The mass spectrum showed M^+, m/e 87, and the isotopic composition given under the appropriate heading of Table I, row 3. Isotopic compositions of cyclopentanol-d_1 obtained in experiments 1 and 2 are given in rows 1 and 2, respectively.

B. Oxidation.—The 520-mg sample of cyclopentanol-d_1 was oxidized to 350 mg of cyclopentanone-d_1 purified by preparative glpc (5 ft, 15% Carbowax 20M, 100°). The mass spectrum showed M^+, m/e 85, and the isotopic composition given under the appropriate heading of Table I, row 3. Isotopic compositions of cyclopentanone-d_1 obtained in runs 1 and 2 are given in rows 1 and 2, respectively.

C. Exchange.—Cyclopentanone-d_1, 350 mg, gave after purification by glpc 40 mg of cyclopentanone, whose isotopic distribution is given in row 3.

Addition of DOAc to Bicyclo[3.1.0]hexane.—In the first experiment, a sealed glass tube containing 3.52 g of bicyclohexane, 400 mg of sulfuric acid-d_2, and 100 ml of acetic acid-*O*-*d* was maintained at 25° for 47 hr. Thereafter the contents of the tube were poured into 800 ml of water and the resulting mixture was extracted continuously with ether for 8 days. The extract was washed with saturated $NaHCO_3$, dried ($MgSO_4$), and reduced in volume to 50 ml by careful distillation of the ether. The concentrated extract was treated immediately with $LiAlH_4$. In the second experiment, 3.32 g of bicyclo[3.1.0]hexane was treated with 400 mg of D_2SO_4 and 100 ml of acetic acid-*O*-*d*; processing as described for the first sample gave 4.14 g of yellow oil after removal of most of the ether by distillation.

A. $LiAlH_4$ Hydrogenolysis.—The ethereal solution of acetates from the first experiment afforded, after purification by glpc (5 ft, 15% Carbowax 20 M, 125°), 250 mg of cyclohexanol-d_1: mass spectrum m/e (rel intensity) 101 (10), 100 (20), 99 (10), 98 (9), 84 (62), 83 (84), 82 (35), 67 (48), 66 (43), 59 (36), 58 (100), 57 (70). In the second experiment, the sample of crude acetates gave a mixture of alcohols from which was isolated by glpc 530 mg of *trans*-2-methylcyclopentanol-d_1, mass spectrum m/e (rel intensity) 101 (20), 100 (3), 83 (38), 82 (12), 68 (20), 67 (26), 58 (23), 57 (100); nmr τ 6.32 (m, 1 H, CHOH), 9.03 (br d, J = 6.5 Hz, 2.3 H, $CHCH_3$), and cyclohexanol-d_1, mass spectrum identical with that of the first sample. The isotopic composition of the cyclohexanol (row 6) was taken to be the same as that of the methylcyclopentanol-d_1 which is given in Table I, row 5.

B. Oxidation.—A sample of the cyclohexanol-d_1 (250 mg) obtained from the first experiment gave after purification by glpc (5 ft, 15% Carbowax 20 M, 100°) 99 mg of cyclohexanone-d_1: mass spectrum m/e (rel intensity) 99 (80), 70 (47), 69 (50), 57 (28), 56 (78). The isotopic composition is given in Table I, row 4. A 100-mg sample of the cyclohexanol-d_1 from the second experiment was oxidized and gave, after purification by glpc, 55 mg of cyclohexanone-d_1 whose isotopic composition is given in Table I, row 6. A 327-mg sample of *trans*-2-methylcyclopentanol-d_1 on oxidation gave, after purification by glpc, 110 mg of 2-methylcyclopentanone-d_1, mass spectrum m/e 99 (M^+), whose isotopic composition is given in Table I, nmr τ 8.96 (d, $CH_3/CH_2 + CH = 0.32$).

C. Exchange.—Samples of cyclohexanone-d_1 originating from first and second experiments, and 2-methylcyclopentanone-d_1, afforded samples of the corresponding exchanged ketones whose isotopic compositions are given in Table I, rows 4, 6, and 5, respectively.

Cyclopentanone-2-d_1 from Cyclopentene Oxide.—Cyclopentene oxide, 4.693 g, was treated with $LiAlD_4$ in ether solution and gave 4.5 g of cyclopentanol-2-d_1 after distillation. A sample was purified further by glpc for mass spectral analysis. The isotopic distribution was d_0, 16 ± 1%; d_1, 80 ± 1%; d_2, 5 ± 2%. Jones oxidation and processing in the usual manner gave 2.7 g of cyclopentanone-2-d_1 whose isotopic distribution was d_0, 18 ± 1%; d_1, 77 ± 1%; d_2, 5 ± 1%. A 1.07-g sample which had been treated with NaOMe–MeOH (~5 *M*) for 8 days at 25° and processed in the usual manner had the following isotopic distribution: d_0, 99 ± 1%; d_1, 2 ± 1%; d_2, 2 ± 1%.

Cyclohexanone-2-d_1 from Cyclohexene Oxide.—Following the procedure used in the preparation of cyclopentanone-2-d_1, cyclohexene oxide (6.34 g) was treated with $LiAlD_4$ and a 986-mg portion of the resulting alcohol (3.03 g) was oxidized by the Jones procedure to give 460 mg of cyclohexanone-2-d_1 whose isotopic distribution was d_0, 20 ± 2%; d_1, 79 ± 2%; d_2, 1 ± 1%. A sample treated with NaOMe–HOMe (~5 *M*) for 8 days at 25° gave cyclohexanone: d_0, 98 ± 2%; d_1, 2 ± 1%; d_2, 0.

Registry No.—**1**, 185-94-4; **2**, 285-58-5; acetic acid, 64-19-7; *trans*-2-methylcyclopentanol, 25144-04-1.

Intramolecular Cyclizations Leading to N-Bridgehead Bicyclics. 5,5-Diphenylhydantoin Derivatives

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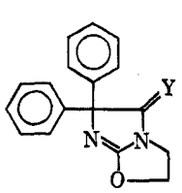
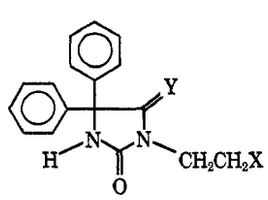
Received January 27, 1972

The synthesis and study of the intramolecular cyclizations of 3-(2-hydroxyethyl)-5,5-diphenylhydantoin mesylate (**2a**) and 1-(2-hydroxyethyl)-4,4-diphenyl-2-imidazolidinone mesylate (**2b**) are described. Although both N- and O-alkylation reactions are possible, only the products resulting from intramolecular O-alkylations were obtained.

The reported high concentrations of 5,5-diphenylhydantoin (DPH) in brain tissue and its preferred localization in primary brain tumors[1,2] suggested the synthesis of highly reactive DPH analogs as potential brain antitumor agents.[3] The nitrogen bridgehead bicyclic compounds **1a** and **1b** are part of the results of this work, and, in addition to their behavior as powerful alkylating agents, these compounds have clarified the course of intramolecular cyclization in the 3-substituted hydantoin and the 1-substituted imidazolidinone ring systems.



1a, Y = O
b, Y = H_2



2a, Y = O; X = OSO_2CH_3
b, Y = H_2; X = OSO_2CH_3
c, Y = O; X = OH

The synthesis of **2a** and **2b** and the determination of the structures of their cyclized products helped to resolve the question of whether intramolecular N-

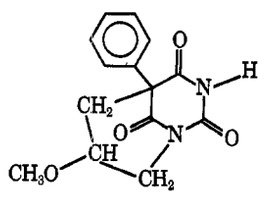
(1) H. Firemark, C. G. Barlow, and L. J. Roth, *Int. J. Neuropharmacol.*, **2**, 25 (1963).
(2) I. Rosenblum and A. A. Stein, *Biochem. Pharmacol.*, **12**, 1453 (1963).
(3) V. E. Marquez, L.-M. Twanmoh, H. B. Wood, Jr., and J. S. Driscoll, Abstracts of Papers, 162nd National Meeting of the American Chemical Society, Washington, D.C., Sept 1971, Division of Medicinal Chemistry, paper no. 36.

alkylation or O-alkylation would take place in the aforementioned ring systems.

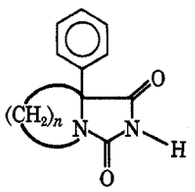
In **2a** the more acidic imide nitrogen (N-3) is substituted and in **2b**, where both nitrogens are amidic, only one is substituted. Both systems, therefore, possess an amide nitrogen as a potential site for alkylation. On the other hand, in their tautomeric forms, intramolecular alkylation can be envisaged to take place at the oxygen atom.

Intermolecular amide nitrogen (N-1) alkylations are well known in 3-substituted hydantoins but they occur under more severe conditions than the simple N-3 imide alkylations usually encountered with unsubstituted hydantoins. In the intramolecular reactions studied here, however, the presence of the alkylating group in the same molecule at the 3 position presents a somewhat different problem because the intramolecular process will be controlled by the thermodynamic stabilities of the two possible bicyclic products resulting from N- or O-alkylation.

Smissman, *et al.*, suggest that the use of NaH and DMF generally favors intramolecular N-alkylation. This group succeeded in preparing the N-alkylated bicyclic derivative of 5-phenyl-5-(2-methoxy-3-bromopropyl)barbituric acid[4] (**3**) and, under similar conditions, they obtained two N-1 alkylated bicyclohydantoins when the alkylating group was located in the 5 position (**4a**,**b**).[5]



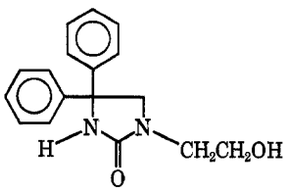
3



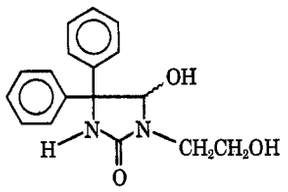
4a, $n = 3$
b, $n = 4$

O-Alkylation in hydantoins bearing the alkylating group on the side chain at the 5 position does not seem to be favored. On the other hand, O-alkylation occurs with ease in the 5-haloalkylbarbituric acids.[6] In our 3-substituted hydantoin system, bicyclic products resulting from both N- or O-alkylation seemed possible.

A common starting material for both 3-(2-hydroxyethyl)-5,5-diphenylhydantoin mesylate (**2a**) and 1-(2-hydroxyethyl)-4,4-diphenyl-2-imidazolidinone mesylate (**2b**) was the known 3-(2-hydroxyethyl)-5,5-diphenylhydantoin (**2c**).[7] The conversion of **2c** to **2a** was easily accomplished by treatment with methanesulfonyl chloride in dry pyridine at room temperature. The sequence leading to **2b** was planned based on the previously reported reductions of hydantoins with $LiAlH_4$. This reaction selectively reduces the amide carbonyl.[8] The reduction of **2c** to **5** with $LiAlH_4$ in refluxing THF, however, failed to proceed to completion. Even with a large excess of $LiAlH_4$ and prolonged reaction times a mixture of **5** and another partially reduced component, **6**, was always obtained. When **2c** was allowed to react with $LiAlH_4$ at room temperature in THF, practically no **5** was formed. Instead, the hydroxy imidazolidinone **6** was obtained. The infrared spectrum of this compound showed absorptions at 3250, 3150, and 1680 cm^{-1}, which indicated that partial reduction of one carbonyl group had taken place. The nmr gave a two-proton set of two doublets (OH,CH coupling) centered at δ 5.80 which collapsed into a one-proton singlet after D_2O exchange. The mass spectrum of **6** presented a molecular ion peak at m/e 298.



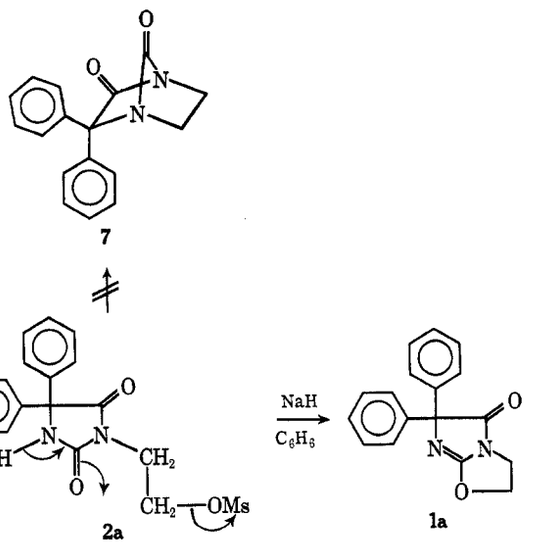
5



6

When excess Red-Al was used in refluxing THF, **2c** was reduced to the desired product, **5**. A characteristic ir band at 1690 cm^{-1}, important nmr signals at δ 4.04 (singlet for the ring methylene hydrogens), 3.30 (A_2B_2X system of the side chain), 4.70 (triplet, hydroxyl proton), and 7.92 (singlet, amide hydrogen), plus a molecular ion at m/e 282, confirmed the structure. Treatment of **2c** with methanesulfonyl chloride afforded **2b** in good yields.

When the mesylate **2a** was caused to react with NaH in refluxing benzene only the O-alkylated hydantoin, 2,3-dihydro-6,6-diphenylimidazo[2,1-*b*]oxazole-5(6*H*)-one (**1a**) plus some polymeric material was observed. The bridged bicyclic compound **7** was not detected in the reaction mixture.



7

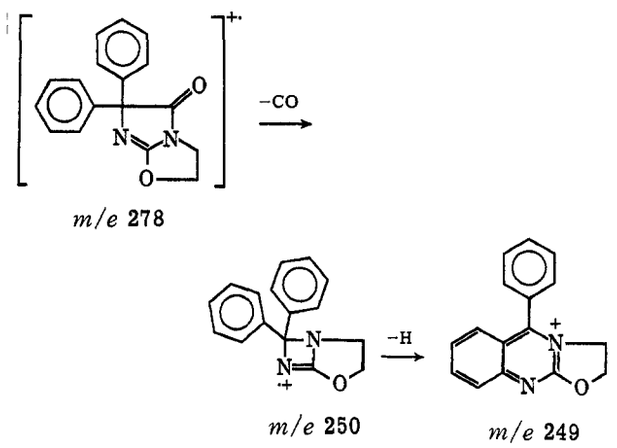
2a

1a

In the nmr spectrum of **1a**, two distinct triplets were observed at δ 3.80 and 4.88 corresponding, respectively, to the methylene hydrogens adjacent to the nitrogen and oxygen. If the N-alkylated bicyclic compound **7** had been obtained, the methylene signals should have been nearly equivalent. When **1a** was dissolved in detuerioacetone with added traces of D_2O and CF_3COOH and its nmr spectrum was observed over a period of time, both triplets gradually collapsed to a

(4) E. E. Smissman, R. A. Robinson, J. B. Carr, and A. J. B. Matuszak, *J. Org. Chem.*, **35**, 3821 (1970).
(5) E. E. Smissman, P. L. Chien, and R. A. Robinson, *ibid.*, **35**, 3818 (1970).
(6) E. E. Smissman, R. A. Robinson, and A. J. R. Matuszak, *ibid.*, **35**, 3823 (1970).
(7) K. Schlögl, F. Wessely, O. Kraupp, and H. Stormann, *J. Med. Pharm. Chem.*, **4**, 231 (1961).
(8) F. J. Marshall, *J. Amer. Chem. Soc.*, **78**, 3697 (1956).

singlet which was characteristic of the spectrum of **2c** in deuterioacetone after D_2O exchange. Therefore, **1a** was hydrolyzed to **2c** in the same manner as the O-alkylated barbiturates hydrolyzed in acid to the corresponding alcohols.[9] In addition to a molecular ion peak at *m/e* 278, the mass spectrum of **1a** showed important peaks at *m/e* 250 and 249 corresponding, respectively, to the loss of CO and further rearrangement to produce a stable ion *via* loss of a hydrogen radical.[10]



m/e 278 *m/e* 250 *m/e* 249

The infrared spectrum of **1a** exhibited strong absorptions at 1745 and 1700 cm^{-1}. The higher wavenumber absorption band was assigned to the carbonyl group, and the 1700-cm^{-1} band, although somewhat high, was attributed to the C=N stretching frequency. The lack of planarity induced by the strained rings in **1a** is responsible for the abnormally high frequency of the C=N bond. This assignment was also confirmed by comparison with **1b**.

Under the same conditions used to cyclize **2a**, the mesylate **2b** afforded 2,3,5,6-tetrahydro-6,6-diphenylimidazo[2,1-*b*]oxazole (**1b**) in good yield. Nmr signals were present at δ 3.80 (singlet, isolated ring methylene hydrogens) and 3.22 and 4.62 (triplets, corresponding to methylenes adjacent to nitrogen and oxygen). In addition to the molecular ion peak at *m/e* 264, important peaks were found at *m/e* 208, 187, 165, and 160. The strong ir band observed at 1680 cm^{-1} was assigned to the C=N bond of this puckered bicyclic compound.

The unsubstituted parent ring system of **1a** and **1b** has been mentioned in the literature, but no spectral data were reported.[11,12] The compound, named as Δ^7-1-oxa-4,7-diazabicyclo[3.3.0]octene, was the reaction product of 1-(2-chloroethyl)-2-imidazolidone with methanolic KOH.

The reaction of both **1a** and **1b** with *p*-nitrobenzylpyridine (see Experimental Section) gave an intense blue color[13] indicating the strong electrophilic character of these compounds. The study of this reactive bridgehead nitrogen ring system is being continued, since its lactim ether functionality is related to certain new types of antitumor agents.[14]

(9) E. E. Smissman and R. A. Robinson, *J. Org. Chem.*, **35**, 3532 (1970).
(10) R. A. Corral, O. O. Orazi, A. M. Duffield, and C. Djerassi, *Org. Mass. Spectrom.*, **5**, 551 (1971).
(11) A. F. McKay, G. Y. Paris, and M. E. Kreling, *J. Amer. Chem. Soc.*, **79**, 5276 (1957).
(12) A. F. McKay and M. E. Kreling, *Can. J. Chem.*, **37**, 427 (1959).
(13) T. J. Bardos, N. Datta-Gupta, P. Hebborn, and D. J. Triggle, *J. Med. Chem.*, **8**, 167 (1965).

Experimental Section[15]

3-(2-Hydroxyethyl)-5,5-diphenylhydantoin Methanesulfonate Ester (2a).—Methanesulfonyl chloride (1.46 ml, 0.018 mol) was added in one portion to a solution of **2c** (5.14 g, 0.017 mol) in 40 ml of dry pyridine and the reaction mixture was stirred overnight with the exclusion of moisture. The solution was added to 40 ml of chilled, concentrated HCl, and the solid formed was vigorously stirred, filtered, washed with water, and dried. Recrystallization from MeOH afforded 4.75 g (73%) of **2a**: mp 174–176°; ir 3200, 1760, 1700, 1170, 910, and 810 cm^{-1}; nmr δ 3.05 (s, 3), 3.82 (t, 2), 4.40 (t, 2), 7.35 (s, 10), and 9.63 (s, 1).

Anal. Calcd for $C_{18}H_{18}N_2O_5S$: C, 57.74; H, 4.84; N, 7.48; S, 8.56. Found: C, 57.79; H, 4.71; N, 7.22; S, 8.26.

2,3-Dihydro-6,6-diphenylimidazo[2,1-*b*]oxazole-5(6*H*)-one (1a).—Compound **2a** (3.85 g, 0.0103 mol) was dissolved in 500 ml of hot benzene. To the cooled solution, 0.435 g of NaH (57% oil suspension) was added in one portion and the mixture was refluxed for 5 hr. Tlc analysis [silica gel, AcOEt–$CHCl_3$ (1:1)] showed complete disappearance of the spot corresponding to starting material (R_f 0.39). One spot (R_f 0.32), which corresponded to product, was observed. The reaction mixture was filtered hot, and a small amount of a polymeric substance was discarded. The filtrate was reduced to dryness, triturated with ether, and filtered. Recrystallization from toluene afforded 2.60 g (91%) of **1a**: mp 188–190°; ir 1750, 1690, 1710, 1270, 1030, 975, 850, 770, 760, 730, 710, and 705 cm^{-1}; nmr δ 3.80 (t, 2), 4.88 (t, 2), 7.25 and 7.54 (multiplets, 10); mass spectrum *m/e* (rel intensity) 278 (37) (parent), 250 (25), 249 (100), 149 (35), 91 (32), and 40 (40).

Anal. Calcd for $C_{17}H_{14}N_2O_2$: C, 73.36; H, 5.07; N, 10.07. Found: C, 73.50; H, 5.24; N, 10.03.

(±)-5-Hydroxy-1-(2-hydroxyethyl)-4,4-diphenyl-2-imidazolidinone (6).—A solution of **2c** (1.5 g, 5.08 mmol) in 25 ml of THF was added dropwise to a slurry of $LiAlH_4$ (0.590 g, 15.2 mmol) in 15 ml of THF. The reaction was stirred for 5 hr at room temperature and the excess of hydride was stirred for 5 hr at room temperature and the excess of hydride was destroyed by the careful addition of CH_3OH and a saturated solution of Na_2SO_4 in water. After the solid was discarded, the organic layer of the filtrate was separated. Following the addition of an equal volume of $CHCl_3$ to the organic layer, it was washed with water and saturated NaCl solution and dried (Na_2SO_4). After removal of the solvents, the oily residue obtained was triturated with ether to give 0.950 g (63%) of **6** as a pure substance, mp 151–152°. The compound was recrystallized from acetone: mp 153–154°; ir 3250, 3150, 1680, 1080 (broad), 865, 768, 750, and 700 cm^{-1}; nmr δ 3.23 (m, 2), 3.42 (m, 2), 4.70 (t, 1), 5.62 (d, 1, J = 7 Hz, resolved into a singlet after D_2O exchange), 5.92 (d, 1, J = 7 Hz, disappeared after D_2O exchange), 7.24 (m, aromatic), and 7.91 (s, 1, amide NH); mass spectrum *m/e* (rel intensity) 298 (8) (parent), 280 (98), 262 (13), 249 (47), 236 (66), 221 (25), 209 (27), 208 (58), 182 (98), 165 (100), 104 (99), 77 (99), and 72 (99).

Anal. Calcd for $C_{17}H_{18}N_2O_3$: C, 68.43; H, 6.08; N, 9.39. Found: C, 68.44; H, 6.08; N, 9.41.

1-(2-Hydroxyethyl)-4,4-diphenyl-2-imidazolidinone (5).—A solution of **2c** (1.86 g, 6.3 mmol) in 40 ml of THF was added dropwise to a mixture of Red-Al[16] (12.5 ml, 45 mmol of H_2) and

(14) A. Hoshi, F. Kanzawa, K. Kuretani, M. Saneyoshi, and Y. Arai, *Gann*, **62**, 145 (1971).
(15) Melting points were determined on a Thomas-Hoover apparatus and are uncorrected. Infrared spectra were measured with Perkin-Elmer 621 and 137 spectrometers as Nujol mulls unless otherwise specified. Nmr spectra were recorded on a Varian HA-100D spectrometer and chemical shifts are given in parts per million from tetramethylsilane. Nmr spectra were determined as approximately 5% solutions in DMSO-d_6 unless otherwise stated. Elemental analyses were carried out by Dr. W. C. Alford, NIAMD, NIH. Electron bombardment mass spectra were determined by Mr. W. R. Landis, NIAMD, NIH, on a Hitachi Perkin-Elmer RMU-7 instrument at 80 eV. Developed tlc plates were visualized by spraying with a 4% solution of *p*-nitrobenzylpyridine in 4:1 methanol–water. The plates were heated at 120° for 10 min and then sprayed with a 0.1 *N* KOH in 4:1 methanol–water solution. Blue spots indicate compounds with alkylating properties.
(16) 70% solution of sodium bis(2-methoxyethoxy)aluminum hydride in benzene.

THF (20 ml). The mixture was refluxed for 5 hr. The excess of hydride was destroyed by the addition of an aqueous concentrated solution of Na_2SO_4 and the purification procedure followed was identical with that described for compound **6**. The yield of product after ether trituration was 0.9 g (51%), mp 159–160°. The compound recrystallized from acetone as white prisms: mp 161–162°; ir 3450, 3200, 1680, 1675 (shoulder), 1300, 1070, 1030, 860, 850, 790, 765, 745, and 710 cm^{-1}; nmr δ 3.48 (t, 2), 3.53 (q, 2), 4.04 (s, 2), 4.70 (t, 1), 7.32 (m, 10), and 7.92 (s, 1); mass spectrum *m/e* (rel intensity) 282 (33) (parent), 252 (34), 251 (76), 209 (15), 208 (69), 205 (24), 178 (34), 108 (40), 105 (56), 91 (55), 77 (45), 74 (54), 72 (42), 58 (64), and 43 (100).

Anal. Calcd for $C_{17}H_{18}N_2O_2$: C, 72.31; H, 6.42; N, 9.92. Found: C, 72.17; H, 6.60; N, 9.87.

1-(2-Hydroxyethyl)-4,4-diphenyl-2-imidazolidinone Methanesulfonate Ester (2b).—Following the procedure for the preparation of **2a**, compound **5** (0.58 g, 2.07 mmol) was treated with methanesulfonyl chloride (0.19 ml, 2.17 mmol) in 5 ml of pyridine. After the addition of concentrated HCl, the solution was extracted with $CHCl_3$. The chloroform layer was washed with water and dried (Na_2SO_4). The oil recovered after removal of the solvent was triturated with ether and the solid formed was recrystallized from benzene to yield 0.40 g (54%) of **2b**: mp 124–125°; ir 3200, 1680, 1370, 1340, 1180, 1000, 990, 900, 805, 750, 715, and 705 cm^{-1}; nmr δ 3.02 (s, 3), 3.42 (t, 2), 4.00 (s, 2), 4.27 (t, 2), 7.28 (m, 10), and 8.10 (s, 1).

Anal. Calcd for $C_{18}H_{20}N_2O_4S$: C, 59.98; H, 5.59; N, 7.77; S, 8.89. Found: C, 59.83; H, 5.71; N, 7.65; S, 8.92.

2,3,5,6-Tetrahydro-6,6-diphenylimidazo[2,1-*b*]oxazole (1b).—Following a similar procedure for the synthesis of **1a**, compound **2b** (0.40 g, 1.15 mmol) was treated with 0.2 g of NaH (57% oil suspension) in toluene. The reaction was completed in 1.5 hr according to tlc analysis [one spot, R_f 0.33, silica gel, $CHCl_3$–EtOAc (1:1)]. The starting material in the same system had an R_f value of 0.18. After work-up, 0.25 g (85%) of **1b** was obtained. One recrystallization from toluene afforded an analytical sample: mp 197–198°; ir 1670, 1260, 1210, 980, 780, 755, 732, 710, and 700 cm^{-1}; nmr δ 3.22 (t, 2), 3.80 (s, 2), 4.64 (t, 2), and 7.26 (m, 10); mass spectrum *m/e* (rel intensity) 264 (100) (parent), 208 (96), 187 (60), 180 (30), 165 (38), 160 (100), 132 (22), 105 (31), 91 (33), and 77 (83).

Anal. Calcd for $C_{17}H_{16}N_2O$: C, 77.24; H, 6.10; N, 10.60. Found: C, 77.40; H, 6.15; N, 10.70.

Registry No.—**1a**, 34806-22-9; **1b**, 34792-37-5; **2a**, 34806-23-0; **2b**, 34792-38-6; **5**, 34806-24-1; **6**, 34806-21-8.

^1H and ^{13}C Nuclear Magnetic Resonance Spectra of Cyclopentadienylmagnesium Compounds in Tetrahydrofuran

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Received February 11, 1972

Low-temperature pmr spectra of mixtures of magnesium cyclopentadienide and magnesium chloride and of magnesium cyclopentadienide and magnesium bromide, 0.05–0.56 *M* in tetrahydrofuran, indicate that the cyclopentadienylmagnesium halides consist of Schlenk equilibrium mixtures, $(C_5H_5)_2Mg + MgX_2 \rightleftarrows 2C_5H_5MgX$, in which the C_5H_5MgX predominates. A rapid exchange between cyclopentadienylmagnesium chlorides and cyclopentadienyl impurities (presumedly alkoxides) has been detected. ^{13}C nmr chemical shifts of cyclopentadienyl-, methylcyclopentadienyl-, 1,3-dimethylcyclopentadienyl-, and trimethylsilylcyclopentadienylmagnesium chlorides are reported and discussed in terms of the charge distributions in substituted cyclopentadienides.

The observation that benzyne adds to cyclopentadienylmagnesium bromide ("C_5H_5MgBr")[2] to give benzonorbornadien-9-ylmagnesium bromide[3] has stimulated investigation of the structure of cyclopentadienylmagnesium compounds. Ir and uv spectra of "C_5H_5MgBr" and "C_5H_5MgCl" and magnesium cyclopentadienide [$(C_5H_5)_2Mg$] in tetrahydrofuran (THF) indicated that the principal components of these compounds in solution all have magnesium atoms located on or near the C_5 axes of the cyclopentadienide ions.[4] They do not have carbon–magnesium σ bonds. X-Ray analysis proved that a solvated C_5H_5MgBr crystal had a similar structure,[5] and the crystallographic unit cell parameters of $(C_5H_5)_2Mg$ suggested that it was isostructural with ferrocene.[6] This spectroscopic and X-ray data, however, provide no clue as to the nature of aggregation of cyclopentadienylmagnesium compounds in solution.

In 1929 Schlenk[7] suggested that Grignard reagents were equilibrium mixtures as shown in eq 1, because

$$R_2Mg + MgX_2 \rightleftarrows 2RMgX \quad (1)$$

addition of dioxane to "RMgX" precipitated MgX_2. In spite of numerous attempts to detect Schlenk equilibria,[8] only recently has direct identification of RMgX and R_2Mg in solution by nmr established positions of equilibrium quantitatively.[9,10] Evans and Fazakerley[9] reported ^{19}F and ^1H spectra of RMgX and R_2Mg for over 20 different Grignard reagents and found the position of equilibrium to be highly dependent on the alkyl or aryl group and the solvent. Temperatures of −68° and below were needed to observe slow exchange pmr spectra of CH_3MgBr and $(CH_3)_2Mg$ in THF. A similar study of "C_5H_5MgCl" and "C_5H_5MgBr" in THF is reported here.

In an extension of our cycloaddition research benzyne was generated in solutions of several substituted "cyclo-

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(2) In this paper "C_5H_5MgBr" denotes cyclopentadienyl Grignard reagent without specification of its composition, and C_5H_5MgBr denotes cyclopentadienylmagnesium bromide, a specific component of the Schlenk equilibrium mixture.

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