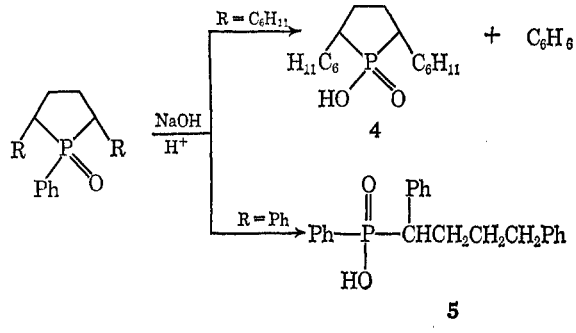
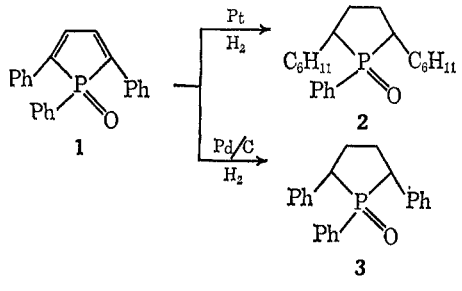
SCHEME I



SCHEME II



of serious coulombic repulsion between the approaching hydroxide ion and the oxide oxygen atom. Although there is some increase in ring strain in going to intermediate **7**, its formation is favored by minimum coulombic repulsion and by the fact that the electronegative oxygen atoms in **7** occupy apical positions.[6]

It seems reasonable to conclude that the reaction of tertiary phosphine oxides with fused sodium hydroxide normally proceeds through trigonal-bipyramidal intermediates in which oxygen atoms occupy the apical positions. Exceptions to this rule must occur in the case of those heterocyclic compounds in which there would be a large increase in ring strain in going to an intermediate in which the phosphorus atom must span two equatorial positions. In general, however, cleavage probably takes place at an equatorial position of a trigonal-bipyramidal intermediate. By contrast, the alkaline cleavage of quaternary phosphonium salts normally involves the loss of a carbanion from an apical position of a trigonal-bipyramidal intermediate.[2]

Experimental Section[7]

1,2,5-Triphenylphosphole 1-Oxide (1).—1,2,5-Triphenylphosphole[4] (12.0 g, 0.039 mol) was dissolved in tetrahydrofuran (150 ml) and the stirred solution was treated dropwise with 30% hydrogen peroxide (15 ml). The phosphine oxide began crystallizing during the addition. After the addition, the solution was evaporated to 50 ml, cooled, and filtered: yield 11.4 g (91%); mp 234–237° (lit.[4] mp 237–239°).

1-Phenyl-2,5-dicyclohexylphospholane 1-Oxide (2).—1,2,5-Triphenylphosphole 1-oxide (3.4 g, 0.010 mol) was dissolved in a 2:1 mixture of acetic acid–ethyl acetate. Platinum oxide (2 g) was added, and the phosphole oxide was reduced at room temperature and 4 atm in a Parr hydrogenation apparatus. After 2 hr, the uptake of hydrogen was equivalent to eight double bonds. The catalyst was separated by filtration, and the solvent was evaporated. The product was obtained by recrystallization of the residue from ethyl ether–petroleum ether: yield 2.6 g (72%); mp 178–180°; nmr τ 7.5–9.0 (m, 28, aliphatic H) and 2.0–2.7 (m, 5, aromatic H).

Anal. Calcd for $C_{22}H_{33}OP$: C, 76.71; H, 9.66; P, 8.99. Found: C, 77.00; H, 9.46; P, 9.42.

1,2,5-Triphenylphospholane 1-Oxide (3).—1,2,5-Triphenylphosphole 1-oxide (5.0 g, 0.015 mol) was dissolved in a 2:1 acetic acid–ethyl acetate mixture. Palladium (0.75 g of 10% palladium on carbon) was added, and the compound was reduced at room temperature and 4 atm. After 3 hr, the uptake of hydrogen was equivalent to two double bonds. The catalyst was separated, and the solvent was evaporated. The residue was recrystallized from carbon tetrachloride: yield 4.05 g (80%); mp 151–153° (lit.[4] mp 205–207°); nmr τ 7.1–7.6 (m, 4, CH_2CH_2), 6.02 (d, J_{PH} = 22.5 Hz, further split into triplets, J = 9.0 Hz, 2, HCPCH), and 2.7–3.1 (m, 15, aromatic H).

Anal. Calcd for $C_{22}H_{21}OP$: C, 79.50; H, 6.37; P, 9.32. Found: C, 79.40; H, 6.30; P, 9.28.

Cleavage of 1-Phenyl-2,5-dicyclohexylphospholane 1-Oxide (2).—The phosphine oxide **2** (2.7 g, 0.0079 mol) was thoroughly mixed with finely powdered sodium hydroxide (0.05 mol) in a 25-ml pear-shaped flask fitted with a condenser. The flask was slowly heated to 300° and maintained between 300 and 310° for 1.5 hr. About 0.7 ml of benzene (identified by nmr and ir), essentially the calculated amount for exclusive phenyl cleavage, distilled during this time. The contents of the flask were dissolved in water, treated with charcoal, and acidified to give 1-hydroxy-2,5-dicyclohexylphospholane 1-oxide (**4**): yield 1.75 g (79%); mp 272–276° after recrystallization from glacial acetic acid. The ir did not show any aromatic CH stretches, but had aliphatic CH stretches at 2850 and 2920 cm^{-1} and a wide band centered at 950 cm^{-1}. The nmr spectrum showed a wide multiplet at τ 7.6–9.1.

Anal. Calcd for $C_{16}H_{29}O_2P$: C, 67.58; H, 10.28; P, 10.89. Found: C, 67.57; H, 10.31; P, 11.00.

Cleavage of 1,2,5-Triphenylphospholane 1-Oxide (3).—This phosphine oxide (3.0 g, 0.0090 mol) was cleaved with sodium hydroxide (1.5 g) at 300° for 1.5 hr by the procedure described for 1-phenyl-2,5-dicyclohexylphospholane 1-oxide. No hydrocarbon distilled during the reaction. The usual isolation procedure gave (1,4-diphenylbutyl)phenylphosphinic acid (**5**): yield 2.8 g (89%); mp 143–147° after recrystallization from ethanol; nmr τ 8.64 (t, J = 7.0 Hz, 2, $PCCH_2$), 8.08 (m, 2, CCH_2C), 7.65 (m, 2, CH_2Ph), 7.10 (t, with further splitting, J_{PH} = 14.0 Hz, 1, PCH), and 2.5–3.2 (m, 15, aromatic H).

Anal. Calcd for $C_{22}H_{22}O_2P$: C, 75.41; H, 6.62; P, 8.84. Found: C, 75.29; H, 6.73; P, 8.85.

Registry No.—**2**, 22137-71-9; **3**, 1045-11-0; **4**, 22155-43-7; **5**, 22137-73-1.

(7) Melting points were taken with a Mel-Temp capillary melting point apparatus and are uncorrected. Infrared spectra were taken on a Perkin-Elmer Model 521 spectrophotometer. Nmr spectra were taken with either a Varian HA-100 or Varian T-60 instrument; deuteriochloroform was used as a solvent with tetramethylsilane as an internal standard. Elemental analyses were performed by Galbraith Laboratories.

Leguminosae Alkaloids. VII. The Synthesis of (±)-Lamprolobine[1a-c]

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Received June 23, 1969

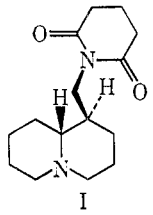
The alkaloid lamprolobine, isolated from *Lamprolobium fruticosum*, was recently assigned the structure (−)-(1*R*,5*R*,10*R*)-1-(glutarimidomethyl)quinolizidine (**I**) on the basis of evidence obtained from a degradative study.[2] Lamprolobine represents the first natural

(1) (a) We thank the National Institute of Mental Health for the grant under which this work was supported; (b) we gratefully acknowledge the departmental grant awarded by the National Science Foundation which contributed toward the purchase of the mass spectrometer used in this work; (c) we wish to express our warmest thanks to Dr. J. A. Lamberton of CSIRO, Australia, for his courtesy in providing a generous sample of (−)-lamprolobine.

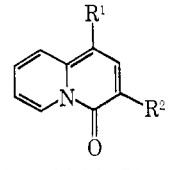
(2) N. K. Hart, S. R. Johns, and J. A. Lamberton, *Aust. J. Chem.*, **21**, 1619 (1968).

example of a logical, but unsubstantiated, variation[2] in the established[3,4] biogenetic route common for the sparteine and matrine ring systems of the *Leguminosae* family of alkaloids.

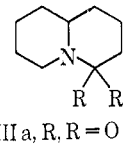
We report herein the synthesis of (±)-lamprolobine, carried out as indicated in the illustration. 1-Carbomethoxy-3-carbethoxy-4-quinolizone (IIa) was prepared by condensation of methyl 2-pyridylacetate and diethyl ethoxymethylidenemalonate. Its hydrolysis and didecarboxylation to 4-quinolizone (IIb) was accomplished *via* a procedure modified slightly from the original.[5] Catalytic hydrogenation of 4-quinolizone (IIb) over platinum oxide catalyst gave 4-quinolizidone (IIIa), which was reduced by lithium aluminum hydride to quinolizidine (IIIb). 1,10-Dehydroquinolizidine (IVa) resulted from mercuric acetate treatment[6] of



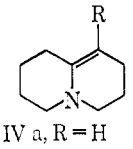
I



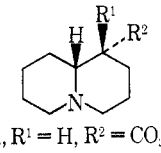
II a, $R^1 = CO_2Me$; $R^2 = CO_2Et$
b, $R^1 = R^2 = H$



III a, R, R = O
b, R = R = H



IV a, R = H
b, R = CO_2Et



V a, $R^1 = H$, $R^2 = CO_2Et$
b, $R^1 = CO_2Et$; $R^2 = H$
c, $R^1 = CH_2OH$; $R^2 = H$
d, $R^1 = CH_2Br$; $R^2 = H$

IIIb, and the former gave ethyl 1,10-dehydrolupininate (IVb)[7] upon reaction with ethyl chloroformate. Sodium borohydride was used to reduce IVb to ethyl lupininate (Va), which was epimerized by base to the epimeric ester (Vb). Epilupinine (Vc) was obtained from reduction of Vb with lithium aluminum hydride. In the final step of the synthesis, *trans*-1-bromomethylquinolizidine (Vd),[8] prepared by treatment of Vc with phosphorus tribromide, was brought into reaction with *N*-potassioglutarimide to give (±)-lamprolobine (I). Analytical data determined from the synthetic material were in accord with the expected structure (I), and its infrared spectrum (CCl_4) was found to be superimposable upon that determined from the natural (−)-lamprolobine.[1c] The picrate salt of synthetic (±)-I melted at 192–193°, revealing the presence of a racemic compound, since the picrate of (−)-I melted at 153–154°.[2]

Experimental Section

General.—Temperatures were uncorrected. Combustion analyses were by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. Infrared (ir) spectra were obtained with a Perkin-Elmer Model 337 grating spectrometer. Nuclear magnetic resonance (nmr) spectra were determined in chloroform-*d* solutions, containing 1–4% (v/v) tetramethylsilane (TMS) internal standard, with a Varian A-60 nmr spectrometer. Chemical shifts are reported under the δ convention in parts per million (ppm) relative to TMS (0 ppm). A Perkin-Elmer-Hatachi Model RMU-6 mass spectrometer[1b] was used to obtain mass spectra.

1-Carbomethoxy-3-carbethoxy-4-quinolizone (IIa) was prepared from methyl 2-pyridylacetate (61.7 g, 0.408 mol) and diethyl ethoxymethylidenemalonate (98.0 g, 0.431 mol).[5] It was obtained as a crystalline product: yield 81.5 g (72.6%), mp 154–156°. Recrystallization from acetone gave material that had mp 159–160° (lit.[5] mp 159–160°); $\nu_{max}^{CHCl_3}$ 1710, 1610, 1485, 1390, 1290, and 1225 cm^{-1}; $\lambda_{max}^{CHCl_3}$ 267 (ε 18,100), 350 (ε 13,000), 400 (ε 19,500), and 410 mμ (ε 19,500); nmr ($CDCl_3$) δ 7–10 (m, 5, aromatic H), 4.40 (q, 2, CH_2), 3.91 (s, 3, OCH_3), and 1.43 (t, 3, CCH_3).

The lower-melting material was, however, sufficiently pure to be used successfully in the next step of the over-all synthesis.

4-Quinolizone (IIb).—1-Carbomethoxy-3-carbethoxy-4-quinolizone (IIa, 25 g, 0.12 mol) dissolved in concentrated hydrochloric acid (250 ml), was stirred and heated under reflux for 1 hr. Troublesome foaming of the reaction mixture was surpressed by an antifoam agent.[9] After the yellow mixture was cooled, it was made basic by addition of potassium carbonate and passed through a filter. The filtrate was exhaustively extracted with benzene (until the extract was no longer yellow), and the combined extracts were dried and evaporated to a solid residue. Sublimation of this residue gave a brilliant yellow crystalline sublimate of **4-quinolizone** (IIb): mp 69–71°; $\nu_{max}^{CCl_4}$ 1671, 1636, 1480, and 1157 cm^{-1}; $\lambda_{max}^{ethanol}$ 205 (ε 3000), 215 (ε 3000), 247 (ε 2400), 254 (ε 2200), and 384 mμ (ε 2500); nmr (CCl_4) δ 7.60 (d, 1, aromatic H) and 5.94 (m, 6, aromatic H). The product, which was difficult to handle because of its deliquescence, was dissolved in ethanol and hydrogenated as described below.

4-Quinolizidone (IIIa).—All of the sublimate (4-quinolizone), obtained from hydrolysis–decarboxylation of 1-carbomethoxy-3-carbethoxy-4-quinolizone (25 g, 0.12 mol), was dissolved in 95% ethanol (250 ml), placed in a Parr bottle along with platinum oxide catalyst (450 mg), and shaken overnight at room temperature while contained under hydrogen (55 psi initial pressure). After the catalyst was separated and the reaction mixture was evaporated, the residue was distilled to give **4-quinolizidone** (IIIa): yield 10 g (54% over two steps); bp 83° (0.05 mm); ν_{max}^{neat} 3000, 2945, 2860, 1620, 1470, 1450, and 1279 cm^{-1}.

Quinolizidine (IIIb).—4-Quinolizidone (10.0 g, 0.653 mol), dissolved in absolute ether (50 ml), was added to a solution of lithium aluminum hydride (5 g in 75 ml of absolute ether) at a rate that caused and maintained a brisk reflux. The reflux was continued for 1.5 hr by external heating after the addition was complete. The cooled reaction mixture was hydrolyzed by careful initial addition of water (5 ml), followed by addition of 15% aqueous sodium hydroxide solution (5 ml), and finally addition of water (15 ml). The ethereal layer was separated, dried, and evaporated to give **quinolizidine** (IIIb) in near-quantitative yield: bp 91° (40 mm); ν_{max}^{neat} 2937, 2860, 2795, 2760, 1445, 1300, and 1122 cm^{-1}.

1,10-Dehydroquinolizidine (IVa) was prepared by treatment of quinolizidine (1.09 g, 7.83 mmol) with mercuric acetate (10.0 g, 31.4 mmol) in the manner previously reported.[6] The crude product was converted to its perchlorate salt, 5,10-dehydroquinolizinium perchlorate: yield 1.0 g (52%); mp 225–226° (lit.[6] mp 226–227°); ν_{max}^{nujol} 2015 and 1695 cm^{-1}.

Ethyl lupininate (Va) was prepared by treatment of **ethyl 1-10-dehydrolupininate** (IVb),[7] obtained from the reaction of IVa (3.0 g, 13 mmol) with ethyl chloroformate (1.4 g, 11 mmol), with sodium borohydride (2.5 g, 66 mmol) in methanol (15 ml) at 5°. The pure desire ester[7] was obtained by distillation: yield 0.75 g (57%); bp 79–81° (0.025 mm); nmr (CCl_4) δ 4.05 (q, 2, OCH_2), 3.0–1.2 (complex, 16, quinolizidine H), and 1.13 (t, 3, CCH_3).

Ethyl Epilupininate (Vb).—Ethyl lupininate (3.44 g, 17.7 mmol) was added to ethanol (150 ml) in which sodium (1.5 g, 56 mg-atoms) was previously dissolved. Examination of the reaction mixture by means of thin layer chromatography indicated that the epimerization was completed after overnight refluxing. The reaction mixture was acidified by addition of 10% aqueous hydrochloric acid (100 ml), and the ethanol was removed by distillation under reduced pressure. Basification and ether extraction of the aqueous residue gave, after evaporation of the ether, a

(3) H. R. Schutte, F. Bohlmann, and W. Reusche, *Arch. Pharm.* (Weinheim), **294**, 610 (1961).
(4) H. R. Schutte, H. Aslanow, and C. Schafer, *ibid.*, **295**, 34 (1962).
(5) V. Boekelheide and J. P. Lodge, Jr., *J. Amer. Chem. Soc.*, **73**, 3681 (1951).
(6) N. J. Leonard, A. S. Hay, R. W. Fulmer, and V. W. Gash, *ibid.*, **77**, 439 (1955).
(7) S. I. Goldberg and I. S. Ragade, *J. Org. Chem.*, **32**, 1064 (1967).
(8) G. R. Clemo and J. Rudinger, *J. Chem. Soc.*, 2714 (1951).
(9) General Electric Antifoam No. 60.

residue which was distilled to give **ethyl epilupininate** (Vb); ν_{max}^{neat} (conspicuous peaks not present in ir of ethyl lupininate) 1320, 1260, and 1150 cm^{-1}.

Epilupinine (Vc).—The entire quantity of ethyl epilupininate (Vb) prepared from ethyl lupininate (4.22 g, 21.6 mmol), was dissolved in absolute ether (15 ml) and added to a solution of lithium aluminum hydride (200 g, 52.7 mmol) in ether (75 ml). After the mixture was heated under gentle reflux for 1 hr, it was hydrolyzed by successive additions of water (2 ml), 15% aqueous sodium hydroxide solution (2 ml), and finally water (6 ml). The hydrolyzate was passed through a filter, and the ethereal phase was separated and dried. Evaporation of the ether left a residue which crystallized in the refrigerator, **epilupinine** (Vc): yield 2.80 g (76.4% over two steps); mp 78–79° (lit.[10] mp 77–78°).

trans-**1-Bromomethylquinolizidine** (Vd).[8]—Epilupinine (2.27 g, 14.0 mmol) was dissolved in benzene (15 ml), treated with phosphorus tribromide (1 ml), and heated under reflux for 2 hr. The mixture was cooled (ice added) and basified by careful addition of a 20% aqueous potassium hydroxide solution (30 ml). After separation of the benzene layer, the aqueous layer was extracted with several small portions of benzene. The combined and dried benzene solutions were evaporated, and the residue was distilled to provide *trans*-**1-bromomethylquinolizidine** (Vd): yield 2.43 g (75.0%); bp 100° (1 mm); ν_{max}^{neat} 2940, 2860, 2800, 2760, 2680, 1470, 1445, 1400, 1370, 1350, 1300, 1285, 1275, 1260, 1250, 1230, 1215, 1190, 1170, 1130, 1115, 1075, 1055, 1020, 970, 945, 880, 865, 845, and 775 cm^{-1}; nmr ($CDCl_3$) δ 3.34 (apparent d, $J \cong 4$ Hz, 2 H of bromomethyl group), 2.67 (m, 4 H), and 2.2–1.2 (complex envelope, 12 H).

(±)-**Lamprolobine** (I).—Potassium (700 mg, 17.9 mg-atoms) was dissolved in absolute ethanol (40 ml) and added to glutarimide (2.00 g, 17.7 mmol), and the solution was heated under reflux for 1 hr before it was evaporated to a residue of N-potassioglutarimide. *trans*-1-Bromomethylquinolizidine (3.00 g, 12.9 mmol) dissolved in dimethylformamide (30 ml) was added to the N-potassioglutarimide, and the mixture was heated under gentle reflux for 0.5 hr. After the mixture was allowed to cool to room temperature, it was cautiously added to water (150 ml), and the whole was extracted with several volumes of ether. The combined and dried ether extracts were evaporated to a residue which was taken up in a minimum volume of benzene and carefully washed onto the top of a column of alumina (Woelm, nonalkaline). Elution of the column with benzene, followed by careful evaporation of the solvent, gave (±)-lamprolobine (I) as a colorless oil: yield 1.78 g (52.1%); mass spectrum *m/e* 264 (M^+); infrared spectrum (CCl_4) superimposable upon that determine from a sample[10] of authentic (−)-lamprolobine. The synthetic material was further characterized as its picrate salt and was recrystallized from ethanol; mp 192–193° (racemic compound, since (−)-lamprolobine picrate has mp 153–154°[2]).

Anal. Calcd for $C_{21}H_{27}N_5O_9$: C, 51.11; H, 5.52; N, 14.33. Found: C, 51.38; H, 5.43; N, 14.33.

Registry No.—(±)-I, 22142-02-5; (±)-I picrate, 22142-03-6; IIb, 491-42-9; IIIa, 491-40-7; IIIb, 493-10-7.

(10) S. Okuda, I. Murakoshi, H. Kamata, Y. Kashida, J. Haginiwa, and K. Tsuda, *Chem. Pharm. Bull.* (Tokyo), **13**, 482 (1965).

A Short Synthesis of the Sex Pheromone of the Pink Bollworm Moth

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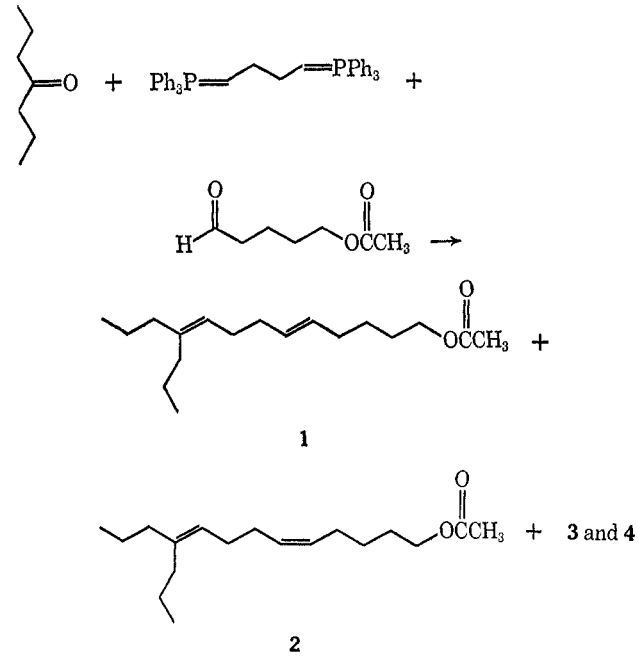
Contribution No. 571 from the Central Research Laboratories, 3M Company, St. Paul, Minnesota 55101

Received July 9, 1969

A valuable new technique for the survey of insect populations involves the use of sex pheromones to lure them to traps. The potency of these compounds is high; for example, the behavioral response threshold is in the region of 10^{-7}–10^{-11} g on the stimulus source for the silkworm moth, gypsy moth, and cabbage looper moth.[1]

In 1966, Jones, Jacobson, and Martin reported the isolation, structure determination, and synthesis of the sex pheromone of the pink bollworm moth, *Pectinophora gossypiella* (Saunders), 10-*n*-propyl-*trans*-5,9-tridecadienyl acetate (**1**).[2] This 11-step synthesis afforded a 0.2% overall yield. Another synthesis of this compound was reported[3] but the product was not biologically active, due to masking by the *cis* isomer.[4] A third synthesis was reported[5] involving seven steps and giving an 18% overall yield (1% overall conversion).



We have prepared compound **1** in 7% yield (overall conversion). The reaction of the difunctional Wittig reagent from tetramethylene-1,4-bistriphenylphosphonium bromide with 4-heptanone and 5-acetoxyvaleraldehyde gave the *cis*- and *trans*-10-*n*-propyl-5,9-tridecadienyl acetate (**1** and **2**) in addition to small amounts of 4,9-di-*n*-propyl-4,8-dodecadiene (**3**) and 5,9-tetradecadiene-1,14-diol diacetate (**4**). Isomerization of the mixture of **1** and **2** with selenium followed by silver nitrate–silica gel chromatography gives the pure *trans* isomer, while chromatography without isomerization affords the pure *cis* isomer and some pure *trans* isomer. The pure **1** from the Wittig reaction, the pure **1** from the isomerization reaction, and the isomerization product mixture were tested. Each gave a response in 75% of males exposed to the samples by the pipet method by which known pure **1** gives a 75% response.[4]

(1) H. H. Shorey, L. K. Gaston, and R. N. Jefferson, *Advan. Pest Control Res.*, **8**, 104 (1968).
(2) W. A. Jones, M. Jacobson, and D. F. Martin, *Science*, **152**, 1516 (1966); W. A. Jones and M. Jacobson, *ibid.*, **159**, 99 (1968).
(3) K. Eiter, E. Truscheit, and M. Boness, *Ann.*, **709**, 29 (1967).
(4) M. Jacobson, *Science*, **163**, 190 (1969).
(5) G. Pattenden, *J. Chem. Soc., C*, 2385 (1968).