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SELECTIVE INSERTION IN THE FORMATION OF BICYCLOBUTANES FROM TETRAALKYLSUBSTITUTED GEM-DIBROMOCYCLOPROPANES[1a]

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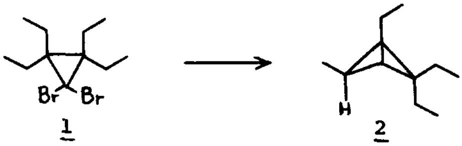
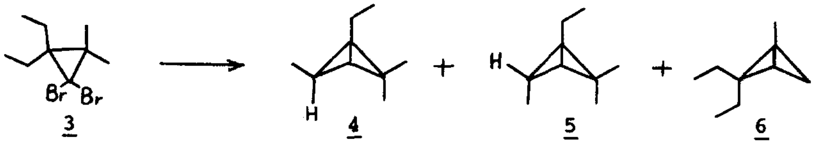
While the reaction of the dibromocarbene adduct of trimethylethylene with methyllithium gives only trimethylallene, the dibromocarbene adduct of tetramethylethylene reacts with methyllithium to give a nearly quantitative yield of 1,2,2-trimethylbicyclobutane.[2] We have examined a number of other systems to determine to what extent this pattern of reactivity for tetrasubstituted gem-dibromocyclopropanes is general and report on two herein.

Treatment of 1, the dibromocarbene adduct of tetraethylethylene, with methyllithium in ether at 0° gave a single product (>96% yield based on glc) to which we assign structure 2, exo-4-methyl-1,2,2-triethylbicyclobutane.[3] The exo assignment of the C-4 methyl group is based on the nmr spectrum[3] as well as on steric considerations and results obtained from a related system (below). An endo methyl group at C-4 would result in extreme crowding with the endo ethyl at C-2. This severe interaction (absent in 2) must be developed sufficiently in the transition state leading to endo-2 to preclude C-H insertion in this sense.



The behavior of the dibromocarbene adduct of 2-ethyl-3-methylpentene-2 presents a direct comparison of the reactivities of methyl and methylene groups. Dibromide 3 reacts with methyllithium in ether at 0° to give a mixture (ca. 95% yield) of three bicyclobutanes 4, 5, 6 in ratios of 96 : 1 : 3.[4] No detectable allene formation occurred nor was any evidence found for insertion into a β-methyl group, a reaction mode which would lead to a bicyclopentane derivative. The major isomer 4, 1-ethyl-exo-2,2,4-trimethylbicyclobutane, can be isolated (87%



3 4 5 6

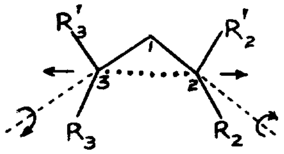
yield) by distillation through a Teflon spinning band column; the minor products were obtained by preparative glc. The structural assignments are confirmed by the spectral properties of the compounds.[5] Additionally, treatment of 4 with magnesium bromide in ether caused rearrangement to a mixture of three products; the major one (79%) was isolated and characterized as 7 showing that the main rearrangement path for 4 is the same as that found for 1,2,2-trimethylbicyclobutane.[2]

4 7

Clearly there is a strong preference for insertion into a CH_2 rather than a CH_3 group, with steric interactions directing attack on the CH_2 group in a manner which leads to an exo configuration for the methyl group at C-4. This striking selectivity cannot reflect a conformational effect; a methyl group certainly must have one hydrogen proximate to the carbenoid center. However, as molecular models will show, certain conformations of the ethyl groups reduce the probability of attack on the hydrogen of a CH_2 group; hence the intrinsic reactivity of the latter may be even higher than is indicated by these results. The selectivity means that, as in other systems, insertion into a CH bond is facilitated by alkyl substitution, implying that a charge deficiency arises at the carbon atom being attacked.

These reactions involve formation of 1-lithio-1-bromocyclopropane intermediates which may or may not lose lithium bromide to form cyclopropylidenes prior to the product-determining transition states. At this time we hold the view (which will be expanded elsewhere) that the transition state can best be regarded as being derived from a carbene, somewhat, but not greatly, perturbed by an adjacent molecule of lithium bromide. Irrespective of the timing of the loss of LiBr, it is clear that the allene/bicyclobutane product ratios reflect the relative rates of competing modes of reaction for carbene or carbenoid intermediates. The fact that mono-, di-, and trisubstituted systems open to allenes while tetrasubstituted systems give bicyclobutanes cannot reflect a significantly enhanced rate of C-H insertion for the latter; rather, putting four substituents on a cyclopropylidene must greatly *decelerate* ring opening to an allene, a deceleration which must be steric in origin. In one sense, then, insertion wins by default.

Operationally, the *direct*[6] opening of a cyclopropylidene, be it free or complexed, to an allene (no intermediates) must occur by either a conrotatory or monorotatory process, both of which represent minimum motion paths. Consider conrotatory opening.[7] If the transition state 8 involves relatively little C_2-C_3 stretching, but there is a significant degree of rotation about C_1-C_2 and C_1-C_3 bonds, each of the substituents R_2 and R'_3 will experience a repulsive steric interaction with the opposing center (and its substituents) undergoing rehybridization, viz. $R_2 \ldots CR'_3R_3$ and $R'_3 \ldots CR_2R'_2$. Monorotatory opening (rotation at only one end of the molecule), which may be important with unsymmetrically substituted systems, would involve only one related interaction, but this would presumably be larger than the individual conrotatory interactions. When one of the substituents R_2 or R'_3 in 8 is hydrogen, such repulsion must be minimized sufficiently to allow ring opening. But in tetrasubstituted systems, repulsive interactions must slow ring opening sufficiently to allow complete C-H insertion to occur.



8

REFERENCES

1. (a) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society (1549-A4) and to the National Science Foundation (GP8181) for support of this research; (b) National Institutes of Health Predoctoral Fellow 1965-1968.

2. (a) W. R. Moore, K. G. Taylor, P. Muller, S. S. Hall, and Z. L. F. Gaibel, *Tetrahedron Lett.*, 2365 (1970); (b) L. Skattebøl, *ibid.*, 2361 (1970).

3. (a) Mass spectrum m/e 152 (M^+); ir 3040, 1375 cm^{-1}; nmr (CCl_4) δ 0.7-1.5 (18H, very complex but having a singlet at 0.77 (1H) CH at C-3), 1.78 (2H, broad q $C\underline{H}_2CH_3$ at C-1); (b) The absence of a methyl doublet at *ca.* δ 0.8 precludes an *endo*-methyl at C-4; the *exo*-methyl must fall at *ca* 1.0. For a related argument see W. G. Dauben and J. S. Ritscher, *J. Amer. Chem. Soc.*, *92*, 2925 (1970).

4. The ratios are somewhat dependent upon the temperature and the nature of the halide (LiBr or LiI) in the methyllithium.

5. (a) *4*: mass spectrum m/e 124 (M^+); ir 3040, 1385, 1375, 1365 cm^{-1}; nmr (CCl_4) δ 0.78 (3H, s, *endo*-2-CH_3), 0.80 (1H, CH at C-3), 0.96 (3H, d, *exo*-4-CH_3), 1.00 (3H, t, $CH_2C\underline{H}_3$), 1.01 (3H, s, *exo*-2-CH_3), 1.46 (1H, q, *endo*-$C\underline{H}CH_3$), 1.75 (2H, q, $C\underline{H}_2CH_3$). (b) Complete spectral data for all compounds will be reported in a subsequent paper.

6. (a) If rearrangement of an organometallic intermediate occurred, a disrotatory opening is possible, giving a new organometallic species (a 2-lithio-3-bromoalkene) which in turn could lose LiBr to form an allene. As we have noted, such a path may well hold for the formation of 1,2-cyclohexadiene from 6,6-dibromobicyclo[3.1.0]hexane,[6b] but it does not appear to be generally followed. (b) W. R. Moore and W. R. Moser, *J. Amer. Chem. Soc.*, *92*, 0000 (1970); W. R. Moore and W. R. Moser, *J. Org. Chem.*, *35*, 908 (1970).

7. Consideration of orbital symmetries suggests that conrotatory opening of a singlet cyclopropylidene to an allene is "forbidden". However we believe that the energy barrier cannot be high ("mildly forbidden") and that in the absence of steric effects the opening should be expected to be fast. These points will be developed elsewhere.