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SYNTHESIS OF 2,5-DISUBSTITUTED PROTOADAMANTANES. SILVER ION-ASSISTED ACETOLYSIS OF 2-EXO-BROMO-5-PROTOADAMANTANONE

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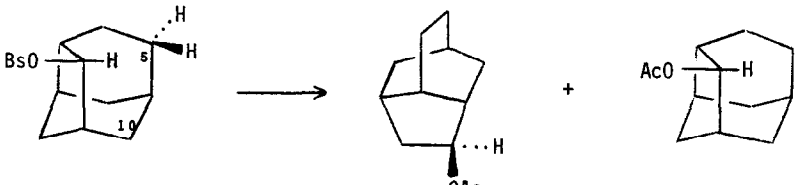
Although a number of monosubstituted protoadamantanes have been synthesized, reports of the rational preparation of disubstituted protoadamantanes remain at a premium. Thus, although both 2-substituted[1-3] and 5-substituted[3-5] protoadamantanes are known, no 2,5-disubstituted protoadamantanes have been synthesized. We now wish to report that: (a) 2,5-disubstituted protoadamantanes can readily be prepared by the acid-catalyzed additions of electrophilic reagents to 8,9-dehydro-2-adamantanone (1), and (b) 2,5-disubstituted protoadamantanes can serve as precursors for the synthesis of 2,7-disubstituted isotwistanes.[6]

Reaction of (1)[7] with hydrobromic acid in glacial acetic acid provides 2-exo-bromo-5-protoadamantanone (2),[8] mp 126-127°, in 95% yield. Treatment of (2) with alkali regenerates (1). The skeletal framework of (2) and the position of the keto substituent in (2) were established by hydrogenolysis of (2) with palladium on calcium carbonate to give the known ketone, 5-protoadamantanone (3).[3,4]

Perchloric acid-catalyzed acetolysis of (1) affords 2-exo-acetoxy-5-protoadamantanone (4),[8] mp 66-68°, in 80% yield.[9] The skeletal position and stereochemistry of the acetoxy substituent in (4) follow from the conversion of (4) to the known alcohol, 2-exo-protoadamantanol (6).[1,10] Hydrolysis of (4) gives 2-exo-hydroxy-5-protoadamantanone (5),[8] mp 244-249° (dec), and Wolff-Kishner reduction of (5) provides (6).

Silver-ion assisted acetolysis of (2) affords 2-exo-acetoxy-7-isotwistanone (7),[8] mp 79.5-80.5°, in 55% yield and (1)[11] in 15% yield.[12] The skeletal framework of (7) and the skeletal position of the acetoxy substituent in (7) were established by the conversion of (7) to the known ketone, 2-isotwistanone (10).[1] Hydrolysis of (7) affords 2-exo-hydroxy-7-isotwistanone (8),[8] mp 61-62°, and Wolff-Kishner reduction of (8) provides 2-exo-isotwistanol (9),[8] mp 57.5-58.5°. Jones oxidation of (9) gives (10). The stereochemistry of the acetoxy substituent and the position of the keto substituent in (7) are consistent with the spectral data and the mode of formation of (7).

Recently, Spurlock and Clark have reported an analogous skeletal rearrangement in the acetolysis of 2-exo-protoadamantyl brosylate (11), which affords 2-exo-isotwistyl acetate (12) and 2-exo-protoadamantyl acetate (13) as the major products of the reaction.[1] It was



(11) (12) (13)

suggested that 2-endo-protoadamantyl acetate is not realized in this reaction because endo attack by nucleophile on the 2-protoadamantyl cation formed in the solvolysis is sterically hindered by the C-5 endo hydrogen.[1] It is to be noted that 2-endo-acetoxy-5-protoadamantanone also is not obtained in the silver-ion assisted acetolysis of bromoketone (2), which lacks C-5 hydrogens. Thus, it appears that endo protoadamantyl derivatives are not realized in these reactions because endo attack by nucleophile on the 2-protoadamantyl cation is not competitive with the 1,2-carbon shift of the C-1 to C-10 σ bond, which undoubtedly anchimerically assists in the ionizations.

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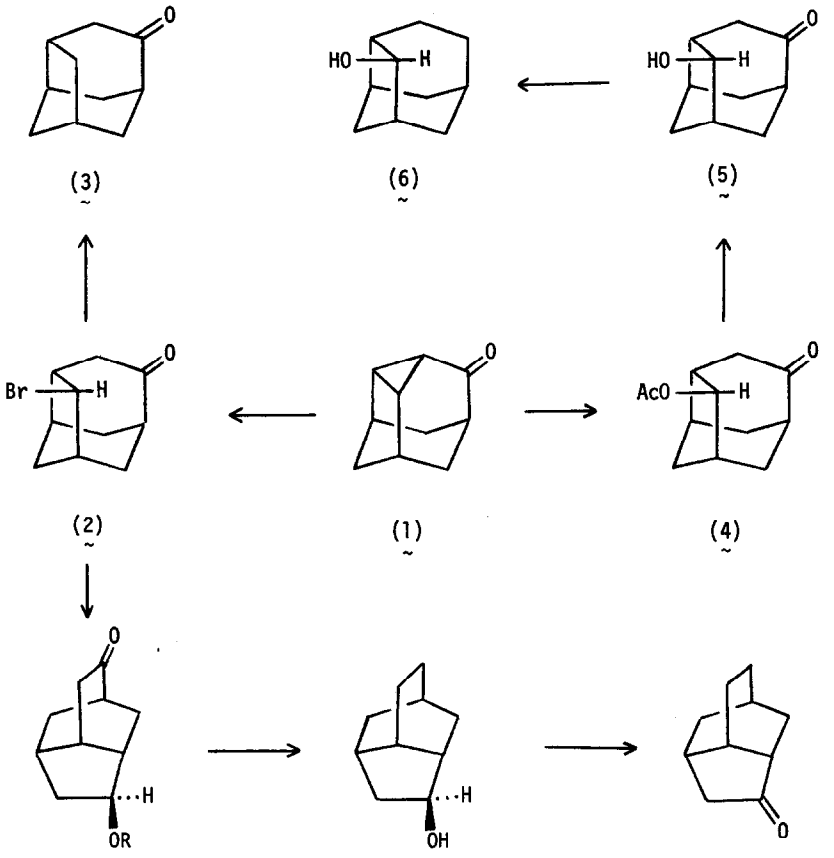

(3) (6) (5)

(2) (1) (4)

(7) R = Ac

(8) R = H

(9) (10)

Footnotes and References

1. L. A. Spurlock and K. P. Clark, J. Amer. Chem. Soc., 94, 5349 (1972).
2. C. A. Cupas, W. Schumann, and W. E. Heyd, ibid., 92, 3237 (1970).
3. H. W. Whitlock, Jr. and M. W. Siefken, ibid., 90, 4929 (1968).
4. J. Boyd and K. H. Overton, J. Chem. Soc., Perkin Trans. I, 2533 (1972).
5. D. Lenoir, R. Glaser, P. Mison, and P. v. R. Schleyer, J. Org. Chem., 36, 1821 (1971).
6. Isotwistane is the trivial name suggested by Spurlock and Clark[1] for the hydrocarbon tricyclo[4.3.1.$0^{3,7}$]decane.
7. J. E. Baldwin and W. D. Foglesong, J. Amer. Chem. Soc., 90, 4303 (1968).
8. Satisfactory elemental analyses and spectral data consistent with the structural assignments have been obtained for all new compounds.
9. Acetoxyketone (7) also was obtained in 12% yield.
10. We are grateful to Professor Spurlock of Brown University for supplying us with a copy of the ir spectrum of (6).
11. Ketone (1) proved to be inert when treated under identical reaction conditions and thus (7) is not derived from (1).
12. Two minor products (ca. 5% yield each), which are not acetates, also were obtained.