

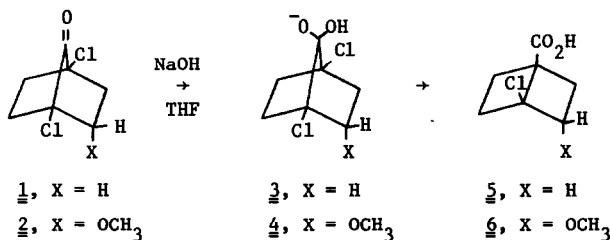
STRAINED RING SYSTEMS. XV.¹ A REGIOSPECIFIC,
NONCONCERTED SEMI-BENZILIC ACID REARRANGEMENT OF
ENDO-2-METHOXY-1,4-DICHLOROBICYCLO[2.2.1]HEPTAN-7-ONE

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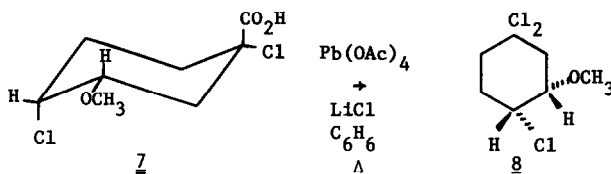
Of the several methods now available for preparing derivatives of bicyclo[2.2.0]hexane, the Scherer synthesis^{2,3} offers certain practical advantages. The key step in the synthetic sequence is the semi-benzilic acid ring contraction of 1,4-dichlorobicyclo[2.2.1]heptan-7-one (1) with powdered sodium hydroxide in THF to 4-chlorobicyclo[2.2.0]hexane-1-carboxylic acid (5). We wish to report evidence which supports the mechanistic premise that rearrange-



ment of oxy-anion 3 (and 4) occurs in a two-step process via a C₄ anion rather than by a direct, concerted step involving C₄-C₇ bond rupture with ejection of chloride ion at C₁ as the C₁-C₄ bond in 5 (and 6) is formed.

The substrate with which we chose to examine this interesting ring contraction process was endo-2-methoxy-1,4-dichlorobicyclo[2.2.1]heptan-7-one (2).⁴ It would not only be reasonably representative of 1 in this reaction, but would have present in the product [2.2.0] system a versatile function at C₃ for future conversions. Reaction of 2 with powdered sodium hydroxide in THF at 40° produced a mixture of acid 6 (89%) and the trisubstituted cyclohexanecarboxylic acid 7 (11%) in quantitative yield.

The structure of acid 7 was arrived at from analysis of its spectral data - mass spectrum (70 eV, heated inlet): 226 m/e (M⁺); pmr (CDCl₃ + DMSO-d₆, internal TMS): τ 1.50 (s, CO₂H, 1), 5.50 (t of d's, C₄-H, 1), 6.61 (6 of 8 lines, C₃-H, 1), 6.65 (s, OCH₃, 3), and 7.2-8.3 (m, C_{2,5,6}-H's, 6); and ¹³C nmr (see Table I). Reaction of acid 7 with Pb(OAc)₄ and LiCl (Kochi reaction)⁵ gave cis-3-methoxy-1,1,4-trichlorocyclohexane (8) in 95% yield where now the full 8-line pmr pattern of C₃-H was observed; pmr (CDCl₃, internal TMS): τ 5.50 (t of d's, C₄-H, 1),

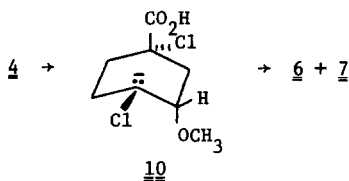


6.40 [8 lines ($J_{C_3H(a)}-C_2H(a)} = 10.2$ Hz, $J_{C_3H(a)}-C_2H(e)} = 4.7$ Hz, and $J_{C_3H(a)}-C_4H(e)} = 3.4$ Hz C_3 -H, 1], 6.66 (s, OCH_3 , 3), and 7.2-8.1 (m, $C_{2,5,6}$ -H's, 6); mass spectrum (70 eV, heated inlet): 216 m/e (M^+); and ^{13}C nmr (see Table I).

The relative stereochemistries of C_1 and C_3 in acid 7 are assigned since these positions are untouched in the semi-benzilic acid rearrangement of 2. The stereorelationship of C_4 in 7 comes from the observed 8-line pmr pattern for the axial C_3 -H. Further, the magnitudes of the J values in the 8-line pattern require that C_4 -H be equatorial which leads to the conformational assignment of acid 7.

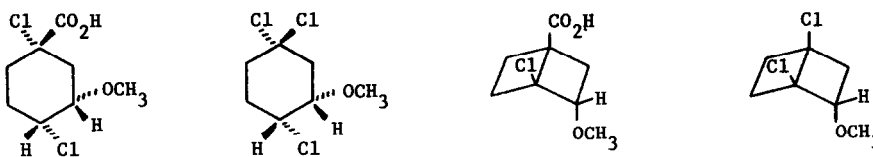
In the [2.2.0] acid 6, the site of attachment of the endo-methoxyl group was established from the ^{13}C nmr spectra (Table I) of 6 and the Kochi reaction⁵ product, 9, derived from 6. Their pmr spectra were also consistent with the assigned structures with the endo-methoxyl group present in both compounds.

Since we were unable to observe the isomers of acids 6 and 7 even in the pmr spectrum of the crude reaction product, the semi-benzilic acid ring contraction of 2 to 6 via 4 occurs regiospecifically. While we would expect the endo-2-methoxyl group in 4 to have little effect on the concerted mechanism of ring contraction leading to a mixture of [2.2.0] acids, 6 + 4-chloro-endo-2-methoxybicyclo[2.2.0]hexane-1-carboxylic acid, a relatively large methoxyl substituent group effect should be expected if the ring contraction is stepwise with the involvement of the intermediate carbanion 10.



The stereochemistry at C_4 of 7 leads us to believe that 7 is not formed by way of an additional intermediate involving the conformational flip from boat-10 to the chair conformer which we would expect to yield a mixture of C_4 epimers with the equatorial C_4 -Cl epimer possibly dominant. Thus it appears that partitioning of anion 10 between protonation (\rightarrow 7) or intramolecular displacement (\rightarrow 6) are the subsequent steps in the mechanism.

In the absence of definitive data in the parent systems ring contraction, 1 \rightarrow 5, we suggest that a nonconcerted ring contraction is operating here also. We then rationalize the observation of cyclohexanecarboxylic acid products in the present case and in the ring contraction of endo-2-benzoyl-exo-2-methyl 1^{3f} as the result of a longer life-time of the

Table I. ^{13}C NMR Data for Compounds 6-9.


	<u>7</u>		<u>8</u>		<u>6</u>		<u>9</u>					
	Chem. ^a Shift (ppm)	$J_{\text{C}_\alpha\text{H}}^{\text{b}}$ Mult. ^b (Hz)	Chem. ^a Shift (ppm)	$J_{\text{C}_\alpha\text{H}}^{\text{b}}$ Mult. ^b (Hz)	Chem. ^{a,e} Shift (ppm)	$J_{\text{C}_\alpha\text{H}}^{\text{b}}$ Mult. ^b (Hz)	Chem. ^{a,e} Shift (ppm)	$J_{\text{C}_\alpha\text{H}}^{\text{b}}$ Mult. ^b (Hz)				
C ₁	64.68	s	87.70	s	47.45	s	71.72	s				
C ₂	36.86	t	44.84	t	34.43	t	79.70	d				
C ₃	76.85	d	76.31	d	80.34	d	43.23	t				
C ₄	57.88	d	57.14	d	69.41	s	62.18	s				
C ₅	[29.53	t	125] ^c	29.36	t	140	[26.76	t	136] ^c	37.21	t	141
C ₆	[31.12	t	125]	39.29	t	136	[26.23	t	136]	26.46	t	141
OCH ₃	55.79	q	140	55.91	q	142	56.51	q	142	56.60	q	140
CO ₂ H	171.10	s			176.03	s						

^aFrom $\text{Si}(\text{CH}_3)_4$. ^bDetermined from proton coupled spectra. For multiplicities: singlet (s), doublet (d), triplet (t), and quartet (q). ^cSpecific C assignments are not made for C₅ and C₆ in 6 and 7. ^dNote different numbering of ring C's in 6 and 9 for comparison of the ^{13}C nmr data. ^eThe assignments of the two bridge-head positions in 6 and 9 were based on their T₁'s [6, C₁ (15.8 sec), C₄ (17.5 sec); 9, C₁ (81.8 sec), C₄ (71.8 sec)] and their chemical shifts.⁶

intermediate ring-opened carbanion (e.g. 10) due to the substituent effects.

Scherer⁷ had suggested that carbanions were involved in analogous semi-benzylic ring contractions of certain cage α,α' -dichloro ketones when the reaction was carried out with aqueous base. We wish to emphasize the point that the above results were obtained in the aprotic medium NaOH/THF. To determine the effect of water on the reaction of 2 + 6 + 7, the process was carried out in 95% aqueous THF at 40°. As before only 6 and 7 were produced, but their individual yields were significantly altered; 64% of 6 and 36% of 7. From this result, it appears that water serves as a proton source for carbanion 10 thus increasing the contribution of this reaction channel in the overall process

Analysis of the ^{13}C nmr spectra of compounds 6-9 along with those of other [2.2.0] derivatives will be presented in a full paper.

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References and Footnotes

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- (4) Ketone 2 or its hydrate is synthetically available from Diels-Alder of 5,5-dimethoxy-tetrachlorocyclopentadiene + vinyl acetate \rightarrow adduct-endo-OAc \rightarrow adduct-endo-OCH₃, then analogous reactions reported for the synthesis of 1.² All new compounds have given satisfactory elemental analyses.
- (5) See R. A. Sheldon and J. K. Kochi in "Organic Reactions," vol. 19, W. G. Dauben, Ed., Wiley, New York, N.Y., 1972.
- (6) (a) J. B. Grutzner, M. Jautelat, J. B. Dence, R. A. Smith, and J. D. Roberts, J. Amer. Chem. Soc., **92**, 7107 (1970); (b) J. B. Stothers, " ^{13}C NMR Spectroscopy," Academic Press, New York, N.Y., 1972, pp 178-180.
- (7) See K. V. Scherer, R. S. Lunt, and G. A. Ungefug, Tetrahedron Letters, 1199 (1965) for suggested carbanion involvement in related base reactions of cage α, α' -dihalo ketones.