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A FACILE ENTRY INTO THE TRICYCLO[3.2.0.0^{2,7}]HEPTANE SYSTEM

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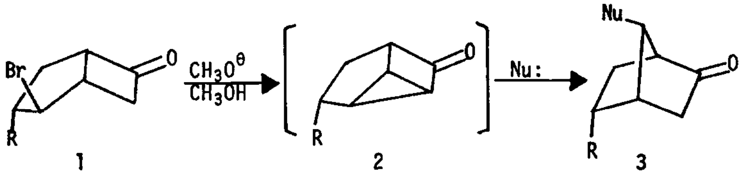
Recently, Roberts described extension of a reaction, first reported by Mitch and Dreiding,[1] by which *exo*-2-bromobicyclo[3.2.0]heptan-6-ones, **1**, are transformed by base into *anti*-7-substituted bicyclo[2.2.1]heptan-2-ones, **3** [equation (1)].[2] In both the earlier[1] and the more recent[2] work, a tricyclo[3.2.0.0^{2,7}]heptan-6-one, **2**, has been suggested as a reactive intermediate, although such a species has not been isolated. We wish to report a high yield synthesis of such an intermediate, *viz.*, *endo*-3-bromotricyclo-[3.2.0.0^{2,7}]heptan-6-one (**2**, R=Br), from *exo*-2-*endo*-3-dibromobicyclo[3.2.0]heptan-6-one (**1**, R=Br).



1 **2** **3** (1)

Treatment of **1** (R=Br)[2,3] with one equivalent of sodium hexamethyldisilazide[5] in anhydrous ether afforded, in 95% crude yield, a yellow solid which was purified by recrystallization from ether and sublimation (0.1 mm). The resulting labile product was colorless and had mp 62.5-64.0°. The purified material was isolable in 81% overall yield based on dibromide **1**.

The structural assignment of the product as **2** (R=Br) is based on its spectroscopic and chemical properties. The strong carbonyl band at 1750 cm^{-1} in the ir spectrum (KBr) is in the range typical for bicyclo[2.2.1]heptanones (*e.g.*, camphor has its carbonyl stretching vibration at 1745 cm^{-1})[6] and suggests that the added strain present in the tricyclic system, which should increase the stretching frequency,[7] is compensated for by conjugation of the carbonyl moiety with the cyclopropyl ring.[8] The pmr spectrum ($CDCl_3$), presented in Table 1, is consistent with the assigned structure, as is the cmr spectrum which reveals seven chemically non-equivalent carbon atoms.[9] However, completely definitive affirmation of the structure as being **2** (R=Br) was desired and was obtained by a single crystal x-ray structure determination.

Table 1. PMR Data for **2** (R=Br)

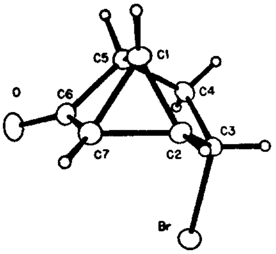
Chemical Shift (δ)	Assignment[a]	Multiplicity, Coupling Constants, J(Hz)
2.14-2.3	H_4-endo	multiplet, $J_{H_4\text{-exo}-H_4\text{-endo}} = 14.5$
2.66-3.0	H_4-exo	d x d x d, $J_{H_3-H_4\text{-exo}} = 8.2$, $J_{H_5-H_4\text{-exo}} = 4.5$
2.9-3.1	H_2,H_7	multiplet
3.2-3.4	H_5	multiplet
3.5-3.7	H_1	d x t, J=2.5, 2.5, 1.5
4.7-4.9	H_3	multiplet

[a] These assignments are based on chemical shifts observed in related systems, *e.g.*, **1** (R=Br) and tricyclo[2.2.0.$0^{2,6}$]hexan-2-one (C-Y. Ho and F. T. Bonds, *J. Amer. Chem. Soc.*, **96**, 7355 (1974).

Crystals of **2** (R=Br) suitable for single crystal diffraction studies were grown by sublimation at 0.1 mm (Hg) pressure and ambient temperatures (∿ 23°). The crystals are triclinic, $P\bar{1}$, $\underline{a}$ = 6.920, $\underline{b}$ = 9.144, $\underline{c}$ = 5.718 Å, α = 102.68, β = 107.18, γ = 77.16°, Z = 2. All diffraction work was carried out with graphite-monochromatized MoKα radiation on a Syntex $P2_1$ autodiffractometer. The crystal was cooled at $-32 \pm 2°$ by a stream of dry N_2 gas supplied by a Syntex LT-1 low temperature attachment.

Despite this low temperature, inert atmosphere, the crystal suffered considerable radiation damage during the course of collection of intensity data (1337 unique reflections to 2θ = 53°, 19.6 hours total exposure). All four periodically measured standard reflection decreased in intensity, at very nearly the same rate, by about 45%. This apparently isotropic loss of effective scattering volume caused no difficulty in the subsequent structure determination and refinement.[10]

The structure was determined by the heavy atom method and has been refined by full matrix least squares methods. The final agreement factors, based on the 1124 reflections with I>2σ(I), are R = 0.050 and wR = 0.051. The overall molecular structure (Fig.1) is that of 2 (R=Br), with the five-membered ring in the envelope conformation, and the four-membered ring being folded by 21° across the C5-C7 line.



Distances	(Å)
C1 - C2	1.484(8)
C2 - C7	1.542(8)
C1 - C7	1.558(8)
C1 - C5	1.528(8)
C5 - C6	1.524(8)
C6 - C7	1.450(8)

Figure 1. Molecular Geometry and Selected Distances in 2 (R=Br)

Treatment of 2 (R=Br) at room temperature with a catalytic amount of sodium methoxide in methanol saturated with potassium cyanide afforded, in high yield, anti-7-cyano-endo-5-bromobicyclo[2.2.1]heptan-2-one (3, R=Br, Nu=CN).[2] This same product was obtained under identical reaction conditions from 1 (R=Br), the precursor to the tricyclic derivative. Consequently, 2 (R=Br) is indeed a viable intermediate in the rearrangement of exo-2-bromobicyclo[3.2.0]heptan-6-ones to anti-7-substituted bicyclo[2.2.1]heptan-2-ones.[1,11]

The availability of derivatives of 2 by way of ring closure from the bicyclic system, 1, not only makes the tricyclic system itself readily accessible but also greatly increases the scope of nucleophiles that can be introduced stereoselectively at C-7 of the bicyclo-[2.2.1]heptan-2-one system. Furthermore, the possibility that useful electrophilic reactions leading to 7-substituted bicyclo[2.2.1]heptan-2-ones can be found is now subject to investigation. Consequently, the potential value of this route to the [2.2.1] skeleton and ultimately to the synthesis, for example, of prostanoids[2,12] is significantly enhanced.[13]

References and Notes

1. E.L. Mitch and A.S. Dreiding, *Chimia* (Switz.), **14**, 424 (1960).
2. S.M. Roberts, *Chem. Commun.*, 948 (1974).
3. That the stereochemistry of dibromide **1**, obtained in our laboratories by bromination of bicyclo[3.2.0]hept-2-en-6-one[4] in the presence of acetamide is *exo*-2-*endo*-3-dibromo is readily demonstrated by analysis of europium-shifted nmr spectra of the dibromide. The detailed spectra will be reported in the full paper (J.C.G. and T.L.).
4. W.T. Brady and E.F. Hoff, *J. Amer. Chem. Soc.*, **90**, 6256 (1966).
5. U. Wannagat and H. Niederprum, *Chem. Ber. Jahrg.*, **94**, 1540 (1961).
6. "The Sadtler Standard Spectra," Sadtler Research Laboratories, Philadelphia, Pa., no. 244.
7. R.M. Silverstein, G.C. Bassler, and T.C. Morrill, "Spectrometric Identification of Organic Compounds," 3rd ed., J. Wiley and Sons, Inc., New York, 1974.
8. a) L.N. Ferguson, *J. Chem. Ed.*, **44**, 17 (1967).
   b) H. Erdtman and T. Norin, *Chem. Ind.* (London), 644 (1960).
   c) L.A. Paquette, K.H. Fuhr, S. Porter, and J. Clardy, *J. Org. Chem.*, **39**, 467 (1974).
9. Absorptions of the ^{13}C nuclei in **2** (R=Br) are at δ 34.0, 42.9, 44.4, 49.3, 51.3, 58.3, and 187.7 ppm relative to tetramethylsilane as the standard.
10. Details of the crystallographic work will appear elsewhere (R.E.D.).
11. Although consideration of factors presented in **2** (R=Br) and of strain in possible products would lead to the prediction that nucleophiles would attack the tricyclic ketone at C_1, it is also of interest that the C_1-C_7 bond appears to be longer, and therefore presumably weaker, than the C_2-C_7 bond.
12. a) J.S. Bindra and A. Grodski, T.K. Schaaf, and E.J. Corey, *J. Amer. Chem. Soc.*, **95**, 7522 (1973), and references therein cited; b) R. Peel and J.K. Sutherland, *Chem. Commun.*, 151 (1974).
13. The partial support of this research by the Robert A. Welch Foundation is gratefully acknowledged. We are also indebted to the National Science Foundation for the purchase of the Syntex $P2_1$ diffractometer (Grant No. GP-37028).