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Carbenoids with Neighboring Heteroatoms. II. Stereoselective Synthesis and Nucleophilic Reactions of α-Halocyclopropyllithium Reagents[1a,b]

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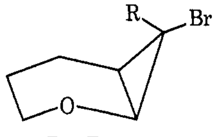
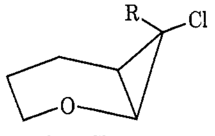
Exploratory investigations into the effect of neighboring n electron donors on the reactivity of carbenoid species were begun. The neighboring oxygen atoms in the 7,7-dihalo-2-oxabicyclo- and -3-oxabicyclo[4.1.0]heptyl ring systems were seen to direct halogen–metal interchange with methyl- and butyllithium to the more sterically hindered (endo) halogen. In addition, the neighboring oxygen stabilized the resulting α-halolithium compound toward α elimination rendering it useful as a nucleophilic reagent. This utility was investigated by reaction with the electrophiles H, D, benzophenone, benzaldehyde, phenyl isocyanate, methyl iodide, mercuric chloride, and carbon dioxide which afforded adducts **1c–h**, **2c–g**, **3**, **6c–f**, and **7d** in moderate to good yields. The 3-oxabicyclo[3.1.0]hexyl ring system was also investigated and found to yield the stable carbenoid **8b** but in low yield.

α-Halo organometallic compounds, particularly lithium reagents, are receiving increased attention both as proposed reactive intermediates in carbenoid reactions[2] and as synthetically useful organometallic reagents.[3] In brief summary, Miller and Whalen[2b] and Closs[2a,d] and Moss[2a] obtained firm evidence implicating α-haloalkyllithium compounds, not free carbenes, as the intermediates directly involved in cyclopropane formation when aryldihalo- and -polyhalomethanes were treated with alkyllithium reagents in the presence of olefins. The findings of Hoeg, Lusk, and Crumbliss[2c] essentially reinforced the conclusions of the previous authors regarding cyclopropane formation.[2e] In addition, they reported[2c] their discovery, made almost simultaneously with Köbrich,[3] that tetrahydrofuran solvent exhibited a marked stabilizing effect on α-haloalkyllithium compounds. Köbrich[3] has reported extensively on a variety of reactions of THF-stabilized lithium carbenoids. The direct intermediacy of lithium carbenoids in an intramolecular C–H insertion reaction has been indicated by the results of Goldstein and Dolbier[2f] who showed that the formation of hexadeuterated 1,1-dimethylcyclopropanes from 1-halo-2,2-di(methyl-d_3)-propyllithium was accompanied by a halogen-dependent (I, Br, Cl) deuterium isotope effect. Thus, the reactions of a number of the "carbenes" produced by α elimination are now attributable to organometallic compounds, and the study of such compounds has revealed that carbenoids can exhibit both nucleophilic and electrophilic reactivity. In this paper we discuss some exploratory work on the effect of oxygen as a neighboring n electron donor on carbenoid reactivity and report on a stereoselective synthesis of intramolecularly stabilized lithium carbenoids and some of their nucleophilic reactions. Their thermal and electrophilic reactions will be discussed at a later date.

The lithium carbenoids **1b**, **2b**, **6b**, **7b**, and **8b** were prepared by halogen–metal exchange between methyl- or butyllithium and the appropriate *gem*-dihalocyclopropane.[4] The dihalocyclopropanes were, with one exception, **1a**, distillable and obtainable in high purity from dihalocarbene additions to the corresponding ole-



1a, R = Br
b, R = Li
c, R = H
d, R = D
e, R = $(C_6H_5)_2COH$
f, R = C_6H_5NHCO
g, R = CH_3
h, R = Hg
i, R = COOH



2a, R = Cl
b, R = Li
c, R = H
d, R = D
e, R = $(C_6H_5)_2COH$
f, R = C_6H_5NHCO
g, R = Hg
h, R = COOH

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[1] (a) Supported in part by Grant 970-G1 from the Petroleum Research Fund administered by the American Chemical Society. (b) Part I: K. G. Taylor and W. E. Hobbs, *Tetrahedron Lett.*, 1221 (1968), a preliminary account. (c) National Aeronautics and Space Administration Trainee, 1966–1968.

[2] (a) G. L. Closs and R. A. Moss, *J. Amer. Chem. Soc.*, **86**, 4042 (1964). (b) W. T. Miller and D. M. Whalen, *ibid.*, **86**, 2089 (1964). (c) D. F. Hoeg, D. I. Lusk, and A. L. Crumbliss, *ibid.*, **87**, 4147 (1965). (d) G. L. Closs, presented at the 20th National Organic Chemistry Symposium of the American Chemical Society, Burlington, Vt., June 1967, Abstracts, p 57. (e) Recent evidence indicates that free dichlorocarbene, however, is involved in electrophilic reactions of trichloromethyllithium: G. Köbrich, H. Büttner, and E. Wagner, *Angew. Chem., Int. Ed. Engl.*, **9**, 169 (1970). (f) M. J. Goldstein and W. R. Dolbier, *J. Amer. Chem. Soc.*, **87**, 2293 (1965).

[3] (a) G. Köbrich, *Angew. Chem., Int. Ed. Engl.*, **6**, 41 (1967), a review; (b) G. Köbrich and H. Büttner, *Tetrahedron*, **25**, 2223 (1969), a recent leading reference.

[4] W. R. Moore and H. R. Ward, *J. Amer. Chem. Soc.*, **82**, 6200 (1960).

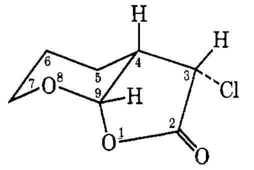
fin. Compound **1a** could not survive distillation but could be purified by column chromatography and low-temperature crystallization.

The 2-Oxabicyclo[4.1.0]heptyl System.—Some of the chemistry of **1b** was the subject of a preliminary communication[1b] and can be summarized as follows. The reaction of **1a** with ethereal methyllithium at −80 or −20° proceeded *via* exchange of the endo bromine giving **1b** in high yield as evidenced by the formation of **1c** or **1d** upon water or deuterium oxide quench, respectively. The stereochemistry of **1c** and **1d** was deduced from features of their nmr spectra. For **1c**, the C-7 H was a quartet at δ 2.83 with two trans couplings[5] (1.3 and 5.0 Hz) and the C-1 H was also a quartet, at δ 3.78 with a cis (8.0 Hz) and a trans (1.3 Hz) coupling. In the spectrum for **1d**, with the C-7 H signal gone, the C-1 H signal remained at δ 3.78 (indicating the same stereochemistry for Br) and was a sharp doublet with $J = 8.0$ Hz (loss of trans coupling). At −80°, **1c** was formed in 95% yield (by vpc) and could be isolated by distillation in 78% yield. At −20° the yield of **1c** was 60–70% by vpc (55% isolated). The above results indicated the presence of **1b** in the reaction mixture as a stable entity, and facets of its nucleophilic utility were studied. Reaction of **1b** with benzophenone, phenyl isocyanate, methyl iodide, and mercuric chloride gave **1e** (75%), **1f** (37%), **1g** (~90%), and **1h** (10%), respectively, with yields as indicated in parentheses. The ir spectrum of **1e** showed an intramolecularly hydrogen-bonded OH thereby confirming the expected endo configuration for the diphenylcarbinol moiety. The reduced yield of **1c** at −20° as opposed to −80° may reflect either thermal instability of **1b** or a decrease in the stereoselectivity of the exchange reaction with increasing temperature.

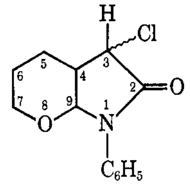
The chemistry of the chloro carbenoid **2b** was similar to that of **1b**. It was prepared from the known[6] **2a** by exchange with ethereal butyllithium at −20°. Water quench of **2b** afforded the known[6,7] monochloro derivative **2c** in 70% yield, and a deuterium oxide quench gave **2d**. Again, reaction of **2b** with benzophenone, phenyl isocyanate, and mercuric chloride gave the products **2e** (56%), **2f** (69%), and **2g** (2%), respectively.

Carbonation of **2b** gave an unexpected result in that a neutral product, lactone **3**, was isolated from the reaction after work-up.

The structure and stereochemistry of **3** rests on the following data and reasoning. Elemental analysis indicated **3** to be isomeric with the anticipated acid **2h**. The ir spectrum of **3** had a strong band at 1780 cm^{-1} consistent with the presence of a γ lactone (1770 cm^{-1}) bearing an α-chloro group (+10 to 40 cm^{-1}).[8] The nmr signals could be assigned as follows: C-9, doublet ($J = 4.0$ cps), 1 H at δ 5.79; C-3, doublet ($J = 6.5$ cps), 1 H at 4.78; C-7, multiplet, 2 H centered at 3.83. The presence of a potential aldehyde function in **3** was indicated by a positive test using acidic dinitrophenylhydrazine reagent. Further, a cis ring juncture was indicated by the coupling constant (4.0 cps) of the C-9 proton located at that potential aldehyde site. An axial orientation for the lactone oxygen would be predicted on the basis of the relative conformational energies of an oxygen function as opposed to a carbon function attached to a six-membered ring.[9] Such a prediction found support in the ir spectrum of **3** which showed bands at 1160 (strong) and 1130 cm^{-1} (weak). Exactly this type of C–O stretch is seen in carbohydrate derivatives bearing axial C-1 acetate groups.[10] Inspection of a Dreiding model of **3** in the conformation shown revealed that an exo hydrogen (endo chlorine) at position 3 has an H-3–H-4 dihedral angle close to 30° which would predict a coupling constant close to 6.5 Hz, the experimental value. Conversely, an endo hydrogen (exo chlorine) at that position should have a dihedral angle of about 90° and, as a result, a coupling constant close to 0 Hz.



3



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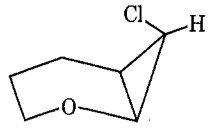

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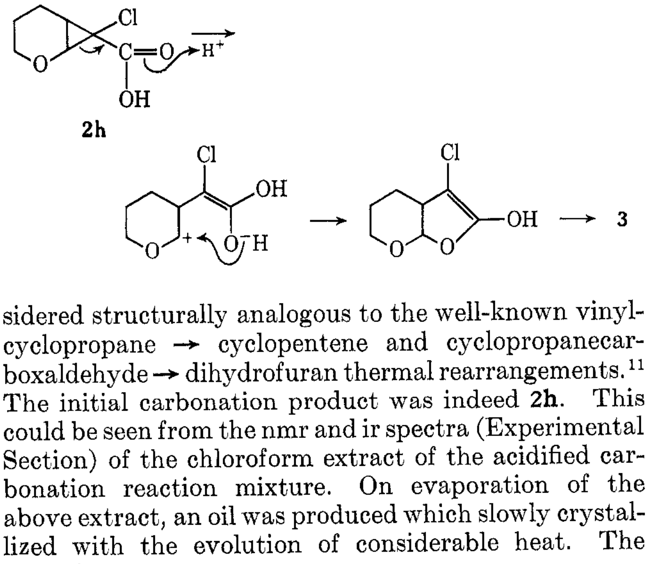
The lactone **3** can be envisioned as arising *via* a rearrangement of the initial carbonation product, acid **2h**, as shown in Scheme I. Such a pathway might be considered structurally analogous to the well-known vinylcyclopropane → cyclopentene and cyclopropanecarboxaldehyde → dihydrofuran thermal rearrangements.[11] The initial carbonation product was indeed **2h**. This could be seen from the nmr and ir spectra (Experimental Section) of the chloroform extract of the acidified carbonation reaction mixture. On evaporation of the above extract, an oil was produced which slowly crystallized with the evolution of considerable heat. The crystals were **3**.

SCHEME I



Carbonation of the bromo carbenoid **1b** also produced an acidic oil which crystallized (mp 57–59°). The oil

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[5] W. G. Dauben and T. Wipke, *J. Org. Chem.*, **32**, 2976 (1967); K. B. Wiberg and B. J. Nist, *J. Amer. Chem. Soc.*, **85**, 2788 (1963).

[6] W. E. Parham and E. E. Schweizer, *ibid.*, **82**, 4085 (1960).

[7] T. Ando, H. Yamanoka, and W. Funasaka, *Tetrahedron Lett.*, 2587 (1967), reports nmr data which shows that the chlorine atom of **2c** is exo. This is a reversal of the endo assignment originally made (without nmr) by Parham and Schweizer.[6]

[8] K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, San Francisco, Calif., 1962, p 44.

[9] E. Eliel, N. Allinger, S. Angyal, and G. Morrison, "Conformational Analysis," Wiley, New York, N. Y., 1965, p 436.

[10] Reference 9, p 396.

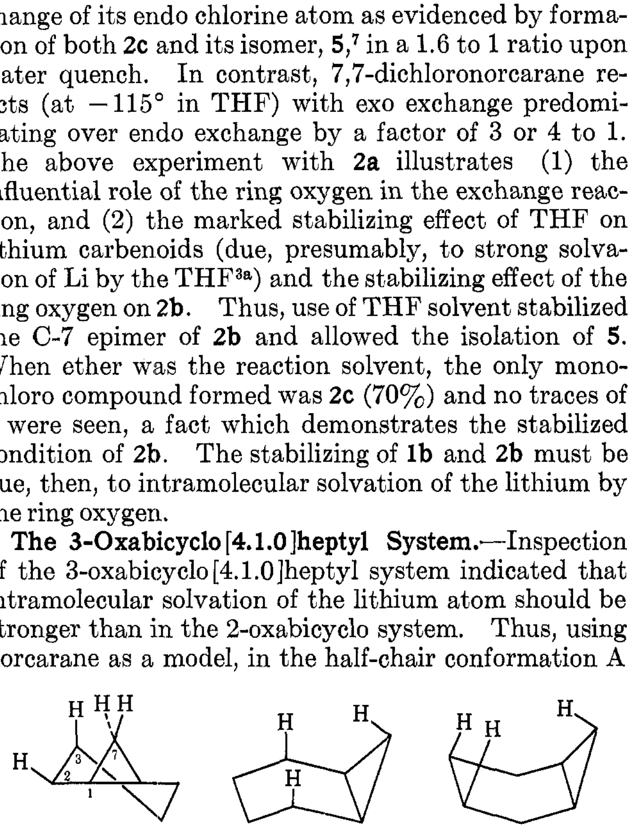
[11] R. Breslow in "Molecular Rearrangements," Vol. I, P. De Mayo, Ed., Wiley-Interscience, New York, N. Y., 1963, pp 236–239.

had ir features similar to those of **2h**, and the crystals had ir and nmr features similar to **3**. The crystals readily liberated HBr at room temperature and decomposition occurred while taking spectra. The crystals had been assigned structure **1h** in ref 1b prior to starting work on **2b**.

Interestingly, the anilide **2f** also appeared to rearrange under mild conditions. Thus, either warming a $CDCl_3$ solution of **2f** in the nmr probe or letting a chloroform solution of **2f** containing a trace of acid stand at room temperature resulted in the formation of a new product which can be formulated as **4** (or its isomeric iminolactone). Only spectral characterization is available for **4**: ir 1703 cm^{-1} consistent with an α-chloro-γ-lactam;[8] nmr loss of the NH proton seen at δ 8.24 in **2f**; appearance of signals of δ 5.9, 5.4, and 2.7 which could be assigned to the C-9, C-3, and C-4 protons of **4**, respectively. All attempts to purify **4** by recrystallization, column chromatography, or preparative tlc were unsuccessful. On one attempt to chromatograph **4** over silica gel a 15% yield of lactone **3** was obtained as the only pure component.

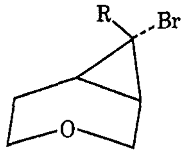
A brief study of the exchange reaction of **2a** with butyllithium in tetrahydrofuran solvent was done to allow a comparison with results in the 7,7-dichloronorcarane system studied by Köbrich and Goyert.[12] At both −20 and −80°, **2a** reacted with predominate exchange of its endo chlorine atom as evidenced by formation of both **2c** and its isomer, **5**,[7] in a 1.6 to 1 ratio upon water quench. In contrast, 7,7-dichloronorcarane reacts (at −115° in THF) with exo exchange predominating over endo exchange by a factor of 3 or 4 to 1. The above experiment with **2a** illustrates (1) the influential role of the ring oxygen in the exchange reaction, and (2) the marked stabilizing effect of THF on lithium carbenoids (due, presumably, to strong solvation of Li by the THF[3a]) and the stabilizing effect of the ring oxygen on **2b**. Thus, use of THF solvent stabilized the C-7 epimer of **2b** and allowed the isolation of **5**. When ether was the reaction solvent, the only monochloro compound formed was **2c** (70%) and no traces of **5** were seen, a fact which demonstrates the stabilized condition of **2b**. The stabilizing of **1b** and **2b** must be due, then, to intramolecular solvation of the lithium by the ring oxygen.

The 3-Oxabicyclo[4.1.0]heptyl System.—Inspection of the 3-oxabicyclo[4.1.0]heptyl system indicated that intramolecular solvation of the lithium atom should be stronger than in the 2-oxabicyclo system. Thus, using norcarane as a model, in the half-chair conformation A

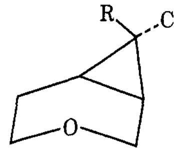


A B C

the C-7 and C-3 hydrogens can approach each other to within 2.1 Å without undue strain. In the same conformation the C-7 and C-2 hydrogens can approach to within 2.4 Å. Further, in the boat (or twist boat) form B, the C-7–C-2 hydrogen distance can shorten to about 2.2 Å, while in the boat form C, the C-7–C-3 hydrogen distance can be as short as 1.9 Å. The above would indicate that the oxygen n electrons in the 3-oxa system have a more favorable bonding distance and geometry for coordination with the C-7 lithium than would the oxygen n electrons of the 2-oxa system. It was deemed of interest, then, to determine what reactivity changes in the carbenoid would, in fact, result from this relatively minor structural change.



6a, R = Br
b, R = Li
c, R = H
d, R = D
e, R = C_6H_5CHOH
f, R = COOH



7a, R = Cl
b, R = Li
c, R = H
d, R = COOH

The stoichiometry of the exchange reaction of dibromocyclopropane **6a** with methyllithium was seen to change with change in reaction solvent. In ether solvent (at −80°) 1 equiv of methyllithium was sufficient to consume all of **6a**. In pentane, however, use of 1 equiv of methyllithium[13] for as long as 1.5 hr left 30% of starting **6a** unreacted. Use of 1.7 equiv of methyllithium reduced the amount of unreacted **6a** to about 10% and 2.0–2.5 equiv of methyllithium proved to be a practical quantity which ensured complete reaction of **6a**. On going from ether to pentane, the yield of the monobromo **6c** (obtained from a water quench of **6b**) increased from 60% by vpc (47% isolated) to 91% by vpc. In a like manner, the yield of carbonation product **6f** increased from 54 to 65%. Often, in practice, a 3:2 pentane–ether mixture, which gave good solubility for starting **6a**, a high yield of **6b**, and 1:1 stoichiometry for the exchange reaction, was used. These yield increases can logically be attributed to an increase in stereoselectivity in the exchange reaction in pentane solvent where the directing influence of the ring oxygen of **6a** would be more important. The change in stoichiometry with change in solvent requires a longer explanation. The following experiments were conducted to shed some light on the nature of the required second equivalent of methyllithium. The reaction of **6b** in ether–pentane (stoichiometry 1:1) with 1 equiv of benzaldehyde afforded the carbinol **6e** as a mixture of diastereomers in 40% yield. In pentane (stoichiometry 2:1), successive treatment of **6a** with 2.5 equiv of methyllithium and 2 equiv of benzaldehyde gave approximately equal amounts of carbinol **6e** and 1-phenylethanol. In addition, successive treatment of **6a** with 2.0 equiv of methyllithium, 1.0 equiv of water, and 1.0 equiv of benzaldehyde yielded (by vpc) about 50% of the monobromo **6c**, about 33% of 1-phenylethanol, and only 0–2% of carbinol **6e**. The above experiments showed that the second mole of methyllithium required for the exchange reaction in pentane was still reactive toward the electrophile benzaldehyde and apparently less reactive (less basic?) toward water than the carbenoid **6b**. The carbenoid **6b** appears insoluble in pentane at −80°, and most likely the second methyllithium is coordinated with it as **6b** precipitates from solution.

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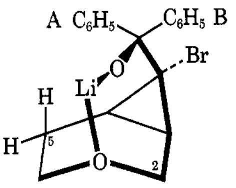
[12] G. Köbrich and W. Goyert, *Tetrahedron*, **24**, 4327 (1968).

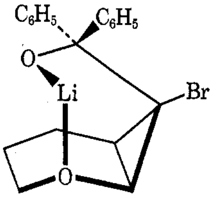
[13] Commercial methyllithium–lithium bromide 1.2 *M* in ether was used; hence, small amounts of ether were always present.

In ether wherein the carbenoid is soluble, the solvent may play the solvating role that methyllithium does in pentane.

Perhaps the most dramatic reactivity difference between **1b** and **6b** was seen in their reactivity toward benzophenone. While **1b** reacted smoothly at -80° to give **1e** in 63% yield, **6b** *failed* to react with benzophenone under a wide variety of concentration, solvent, and temperature conditions with side reactions, one of which was hydrogen abstraction, consuming **6b**.[14] The reasons for this failure must be steric in origin since, as mentioned above, **6b** reacted readily with benzaldehyde to yield **6e**. The failure of **6b** to react with benzophenone is striking when it is recalled that alkyllithium reagents have been seen to react $\sim 10^3$ times faster with ketones than Grignard reagents,[15] and also that ethereal *tert*-butyllithium affords an 81% yield of tri-*tert*-butylcarbinol upon reaction with hexamethylacetone at -65°.[16] If the assumptions are made that the addition step of **6b** to benzophenone is irreversible and that the lithium atom of **6b** (and **1b**) remains bonded to the ring oxygen in the transition state,[17] then the following might be suggested as an explanation for the reactivity difference between **6b** and **1b**. Using Drieding models to approximate the structure of the addition product, I,



I

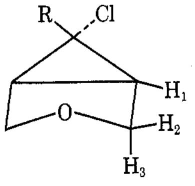


II

of **6b** and benzophenone, the geometry of the seven-membered ring which incorporates the OLi–O link forces phenyl A over the pyran ring to within about 1.7 Å of H-5 (or phenyl B to within about 1.6 Å of H-2 if the 7-ring is inverted) and causes phenyl B to almost eclipse the bromine.[20] The six-membered OLi–O-containing ring in II, conversely, allows the two phenyls and the bromine to be staggered, and neither phenyl is forced over the pyran ring. Thus, if the unfavorable steric factors seen in I build up in the transition state leading to it, the rate of addition of **6b** may be retarded to the point where other reactions[22] of **6b** compete successfully.

The preparation and reactions of the chloro carbenoid **7b** were only briefly investigated because the exchange reaction of **7a** with butyllithium proved quite complex with butyl groups becoming incorporated into several of the products formed. In fact, the monochloro derivative **7c**, although identifiable by nmr, could not be purified due to a butyl-containing impurity with a very similar vpc retention time. Carbonation of **7b**, however, gave the carboxylic acid **7d** in 40% yield.

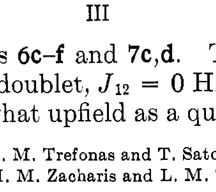
The 3-Oxabicyclo[3.1.0]hexyl System.—Again, the chemistry of carbenoid **8b** was studied only briefly due



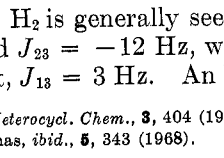
8a, R = Cl
b, R = Li
c, R = H
d, R = COOH

to the relative tediousness in obtaining the known **8a** in sufficient quantity and purity and due to the complex nature of its reactions with butyllithium. A water quench of a preparation of **8b** in ether at -80°, however, did afford **8c**, readily identified by its C-6 H nmr signal at δ 2.88 (triplet, $J_{\text{trans}} = 2.5$ Hz) but only in about 10% yield (starting material remained and butyl-containing products were beginning to form). Carbonation of a similar preparation of **8b** yielded the carboxylic acid **8d** in 9% yield.

Nmr Spectra.—The nmr spectra of the 3-oxabicyclo systems had some common features which bear further comment on two aspects. First, the nmr spectra of **8c** and **8d** were more consistent with a boat, rather than chair, conformation for those compounds. Thus, one hydrogen on C-2 was seen as a sharp doublet with $J_{\text{gem}} = -9.0$ Hz and $J_{21} = 0$ Hz indicating a vicinal dihedral angle close to 90°. In a boat conformation the H_2 hydrogen describes such an angle with H_1, and in this conformation better staggering of the vicinal C–H's and cyclopropane C–C bonds occurs. In a chair conformation no 90° dihedral angle occurs and eclipsing exists between H_2 and the vicinal (banana) bonds of the cyclopropane ring, and between H_3 and H_1. Boat conformations have been observed for the 3-oxa-6-azabicyclo[3.1.0]hexane[23] and 6-azabicyclo[3.1.0]hexane[24] ring systems in the solid state. A similar analysis allows the assignment of half-chair conformation III rather than IV as the predominate one for the compounds **6c–f** and **7c,d**. Thus H_2 is generally seen as a sharp doublet, $J_{12} = 0$ Hz and $J_{23} = -12$ Hz, with H_3 somewhat upfield as a quartet, $J_{13} = 3$ Hz. An H_1–H_2



III



IV

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[14] In one of seven attempts, a 0.7% yield of a product, mp 91–93°, was obtained whose faint nmr was not inconsistent with that expected for the desired carbinol product.

[15] S. G. Smith, *Tetrahedron Lett.*, 6075 (1966).

[16] P. D. Bartlett and E. B. Lefferts, *J. Amer. Chem. Soc.*, **77**, 2804 (1955).

[17] These assumptions appear intuitively valid but their importance to the success of the reaction with benzophenone can only, at present, be suggested. These suggestions, however, imply an additional significant role for basic solvents in the usual organolithium reactions, besides that of assistance in RLi aggregate dissociation,[18] and charge-transfer support in a one-electron process.[19]

[18] T. L. Brown, *Advan. Organometal. Chem.*, **3**, 392 (1966).

[19] C. G. Screttas and J. F. Eastham, *J. Amer. Chem. Soc.*, **88**, 5668 (1966).

[20] An O–Li distance of 1.9 Å and O–Li–O angles of 100 and 109° were used.[21] The basic geometry of the tricyclic systems of I and II is relatively insensitive to these factors and the nonbonded interactions mentioned above cannot be relieved without imparting angle strain to the framework of the 3-oxabicyclo[4.1.0]heptane system.

[21] P. J. Wheatley, *Nature*, **185**, 681 (1960), reports for lithium methoxide a four-coordinate lithium with Li–O distance of 1.95 Å and O–Li–O angles of 131.7 and 101.7°.

[22] To be reported at a later date.

[23] L. M. Trefonas and T. Sato, *J. Heterocycl. Chem.*, **3**, 404 (1966).

[24] H. M. Zacharis and L. M. Trefonas, *ibid.*, **5**, 343 (1968).

dihedral angle approaching 80° can be accommodated in chair III, but not in chair IV, without increase in nonbonded interactions.

The second feature of the nmr spectra of the 3-oxabicyclo systems that was somewhat unusual was the chemical shift changes of H_2 and H_3 that occurred upon changing the substitution on the cyclopropane ring. As can be seen from Table I, when the substituents on the cyclopropane methylene group were both halogen (**6a**, **7a**, **8a**), the chemical shifts of H_2 and H_3 were nearly identical, with the signal appearing as a sharp narrowly spaced doublet, or, as in the case of **9a**, a narrow triplet (half-height width, 6 Hz). This held true, also, when the substituents were both hydrogen. In the case of 3-oxabicyclo[4.1.0]heptane (**9**), the signal was a narrow doublet, and for 3-oxabicyclo[3.1.0]hexane (**10**),[25] the signal was reported as a narrow quartet. However, when the substituents were not identical, as exemplified by the monohalo compounds **6c**, **7c**, and **8c**, H_2 always appeared distinctly downfield from H_3. In another way of looking at the data of Table I, when the endo halogen was replaced by hydrogen, it was H_3, the hydrogen further removed from the substituent change, which was affected the most. An attempt was made to calculate the H_2–H_3 chemical-shift difference, by methods previously used with some success by others, to see if the observed shifts could easily be accounted for.

TABLE I

CHEMICAL SHIFTS (δ) OF H_2 AND H_3 IN THE 3-OXABICYCLO[*n*.1.0] RING SYSTEMS

Compd	H_2		H_3	Δδ H_3–H_2
9[a]		3.77		~0
6a[a]		~3.98		<0.06
6c[a]	4.08		3.77	0.31
7a[b]		4.08		~0
7c[a]	4.09		3.78	0.31
10[c]	3.54		3.41	0.13
8a[d,e]		~4.17		~0
8c[d]	4.08		3.79	0.28

[a] CCl_4 solvent, internal TMS. [b] Neat, external TMS. [c] Taken from ref 25, in CCl_4. [d] $CDCl_3$ solvent, internal TMS. [e] In CCl_4, δ 4.08; ref 25.

Using the method of Tori and Kitahonoki,[26] the shielding effect of the cyclopropane ring on H_2 and H_3 of **9** and **10** was calculated. For conformation III of **9** and the boat form of **10**, H_2–H_3 differences of δ 0.28 and 0.34, respectively, were calculated with H_3 predicted to be downfield from H_2. The effect of a neighboring ether oxygen atom cannot be reliably calculated,[27] but it can be predicted from data from numerous sources[28] that H_3, anti to a nonbonding electron pair of oxygen in the conformations chosen, should be shifted upfield relative to H_2. To fit the observed spectra, the compensating upfield shifts needed to offset the calculated effect of the cyclopropane ring are about δ 0.30 for H_3 of **9** and about δ 0.45 for H_3 of **10**, values which are well within the usually observed range of δ 0.20–0.5.[27,28] By way of contrast, for conformation IV of **9** and the chair form of **10**, H_2–H_3 shift differences due to the cyclopropane ring of δ 1.31 and 1.07, respectively, are calculated. Here, again, H_3 is predicted to be downfield from H_2, and this difference should be accentuated rather than cancelled by the effect of the neighboring oxygen since H_2 is now anti to a nonbonding electron pair. Thus, the observed similarity in chemical shifts for H_2 and H_3 of **9** and **10** can be readily rationalized on the basis of conformation III for **9** and a boat for **10**.

On the basis of the above, it would appear to follow that the observed H_2–H_3 shift differences in **6c**, **7c**, and **8c** should be attributable to the effect of the exo halogen. Zürcher[29] has, with some success, calculated the chemical-shift changes of methyl groups in rigid, aliphatic molecules. He found that, in the compounds studied, changes induced by the neighboring chlorine could be satisfactorily accounted for on the basis of electrical effects alone. Calculations by the method of Zürcher, when applied to conformation III of **6c** and the boat form of **8c**, predicted that H_2 and H_3 should be deshielded by the chlorine substituent to practically the same extent (δ 0.18–0.20) and consequently should differ in chemical shift by only δ 0.02 in both compounds. Assuming conformation IV for **6c** and a chair for **8c** yielded different predictions but no better a correlation. A number of reasons could be cited for the above failure of Zürcher's method. Further comment, however, should be reserved until further work, such as variable temperature nmr studies, testing the flexibility of **6c** and **8c** is done.

Experimental Section

General.—All melting points were taken on a Thomas–Hoover melting point apparatus and are uncorrected. Vpc analyses were performed on an F & M Scientific Corp. instrument, Model 5750, fitted with a flame ionization detector, or Model 700, fitted with a thermal conductivity detector. The following columns were used: A, 15% polytetramethylene ether glycol 3000 on Chromosorb G-NAW; B, 10% Carbowax 20M on Chromosorb G-NAW; C, 2% polytetramethylene ether glycol on Chromosorb G-NAW; D, 10% silicone rubber UCW 98 on Chromosorb G-NAW; E, 2% silicone rubber UCW 98 on Chromosorb G-NAW; F, 2% silicone rubber UCW 98 on Diatoport S; G, 5% ethylene glycol adipate on Diatoport S; H, 20% SE 52 silicone on Chromosorb G-NAW. When necessary, peak identification was done by spiking with known compounds. Nmr spectra were obtained with a Varian Associates A-60A spectrometer with tetramethylsilane as an internal standard and, unless otherwise specified, deuteriochloroform was the solvent. Infrared spectra were determined on a Perkin-Elmer Model 337 grating spectrophotometer. Ultraviolet spectra were obtained with a Cary Model 14 spectrophotometer in 95% ethanol. Elemental analyses were performed as direct analyses by Midwest Microlab, Inc., Indianapolis, Ind.

All the reactions which involved the use of potassium metal, carbene addition, or the use of alkyllithium reagents were conducted in an atmosphere of dry nitrogen. The methyllithium and butyllithium reagents were titrated when required by the method of Gilman and Haubein substituting ethylene dibromide for benzyl chloride.[30]

7,7-Dibromo-2-oxabicyclo[4.1.0]heptane (1a).—To 250 ml of *tert*-butyl alcohol (distilled from sodium) was added 8.6 g (0.22 g-atom) of potassium. The mixture was heated until dissolution occurred. The excess *tert*-butyl alcohol was removed *in*

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[25] T. Shono, A. Oku, T. Morikawa, M. Kimura, and R. Oda, *Bull. Chem. Soc. Jap.*, **38**, 940 (1965).

[26] K. Tori and K. Kitahonoki, *J. Amer. Chem. Soc.*, **87**, 386 (1965).

[27] L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1969, pp 80–81.

[28] (a) C. Altona and E. Havinga, *Tetrahedron*, **22**, 2275 (1966); (b) C. B. Anderson and D. T. Sepp, *ibid.*, **24**, 1707 (1968); (c) D. T. Sepp and C. B. Anderson, *ibid.*, **24**, 6873 (1968); (d) F. W. Nader and E. L. Eliel, *J. Amer. Chem. Soc.*, **92**, 3050 (1970), and references therein; (e) L. D. Hall, *Tetrahedron Lett.*, 1457 (1964).

[29] R. F. Zürcher in "Progress in Nuclear Magnetic Resonance Spectroscopy," Vol. 2, J. W. Emsley, J. Feeny, and L. H. Sutcliffe, Ed., Pergamon Press, New York, N. Y., 1967, Chapter 5.

[30] H. Gilman and A. H. Haubein, *J. Amer. Chem. Soc.*, **66**, 1515 (1944).

vacuo with mild heating. The remaining potassium *tert*-butoxide was broken up and 25.22 g (0.3 mol) of 3,4-dihydro-2*H*-pyran in 90 ml of pentane was added. The resulting slurry was cooled to −20° (ice–acetone) and 38.4 g (0.15 mol) of bromoform in 75 ml of pentane was added dropwise over a period of 1 hr. The mixture was stirred an additional hour at −20° and quenched with water. The organic layer was washed with two portions of water, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was evacuated to 0.8 mm and heated (50–60°) until vigorous boiling occurred. The heating bath was removed and the compound was allowed to cool under reduced pressure. The remaining yellow oil was dissolved in pentane and passed over a column (40.0 g) of neutral alumina. The first 150 ml of eluent was collected and concentrated *in vacuo*. This yielded 28.8 g (75%) of a clear colorless oil: $n^{27}D$ 1.5514; nmr δ 3.84 (d, J = 8.0 Hz, H_1), 3.57 (m, CH_2O), 1.67 (m, 5 H).

It was subsequently found that this compound could be purified by low-temperature (−80°) recrystallization from pentane in about a 40.0% yield. The recrystallized material when stored at −20° was a white crystalline solid and appeared to be stable indefinitely at that temperature.

exo-**7-Bromo-2-oxabicyclo[4.1.0]heptane (1c).**—To a cooled (−20°) solution of 10.0 g (38.4 mmol) of **1a** in 150 ml of ether was added methyllithium–lithium bromide (55.5 mmol) during a period of 30 min. The solution was stirred for an additional 15 min and quenched by the slow addition of water. The organic layer was washed with two portions of water, dried ($MgSO_4$), and concentrated *in vacuo* (the usual work-up). This yielded a yellow oil. Distillation gave 3.97 g (55.5%) of **1c**: bp 58–61.5° (0.32 mm); ir (neat) 3050 cm^{-1} (-CH, cyclopropane); nmr δ 3.78 (q, J = 1.3 and 8.0 Hz, H_1), 3.4 (m, $-CH_2O-$), 2.83 (q, J = 1.3 and 5.0 Hz, H_7), 1.8 (m, 5 H); d^{27}_4 1.55.

When the above procedure was repeated at −80° using 5.0 g of **1a**, the isolated yield was 77.8%.

The yield at −20° was determined by vpc (column A, 6 ft × 0.25 in.), using ethylene glycol as an internal standard, to be 62.0%. At −80° the yield was 95.0%.

Anal. Calcd for C_6H_9BrO: C, 40.70; H, 5.12; Br, 45.13; O, 9.03. Found: C, 40.99; H, 5.12; O, 9.28.

exo-**7-Bromo-***endo***-7-deuterio-2-oxabicyclo[4.1.0]heptane (1d).**—The above procedure was repeated and quenched by the slow addition of deuterium oxide (99.8%). The major component was collected from preparative vpc (column A, 6 ft × 0.25 in.): ir (neat) 2270 cm^{-1} (w) (C–D); the 3050 cm^{-1} (w) (CH, cyclopropane) absorption which was present in **1c** was absent; nmr δ 3.78 (d, J = 8.0 Hz, H_1), 3.57 (m, $-CH_2O-$), 1.67 (m, 5 H).

exo-**7-Bromo-***endo***-7-(diphenylmethanol)-2-oxabicyclo[4.1.0]heptane (1e).**—To a cooled (−80°) solution of 4.0 g (15.64 mmol) of **1a** in 60 ml of ether was added methyllithium–lithium bromide (15.64 mmol) during a period of 15 min. A precipitate formed after about 3 min and the slurry was stirred for an additional 7 min. After this period 2.84 g (15.64 mmol) of benzophenone dissolved in 20 ml of ether was added. The reaction mixture was stirred 1 hr at −80° and quenched by addition of methanol. The usual work-up yielded a clear colorless oil which crystallized on standing. Recrystallization from methanol yielded 4.20 g (75.0%) of white prisms: mp 88–90.0°; ir (CCl_4) 3450 cm^{-1} (OH) which did not change upon dilution; nmr (CCl_4) δ 7.4 (m, phenyl H), 4.33 (s, -OH), 4.05 (d, J = 7.0 Hz, H_1), 3.58 (m, CH_2O), 1.64 (m, 5 H).

Anal. Calcd for $C_{19}H_{19}BrO_2$: C, 63.51; H, 5.33; O, 8.90. Found: C, 63.66; H, 5.45; O, 8.83.

exo-**7-Bromo-***endo***-7-(***N***-phenylcarboxamido)-2-oxabicyclo-[4.1.0]heptane (1f).**—To a cooled (−80°) solution of 4.0 g (15.64 mmol) of **1a** in 60 ml of ether was added methyllithium–lithium bromide (15.64 mmol) during a period of 15 min. The mixture was stirred for an additional 10 min and 1.86 g (15.64 mmol) of phenyl isocyanate in 20 ml of ether was added. The mixture was stirred at −80° for 1 hr and quenched by addition of methanol. The reaction mixture was filtered to yield a white microcrystalline solid. The usual work-up yielded an additional amount of white solid. Recrystallization of the combined solids from methanol yielded 1.73 g (37.4%) of white needles: mp 112.5–113°; ir ($CHCl_3$) 3400 and 3350 (broad) (-NH-), 1680 and 1600 cm^{-1} (amide I and II); nmr δ 8.1 (broad, NH), 7.39 (m, phenyl), 4.05 (d, J = 7.5 Hz, H_1), 3.64 (m, CH_2O), 1.34 (m, 5 H).

Anal. Calcd for $C_{13}H_{14}BrNO_2$: C, 52.70; H, 4.77; O, 10.80. Found: C, 52.89; H, 4.73; O, 10.89.

exo-**7-Bromo-2-oxabicyclo[4.1.0]heptyl-***endo***-7-carboxylic Acid (1i).**—To a cooled (−80°) solution of 4.14 g (16.2 mmol) of **1a** in 60 ml of ether was added methyllithium–lithium bromide (16.8 mmol) during a period of 10 min. The solution was stirred for an additional 10 min and dry carbon dioxide was passed into the stirred solution for a period of 1 hr. The reaction was quenched by the addition of methanol. After it was washed with ether the basic water layer was acidified with concentrated hydrochloric acid and extracted with ether. The ether extracts of the acidic layer were dried ($MgSO_4$) and concentrated *in vacuo* to yield an oil [ir (neat) 3600–2300 (OH) and 1698 cm^{-1} (C=O)] which crystallized to a white solid. Recrystallization from cold benzene–hexane yielded 3.14 g (87.5%) of white crystals: mp 57.5–59.5°; ir (KBr) 1750 cm^{-1} broad (C=O); nmr δ 1.7, 2.6, 3.9, 5.7, and 6.9. The compound was too unstable for further characterization.

exo-**7-Bromo-***endo***-7-methyl-2-oxabicyclo[4.1.0]heptane (1g).**—To a cooled (−80°) solution of 1.3 g (5.12 mmol) of **1a** in 20 ml of ether was added methyllithium–lithium bromide (5.2 mmol) during a period of 10 min. The mixture was stirred for an additional 10 min and 5.7 g (40 mmol) of methyl iodide in 20 ml of ether was added. The bath was removed and the solution was allowed to attain 25°. The solution was stirred at 25° for a period of 1 hr and quenched with water. The usual work-up gave a major component which was collected from preparative vpc (column H, 6 ft × 0.25 in.). The yield was about 90.0% as estimated from vpc: nmr δ 3.82 (d, J = 8.0 Hz, H_1), 3.52 (m, CH_2O), 1.79 (s, CH_3), 1.88 (m, 5 H).

Anal. Calcd for $C_7H_{11}BrO$: C, 44.00; H, 5.80; O, 8.37. Found: C, 44.22; H, 5.78; O, 8.60.

2-Oxabicyclo[4.1.0]heptane (9). A. From 2a.—To a cooled (−80°) mixture of 5.0 g (0.22 g-atom) of sodium in 60 ml of liquid ammonia was added 5.96 g (35.7 mmol) of **2a** in 20 ml of ether during a period of 2 hr. The bath was removed and the ammonia allowed to evaporate. An additional 50 ml of ether was added followed by the careful addition of 2 ml of ethanol. Decomposition was completed by addition of ammonium chloride. The usual work-up gave a major component which was collected from preparative vpc (column A, 6 ft × 0.25 in.): $n^{25}D$ 1.4489 (lit.[19] $n^{25}D$ 1.4488); the ir was identical with that of the published spectrum;[19] nmr δ 3.42 (m, 3 H), 1.84 (m, 2 H), 1.41 (m, 2 H), 0.72 (m, 3 H).

B. From 1a.—From 3 g (0.13 g-atom) of sodium, 35 ml of liquid ammonia, and 3.0 g (11.7 mmol) of **1a** in 20 ml of ether at −80° was obtained **9** as the major component of the reaction, collected from preparative vpc (column H, 6 ft × 0.25 in.). The ir of **9** was identical with that of **9** obtained from the reduction of **2a**.

C. From 1c.—From 0.5 g (21.7 g-atom) of sodium in 10 ml of liquid ammonia and 0.39 g (2.22 mmol) of **1c** in 10 ml of ether at −80°, **9** was obtained and was collected from preparative vpc (column H, 6 ft × 0.25 in.). The ir of **9** was identical with that of **9** obtained from the reduction of **2a**.

Bis{*endo***-7-(***exo***-7-bromo-2-oxabicyclo[4.1.0]heptyl)}mercury (1h).**—To a cooled (−80°) solution of 0.5 g (1.9 mmol) of **1a** in 8 ml of ether was added methyllithium–lithium bromide (2.0 mmol) during a period of 5 min. The mixture was stirred for an additional 10 min and 0.26 g (0.97 mmol) of mercuric chloride in 5 ml of tetrahydrofuran was added dropwise. The mixture was stirred for 45 min and quenched by the addition of water. An insoluble yellow solid (60 mg, mp >225°) was filtered from the two-phase reaction mixture. The usual work-up yielded an oily white solid. Recrystallization from ethanol (95%) yielded 84 mg (10.5%) of white needles, mp 154–155°.

Anal. Calcd for $C_{12}H_{16}Br_2HgO_2$: C, 26.08; H, 2.92. Found: C, 26.12; H, 3.14.

7,7-Dichloro-2-oxabicyclo[4.1.0]heptane (2a)[6] had the following nmr: δ 3.78 (d, J = 8.0 Hz, H_1), 3.52 (m, CH_2O), 1.66 (m, 5 H).

exo-**7-Chloro-2-oxabicyclo[4.1.0]heptane (2c).**—To a cooled (−20°) solution of 1.0 g (5.98 mmol) of **2a** in 15 ml of ether was added butyllithium (5.98 mmol) during a period of 10 min. The solution was stirred for an additional 30 min and quenched by the slow addition of water. The usual work-up yielded an oil. The vpc yield of **2c** was determined (column D, 6 ft × $^1/_8$ in.), using an internal standard (acetophenone), to be 69.5%. The major component was collected: its ir was identical with that of the published spectrum;[6] nmr δ 3.69 (q, J = 1.3 and 8.0 Hz, H_1), 3.4 (m, CH_2O), 2.91 (q, J = 1.3 and 4.5 Hz, H_7), 1.94 (m, 2 H), 1.33 (m, 3 H), is in agreement with previously published features.[7]

exo-**7-Chloro-***endo***-7-deuterio-2-oxabicyclo[4.1.0]heptane** (**2d**).—To a cooled (−20°) solution of 1.0 g (5.98 mmol) of **2a** in 15 ml of ether was added butyllithium (5.98 mmol) during a period of 10 min. The solution was stirred for an additional 30 min and quenched by the slow addition of deuterium oxide (99.8%). The major component was collected from preparative vpc (column H, 6 ft × 0.25 in.): ir (neat) 2270 (w) (C–D), the 3050 cm^{-1} (w) –CH band which was present in **2c** was absent; nmr δ 3.69 (d, J = 8.0 Hz, H_1), 3.4 (m, CH_2O), 1.57 (m, 5 H).

exo-**7-Chloro-***endo***-7-(diphenylmethanol)-2-oxabicyclo[4.1.0]heptane** (**2e**).—To a cooled (−20°) solution of 2.0 g (12.0 mmol) of **2a** in 30 ml of ether was added butyllithium (12.0 mmol) during a period of 10 min. The solution was stirred for an additional 30 min and 2.16 g (12.0 mmol) of benzophenone dissolved in 15 ml of ether was added. The reaction mixture was stirred 1 hr at −20° and quenched with water. The usual work-up yielded a yellow oil. Trituration with pentane produced a white crystalline solid. Recrystallization from methanol yielded 2.14 g (56.7%) of white prisms: mp 93.5–95.0°; ir 3430 cm^{-1} (OH); nmr (CCl_4) δ 7.42 (m, phenyl H's), 4.33 (s, OH), 4.05 (d, J = 7.5 Hz, H_1), 3.63 (m, CH_2O), 1.74 (m, 5 H).

Anal. Calcd for $C_{19}H_{19}ClO_2$: C, 72.48; H, 6.08; O, 10.16. Found: C, 72.28; H, 6.06; O, 10.43.

exo-**7-Chloro-2-oxabicyclo[4.1.0]heptyl-***endo***-7-carboxylic acid** (**2h**).—To a cooled (−20°) solution of 2.0 g (12.0 mmol) of **2a** in 30 ml of ether was added butyllithium (12.0 mmol) during a period of 10 min. The solution was stirred for an additional 30 min and dry carbon dioxide was passed into the stirred (magnetic) solution for a period of 1 hr. The reaction was quenched with water. The basic water layer was acidified with concentrated hydrochloric acid and extracted with chloroform. The chloroform extract was dried ($MgSO_4$) and used for spectral determinations: ir 3600–3400 (OH) and 1715 cm^{-1} (–C═O); nmr ($CHCl_3$) δ 9.23 (s, OH), 3.97 (d, J = 7.5 Hz, H_1).

2-Oxo-3-chlorotetrahydrofuro[2,3-*b*]tetrahydropyran (**3**).—The chloroform extract from above was concentrated *in vacuo*. This yielded a yellow oil which solidified on standing with evolution of heat to yield pale yellow crystals. Recrystallization from ether–pentane yielded 1.17 g (55.2%) of white needles: mp 88–89°; ir 1780 (–C═O), 1160 (s) and 1130 cm^{-1} (w) (axial -CO); nmr δ 5.79 (d, J = 4.0 Hz, H_9), 4.78 (d, J = 6.5 Hz, H_3), 3.83 (m, CH_2O), 2.72 (m, H_4), 1.76 (m, 4 H).

Anal. Calcd for $C_7H_9ClO_3$: C, 47.60; H, 5.14; O, 27.17. Found: C, 47.48; H, 5.07; O, 27.17.

exo-**7-Chloro-***endo***-7-(*N*-phenylcarboxamide)-2-oxabicyclo[4.1.0]heptane** (**2f**).—To a cooled (−20°) solution of 5.0 g (29.5 mmol) of **2a** in 75 ml of ether was added butyllithium (29.5 mmol) during a period of 15 min. The solution was stirred for an additional 30 min and 3.52 g (29.5 mmol) of phenyl isocyanate in 15 ml of ether was added. The resulting slurry was stirred for a period of 1 hr and quenched with water. The reaction mixture was filtered to yield a white microcrystalline solid. The usual work-up of the organic layer yielded an additional amount of white solid. Recrystallization of the combined solids from ether yielded 5.14 g (69.3%) of white needles: mp 111–113°; ir 3400 and 3320 (broad) (NH), 1680 and 1601 cm^{-1} (amide I and II); nmr δ 8.23 (broad, NH), 7.37 (m, phenyl), 3.99 (d, J = 7.0 Hz, H_1), 3.62 (m, CH_2O), 1.64 (m, 5 H).

Anal. Calcd for $C_{13}H_{14}ClNO_2$: C, 62.03; H, 5.61; O, 12.71. Found: C, 62.30; H, 5.85; O, 12.94.

2-Oxo-3-chloro-*N*-phenylpyrrolidino[2,3-*b*]tetrahydropyran (**4**).—To 0.5 g of **2h** dissolved in chloroform was added one drop of isopropyl alcohol saturated with hydrogen chloride. The solution was stored at room temperature for 12 hr. The solvent was stripped *in vacuo* yielding 0.51 g of a tan oil: ir 1703 cm^{-1} (–C═O for γ-lactam); nmr δ 7.32 (m, phenyl), 5.85 (d, J = 1.5 Hz, H_9), 5.34 (s, H_3), 3.86 (m, CH_2O), 2.27 (m, 5 H).

Bis{*endo*-7-(*exo*-7-chloro-2-oxabicyclo[4.1.0]heptyl)}mercury (**2g**).—To a cooled (−20°) solution of 0.5 g (2.9 mmol) of **2a** in 8 ml of ether was added butyllithium (2.9 mmol) during a period of 5 min. The solution was stirred for an additional 30 min and 0.26 g (0.97 mmol) of mercuric chloride in 5 ml of tetrahydrofuran was added dropwise. The mixture was stirred for 15 min at −20° and allowed to attain 25° during 15 min. The mixture was then quenched by the addition of water. An insoluble, high melting, grayish green solid was filtered from the two-phase mixture. The ether layer was washed with two portions of water and concentrated *in vacuo*. This yielded a yellow oil which when triturated with pentane produced a white crystalline solid. The crystals were filtered and recrystallized from ethanol (95%) to yield 20 mg (1.85%) of white needles, mp 131–132°.

Anal. Calcd for $C_{12}H_{16}Cl\,HgO$: C, 31.08; H, 3.48. Found: C, 31.12; H, 3.68.

endo-**7-Chloro-2-oxabicyclo[4.1.0]heptane** (**5**).—To a cooled (−80°) solution of 1.0 g (5.98 mmol) of **2a** in 8 ml of tetrahydrofuran was added butyllithium (5.98 mmol) during a period of 10 min. The solution was stirred for an additional 30 min and quenched by the slow addition of methanol. The organic layer was washed with two portions of water, dried ($MgSO_4$), and concentrated *in vacuo*. Vpc (column D, 6 ft × $^1/_8$ in.) showed **2c** to be 60% of a two-component mixture. The second component was collected using preparative vpc (column D, 6 ft × 0.25 in.). Its nmr was identical with that of the published spectrum[7] for **5**.

6,6-Dichloro-3-oxabicyclo[3.1.0]hexane (**8a**).—A modification of the method of Anderson and Reese was used.[31] A stirred slurry of 42.4 g (0.6 mmol) of 2,5-dihydrofuran and 39.0 g (0.72 mol) of sodium methoxide in 200 ml of pentane at 0° was treated dropwise with 134 g (0.70 mol) of ethyl trichloroacetate during 1 hr. The mixture was stirred at 0–5° for 15 hr, at room temperature for 4 hr, cooled, and quenched with water. This resulted in a dark emulsion and it was necessary to add Norit and filter the mixture before the layers could be distinguished. The organic layer was washed with one portion of water, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was distilled to yield 17.12 g (18.4%) of a colorless liquid, bp 73.5–75° (17 mm). Vpc (column C, 6 ft × $^1/_8$ in.) showed a two-component mixture in a 1:2.1 ratio. The title compound was the more abundant component. An aliquot of 15.08 g of the above mixture was dissolved in 150 ml of methanol and enough water was added to produce cloudiness. To this cooled, stirred solution was added 25 g of potassium hydroxide. The mixture was stirred at room temperature for 6 days. Vpc (column C, 6 ft × 0.25 in.) showed that the hydrolysis of the 2-dichloromethyl-2,5-dihydrofuran isomer was essentially complete. The mixture was saturated with sodium chloride and extracted with two portions of ether. The ether extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Distillation of the residue yielded 8.09 g of a colorless liquid: bp 73–77.5 (20 mm); the nmr [δ 4.11 (d, 4 H), 2.55 (m, 2 H)] agreed with published[25,31] spectra; ir 3060 cm^{-1} (–CH, cyclopropane).

exo-**6-Chloro-3-oxabicyclo[3.1.0]hexyl-***endo***-6-carboxylic Acid** (**8d**).—To a cooled (−80°) solution of 0.5 g (3.3 mmol) of **8a** in 8 ml of ether was added butyllithium (6.6 mmol) during a period of 5 min. The mixture was stirred for 1 hr and dry carbon dioxide was passed into the stirred solution for a period of 1 hr. The reaction was quenched by the slow addition of methanol. The reaction was allowed to warm and water was added. The basic water layer was acidified with concentrated hydrochloric acid and extracted with ether. The ether extracts were dried ($MgSO_4$) and concentrated *in vacuo* to yield a pale yellow semicrystalline solid, which had a strong odor of valeric acid. Recrystallization from ether–petroleum ether (bp 30–60°) yielded 46 mg (8.6%) of white crystals: mp 174–175°; ir (KBr) 3650–2350 (–OH), 1730 cm^{-1} (–C═O); nmr (D_2O, Na_2CO_3, external TMS) δ 2.38 (m, 2 H), 4.30 (d, $J_{\text{gem}} = -9.0$ and $J_{\text{vic}} = 0$ Hz, $H_{2,4}$ endo), 3.91 (d, $J_{\text{gem}} = -9.0$ and $J_{\text{vic}} = 1.0$ Hz, $H_{2,4}$ exo).

Anal. Calcd for $C_6H_7ClO_3$: C, 44.32; H, 4.34; O, 29.52. Found: C, 44.50; H, 4.49; O, 29.26.

exo-**6-Chloro-3-oxabicyclo[3.1.0]hexane** (**8c**).—To a cooled (−80°) solution of 0.5 g (3.3 mmol) of **8a** in 7.5 ml of ether was added butyllithium (6.6 mmol) during a period of 10 min. The reaction was stirred for an additional 20 min and quenched by the slow addition of methanol. The mixture was allowed to warm to 25° and water was added. The ether layer was washed with two portions of water, dried ($MgSO_4$), and concentrated *in vacuo*. Vpc (column C, 6 ft × $^1/_8$ in.) showed starting **8a** and a component with a lower retention time. The first component was collected from preparative vpc (column F, 6 ft × 0.25 in.): nmr δ 4.08 (d, $J_{\text{gem}} = -9.0$ and $J_{\text{vic}} = 0$ Hz, H_2), 3.79 (d, $J_{\text{gem}} = -9.0$ and $J_{\text{vic}} = \sim 1.0$ Hz, H_3), 2.88 (t, J = 2.5 Hz, H_6), 2.02 (m, 2 H).

7,7-Dibromo-3-oxabicyclo[4.1.0]heptane (**6a**).—A slurry of solid potassium *tert*-butoxide (prepared by dissolving 6 g (0.15 g-atom) of potassium in *tert*-butyl alcohol, evaporating the solvent, and drying under N_2 at room temperature *in vacuo*) in 50

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(31) J. C. Anderson and C. B. Reese, *Chem. Ind.* (*London*), 575 (1963).

ml of pentane and 8.4 g (0.10 mol) of 5,6-dihydro-2*H*-pyran[32] at −20° was treated dropwise with 25.3 g of bromoform in 25 ml of pentane over 45 min. After stirring overnight at room temperature, water was added and the organic layer separated, washed with saturated NaCl solution, and dried ($MgSO_4$). Evaporation of the pentane *in vacuo* yielded 18.3 g of a yellow liquid (which contained starting olefin, 31%; **6a**, 47%; and bromoform, 22%) which was fractionated *in vacuo*. The second fraction, bp 122° (14 mm), was redistilled to yield 7.53 g (30%) of **6a**, bp 122° (14 mm), of about 95% purity: nmr (CCl_4) δ 3.98 (t, $W_{1/2}$ = 6 Hz, $H_{2,3}$), 3.55 (m, 1 H), 3.10 (m, 1 H), 1.9 (m, 4 H). A third distillation yielded an analytical sample, bp 95° (4 mm)

Anal. Calcd for $C_6H_8Br_2O$: C, 28.15; H, 3.15; Br, 62.44 Found: C, 28.35; H, 3.20; Br, 61.46.

exo-**7-Bromo-3-oxabicyclo[4.1.0]heptane (6c).**—A solution of 2.4 g (9.3 mmol) of **6a** in 45 ml of ether was cooled to −80° and ethereal methyllithium–lithium bromide (9.4 mmol) was added. The mixture was stirred for 20 min at −80° and then quenched with water. The organic layer was dried ($MgSO_4$), the ether evaporated, and the liquid residue distilled to yield 0.8 g of a colorless liquid, bp 94° (30 mm), which was shown by vpc (column G) to be 94% pure **6c**: yield 47%; nmr (CCl_4) δ 4.08 (d, $J_{\text{gem}} = -12.0$, $J_{\text{vic}} = 0$ Hz, H_2), 3.77 (q, $J_{\text{gem}} = -12.0$, $J_{\text{vic}} = 3.5$ Hz, H_3), 3.4 (m, 2 H), 2.85 (t, $J_{\text{trans}} = 3.5$ Hz, HCBr), 1.85 (m, 2 H), 1.4 (m, 2 H).

The vpc yield of **6c** prepared as above was determined to be 60% (column G, with bromobenzene as internal standard). Using 0.26 g (1 mmol) of **6a** in 10 ml of pentane at −80° required 2.5 mol equiv (~2 ml) of ethereal methyllithium–lithium bromide for complete reaction of **6a**. After the resulting slurry stirred at −80° for 30 min, a water quench afforded **6c** in 91% yield by vpc (columns B, D, G; bromobenzene internal standard; average of three reactions). When the results were corrected for purity of **6a**, the yield of **6c** was 96%. Preparative vpc (column F) afforded an analytical sample.

Anal. Calcd for C_6H_9BrO: C, 40.70; H, 5.12; Br, 45.13. Found: C, 40.67; H, 5.21; Br, 44.95.

exo-**7-Bromo-*endo*-7-deuterio-3-oxabicyclo[4.1.0]heptane (6d).**—A solution of 0.512 g (2 mmol) of **6a** in 10 ml of ether at −80° was treated with 1 equiv of methyllithium–lithium bromide, added all at once. After stirring at −80° for 30 min, the reaction was quenched with D_2O (99.5%). The organic layer separated, dried ($MgSO_4$), and evaporated to yield 0.23 g of a colorless oil, the nmr and vpc (column F) of which indicated that it was almost entirely a mixture of **6c** and **6d** in 33:67 ratio. Preparative vpc (column F) afforded a pure sample, and nmr integration confirmed the presence of 33% of **6c** in **6d**:[33] nmr (CCl_4) δ 4.08 (d, $J = -12$ Hz, 1 H) 3.77 (q, $J = -12$ and 3.5 Hz, 1 H), 3.4 (m, 2 H), 2.80 (t, $J = 3.5$ Hz, 0.3 HCBr), 1.85 (m, 2 H), 1.4 (m, 2 H).

exo-**7-Bromo-*endo*-7-(phenylmethanol)-3-oxabicyclo[4.1.0]-heptane (6e).**—A solution of 0.51 g (2 mmol) of **6a** in 15 ml of pentane and 10 ml of ether was cooled to −80° and treated with 1 equiv of methyllithium–lithium bromide. After stirring at −75° for 30 min, 0.26 g (2.4 mmol) of benzaldehyde in 10 ml of ether was added, and the mixture was allowed to warm to room temperature during 1 hr. After a water quench, the organic layer was washed twice with water, dried ($MgSO_4$), and evaporated to yield 0.45 g (80%) of crude, yellow crystals of **6e**, mp 69–75°. One recrystallization from pentane–ether afforded 0.216 g (40%) of white crystals, mp 80–83°. A second recrystallization gave an analytical sample: mp 84.5–85.5; ir (CCl_4) 3550 (with shoulder at 3570, free OH), 3440 cm^{-1} (broad, intramolecularly bonded OH) which did not change upon dilution; nmr (on **6e**, mp 80–83°) δ 7.3 (m, C_6H_5), 5.08 (broad d, $J = 6$ Hz, OH), 4.37 (d, $J_{\text{gem}} = -12$ Hz, 0.3 H endo on C_2), 4.12 (d, $J_{\text{gem}} = -12$ Hz, 0.7 H endo on C_2), 3.67 (m, 2 H), 3.17 (d, $J = 6$ Hz, 0.3 H benzylic), 2.88 (m, 1.7 H), 1.9 (m, 2 H) 1.6 (sextet, cyclopropane H). The spectrum is best interpreted as a mixture of diastereomers of **6e**.

Reactions of 6b–Methyllithium Complex. A. With 2 Equiv of Benzaldehyde.—A solution of 0.095 g (0.37 mmol) of **6a** in 5 ml of pentane at −80° was treated with 2.5 equiv (about 0.9 ml) of methyllithium–lithium bromide. After stirring at −80° for 30 min, 0.079 g (0.74 mmol) of benzaldehyde in 2 ml of ether was added, and the mixture was allowed to warm to room temperature during 1 hr. A water quench followed by the usual work-up afforded 0.075 g of a yellow oil. Vpc of the oil (columns A and D, no internal standard) indicated three major components: **6c** (7%), **6e** (40%), and 1-phenylethanol (51%).

B. With 1 Equiv of H_2O Followed by 1 Equiv of Benzaldehyde.—A solution of 0.105 g (0.41 mmol) of **6a** in 5 ml of pentane at −80° was treated with 2.0 equiv of methyllithium–lithium bromide and stirred at −80° for 30 min. A solution of 0.0074 g (0.41 mmol) of H_2O in 1 ml of ether was added, and the mixture was allowed to stir without the cooling bath for 15 min. At this point, 0.0435 g (0.41 mmol) of benzaldehyde in 1 ml of ether was added and stirring continued for 1 hr. Work-up as in part A yielded 0.050 g of yellow oil. Vpc (columns A and D, no internal standard) indicated two major peaks: **6c** (50%) and 1-phenylethanol (33%). Less than 2% of **6e** was detected.

exo-**7-Bromo-3-oxabicyclo[4.1.0]heptyl-*endo*-7-carboxylic Acid (6f).**— Carbenoid **6b** was prepared in 20 ml of pentane from 0.43 g (1.7 mmol) of **6a** at −80°. Carbon dioxide was passed through the reaction mixture for 1 hr at −80°. A water quench, followed by extraction with ether, yielded 0.21 g of white, crystalline **6f**. Acidification of the aqueous layer followed by ether extraction yielded an additional 0.03 g, total yield 65%, mp 153–155°. Recrystallization from ether gave an analytical sample: mp 155°; ir (KBr) 3000 (broad, OH), 1725 cm^{-1} (strong, C=O); nmr δ 9.35 (s, COOH), 4.58 (d, $J_{\text{gem}} = -12$ Hz, endo H on C_2), 3.93 (m, 1 H), 3.87 (q, $J_{\text{gem}} = -12$ Hz, $J_{\text{vic}} = 3$ Hz, exo H on C_2), 3.28 (sextet, 1 H), 2.55 (m, 1 H), 1.8 (m, 3 H).

Anal. Calcd for $C_7H_9BrO_3$: C, 38.03; H, 4.10; O, 21.71. Found: C, 38.15; H, 4.22; O, 21.66.

7,7-Dichloro-3-oxabicyclo[4.1.0]heptane (7a).—Using the method of Parham,[6] dichlorocarbene, generated from 28.7 g of ethyl trichloroacetate, was added to 12.6 g of 5,6-dihydro-2*H*-pyran[32] at −15° yielding a crude product which on fractionation yielded 8.25 g (33%) of colorless **7a**: bp 103–105° (28 mm); nmr (neat, external TMS) δ 4.08 (d, $H_{2,3}$), 3.5 (m, 2 H), 2.1 (m, 4 H). A redistillation afforded an analytical sample, bp 105° (30 mm).

Anal. Calcd for $C_6H_8Cl_2O$: C, 43.14; H, 4.82. Found: C, 42.88; H, 4.86.

exo-**7-Chloro-3-oxabicyclo[4.1.0]heptyl-*endo*-7-carboxylic Acid (7d).**—A solution of 1.51 g (9.00 mmol) of **7a** in 50 ml of tetrahydrofuran at −80° was treated with 1.4 equiv of butyllithium in hexane. The reaction turned yellow but remained homogeneous during stirring for 30 min. Dry CO_2 was bubbled through the reaction for 1 hr after which the reaction was quenched with water and the aqueous and organic layers separated. The aqueous layer was acidified and extracted with ether. Drying ($MgSO_4$) and evaporation of the ether yielded 0.88 g of yellow crystals, mp 130–138°. Recrystallization from petroleum ether–ether gave white, crystalline **7a**, mp 138–141°, 0.53 g (30%). Further recrystallization from ether gave an analytical sample: ir (KBr) 3000 (broad and strong, OH), 1740 cm^{-1} (C=O); nmr (D_2O, Na_2CO_3, external TMS) δ 4.42 (d, $J_{\text{gem}} = -12$ Hz, endo H on C_2), 4.10 (q, $J_{\text{gem}} = -12$, $J_{\text{vic}} = 4$ Hz, exo H on C_2), 3.58 (m, 2 H), 2.13 (m, 2 H), 1.83 (m, 2 H).

Anal. Calcd for $C_7H_9ClO_3$: C, 47.60; H, 5.13; Cl, 20.07; O, 27.18. Found: C, 47.66; H, 5.12; Cl, 20.08; O, 26.91.

exo-**7-Chloro-3-oxabicyclo[4.1.0]heptane (7c).**—A solution of 0.50 g (3.0 mmol) of **7a** in 9 ml of tetrahydrofuran was treated at −80° with 2 equiv of butyllithium in hexane. After stirring for 90 min at −80°, a water quench produced an organic layer which after drying and evaporation gave 0.63 g of a yellow liquid. Preparative vpc (column F) of the major component (64%) yielded impure **7c**, contaminated by a butyl-containing product of identical retention time: nmr (CCl_4) δ 4.09 (d, $J_{\text{gem}} = -12$ Hz, H_2), 3.78 (q, $J_{\text{gem}} = -12$, $J_{\text{vic}} = 3.5$ Hz, H_3), 3.5 (m, 2 H), 2.95 (t, $J_{\text{trans}} = 3$ Hz, HCCl), 1.9 (m, 2 H), 1.3 (m, 2 H), 0.8 (m, ~1 H).

3-Oxabicyclo[4.1.0]heptane (10).—A solution of 2.0 g of **6a** in 32 ml of ether was added dropwise to a solution of 8 g of sodium in 100 ml of liquid ammonia. After the addition the solution was stirred at −80° for 1 hr and at reflux (about −30°) for 30 min. Addition of NH_4Cl discharged the color, and evaporation of the ammonia left a residue which was partitioned between 80 ml of ether, 5 ml of methanol, and 60 ml of H_2O. The organic layer was dried ($MgSO_4$) and evaporated to 5 g at 0° under modest vacuum. Preparative vpc (column D) of the one major component (90% of the total excluding solvent) yielded **10**: ir (neat)

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[32] J. Colonge and P. Boisde, *Bull. Soc. Chim. Fr.*, 824 (1956).

[33] Incorporation of H into **1d** after stirring at −20° for 70 min was only about 8%. The source of H which is incorporated into **6d** is, at present, not known.

3060, 3020 cm^{-1} (cyclopropane, CH); nmr (CCl_4) δ 3.77 (d, $H_{2,3}$), 3.4 (m, 2 H), 1.8 (m, 2 H), 0.8 (m, 2 H), 0.35 (m, 1 H).

Anal. Calcd for $C_6H_{10}O$: C, 73.42; H, 10.27; O, 16.30. Found: C, 73.11; H, 10.18; O, 16.43.

Registry No.—**1a**, 27024-90-4; **1c**, 17879-78-6; **1d**, 17879-77-5; **1e**, 17879-76-4; **1f**, 17879-75-3; **1g**, 17879-74-2; **1h**, 27024-96-0; **1i**, 18022-11-2; **2d**, 27024-98-2; **2e**, 27024-99-3; **2f** 27025-00-9; **2g**, 27062-09-5; **2h**, 27025-01-0; **3**, 27025-02-1; **4**, 27025-03-2; **6a**, 27025-04-3; **6c**, 27025-05-4; **6d**, 27025-06-5; **6e**, 27025-07-6; **6f**, 27025-08-7; **7a**, 932-61-6; **7c**, 27193-01-7; **7d**, 27193-02-8; **8a**, 931-28-2; **8c**, 27025-11-2; **8d**, 27025-12-3; **10**, 286-10-2.

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2-Metalation of Dimethylaminoethylferrocene with Butyllithium and Condensations with Electrophilic Reagents. Synthesis of 2-Substituted Vinylferrocenes[1a]

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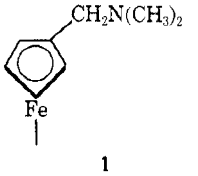
N,N-Dimethylaminoethylferrocene (DMAEF) was metalated in good yield with *n*-butyllithium in ether-hexane, and the intermediate 2-lithioamine was condensed with benzophenone, benzonitrile, phenyl isocyanate, phenyl isothiocyanate, hexachloroethane, and mercuric chloride to form the corresponding 2 derivatives. Methiodides of the above 2 derivatives were formed and converted to the corresponding 2-substituted vinylferrocene derivatives by treatment with potassium hydroxide. Metalation of DMAEF for extended time with excess *n*-butyllithium gave fair yields of the 2,1′-dilithioamine intermediate. That metalation occurred at the 2 position was established by converting the 2-benzoyldimethylaminomethylferrocene methiodide salt with KNH_2–NH_3 to give *via* a Stevens rearrangement the identical phenone derivative obtained from metalation of DMAEF. The successful 2-lithiation reported here for dimethylaminoethylferrocene is in direct contrast to the poor yield of lithiation found in the analogous benzene derivative, *N,N*-dimethyl-β-phenethylamine. The difference in behavior is attributed to the relative acidities of the 2 position and α protons in the respective systems.

Recently, we reported that metalation of dimethylaminomethylferrocene (DMAMF) (**1**) with *n*-BuLi apparently proceeded *via* the cyclic 2-lithiated species **1a**.[2] The analogous 2 position lithiation of benzyldimethylamine (**2**) to give the lithio intermediate **2a** had been reported earlier.[3] Hauser and other coworkers also published a study of the metalation of the homologous β-phenethyldimethylamine system but record only a tarry product from the reaction of β-phenethyldimethylamine (**3**) with *n*-BuLi followed by treatment with benzophenone.[4] In contrast to this are two recent observations[5] that metalation of β-phenethyldimethylamine (**3**) with *n*-BuLi apparently does proceed through the six-membered cyclic lithioamine intermediate (**3a**) to give the anticipated carbinolamine **4** when treated with benzophenone, although the yield of such an intermediate must be very low. In a noteworthy extension of this method, the oxygen analog of amine **1**, namely, ferrocenylmethyl methyl ether, has been found to undergo the 2-lithiation reaction.[6]



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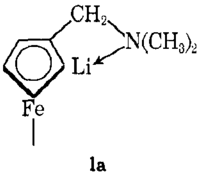
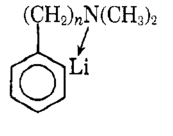
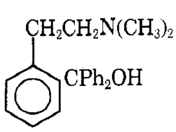


1a



2a, $n = 1$
3a, $n = 2$



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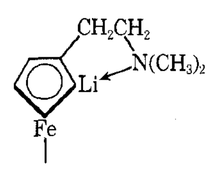
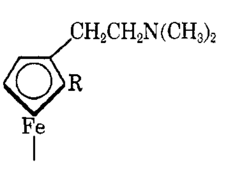


5a



5, R = –H
6, R = –CPh_2OH
8, R = –CONHPh
9, R = –CSNHPh
10, R = –COPh
11, R = –Cl
12, R = –HgCl

We would now like to report that metalation of dimethylaminoethylferrocene (DMAEF) (**5**) with *n*-BuLi for 2 hr gave an optimum yield of 68% of the 2-lithio intermediate **5a** as demonstrated by its condensation with benzophenone to produce carbinolamine **6** (*cf.* Table I). Longer metalation periods brought considerable concentration of dilithio intermediate **5b**. Struc-

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(2) D. W. Slocum, B. W. Rockett, and C. R. Hauser, *J. Amer. Chem. Soc.*, **87**, 1241 (1965).

(3) (a) F. N. Jones, M. F. Zinn, and C. R. Hauser, *J. Org. Chem.*, **28**, 663 (1963); (b) F. N. Jones, R. L. Vaulx, and C. R. Hauser, *ibid.*, **28**, 3461 (1963).

(4) R. L. Vaulx, F. N. Jones, and C. R. Hauser, *ibid.*, **30**, 58 (1965).

(5) (a) N. S. Narasimhan and A. C. Ranade, *Tetrahedron Lett.*, 603 (1966); (b) D. W. Slocum, T. R. Engelmann, and C. A. Jennings, *Aust. J. Chem.*, **21**, 2319 (1968).

(6) D. W. Slocum and B. P. Koonsvitsky, *Chem. Commun.*, 846 (1969).