draw about the reactions of the carbanion **8** are that the nature of the acylating agent does play some role in the determination of the product in a way that we cannot as yet interpret. Also, we note that this system is a case of a demonstrably tridentate carbanion.

With ester **11**, the first simple member of the 3H-pyrrolo[1,2-*a*]indole class, in hand, we set out to study its chemistry to determine whether an aziridine function could be introduced as had been planned originally. Hydrogenation of the vinylic double bond of **11** to afford indole ester **23** proceeded in 99% yield. This was



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the only usable reaction we could perform with **11**. Our first attempts at aziridine introduction at the vinylic bond were based on the method of triazoline formation (*vide supra*).[4,5] No useful result was obtained upon reaction of **11** with methyl azide, *p*-bromophenyl azide, or carbethoxy azide, over a gamut of conditions and solvents. Since the dipolar addition reaction of azides has been shown to be sensitive to steric effects, ring strain features, and bond polarities,[4] and since none of the favorable sort of features is incorporated in **11**, the failure of this approach was not totally unexpected. We then turned to the less discriminate method of nitrene insertion as a means of aziridine synthesis.[15] Both photochemical and ordinary methods of nitrene generation were used. Many products were detected by tlc. One preparative tlc fraction was isolated which had ir and uv spectra (see Experimental Section) which were in agreement with what one would have predicted for the desired product, but a satisfactory nmr spectrum could not be obtained. The iodine isocyanate method of aziridine synthesis was examined[16] and found wanting. This was expected since the simpler electrophilic attack of ester **11** by bromine had given a very complex mixture. Our investigations with ester **11** have been suspended at this point while our laboratory turns to other varieties of unsaturated tricyclics.

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(15) (a) J. S. McConaghy, Jr., and W. Lwowski, *ibid.*, **89**, 2357 (1967); (b) W. Lwowski and T. J. Maricich, *ibid.*, **87**, 3630 (1965); (c) W. Lwowski and T. W. Mattingly, Jr., *ibid.*, **87**, 1947 (1965).

(16) A. Hassner, M. E. Lorber, and C. Heathcock, *J. Org. Chem.*, **32**, 540 (1967).

Experimental Section[17,18]

9H-Pyrrolo[1,2-a]indole (7).—Material of mp 90–91°, prepared as previously described, was used in the following experiments.[19]

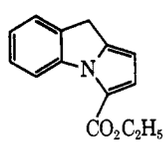
Lithium Anion of 9H-Pyrrolo[1,2-a]indole (8).—The anion employed in the subsequent condensations was prepared by addition of a 10 *M* % excess of a hexane solution of *n*-butyllithium (Foote) to an approximately 0.3 *M* solution of 9H-pyrrolo[1,2-*a*]indole in anhydrous diethyl ether. The solution was stirred for 15 min before further reaction at which time it appeared a Brunswick green.

Condensation of the Anion with β-Chloroethyldiethylamine.[11]—To a solution of the anion (3.00 mmol) in 20 ml of anhydrous diethyl ether was added a solution of 410 mg (3.02 mmol) of β-chloroethyldiethylamine in 2 ml of diethyl ether. The mixture was stirred for 20 hr after which the lithium chloride was filtered off and the solvent was removed. The resulting oil was evaporatively distilled at 140–150° (0.30 mm) yielding 20 mg of starting hydrocarbon followed by 645 mg of a pale yellow distillate whose tlc, vpc, and nmr spectrum revealed it to contain a trace of **7** and a mixture of alkylated products. A benzene solution of the distillate was subjected to gas chromatography at 247°. The mixture was resolved into three components of retention times of 4.4, 5.5, and 7.7 min in a ratio of 15:1:3.5, respectively. Samples of each component were collected and analyzed by nmr. The first component appeared to be the monoalkylated product **9-β-diethylaminoethyl-9H-pyrrolo[1,2-a]indole (9)**: nmr (CCl_4), δ 0.95 (t, 6, CH_3CH_2), 1.97 (m, 2, CH_2CH), 2.50 (m, 6, CH_2N), 3.98 (m, 1, HC-9), 6.03 (dd, 1, HC-1), 6.28 (t, 1, HC-2), 6.95 (dd, 1, HC-3), 7.00–7.33 (m, 4, aromatic). Insufficient amounts of the second component were collected to permit identification. The third component appeared to be the dialkylated product, **9,9-di-β-diethylaminoethyl-9H-pyrrolo[1,2-a]indole (10)**: nmr (CCl_4), δ 0.78 (t, 12, CH_3), 2.00 (broad s, 4, CH_2), 2.29 (m, 12, CH_2N), 6.02 (m, 1, HC-1), 6.32 (m, 1, HC-2), 6.98 (m, 1, HC-3), 7.05–7.38 (m, 4, aromatic).

Condensation of the Anion with Diethyl Carbonate. 9-Carbethoxy-3H-pyrrolo[1,2-a]indole (11).—A solution of the anion **8** (33.82 mmol) in 110 ml of anhydrous ether was added as rapidly as possible to an ice-cooled solution of 4.0 g (34 mmol) of diethyl carbonate, redistilled from P_2O_5, in 40 ml of diethyl ether. The resulting mixture was immediately hydrolyzed with ice and dilute hydrochloric acid. Standard work-up afforded a deep red oil. Tlc of the oil displayed the presence of starting hydrocarbon and one major new product: ir (CCl_4), 1705 cm^{-1} (C=O). The oil was chromatographed on a column of 180 g of alumina. Elution with hexane yielded 1.723 g (32.8%) of starting hydrocarbon. Elution with 1:4 benzene–hexane followed by 1:1 benzene–hexane afforded 2.111 g of a reddish oil which crystallized from hexane–benzene to give 1.158 g of tan crystals, mp 74.5–76.5°. The mother liquors gave a second crop of 0.19 g, mp 75.0–76.5°, for a total yield of 17.6%. An analytical sample of the ester, **9-carbethoxy-3H-pyrrolo[1,2-a]indole**, was prepared by evaporative distillation at 140–160° (0.15 mm) and crystallization from hexane: mp 76.5–78.5°; ir (CCl_4), 1700 cm^{-1} (C=O); ir (CS_2), 692 and 684 cm^{-1} (*cis* C=C); uv max (isooctane), 227 mμ (ε 28,000), 248 (16,000), 253 (16,000), 265 sh (3000), 310 sh (12,000), 320 (13,000), 336 sh (9200), 357 (4200); uv max (95% C_2H_5OH), 229 mμ (ε 33,000), 237 (32,000), 318 (17,000); nmr (CCl_4), δ 1.35 (t, 3, CH_3), 4.02 (t, 2, $J_{13} = J_{23} = 2$ Hz, CH_2N), 4.23 (q, 2, CH_2O), 6.32 (dt, 1, $J_{12} = 6.0$, $J_{23} = 2.0$ Hz, HC-2), 6.77 (dt, 1, $J_{12} = 6.0$, $J_{23} = 2.0$ Hz, HC-1), 6.85–7.13 (m, 3, HC-5, HC-6, HC-7), 8.02 (m, 1, HC-8); nmr (acetone-d_6), δ 1.38 (t, 3, CH_3), 4.33 (q, 2, CH_2O), 4.64 (t, 2, $J_{13} = J_{23} = 2.0$ Hz, NCH_2), 6.87 (dt, 1, $J_{12} = 6$, $J_{23} = 2.0$ Hz, HC-2), 6.98–7.29 (m, 4, HC-1, three aromatic), 8.17 (m, 1, HC-8).

Anal. Calcd for $C_{14}H_{13}NO_2$: C, 74.0; H, 5.8; N, 6.2. Found: C, 74.0; H, 5.8; N, 6.1.

In a subsequent experiment, the crude red oil was analyzed by vpc which indicated the presence of starting **7** and one major product, namely **11**. Several minor peaks were also noted in the chromatogram, but these were small in area relative to the two components noted above. In experiments in which the anion was added over a longer period of time, or in which the anion was added rapidly, but the mixture was allowed to stir with ice cooling for several hr, the amount of ester **11** was found to decrease with time, until it was no longer evident in the reaction mixture upon vpc analysis. No new volatile product developed during this time. In one scaled-up experiment, the anion **8** was added to a large excess of diethyl carbonate. Upon chromatography of the reaction mixture on silica gel, a new ester was eluted from the column after starting **7** had been removed but before the major product **11** was recovered. Evaporative distillation of this new fraction at 120–130° (0.15 mm) produced 40 mg of a pale yellow oil which could not be induced to crystallize. This ester appeared to be **3-carbethoxy-9H-pyrrolo[1,2-a]indole:**



ir (CCl_4), 1712 cm^{-1} (ester C=O); nmr (CCl_4), δ 1.33 (t, 3, CH_3), 3.61 (broad s, 2, $ArCH_2$), 4.25 (q, 2, OCH_2), 5.93 (dt, 1, $J_{12} = 3.4$ Hz, $J_{19} < 0.5$ Hz, HC-1), 6.93–7.27 (m, 4, HC-2, three aromatic), 8.63 (m, 1, HC-5).

9-Carbethoxy-1,2-dihydro-1H-pyrrolo[1,2-a]indole (23).—A solution of 166 mg (0.730 mmol) of ester **11** in 20 ml of absolute ethanol was hydrogenated over 54 mg of a 5% palladium-on-carbon catalyst at room temperature and atmospheric pressure. Hydrogen (1 equiv) was consumed in 2 min and the mixture was stirred for 12 min with no additional gas uptake. Upon removal of the catalyst and solvent, there was obtained 166 mg (99%) of crystals, mp 95–95.5°. An analytical sample was prepared by crystallization from hexane: mp 95.5–96.0°; ir (CCl_4), 1698 cm^{-1} (ester C=O); ir (CS_2), absence of *cis* C=C at 692 and 684 cm^{-1}; uv max (isooctane), 217 mμ (ε 34,000), 229 (26,000), 245 sh (11,000), 275 sh (9700), 283 (12,000), 292 (11,000); nmr (CCl_4), δ 1.30 (t, 3, CH_3), 2.27 (m, 2, NCH_2CH_2), 2.78 (m, 2, $NCH_2CH_2CH_2$), 3.53 (t, 2, $J_{23} = 7$ Hz, NCH_2), 4.17 (q, 2, OCH_2), 6.75–7.11 (m, 3, aromatic), 7.95 (m, 1, HC-8).

Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.3; H, 6.6; N, 6.1. Found: C, 73.3; H, 6.6; N, 6.2.

Condensation of the Anion 8 with Ethyl Chloroformate. 9,9-Biscarbethoxy-9H-pyrrolo[1,2-a]indole (14).—A solution of 12.9 mmol of the anion **8** was added to an ice-cooled solution of 2.8 g (26 mmol) of redistilled ethyl chloroformate in 50 ml of diethyl ether. The mixture was stirred for 20 min and then poured into water. The organic layer was worked up in the usual manner and the solvent was removed to yield a red oil, ir (CCl_4) 1750 cm^{-1}, the vpc of which showed one major product other than regenerated **7**. The reaction product was chromatographed on 100 g of silica gel. Elution with CCl_4 afforded 700 mg (35%) of **7**. Elution with $CHCl_3$ yielded a red oil which was evaporatively distilled at 125–145° (0.01 mm) to afford 573 mg of a pale yellow oil. This oil, diester **14**, was crystallized from hexane–chloroform to yield 475 mg (13%) of crystals, mp 111–113°. An analytical sample was prepared by crystallization from hexane–chloroform: mp 115.0–115.5°; ir (CCl_4), 1755 cm^{-1} (unconjugated ester C=O); uv max (isooctane), 212 mμ (ε 21,000), 269 (13,000); nmr ($CDCl_3$), δ 1.23 (t, 6, CH_3), 4.24 (q, 4, OCH_2), 6.46 (m, 2, HC-1, HC-2), 7.10 (dd, 1, $J_{13} = 1.5$, $J_{23} = 2.6$ Hz, N-HC-3), 7.15–7.43 (m, 3, aromatic), 7.80 (m, 1, HC-8).

Anal. Calcd for $C_{17}H_{17}NO_4$: C, 68.2; H, 5.7; N, 4.7. Found: C, 68.2; H, 5.8; N, 4.7.

(17) All reactions described within were conducted under an atmosphere of nitrogen using the apparatus of Johnson and Schneider.[18] The standard reaction work-up, unless otherwise noted, involved washing the organic reaction solvent with dilute sodium bicarbonate solution, distilled water, and saturated sodium chloride. The organic solvent was then dried with anhydrous sodium sulfate and evaporated at reduced pressure. Column chromatography was performed with neutral Woelm alumina, activity III, and with Davison silica gel (100–200 mesh). Melting points were determined on a Fisher–Johns apparatus and are uncorrected. Analyses were done by Spang Microanalytical Laboratory, Ann Arbor, Mich. Vpc analyses were determined with an F & M instrument on a 6 ft × 0.125 in. 10% SE-30 on a firebrick column. Infrared spectra were obtained with a Perkin-Elmer 337 grating spectrophotometer. Ultraviolet spectra were taken with a Cary 15 spectrophotometer. Nmr spectra were measured with a Varian A-60 instrument, probe temperature 38°, with signals reported relative to internal tetramethylsilane, δ 0.00 ppm.

(18) W. S. Johnson and W. P. Schneider, *Org. Syn.*, **30**, 18 (1950).

(19) V. J. Mazzola, K. F. Bernady, and R. W. Franck, *J. Org. Chem.*, **32**, 486 (1967).

Condensation of Anion 8 with Carbon Dioxide. 9-Carboxy-3H-pyrrolo[1,2-*a*]indole (15).—To a stirred, ice-cooled solution of 32.9 mmol of the anion **8** in 110 ml of diethyl ether was added gaseous CO_2, dried by passing it through a column of molecular sieves, until the green color of the anion was discharged. The mixture was then poured into water and the ethereal layer separated. The aqueous layer was extracted with ether; the combined ether layers were worked up in the usual way to afford 3.36 g of **7**, mp 86–90°. The aqueous layer was acidified with cold, dilute HCl and the resulting precipitate was extracted into ether and worked up as usual to yield 2.20 g of an acid mixture, shown by tlc to consist of one major product. The mixture was chromatographed on silica gel. Elution with $CHCl_3$ yielded 525 mg of **7** (decarboxylation on the column?) to make a total of 74% recovered starting material. Elution with 1:49 acetic acid–chloroform yielded 478 mg (7%) of acid **15** homogeneous on tlc, mp 180–210° (decarboxylation). No other product could be eluted from the column. Acid **15** was sublimed at 165° (0.14 mm) and crystallized from ethanol: mp 213–215° (decarboxylation): ir (KBr), 1645 cm^{-1} (acid C=O); uv max (95% C_2H_5OH), 225 mμ (ε 22,000), 253 (17,000), 318 (12,000).

Anal. Calcd for $C_{12}H_9NO_2$: C, 72.4; H, 4.6; N, 7.0. Found: C, 72.5; H, 4.6; N, 7.0.

Condensation of the Anion 8 with Dimethyl Oxalate.—A solution of 19.3 mmol of the anion **8** was added as rapidly as possible to an ice-cooled solution of 2.36 g (20 mmol) of dimethyl oxalate in 60 ml of ether. After complete addition of the anion, the mixture was hydrolyzed with ice and dilute HCl. The usual work-up gave a red oil, whose tlc showed the presence of **7** and several new spots: ir (CCl_4), 1740 (ester C=O), 1686 cm^{-1} (conjugated C=O). The crude product was chromatographed on a column of 100 g of silica gel. Elution with hexane and 1:1 hexane–benzene yielded 1.01 g (33.6%) of **7**. Elution with benzene afforded 1.13 g of a red oil which crystallized from benzene to yield ester **16** as 320 mg of black crystals, mp 133.5–136°. The mother liquors were chromatographed on alumina with benzene as eluent. Two yellow bands developed. The first one removed afforded 60 mg of an oil which crystallized from hexane–benzene to give 45 mg of crystals, mp 78–81°. The second band gave 320 mg of an oil which could be crystallized from hexane–benzene to afford 280 mg of material, mp 135–136°, which was identical with ester **16** obtained in the initial chromatography. The combined yield of **methyl 9H-pyrrolo[1,2-*a*]indole-1-glyoxalate (16)** was 600 mg (13%). The analytical sample was recrystallized from hexane–benzene: mp 136.5–138.0°; ir (CCl_4), 1745 (ester C=O), 1675 cm^{-1} (conjugated C=O); uv max (isooctane), 239 mμ (ε 13,000), 282 (11,000), 289 (13,000), 299 (13,000); nmr ($CDCl_3$), δ 3.95 (s, 3, OCH_3), 4.08 (s, 2, $ArCH_2$), 6.93 (d, 1, J_{23} = 3.0 Hz, HC-2), 7.20–7.70 (m, 5, HC-3, aromatics).

Anal. Calcd for $C_{14}H_{11}NO_3$: C, 69.7; H, 4.6; N, 5.8. Found: C, 69.6; H, 4.7; N, 5.9.

The lower melting column fraction was evaporatively distilled at 120–140° (0.20 mm) and crystallized from hexane to afford 35 mg of yellow crystals, mp 98.0–98.5°, which were identical in their ir, uv, mp, and tlc characteristics with **methyl 9H-pyrrolo[1,2-*a*]indole-3-glyoxalate (17)** prepared independently. The yield of this ester in this reaction was 1%.

Methyl 9H-Pyrrolo[1,2-*a*]indole-3-glyoxalate (17).—Following the procedure of Remers,[18] 254 mg (2.0 mmol) of oxalyl chloride was added to an ice-cooled, stirred solution of 310 mg (2.0 mmol) of **7** in 5 ml of CH_2Cl_2. After stirring for 15 min, the solvent was removed and the yellow-brown acid chloride was treated with 3 ml of methanol and 300 mg of Na_2CO_3. The mixture was stirred at room temperature for 2.5 hr and then at reflux for 2 min. Insoluble material was filtered off and the solvent was removed. The crude residue was chromatographed through alumina using benzene as eluent. Crystallization of the material from the column with methanol afforded 166 mg (34.4%) of ester **17**, mp 96.5–98.5°. The analytical sample was prepared *via* crystallization from hexane as long, pale yellow needles: mp 98.5–99.5°; ir (CCl_4), 1743 (ester C=O), 1662 cm^{-1} (conjugated C=O); uv max (isooctane), 233 mμ (ε 9500), 279 (7700), 286 (8800), 312 (13,000); nmr (acetone-d_6), δ 3.43 (s, 5, $ArCH_2$, OCH_3), 5.85 (dt, 1, J_{12} = 4.0, J_{19} = 1.0 Hz, HC-1), 6.62–7.05 (m, 4, HC-2, aromatic), 8.15 (m, 1, HC-5).

Anal. Calcd for $C_{14}H_{11}NO_3$: C, 69.7; H, 4.6; N, 5.8. Found: C, 69.7; H, 4.5; N, 5.9.

Condensation of the Anion 8 with Phenyl Isocyanate.—A solution of 3 mmol of anion **8** was added rapidly to an ice-cooled solution of 640 mg (5.37 mmol) of redistilled phenyl isocyanate in 10 ml of ether. The mixture was stirred for 5 min and then hydrolyzed with ice and dilute HCl. Work-up afforded a crude product, ir (CCl_4) 1721 and 1683 cm^{-1}, whose tlc indicated the presence of at least three new compounds. The crude product was chromatographed on alumina. Elution with hexane afforded 57 mg (13%) of **7**. Elution with 1:1 hexane–benzene gave 158 mg of a product which could be crystallized from benzene–ethanol to afford 117 mg (14%) of **N-phenyl-9H-pyrrolo[1,2-*a*]indole-3-carboxamide (21)**, mp 200–202°. The analytical sample was prepared from benzene–ethanol: mp 202–203°; ir (KBr), 3305 (NH) and 1654 cm^{-1} (C=O); uv max (isooctane), 241 mμ (ε 9700), 287 sh (23,000), 293 (24,000); nmr (DMSO), δ 3.95 (broad s, 2, CH_2Ar), 6.30 (dt, 1, J_{12} = 3.5 Hz, J_{19} = 1.0, HC-1), 7.15–7.65 (m, 8, HC-2, NH, aromatics), 7.92 (m, 2, aromatics), 8.57 (m, 1, HC-5).

Anal. Calcd for $C_{18}H_{14}N_2O$: C, 78.8; H, 5.1; N, 10.2. Found: C, 78.9; H, 5.1; N, 10.1.

Elution of the column with benzene afforded 99 mg of a mixture which was fractionally crystallized from ethanol. The product isolated in this manner was 10 mg of **N-phenyl-9H-pyrrolo[1,2-*a*]indole-1-carboxamide (20)** (1% yield), mp 154–156°. An analytical sample was prepared by recrystallization from ethanol: mp 155–156°; ir (KBr), 1712 cm^{-1} (C=O); uv max (isooctane), 235 mμ (ε 14,000), 278 (16,000), 284 (16,000), 288 (15,000); nmr ($CDCl_3$), δ 4.19 (s, 2, CH_2Ar), 6.71 (d, 1, J_{23} = 2.5 Hz, HC-2), 7.00–7.80 (m, 11, HC-3, NH, aromatics).

Anal. Calcd for $C_{18}H_{14}N_2O$: C, 78.8; H, 5.1; N, 10.2. Found: C, 78.9; H, 4.9; N, 10.5.

The mother liquors from the above fractional crystallization were evaporated, and the residue was crystallized from hexane–benzene to afford 30 mg (3%) of **N,N′-diphenyl-9H-pyrrolo[1,2-*a*]indole-9,9-dicarboxamide (19)**, mp 180–184°. An analytical sample was prepared from benzene–hexane: mp 186.5–188.0°; ir (KBr), 1680 cm^{-1} (C=O); uv max (isooctane), 248 mμ (ε 44,700); nmr ($CDCl_3$), δ 6.67 (m, 2, HC-1, HC-2), 7.14–7.72 (m, 16, HC-3, NH, aromatics), 8.08 (m, 1, HC-5).

Anal. Calcd for $C_{25}H_{19}N_3O_2$: C, 76.3; H, 4.9; N, 10.7. Found: C, 76.3; H, 4.9; N, 10.7.

Condensation of the Anion 8, Complexed with Triethylamine, with Diethyl Carbonate.—To a solution of 3.0 mmol of the anion **8** was added 310 mg (3.1 mmol) of triethylamine, and the resulting solution was allowed to stand for 2.5 hr. Then 390 mg (3.3 mmol) of diethyl carbonate was added to the solution. The usual discharge of the deep green color did not take place. The solution was stirred for 2.5 hr and then it was treated with ice and dilute HCl. Work-up yielded an oil whose tlc showed the presence of **7**, **11**, and a new product. The oil was chromatographed on alumina. Benzene elution afforded, in order, 356 mg (76.3%) of **7**, 89 mg of crude **11**, and 60 mg of a new ester, **22**. The crude ester **11** was distilled at 140–160° (0.15 mm) and crystallized from pentane–benzene to yield 60 mg (9%) of pure ester, mp 76–77.5°. The new ester **22** was distilled at 140–160° (0.15 mm) and crystallized from pentane–benzene to yield 26 mg (3%) of **1,9-dicarbethoxy-9H-pyrrolo[1,2-*a*]indole**, mp 92–93°. The analytical sample was recrystallized from pentane–benzene: mp 92.5–93.5°; ir (CCl_4), 1755, 1740, and 1725 cm^{-1} (C=O); uv max (isooctane), 212 mμ (ε 33,000), 230 (17,000), 237 sh (15,000), 272 (17,000); nmr ($CDCl_3$), δ 1.25 (t, 3, CH_3), 1.33 (t, 3, CH_3), 4.33 (q, 4, OCH_2), 5.07 (s, 1, HC-9), 6.89 (d, 1, J_{23} = 3.0 Hz, HC-2), 7.15 (d, 1, J_{23} = 3.0 Hz, HC-3), 7.31–7.59 (m, 4, aromatic).

Anal. Calcd for $C_{17}H_{17}NO_4$: C, 68.2; H, 5.7; N, 4.7. Found: C, 68.1; H, 5.8; N, 4.9.

In a similar experiment, the reaction solution was allowed to stir for 24 hr after the addition of diethyl carbonate. At this time, the green color was discharged. Work-up and chromatography gave 70% of recovered **7** and diester **22** in 6% yield, mp 92.5–93.5°. Only traces of **11** were detected.

Nitrene Addition to 9-Carbethoxy-3H-pyrrolo[1,2-*a*]indole-(11).—A solution of 227 mg (1.00 mmol) of ester **11** and 1.20 g (10.4 mmol) of ethyl azidoformate in 3.8 ml of methylene chloride was irradiated in a Pyrex tube under an atmosphere of N_2 with a Hanovia 100-W high-pressure lamp until 35 ml of N_2 was evolved.[15] The reaction mixture was then worked up by chromatography on alumina. Benzene elution gave recovered **11** (22%). Then 16 mg of material was obtained which exhibited carbonyl bands in the ir different from **11**. This product was chromatographed on tlc plates using silica gel G and 9:1 benzene–ether as developing solvent. A fraction (4 mg) was ob-

tained: mp 164–165.5°; ir (CCl_4), 1735 (carbamate C=O), and 1705 cm^{-1} (conjugated ester C=O); uv max (isooctane), 209 mμ (ε 28,000), 217 sh (26,000), 232 (22,000), 277 (6400), 287 (7100), 294 (6800). An interpretable nmr using a computer of average transients could not be obtained. The compound was not further characterized.

Registry No.—**9,** 16916-03-3; **10,** 16916-04-4; **11,** 16916-05-5; **14,** 16960-03-5; **15,** 16916-07-7; **16,** 16916-08-8; **17,** 16916-09-9; **19,** 16916-10-2; **20,** 16916-11-3; **21,** 16916-12-4; **22,** 16916-13-5; **23,** 16916-14-6; 3-carbethoxy-9H-pyrrolo[1,2-*a*]indole, 16916-06-6.

Displacement Reactions of Dibutyl Iodomethaneboronate and the Synthesis of Boron-Substituted Pyrimidines[1a,b]

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Dibutyl iodomethaneboronate has been synthesized by reaction of iodomethylmercuric iodide with boron tribromide followed by esterification with 1-butanol. Nucleophiles including alkoxides, amines, carbanions, and mercaptides displace iodide from dibutyl iodomethaneboronate to yield the corresponding substituted methaneboronic acid derivatives. Several boron-containing pyrimidines have been prepared by the reaction of the iodomethaneboronic ester with mercaptopyrimidines.

Reasons for studying carbon-functional boronic esters include observations of strong neighboring-group effects of boron[2-4] and the possibility of finding an effective compound for the ^{10}B neutron capture therapy of brain tumors.[5] Displacement of halide from an α-haloalkaneboronic ester is a potentially useful approach to a wide variety of substituted boronic esters.[3,4] However, it turned out that alkoxide ion often reacts much faster than more highly desired other nucleophiles, even mercaptides, in displacement of bromide from such compounds as dibutyl 2-bromopropane-2-boronate, owing to preliminary attack of the more basic anion on the boron atom. We thought it likely that reagents more nucleophilic toward carbon would react faster than those more basic toward boron if the transition state could be given more "SN2 character." Reduction of chain branching would accomplish this end, and a halomethaneboronic ester, $XCH_2B(OR)_2$, was therefore desired. A second advantage of such a compound would be the incorporation of a minimum of extraneous carbon along with the boron in compounds synthesized for potential biological properties.

Synthesis of $ICH_2B(OBu)_2$.—Our previous syntheses of α-haloalkaneboronic esters involved radical[2] or ionic[3] additions to alkeneboronic esters. An entirely new approach was therefore needed to make a halomethaneboronic ester. Chlorination of di-*t*-butyl methaneboronate with *t*-butyl hypochlorite yielded a little chloromethaneboronic ester after a lot of effort.[6] We therefore tried treating iodomethylmercuric iodide[7] with boron tribromide. After esterification of the product with 1-butanol, a low yield of dibutyl iodomethaneboronate (**1**) was obtained. Sodium iodide greatly improved the yield, evidently because it complexes with the mercury atom and makes it a better leaving electrophile.

$$ICH_2HgI + BBr_3 + NaI \longrightarrow HgI_2 + NaBr + ICH_2BBr_2 \xrightarrow{BuOH} ICH_2B(OBu)_2$$
1

After trying numerous variations, it was found that the best reaction conditions were about 1 day of vigorous stirring at 25°, with a large excess of boron tribromide and a moderate amount of methylene iodide, the quantity trapped in the iodomethylmercuric iodide on recrystallization (~20%) being about right. Careful vacuum drying of the ICH_2HgI cut the yield in half, though increasing the amount of methylene iodide did not seem to help. It is possible that the CH_2I_2 functions by increasing the slight solubility of the ICH_2HgI in the boron tribromide or by modifying the surface or mechanical properties of the mercury compound.

Although we are not sure that our yield (40% based on crude ICH_2HgI) is the best possible, it appears that instability of either the iodomethylmercury or boron compound may be a limiting factor. Heat or ultraviolet light increased the amounts of various by-products containing the $B-CH_2-B$ linkage, as shown by the appearance of several nmr peaks at τ 9.5–10. The boron tribromide treatment worked better for conversion of methylenedimercuric iodide,[7] $CH_2(HgI)_2$, into bis(dibromoboryl)methane, $CH_2(BBr_2)_2$,[1a] but this approach to methanediboronic acid has now been superseded by the much more efficient direct reaction of methylene chloride, lithium, and dimethoxyboron chloride.[8]

The crude dibutyl iodomethaneboronate (**1**) contained variable amounts of bromomethaneboronic ester, revealed by the $Br-CH_2-B$ nmr peak at τ 7.6. (For comparison, the corresponding $Cl-CH_2-B$ peak is at τ 7.2,[6] the $I-CH_2-B$ peak at τ 7.95.) The bromo compound has about the same boiling point as tributyl borate and was not isolated. Sodium iodide in acetone converted into the iodo compound (**1**).

Displacement Reactions.—As anticipated, dibutyl iodomethaneboronate (**1**), when treated with a wide

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