and filtered, giving **2a** as an off-white solid (2.01 g, 96%), mp 180–183 °C, after drying in vacuo. An analytical sample had mp 182.5–184 °C (EtOH); NMR δ 2.8 (t, 2 H, J = 7 Hz), 3.9 (t, 2 H, J = 7 Hz), 4.8 (d, 2 H, J = 2 Hz), 5.9 (t, 1 H, J = 2 Hz), 7.8 (m, 4 H); IR (Nujol) 1760 cm^{-1}.

Anal. Calcd for $C_{14}H_{11}NO_4$: C, 65.37; H, 4.31; N, 5.45. Found: C, 65.35; H, 4.21; N, 5.47.

B. From Phosphonium Salt 3f. To a solution of 1.10 g (0.00179 mol) of **3f** in 25 mL of CH_2Cl_2 was added 0.30 mL (1.2 equiv) of freshly distilled Et_3N. After 20 h the solution was evaporated and dried in vacuo to give 1.32 g (100%) of a tan solid whose IR and NMR spectra were the sum of those of **2a**, Ph_3PO, and Et_3N·HBr. The hydrobromide was removed by treatment with H_2O, and the residue was recrystallized once from EtOH to give the product as a white solid (0.327 g, 71%), mp 176–179 °C.

Lactones 2b and 2c. The preparations of **2b** and **2c** from bromo ketones **6a** and **6b**, respectively, were analogous to that for the conversion of **3e** to **2a**, and the yields were essentially quantitative. For **2b**: mp 91–92.5 °C (lit.[16] mp 94 °C); NMR δ 5.2 (d, 2 H, J = 2 Hz), 6.3 (t, 1 H, J = 2 Hz), 7.5 (m, 5 H); IR (Nujol) 1745 cm^{-1}. For **2c**: mp 151–152.5 °C (lit.[17] mp 152–153 °C); NMR δ 6.3 (d, 1 H, J = 2 Hz), 6.6 (d, 1 H, J = 2 Hz), 7.4 (m, 10 H); IR (Nujol) 1740 cm^{-1}.

Isolation of Phosphorane 3g. A suspension of 1.00 g (0.00162 mol) of **3f** in 25 mL of Et_3N was stirred for 17 h. Evaporation of the excess amine in vacuo, stirring with H_2O, and filtration left 0.819 g (94%) of **3g** as a white solid that turned brown on standing in air. On moderately fast heating it partially melted at 97.5–99 °C, resolidified, and slowly decomposed above 120 °C; IR (Nujol) 1725, 1625 cm^{-1}.

IR Analysis of Phosphonium Salt Cyclizations. To a solution of the salt in $CHCl_3$ was added 1.2 equiv of Et_3N. The sample was immediately placed in the spectrophotometer, and the increase in adsorption of the solution at 1175 cm^{-1} (P=O) was continuously recorded via time drive to give a smooth curve; the reaction was taken to be over when the curve leveled off. The equilibrium temperature attained in the IR beam was found to be ca. 41 °C (thermocouple), but since the samples were initially at room temperature the reactions are probably somewhat faster than shown in Table I.

2-Diethylphosphonoacetoxycyclohexanone (9c). A solution of 2.38 g (0.0134 mol) of 2-bromocyclohexanone[19] and 4.12 g (0.0176 mol) of potassium diethylphosphonoacetate[20] in 50 mL of CH_2Cl_2 was allowed to stand for 4 days. Precipitated KBr was filtered off, the filtrate was evaporated, and the residue was partitioned between H_2O and $CHCl_3$. The organic layer was dried ($MgSO_4$), evaporated, and dried in vacuo to give **9c** as a pale yellow spectrally clean liquid: 3.56 g (91%); NMR δ 1.2–2.7 (m, 8 H), 1.35 (t, 6 H, J = 7 Hz), 3.09 (fine split d, 2 H, J = 1 and 21 Hz), 4.20 (fine split quintet, 4 H, J = 1 and 7 Hz), 5.19 (dd, 1 H, J = 6 and 11 Hz); IR (neat) 1750, 1730, 1265, 1025 cm^{-1}.

Registry No.—**3c**, 7504-49-6; **3d**, 66792-68-5; **3e**, 51132-00-4; **3g**, 66792-69-6; **4**, 65465-68-1; **6a**, 70-11-1; **6b**, 1484-50-0; **7a**, 53392-50-0; **7b**, 66792-70-9; **9c**, 66792-71-0; **9** (Y = Br), 822-85-5; bromoacetic acid, 79-08-3; potassium diethylphosphonoacetate, 34170-84-8.

References and Notes

(1) Taken from the Ph.D. Thesis of S.F.K.
(2) R. K. Hill, *Alkaloids (N.Y.)*, **9**, 483 (1967).
(3) K. Wada, S. Marumo, and K. Munakata, *Tetrahedron Lett.*, 5179 (1966).
(4) Y. S. Rao, *Chem. Rev.*, **76**, 625 (1976).
(5) S. F. Krauser and A. C. Watterson, Jr., *J. Org. Chem.*, **43**, 2026 (1978).
(6) J. Cure and M. Gaudemar, *Bull. Soc. Chim. Fr.*, 2471 (1969).
(7) M. W. Rathke and A. Lindert, *J. Org. Chem.*, **35**, 3966 (1970).
(8) R. Deghenghi, A. Philip, and R. Gaudry, *Tetrahedron Lett.*, 2045 (1963).
(9) M. S. Newman, R. W. Wotring, Jr., A. Pandit, and P. M. Chakrabarti, *J. Org. Chem.*, **31**, 4293 (1966).
(10) M. W. Rathke, *J. Am. Chem. Soc.*, **92**, 3222 (1970).
(11) L. Horner, H. Hoffman and H. G. Wippel; *Chem. Ber.*, **91**, 61 (1958); W. S. Wadsworth and W. D. Emmons, *J. Am. Chem. Soc.*, **83**, 1733 (1961).
(12) H. Vieregge, H. M. Schmidt, J. Renema, H. J. T. Bos, and J. F. Arens, *Recl. Trav. Chim. Pays-Bas*, **85**, 929 (1966).
(13) H. G. Lehmann and R. Welchert, *Angew. Chem., Int. Ed. Engl.*, **7**, 300 (1968).
(14) O. Isler, H. Gutmann, M. Montavon, R. Ruegg, G. Ryser, and P. Zeller, *Helv. Chim. Acta*, **40**, 1242 (1957).
(15) Characterized via IR and NMR spectroscopy.
(16) M. Rubin, W. D. Paist, and R. C. Elderfield, *J. Org. Chem.*, **6**, 260 (1941).
(17) A. Padwa and R. Hartman, *Tetrahedron Lett.*, 2277 (1966).
(18) M. S. Newman and C. A. Vanderwerf, *J. Am. Chem. Soc.*, **67**, 233 (1945).
(19) J. Allinger and N. L. Allinger, *Tetrahedron*, **2**, 64 (1958).
(20) R. A. Malevannaya, E. N. Tsvetkov, and M. I. Kabachnik, *Zh. Obshch. Khim.*, **41**, 1426 (1971).
(21) A. J. Kirby and S. G. Warren, "The Organic Chemistry of Phosphorus", Elsevier, New York, N.Y., 1967, p 37.

Formation of 2,3-Dihydro-2,2-diphenylbenzo[*b*]furan-3-one by Reaction of *gem*-Dichloroaziridine with Phenol: Multiplicity of Reactions of *gem*-Dichloroaziridines under Acidic Conditions

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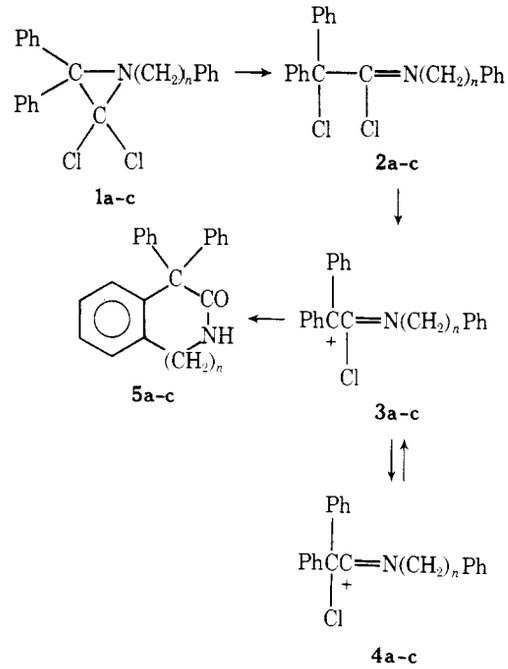
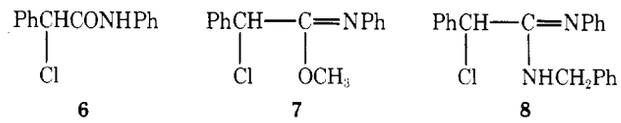
We have observed the formation of 4,4-diphenyl-1,2,3,4-tetrahydroisoquinolin-3-one (**5b**) and 1,1-diphenyl-1,3,4,5-tetrahydro-2*H*-3-benzazepin-2-one (**5c**) by treatment of 1-



a, n = 0; **b**, n = 1; **c**, n = 2

benzyl-2,2-dichloro-3,3-diphenylaziridine (**1b**) and 2,2-dichloro-3,3-diphenyl-1-(2-phenylethyl)aziridine (**1c**), respectively, with sulfuric acid in acetic acid.[1] It was assumed that the reactions proceed through cleavage of the C(3)–N bond and subsequent or simultaneous migration of a chlorine atom to the C(3) position to form *N*-benzyl- or *N*-(2-phenylethyl)-α-chloro-α,α-diphenylacetimidoyl chloride (**2b** or **2c**). The subsequent intramolecular Friedel–Crafts reaction and hydrolysis give the cyclic compounds **5b** or **5c**. In the case of *N*-phenyl compound **1a**, the intermediate (**2a**) was isolated by thermal isomerization. It was converted to 3,3-diphenyloxindole (**5a**) in good yield by treatment with sulfuric acid–acetic acid.[1,2]

Since the hydrolysis, methanolysis, and aminolysis of 2,2-dichloro-1,3-diphenylaziridine were reported to give compounds **6**,[3] **7**,[4] and **8**,[5] both of the two chlorine-carrying



carbon atoms in **2** are considered to be sensitive to nucleophilic attack. Therefore, we expected the formation of heterocyclic compounds by intermolecular reactions of **1** with nucleophilic aryl compounds. We wish now to report the formation of 2,3-dihydro-2,2-diphenylbenzo[*b*]furan-3-one (**12**) by the reaction of **1c** with phenol.

When **1c** was reacted with phenol in benzene in the presence

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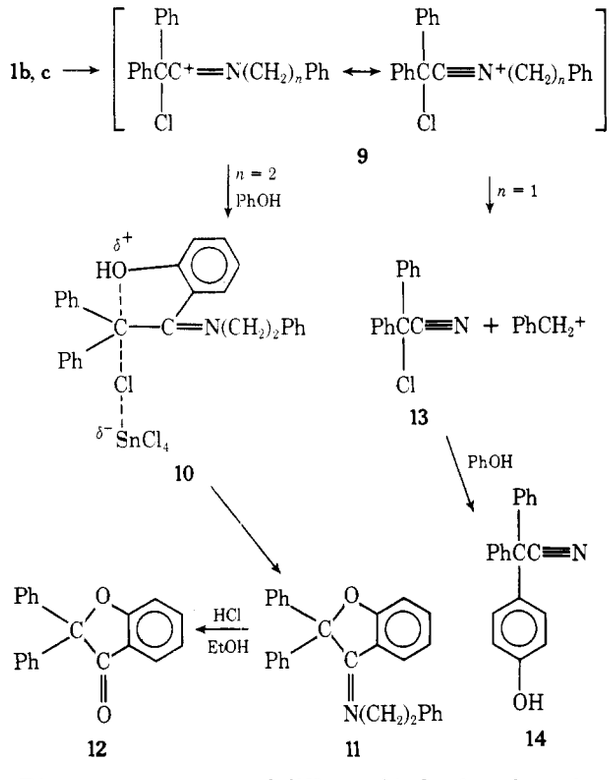
of stannic chloride at room temperature, 2,3-dihydro-2,2-diphenyl-3-(2-phenylethyl)iminobenzo[*b*]furan (**11**) was obtained in 39% yield. By the treatment of an ethanolic solution of **11** with hydrochloric acid solution at reflux temperature, 2,3-dihydro-2,2-diphenylbenzo[*b*]furan-3-one (**12**) was obtained in 55% yield.

A similar reaction of **1b** with phenol in the presence of stannic chloride in benzene afforded the noncyclic compound α-(*p*-hydroxyphenyl)-α,α-diphenylacetonitrile (**14**) in 43% yield. Considering the results of intramolecular cyclization of the *gem*-dichloroaziridines (**1a–c**) under acidic conditions and solvolyses of 1,3-diphenyl-2,2-dichloroaziridine as described above, the following reaction mechanism was tentatively proposed.



Divergent processes and different kinds of products from **1b** and **1c** may be attributed to the difference in nature of the group on the nitrogen atom. Stable carbonium ion forming groups such as a benzyl group would favor the von Braun type of degradation to give the nitrile **13**, which reacts subsequently with phenol to give **14**. The intermediate imidoylcarbonium ion **9** from **1c**, having a 2-phenylethyl group on the nitrogen, would attack phenol at the ortho position to form **11**. It is interesting to note that the alkylation of phenol with **1b** occurs at the para position while that with **1c** occurs at the ortho position. This seems to add an example to the known experimental criteria that secondary carbonium ions predominantly attack the ortho position of phenol while tertiary carbonium ions attack the para position.[8] Alternatively, the ortho substitution by **9** may be favored by the formation of cyclic intermediate **10** in the presence of $SnCl_4$. The reaction of **1c** with phenol is expected to serve as a general method for the synthesis of 2,3-dihydro-2,2-diphenylbenzo[*b*]furan-3-ones.

Experimental Section

Infrared spectra were obtained in KBr disks on a Jasco IRA-2 spectrometer, and NMR spectra were taken on a Hitachi R-20A spectrometer. Mass spectra were recorded on a Hitachi RMU-7M spectrometer. Combustion analyses were performed on a Perkin-Elmer 240 analyzer.

Reaction of 2,2-Dichloro-3,3-diphenyl-1-(2-phenylethyl)-aziridine (1c) with Phenol. To a solution of 3.68 g (0.01 mol) of **1c** in 30 mL of benzene was added slowly a solution of 5.21 g (0.02 mol) of stannic chloride and 1.88 g (0.02 mol) of phenol in 30 mL of benzene. The mixture was stirred at room temperature for 36 h and then poured into water. The organic layer was separated, washed with aqueous sodium hydrogen carbonate and then with water, and dried over anhydrous sodium sulfate. After evaporation of the solvent, the residue was chromatographed on a silica gel column using benzene as an eluent to give pure 2,3-dihydro-2,2-diphenyl-3-(2-phenylethyl)iminobenzo[*b*]furan (**11**) in 39% yield: mp 109–110 °C; IR 1650 cm^{-1} (C=N); NMR ($CDCl_3$) δ (ppm) 3.10 (t, 2, CH_2Ph), 4.17 (t, 2, CH_2N=C), 7.30 (m, 19, Ph); MS 389 (M^+), 298, 284, 270, 165, 105.

Anal. Calcd for $C_{28}H_{23}NO$: C, 86.34; H, 5.95; N, 3.60. Found: C, 86.09; H, 5.94; N, 3.52.

Hydrolysis of 2,3-Dihydro-2,2-diphenyl-3-(2-phenylethyl)-iminobenzo[*b*]furan (11). A solution of 0.2 g (0.51 mmol) of **11** in 11 mL of ethanol was treated with 1 mL of 12 M hydrochloric acid under reflux for 2 h. The acidic solution was neutralized with an ethanolic sodium hydroxide solution, and the sodium chloride that precipitated was removed. After evaporation of the solvent, the residue was chromatographed on a silica gel plate using carbon tetrachloride as an eluent. Isolation of the product band and extraction with acetone followed by evaporation of the solvent gave pure 2,3-dihydro-2,2-diphenylbenzo[*b*]furan-3-one (**12**): mp 91–92 °C (lit.[6] mp 90 °C); IR 1710 cm^{-1} (C=O); NMR ($CDCl_3$) δ (ppm) 7.3 (m, Ph); MS 286 (M^+), 258, 257, 181, 165, 109, 77, 76.

Anal. Calcd for $C_{20}H_{14}O_2$: C, 83.90; H, 4.93. Found: C, 83.14; H, 4.97.

Reaction of 1-Benzyl-2,2-dichloro-3,3-diphenylaziridine (1b) with Phenol. To a solution of 3.54 g (0.01 mol) of **1b** in 30 mL of benzene was added slowly a solution of 5.21 g (0.02 mol) of stannic chloride and 1.18 g (0.02 mol) of phenol in 30 mL of benzene. The mixture was stirred for 36 h at room temperature and worked up by a similar method to that described for the reaction of **1c**. The yield of α-(*p*-hydroxyphenyl)-α,α-diphenylacetonitrile (**14**) was 43%: mp 194.5–195 °C (lit.[7] mp 191–192 °C); IR 3400 (OH), 2225 (C≡N) cm^{-1}; NMR ($CDCl_3$) δ (ppm) 6.5–7.2 (m, Ph); MS 285 (M^+), 208, 190, 181, 165, 153, 152.

Anal. Calcd for $C_{20}N_{15}NO$: C, 84.19; H, 5.30; N, 4.91. Found: C, 84.51; H, 5.33; N, 4.96.

Registry No.—**1b,** 31528-96-8; **1c,** 61123-19-1; **11,** 66749-69-7; **12,** 66479-70-0; **14,** 13343-54-9; phenol, 108-95-2.

References and Notes

(1) M. Senō, S. Shiraishi, Y. Suzuki, and T. Asahara, *Bull. Chem. Soc. Jpn.*, **49,** 1893 (1976).
(2) M. Senō, S. Shiraishi, Y. Suzuki, and T. Asahara, *Bull. Chem. Soc. Jpn.*, in press.
(3) R. E. Brooks, J. O. Edwards, G. Levey, and F. Smith, *Tetrahedron*, **22,** 1279 (1966).
(4) J. A. Deyrup and R. E. Greenwald, *J. Am. Chem. Soc.*, **87,** 4538 (1965).
(5) K. Ichimura and M. Ohta, *Tetrahedron Lett.*, 807 (1966).
(6) A. Shonberg and K. Junghans, *Chem. Ber.*, **97,** 2539 (1964).
(7) H. D. Becker, *J. Org. Chem.*, **32,** 4093 (1967).
(8) S. H. Patinkin and B. S. Friedman, *Friedel–Crafts Relat. React. 1964*, **2,** Part 1, 75 (1964).

A Facile Synthesis of 2-(Trifluoromethyl)histamine and 2-(Trifluoromethyl)-L-histidine

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Our observations of the potent and selective biological activities of 2-fluoro-L-histidine[2] and 2-fluorohistamine[3] stimulated efforts to prepare and test additional analogues of metabolically significant imidazoles, particularly those with other electronegative groups at C-2. The more obvious synthetic approaches begin with a preformed 2-substituted imidazole, followed by elaboration of the histidine or histamine side chain.[4] There are, however, significant advantages to the

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