H, d, J = 9 Hz, H_8), 6.92 (2 H, d, J = 9 Hz, $H_{3'}$ and $H_{5'}$), 7.17 (2 H, d, J = 9 Hz, $H_{2'}$ and $H_{6'}$), 9.51 (1 H, s, CHO); IR ν_{max} (Nujol) 1640 (HC=O); UV (ethanol) λ_{max} 233 (4.30), 346 (4.37). Anal. Calcd for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16. Found: C, 77.56; H, 6.49.

3,9-Dimethoxy-7*H*-benzo[*c*]fluorene (7). The aldehyde **6** (400 mg) was stirred with PPA [prepared from P_2O_5 (10 g) and H_3PO_4 (6 mL)] at 90 °C for 2 h. The reaction mixture was decomposed with ice and the product extracted with ether (2 × 30 mL). Purification by TLC (ethyl acetate/hexane, 1:4) afforded **7**: 175 mg (46%); mp 175–177 °C (methanol–hexane); ^{1}H NMR ($CDCl_3$) 3.80–3.98 (8 H, 3 s, 2 OCH_3, CH_2), 6.76–7.91 (8 H, m, arom H). Anal. Calcd for $C_{19}H_{16}O_2$: C, 82.58; H, 5.84. Found: C, 82.24; H, 5.79.

1-[6-Methoxy-1-(*p*-methoxyphenyl)-3,4-dihydro-2-naphthalenyl]propan-1-ol (8). To C_2H_5MgBr [prepared from Mg (0.4 g) and C_2H_5Br (2.25 g)] in dry ether (20 mL) was added dropwise **6** (3 g) in dry ether (30 mL) under cooling and stirring, and the reaction mixture was left overnight. After the mixture was heated to reflux for 2 h and cooled, the complex was decomposed by the slow addition of ice cold water (20 mL), followed by ice cold saturated aqueous NH_4Cl (30 mL). Processing of the ether extract afforded the allylic alcohol **8**: 3.3 g (quantitative); bt 60 °C (4 mmHg); ^{1}H NMR (CCl_4) 0.75 (3 H, t, J = 7 Hz, CH_2CH_3), 1.37 (2 H, m, CH_2CH_3), 2.0 (1 H, br, OH), 2.20, 2.80 (4 H, 2 m, $2CH_2$), 3.67, 3.73 (6 H, 2 s, $2OCH_3$), 4.03 (1 H, t, J = 7 Hz, CHOH), 6.37 (2 H, br s, H_7 and H_8), 6.53 (1 H, br s, H_5), 6.70 (2 H, d, J = 9 Hz, $H_{3'}$ and $H_{5'}$), 6.93 (2 H, d, J = 9 Hz, $H_{2'}$ and $H_{6'}$); IR ν_{max} (neat) 3420 (OH); UV (ethanol) λ_{max} 224 (4.49), 314 (4.37). Anal. Calcd for $C_{21}H_{24}O_3$: C, 77.75; H, 7.46. Found: C, 77.66; H, 7.51.

3,9-Dimethoxy-7*H*-ethyl-5,6-dihydrobenzo[*c*]fluorene (9). The allylic alcohol **8** (1 g) was stirred with PPA [prepared from P_2O_5 (20 g) and H_3PO_4 (12 mL)] at 90 °C for 2 h. The usual workup furnished **9**: 0.86 g (91%); bt 170 °C (4 mmHg); ^{1}H NMR (CCl_4) 0.60 (3 H, t, J = 7 Hz, CH_2CH_3), 1.90 (2 H, m, CH_2CH_3), 2.46, 2.73 (4 H, m, $2CH_2$), 3.33 (1 H, t, J = 5 Hz, $CHCH_2$), 3.73 (6 H, 2 s, $2OCH_3$), 6.50–6.83 (4 H, m, H_2, H_4, H_8, and H_{10}), 7.46 (2 H, dd, J = 8 Hz, H_1 and H_{11}); IR λ_{max} (neat) 1610 (C=C); UV (ethanol) λ_{max} 254 (4.56), 263 (4.55), 300 (4.11). Anal. Calcd for $C_{21}H_{22}O_2$: C, 82.32; H, 7.24. Found: C, 82.15; H, 7.27.

3,9-Dimethoxy-7-ethylidenebenzo[*c*]fluorene (10). A mixture of **9** (300 mg) in dioxane (8 mL) and DDQ (270 mg) was refluxed for 30 h under N_2 blanket. The hydroquinone was filtered off, and the filtrate after concentration was chromatographed (neutral alumina, benzene) to yield **10**: 155 mg (52%); mp 120–121 °C (ethanol–hexane); ^{1}H NMR ($CDCl_3$) 2.41 (3 H, d, J = 8 Hz, vinyl CH_3), 3.87, 3.92 (6 H, 2 s, $2OCH_3$), 6.7–8.67 (9 H, m, vinylic H and arom H); IR ν_{max} (Nujol) 1610 (C=C); UV (methanol) λ_{max} 262 (4.71), 327 (4.27), 366 (3.91). Anal. Calcd for $C_{21}H_{18}O_2$: C, 83.42; H, 6.0. Found: C, 83.56; H, 6.17.

6-Methoxy-(*p*-methoxyphenyl)-1,2,3,4-tetrahydro-2-naphthaldehyde (11). A solution of **6** (1 g) in anhydrous THF (20 mL) was added to liquid NH_3 (100 mL) under stirring. Anhydrous $FeCl_3$ (20 mg) was then added, followed by lithium (60 mg) in small portions, and the deep blue complex was stirred for 30 min and decomposed with solid NH_4Cl. Ammonia was allowed to evaporate off, water added, and the product extracted with ether (2 × 50 mL). Removal of solvent and purification of the residue by TLC (ethyl acetate–hexane, 1:4) furnished **11**: 0.905 g (90%); bt 180 °C (5 mmHg); ^{1}H NMR (CCl_4) 1.97 (2 H, m, 3-CH_2), 2.86 (3 H, m, CHCHO and 4-CH_2), 3.72, 3.75 (6 H, 2 s, $2OCH_3$), 4.26 (1 H, d, J = 8 Hz, PhCH), 6.47–6.63 (2 H, m, H_5 and H_7), 6.67 (1 H, d, J = 9 Hz, H_8), 6.73 (2 H, d, J = 9 Hz, $H_{3'}$ and $H_{5'}$), 6.97 (2 H, d, J = 9 Hz, $H_{2'}$ and $H_{6'}$), 9.53 (1 H, d, J = 2 Hz, CHCHO); IR ν_{max} (neat) 2840 (HC=O), 1725 (HC=O). Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.81; H, 6.50.

1-[6-Methoxy-1-(*p*-methoxyphenyl)-1,2,3,4-tetrahydro-2-naphthalenyl]propan-1-ol (12). By use of the same procedure as for **8**, Grignard reaction of **11** (0.6 g) with C_2H_5MgBr afforded **12**: 0.66 g (quantitative): bt 155 °C (5 mmHg); ^{1}H NMR (CCl_4) 0.80 (3 H, t, CH_2CH_3), 1.13–1.90 (6 H, m, 2-CH, OH, CH_2CH_3, 3-CH_2), 2.80 (2 H, m, 4-CH_2), 3.26 (1 H, m, H_1), 3.67 (6 H, 2 s, $2OCH_3$), 3.92 (1 H, m, CHOH), 6.40–7.0 (7 H, m, arom H); IR ν_{max} (neat) 3400 (OH). Anal. Calcd for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03. Found: C, 77.13; H, 8.35.

3,10-Dimethoxy-5-methyl-5,6,6a,7,8,12b-hexahydrobenzo[*c*]phenanthrene (13). The alcohol **12** (0.5 g) was stirred with PPA [prepared from P_2O_5 (10 g) and H_3PO_4 (6 mL)] at 90 °C for 2 h. The reaction mixture was decomposed with ice and the product extracted with ether (2 × 30 mL). Purification of the residue left after removal of solvent by TLC (silica gel; ethyl acetate–hexane, 3:7) afforded **13**: 0.37 g (78%); bt 190 °C (3 mmHg); ^{1}H NMR ($CDCl_3$) 0.85 (3 H, d, J = 6 Hz, $CHCH_3$), 1.27–1.9 (5 H, m, 6-CH_2, 6aH, 7-CH_2), 2.23–3.0 (4 H, m, $CHCH_3$, 8-CH_2, 12b-H), 3.77, 3.85 (6 H, 2 s, $2OCH_3$), 6.50–7.50 (6 H, m, arom H). Anal. Calcd for $C_{21}H_{24}O_2$: C, 81.78; H, 7.84. Found: C, 81.42; H, 7.76.

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Synthesis of Tertiary Phosphine Derivatives of Dihydrophenophosphazine[1]

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The interaction of phosphorus trichloride and diarylamines at elevated temperatures yields chlorophosphine derivatives of the 5,10-dihydrophenophosphazine ring system. These compounds react with phenylmagnesium bromide to provide a facile synthesis of tertiary phosphine derivatives of 5,10-dihydrophenophosphazine that bear substituents on the aromatic ring. Further elaboration of the tertiary phosphines may provide compounds of therapeutic interest.

Few papers that describe the synthesis of tertiary phosphine derivatives of 5,10-dihydrophenophosphazine (**1**) can be found in the literature. Baum, Lloyd, and Tamborski[2] in 1964 reported the conversion of *o,o'*-dibromo-*N*-methyldiphenylamine to the corresponding dilithio compound and subsequent reaction of the dilithio

(1) Abstracted in part from the Ph.D. Thesis of H.S.F., North Carolina State University, 1981.

(2) G. Baum, H. A. Floyd, and C. Tamborski, *J. Org. Chem.*, **29**, 3410 (1964).

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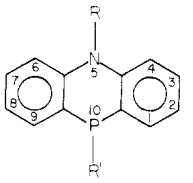
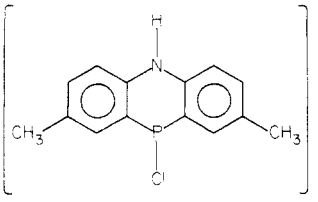


1, R = R′ = H
2, R = CH_3; R′ = Ph
3, R = H; R′ = Cl

compound with phenyldichlorophosphine to give **2**. In another study,[3] 10-chloro-5-methyl-5,10-dihydrophenophosphazine 10-oxide was shown to react with Grignard reagents to give tertiary phosphine oxide derivatives. These oxides were then reduced with trichlorosilane to give tertiary phosphine derivatives of the dihydrophenophosphazine ring system where R = CH_3 and R′ = CH_3 or phenyl. In a more recent paper,[4] the synthesis of this class of compounds was accomplished by heating methyl- or phenyldichlorophosphine with diphenylamine at 230–250 °C.

The resemblance of 5,10-dihydrophenophosphazines to phenothiazines (a well-known class of clinically useful compounds) prompted us to explore a more general entry into the former class of heterocyclic compounds to allow the inclusion of ring substituents. A mechanism proposed by Jenkins and Freedman[5] for the reaction between phosphorus trichloride and diphenylamine suggested that the chlorophosphine derivative **3** was the final product formed before hydrolysis of the reaction mixture. It seemed to us that a compound such as **3** would be readily converted to tertiary phosphines via reaction with a suitable Grignard reagent. Chlorophosphine derivatives of this type have never been isolated, and it has indeed been suggested[6] that a polymer containing phosphorus–nitrogen bonds (rather than **3**) is the product of the reaction between phosphorus trichloride and diphenylamine at 200–220 °C. Shortly after we began work on the synthesis and isolation of compound **3** and ring-substitued derivatives, a paper published by Hellwinkel and coworkers[7] on the synthesis of heterotryptycene compounds described the in situ generation and Grignard reaction of the chlorophosphine **4**. These workers did not report an attempted isolation of **4**, nor were there other examples to show the generality of the method.



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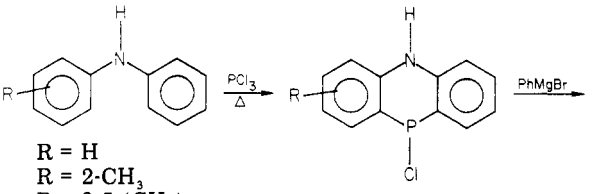
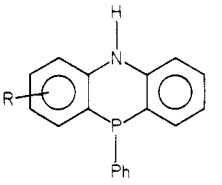
We now report that chlorophosphines **3**, **5**, and **6** have been prepared and subsequently converted (via a Grignard reaction) to tertiary phosphine derivatives of 5,10-dihydrophenophosphazine (**7–9**; cf. Scheme I). Compounds **5** and **6** formed as sublimates in the reaction kettle when

Scheme I



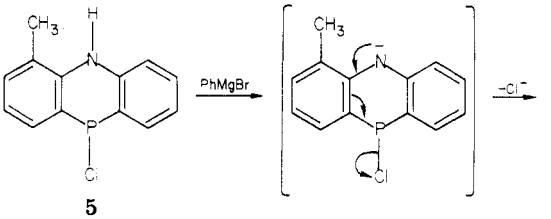
R = H
R = 2-CH_3
R = 3,5-$(CH_3)_2$

3, R = H
5, R = 4-CH_3
6, R = 1,3-$(CH_3)_2$



7, R = H
8, R = 4-CH_3
9, R = 1,3-$(CH_3)_2$

Scheme II



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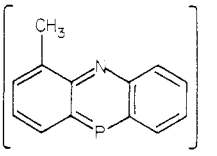

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phosphorus trichloride and the corresponding diarylamine were allowed to react in the absence of a catalyst or solvent at 210–230 °C. These yellow solids were transferred to containers with the aid of a drybox and stored under N_2 in a vacuum desiccator. Mass spectrometric analyses of both products showed intense peaks that corresponded to the molecular ion, and in the case of **5** the molecular ion was the base peak of the spectrum. We were, however, unable to prepare an analytically pure sample of either compound. Attempted purification by sublimation in vacuo caused decomposition, while the insolubility of these derivatives in nonhydroxylic solvents prevented purification by recrystallization. Compound **3** did not sublime out of the reaction mixture, and it could not be separated from the spirophosphonium salt[5] that is a second product of the reaction between diphenylamine and phosphorus trichloride. However, subsequent chemical reactivity of the crude reaction mixture led us to believe that it was formed as was **5** and **6**. The Grignard reactions of compounds **3**, **5**, and **6** with phenylmagnesium bromide took place in Et_2O or THF at 0–25 °C and were essentially complete (by TLC) after 2–6 h. The reaction mixtures were, however, allowed to stir overnight (16 h) as a matter of convenience. The yields[8] varied from a low of 8% for compound **8** to a high of 34% for **9**. The low yield of **8** from the corresponding chlorophosphine may be due to dehydrohalogenation of the chlorophosphine to give the unstable

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(4) K. A. Petrov, V. A. Chauzov, and N. Y. Lebedeva, *Zh. Obshch. Khim.*, **50**, 476 (1980); *Chem. Abstr.*, **92**, 215502 (1980).
(5) R. N. Jenkins and L. D. Freedman, *J. Org. Chem.*, **40**, 766 (1975).
(6) A. I. Bokanov and B. I. Stepanov, *Usp. Khim.*, **46**, 1625 (1977).
(7) D. Hellwinkel, A. Shenk, and W. Blaicher, *Chem. Ber.*, 111, 1798 (1978).

(8) These yields represent the combined amount of tertiary phosphine and the corresponding oxide obtained from each reaction.

phenophosphazine intermediate **10** (cf. Scheme II). Two moles of Grignard reagent per mole of chlorophosphine are required in these reactions. The first mole is presumably consumed by deprotonation of the nitrogen–hydrogen linkage, while the second attacks the phosphorus–chlorine bond. We believe that, for reasons we have not yet determined, **5** undergoes this facile elimination of HCl preferentially to the desired chloride replacement by the phenyl anion. While **10** has not been isolated, there is mass spectrometric evidence for its formation. An electron-impact spectrum of **5** exhibited a large peak (relative intensity of 40%) at *m/e* 211 which corresponds to M – 36. The 34% yield of compound **9** compares very favorably with the 36% yield of 5,10-dihydrophenophosphazine 10-oxide that is obtained when **3** is hydrolyzed with H_2O.[5] The yields from these reactions are better appreciated when one considers that an average of 20% of starting diarylamine can be recovered after the reaction.

The tertiary phosphine derivatives reported in this paper slowly oxidized in air to give the corresponding tertiary phosphine oxides. Therefore, they are kept best when stored under N_2. When this oxidation was carried out in acetone with H_2O_2, a nearly quantitative yield of analytically pure oxide was always obtained in 2–3 min. The phosphines also undergo base-catalyzed addition of acrylonitrile at the 5-position to give the expected N-cyanoethylated derivatives.

We believe that the synthesis of tertiary phosphine derivatives of 5,10-dihydrophenophosphazine via a Grignard reaction with an appropriate chlorophosphine precursor offers an attractive entry into this class of compounds. Advantages of this method over existing ones include the elimination of the necessity for brominated diarylamines, the maintenance of a nitrogen atom capable of functionalization, two relatively simple steps, and the flexibility to incorporate aryl or alkyl groups at the 10-position by varying the Grignard reagent.

Experimental Section

General Methods. Melting points were determined with a Mel-Temp capillary melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 727B spectrophotometer, NMR spectra on a Perkin-Elmer R24A spectrometer, and mass spectra on a Varian MAT CH5 spectrometer. The elemental analyses were performed by Galbraith Laboratories.

The reactions between the diarylamines and phosphorus trichloride were carried out at 210–230 °C in a four-necked resin flask equipped with a condenser protected by a calcium sulfate drying tube, a thermometer reaching to the bottom, and a magnetic stirrer.

2-Methyldiphenylamine. 2′-Methylacetanilide (60.0 g, 0.400 mol) and bromobenzene (52 mL, 0.500 mol) were stirred under reflux for 18 h in the presence of 110 g of potassium carbonate and 8.0 g of cuprous iodide. The cooled reaction mixture was extracted with Et_2O. The Et_2O solution was concentrated to give 69.0 g of crude product. This oil was twice distilled to give 57.3 (78%) of pure 2-methyldiphenylamine: bp 112–114 °C (0.6 mmHg) [lit.[9] bp 143–146 °C (4–5 mmHg)]; ^1H NMR ($CDCl_3$) δ 2.0 (s, 3, Ar CH_3), 5.20 (br s, 1, NH), 6.70–7.30 (m, 9, Ar H); IR (neat) 3400 cm^{-1} (NH).

3,5-Dimethyldiphenylamine. 3′,5′-Dimethylacetanilide (65.2 g, 0.400 mol) and bromobenzene (63 mL, 0.600 mol) were converted to 3,5-dimethyldiphenylamine by the procedure described above for 2-methyldiphenylamine. The amine was purified by recrystallization from petroleum ether: 58 g (74%); mp 52–53 °C (lit.[10] mp 51–52 °C); ^1H NMR ($CDCl_3$) δ 2.25 (s, 6, Ar CH_3), 5.55 (br s, 1, NH), 6.6–7.4 (m, 8, Ar H); IR (Nujol) 3380, 3440 cm^{-1} (NH).

(9) S. P. Massie and P. K. Kadaba, *J. Org. Chem.*, **21**, 347 (1956).
(10) L. J. Kricka and J. M. Vernon, *Can. J. Chem.*, **52**, 299 (1974).

10-Chloro-4-methyl-5,10-dihydrophenophosphazine (5) and 10-Chloro-1,3-dimethyl-5,10-dihydrophenophosphazine (6). 2-Methyldiphenylamine (18.3 g, 0.100 mol) and phosphorus trichloride (9.0 mL, 0.110 mol) were stirred together as the reaction temperature was raised to 210 °C. The temperature was kept near that point for 21 h. The reaction mixture was cooled to room temperature, and the yellow sublimate was transferred to a dry container with the aid of a drybox. This yellow solid could not be purified. Mass spectral analysis of this crude sample (**5**) gave the following results: *m/e* (relative intensity) 249 (57), 248 (22), 247 (100), 246 (5), 229 (8), 228 (53), 213 (18), 212 (86), 211 (40), 210 (12), 209 (10). The ions at *m/e* 249 and 247 represent the molecular ion.

3,5-Dimethyldiphenylamine (19.7 g, 0.100 mol) and phosphorus trichloride (9.0 mL, 0.110 mol) were converted to crude **6** by the procedure outlined for compound **5**. The yellow solid was examined by mass spectrometry and gave the following data: *m/e* (relative intensity) 263 (6), 261 (19), 227 (18), 226 (100), 225 (85), 224 (19), 210 (15), 209 (18), 36 (26). The ions at *m/e* 263 and 261 represent the molecular ion. The base peak (*m/e* 225) corresponds to the dehydrohalogenation product of **6**.

10-Phenyl-5,10-dihydrophenophosphazine (7) and 10-Phenyl-5,10-dihydrophenophosphazine 10-Oxide. Diphenylamine (16.9 g, 0.100 mol) and phosphorus trichloride (9.0 mL, 0.110 mol) were stirred together at room temperature for 5 min. The reaction mixture was heated to 220 °C over the next 2.5 h and kept near that point for another 16 h. The cooled reaction vessel was flushed with N_2 for 40 min to remove HCl and residual PCl_3. The solid (crude **3**) was suspended in 125 mL of dry THF. The suspension was cooled to 5°C and stirred as a solution of 0.3 mol of PhMgBr in 125 mL of THF was added. The reaction was stirred cold for 30 min and then at room temperature for 2 h. The solution was poured into a mixture of 800 mL of cold H_2O and 30 mL of concentrated HCl. The entire mixture was stirred vigorously for 10 min, and the THF layer was collected. The THF solution was concentrated to give 18.0 g of crude **7**. Column chromatography of this material on silica gel with 1% EtOAc–hexane as the eluant gave 1.9 g of diphenylamine and 5.6 g of pure **7**: mp 158–160 °C; IR (Nujol) 3400 cm^{-1} (NH); mass spectrum, *m/e* (relative intensity), 276 (8), 275 (46), 199 (12), 198 (100), 197 (4), 167 (7), 77 (4). Anal. Calcd for $C_{18}H_{14}NP$: C, 78.53; H, 5.13; N, 5.09. Found: C, 78.57; H, 5.14; N, 5.16.

Continued elution of the column, following the isolation of **7**, with 9:1 EtOAc–MeOH gave 4.2 g of the corresponding tertiary phosphine oxide, i.e., 10-phenyl-5,10-dihydrophenophosphazine 10-oxide: IR (Nujol) 3260, 3160 (NH), 1170 cm^{-1} (P=O); mass spectrum, *m/e* (relative intensity) 292 (12), 291 (71), 290 (25), 215 (13), 214 (100), 198 (8), 186 (10), 185 (7), 167 (11), 166 (7), 77 (4). Anal. Calcd for $C_{18}H_{14}NOP$: C, 74.22; H, 4.84; N, 4.81. Found: C, 74.21; H, 4.79; N, 4.82.

4-Methyl-10-phenyl-5,10-dihydrophenophosphazine (8) and 4-Methyl-10-phenyl-5,10-dihydrophenophosphazine 10-Oxide. To a suspension of crude **5** (20 g) in 200 mL of dry Et_2O was added (at 5 °C) a solution of PhMgBr (54 g, 0.300 mol) in 200 mL of Et_2O. The reaction was stirred overnight at room temperature and subsequently for 1 h under reflux. The solution obtained was poured into cold dilute HCl, and the mixture was stirred well. The Et_2O solution was dried ($MgSO_4$) and concentrated to give 17.1 g of a light orange oil. Crude **8** was purified by column chromatography in the manner described for **7** and its oxide to give a 1% yield of pure **8**: mp 138–140 °C; ^1H NMR ($CDCl_3$) δ 2.23 (s, 3, Ar CH_3), 6.2–7.8 (m, 12, Ar H); mass spectrum, *m/e* (relative intensity) 290 (12), 289 (74), 213 (21), 212 (100), 211 (7), 210 (6), 209 (6), 181 (5), 180 (8), 145 (5). Anal. Calcd for $C_{19}H_{16}NP$: C, 78.88; H, 5.57; N, 4.84. Found: C, 78.77; H, 5.61; N, 4.81.

Further elution of the column that afforded **8** with 1:1 EtOAc–MeOH gave a 7% yield of the corresponding phosphine oxide: mp >325 °C; IR (Nujol) 3240, 3160 (NH), 1165 cm^{-1} (P=O); mass spectrum, *m/e* (relative intensity) 306 (17), 305 (80), 304 (25), 229 (15), 228 (100), 212 (12), 200 (6), 185 (9), 181 (6), 180 (13), 152 (8), 77 (5). Anal. Calcd for $C_{19}H_{16}NOP$: C, 74.75; H, 5.28; N, 4.59. Found: C, 74.52; H, 5.23; N, 4.50.

1,3-Dimethyl-10-phenyl-5,10-dihydrophenophosphazine (9) and 1,3-Dimethyl-10-phenyl-5,10-dihydrophenophosphazine 10-Oxide. The crude chlorophosphine **6** was suspended in 200

mL of dry Et_2O and converted to 17.9 g of crude **9** by the procedure described for **7**. Column chromatography of this material on silica gel with 1% EtOAc–hexane afforded 3.1 g of diarylamine, 1.3 g of biphenyl, and a 20% yield of pure **9**: mp 130–132 °C; ^1H NMR ($CDCl_3$) δ 2.22 (s, 3, Ar CH_3), 2.50 (s, 3, Ar CH_3), 6.2–7.8 (m, 11, Ar H); mass spectrum, *m/e* (relative intensity) 304 (10), 303 (45), 227 (15), 226 (100), 225 (5), 209 (5), 151 (4), 77 (3). Anal. Calcd for $C_{20}H_{18}NP$: C, 79.19; H, 5.98; N, 4.62. Found: C, 79.42; H, 5.84; N, 4.82.

Compound **9** (0.303 g, 0.001 mol) was dissolved in 5 mL of acetone. To this solution was added 0.2 g of 30% H_2O_2. The oxide of **9** precipitated immediately. After the mixture was stirred for 2 min, the white solid was collected by filtration to give 0.31 g (97%) of analytically pure material: mp >310 °C; ^1H NMR (TFA) δ 1.88 (s, 3, Ar CH_3), 2.04 (s, 3, Ar CH_3), 6.4–7.6 (m, 12, Ar H); IR (Nujol) 3260 and 3160 (NH), 1175 cm^{-1} (P=O); mass spectrum, *m/e* (relative intensity) 320 (18), 319 (93), 318 (100), 304 (8), 243 (6), 242 (42), 226 (9), 195 (6), 194 (17), 180 (11), 160 (6), 152 (7), 151 (6), 91 (6), 77 (6). Anal. Calcd for $C_{20}H_{18}NOP$: C, 75.22; H, 5.68; N, 4.39. Found: C, 75.16; H, 5.64; N, 4.34.

Registry No. **3**, 79735-27-6; **5**, 79735-28-7; **6**, 79722-68-2; **7**, 79722-69-3; **7** phosphine oxide, 73785-73-6; **8**, 79735-29-8; **8** phosphine oxide, 79735-30-1; **9**, 79735-31-2; **9** phosphine oxide, 79735-32-3; 2′-methylacetanilide, 120-66-1; bromobenzene, 108-86-1; 2-methyldiphenylamine, 1205-39-6; 3′,5′-dimethylacetanilide, 2050-45-5; 3,5-dimethyldiphenylamine, 51786-49-3; phosphorus trichloride, 7719-12-2; diphenylamine, 122-39-4.

In Vitro Reactions of Alkaloids. 2. Selective Decarbalkoxylation of Geminal Diesters, β-Keto Esters, and δ-Keto-β,γ-unsaturated Esters

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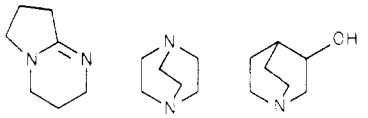
The reactivity of brucine, tropine, nicotine, reserpine, yohimbine hydrochloride, and quinidine has been demonstrated by the decarbalkoxylation of diethyl bis(3,4-dichlorobenzyl)malonate, ethyl β-(1-adamantyl)-β-oxopropionate, and 4-carbethoxy-3-methyl-2-cyclohexen-1-one. All reactions were conducted in dry *o*-xylene at 144–146 °C for 24 h with equivalent ratios (8:1) of base to substrate. These conditions were chosen for the purpose of establishing maximum selectivity. Brucine, nicotine, and yohimbine hydrochloride were shown to be selective toward the β-keto ester system, whereas tropine, reserpine, and quinidine were more selective catalysts toward decarbalkoxylation of δ-keto-β,γ-unsaturated esters. Brucine gave higher yields with all esters decarbalkoxylated and thus is the most reactive. The ability of these alkaloids to decarbalkoxylate esters, with some selectivity, suggests that one of the roles of alkaloids in plants may be to catalyze certain decarboxylation reactions.

We have reported[1-6] the carbalkoxylation of geminal diesters, β-keto esters, and δ-keto-β,γ-unsaturated esters with the tertiary amine bases 1,5-diazabicyclo[4.3.0]non-5-ene (**1**), 1,4-diazabicyclo[2.2.2]octane (**2**), and 3-quinuclidinol (**3**), in nonaqueous solvents in good yields.



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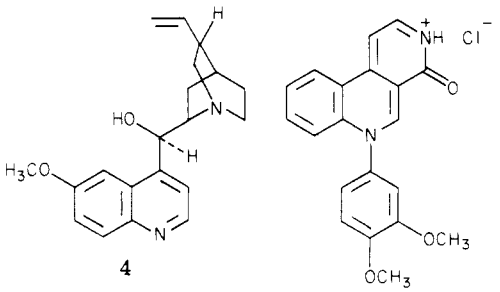
The similarity of the bicyclic moiety of these bases with that found in alkaloids such as quinine and the fact that the substrates (β-keto esters, geminal diesters, and δ-keto-β,γ-unsaturated esters) used are similar to those found in biological systems led us to postulate that one of the roles of alkaloids in plants could be to catalyze metabolic decarboxylation and decarbalkoxylation reactions. Some scientists have speculated[7] that alkaloids are by-products of plant metabolism, while others have proposed that they might serve as protective materials, reservoirs for protein, plant stimulants, plant regulators, and detoxifying agents. However alkaloids are still referred to as secondary metabolites, implying that they have no confirmed role in plant metabolic processes.

We have previously tested[8] our postulation by investigating the in vitro reactivity of quinine (**4**) and perloline hydrochloride (**5**) toward the three types of esters mentioned above. The results showed that decarbalkoxylation of the esters occurred in good yields. However a general statement concerning selectivity could not be made since the reactions were not performed under identical conditions. The conditions chosen were those that would result in the maximization of yields. Therefore an investigation was warranted into whether a broad spectrum of alkaloids would be reactive. Furthermore the question of selectivity needed to be answered in order to allow the postulation of a catalytic role for alkaloids in plants.



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This paper describes an investigation of the relative selectivity of the alkaloids brucine (**6**), tropine (**7**), nicotine (**8**), reserpine (**9**), yohimbine hydrochloride (**10**), and

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