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THERMOLYSIS OF 1-HOMOADAMANTYL HYPOIODITE. CONVENIENT SYNTHESIS OF 10-HOMOPROTOADAMANTAN-4-ONE (TRICYCLO $[4.3.2.0^{3,8}]$UNDECAN-4-ONE)

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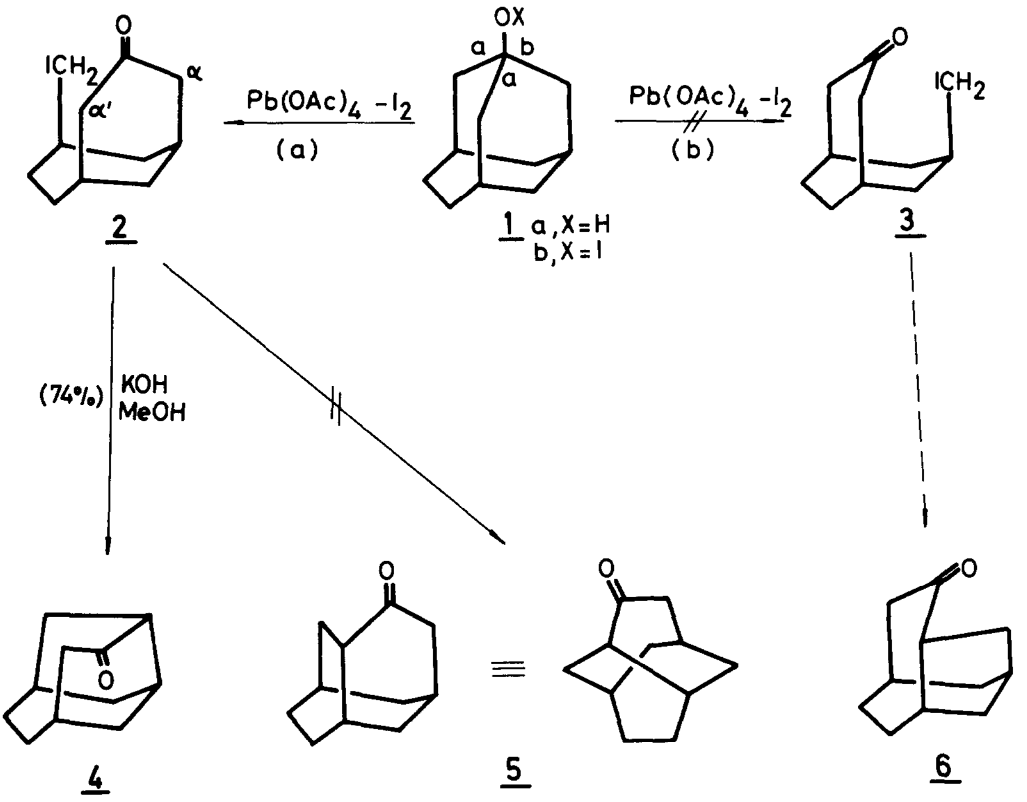
Summary: Thermolysis of 1-homoadamantyl hypoiodite followed by intramolecular cyclization yields 74% of the hitherto unknown 10-homoprotoadamantan-4-one; the hypoiodite thermolysis-cyclization sequence appears to be an excellent method for the preparation of adamantanoid ketones.

β-Scission of tertiary polycyclic hypohalites attracted our attention as a potentially general route to adamantanoid ketones. While thermolysis and photolysis of long chain aliphatic hypohalites yield mainly δ-haloalcohols,[1] short chain aliphatic and cyclic hypohalites give substantial amounts of β-scission products - ketones and halides.[1,2] This has scarcely been used in synthetic chemistry.[1,2] 4-Protoadamantanone was obtained in 35% yield by thermolysis of 1-adamantyl hypohalite followed by cyclization of the resulting haloketone.[3] In spite of the low and erratic yield, this reaction sequence has been the most convenient entry to the protoadamantane system. Recently we found[4] that the yield of 4-protoadamantanone (> 98% pure by GLC) could be increased to a steady 65-75% if the hypoiodite reaction of 1-adamantanol was carried out in a dilute benzene solution at 70° C.[5]

We now report the thermolysis of 1-homoadamantyl hypoiodite (1b) and the intramolecular cyclization of the resulting iodoketone. Contrary to 1-adamantyl hypoiodite, only two of the three β-C,C-bonds in 1 are equivalent ($a \neq b$) and, consequently, two isomeric iodoketones, 2 and 3, could be formed by β-scission. Intramolecular base promoted C-alkylation of 2 and 3 could be expected[3,6] to produce homoprotoadamantane ketones 4 and 5, and 6, respectively.

1-Homoadamantyl hypoiodite (1b) was prepared *in situ* from 1-homoadamantanol[7] (1a) by the modified hypoiodite reaction.[5] Thermolysis of 1b produced only one iodoketone.[8] The crude iodoketone was cyclized by base[5] to give a single product, which was purified by column chromatography.



The overall yield of the pure product (⩾98% by GLC) was 74% (based on 1a). The spectral data of the product[9] are in accord with all three proposed structures, 4, 5, and 6. To assign the correct structure, the ketone was reduced to the parent hydrocarbon by the Wolff-Kishner reaction. The ^{13}C NMR spectrum of the hydrocarbon showed 11 signals indicating the structure corresponding to 4.[10] This new adamantanoid hydrocarbon (tricyclo $[4.3.2.0^{3,8}]$ undecane) can be conveniently named 10-homoprotoadamantane.

Thus, thermolysis of 1-homoadamantyl hypoiodite (1b) followed by base promoted intramolecular cyclization of the resulting iodoketone yields exclusively 10-homoprotoadamantan-4-one (4, tricyclo $[4.3.2.0^{3,8}]$undecan-4-one). Since 1b can be easily prepared *in situ* from readily available 1-homoadamantanol,[7] the hypoiodite thermolysis-cyclization sequence is a convenient entry to the 10-homoprotoadamantane system.[11] Thermolysis of 1b is a highly selective process. Bond a is exclusively cleaved, although the cleavage of both bond a and b would lead to primary free radicals[1,3] and primary iodoketones (2 and 3). The direction of the cleavage may be controlled by the relative strain energies of the two iodoketones. Intramolecular cyclization of iodoketone 2 yields exclusively ketone 4, although both α and α' methylene groups in 2 are activated and structure 5 is at least 5 kcal/mol more stable than structure 4.[12] This could be explained by the closer proximity of the carbon bearing iodide to the enolate formed by enolization toward the α methylene group.

The real significance of the hypoiodite thermolysis-cyclization sequence has never been fully recognized. This reaction sequence is currently being studied in our laboratory on a number of polycyclic hypoiodites. It appears to be an excellent method for the preparation of a variety of adamantanoid ketones.[13]

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References and Notes

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5. A mixture of 1-homoadamantanol (or 1-adamantanol) (5 mmol), dry $Pb(OAc)_4$ (10 mmol), and iodine (11 mmol), was vigorously stirred in 70 ml of dry benzene at 80° C for 5 min and at 60° C (70° C for 1-adamantanol) for additional 2 hr. The solid materials were removed by

filtration and the filtrate was washed successively with aqueous $NaHSO_3$ and $NaHCO_3$ and dried. Evaporation of the solvent without heating yielded the bicyclic iodoketone which was cyclized by KOH (12 mmol) in methanol (25 ml; reflux, 3 hr). The crude product was purified on a neutral alumina (activity III/IV) column using a $0 \rightarrow 100\%$ ether-pentane mixture as eluent.

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8. Ir (film) 1700 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ_{TMS} 3.0 (d, J = 6 Hz, CH_2I), 0.7-2.8 ppm (br m, 15 H).
9. ^{13}C NMR ($CDCl_3$) δ_{TMS} 217.7, 50.6, 44.6, 40.0, 38.6, 38.3, 36.0, 35.5, 31.1, 30.8, and 29.2 ppm; ^{1}H NMR ($CDCl_3$) δ_{TMS} 1.2-3.0 (br m) ppm; ir (KBr) 2900, 2860, 1690, 1450 cm^{-1}; mass spectrum m/e 164(100%), 121(37%), 107(40%), 96(92%), 81(93%); mp 208-209° C.
10. ^{13}C NMR ($CDCl_3$) δ_{TMS} 42.2, 38.9, 35.9, 35.8, 33.8, 33.7, 33.0, 30.1, 27.4, 23.9, and 18.3 ppm; ^{1}H NMR ($CDCl_3$) δ_{TMS} 0.7-2.5 (br m) ppm; ir (KBr) 2900, 2860, 1450 cm^{-1}; mass spectrum m/e 150(100%), 135(41%), 121(73%), 107(70%), 95(72%), 79(65%); mp 233-234° C. The ^{13}C NMR spectra of the hydrocarbons corresponding to ketones 5 and 6 would show 6 and 7 signals, respectively.
11. Recently, 10-homoprotoadamant-4-en-2-one was obtained by the photoisomerization of tricyclo-[4.4.1.$0^{3,8}$]undec-4-en-2-one: R.K. Murray, Jr., D.L. Goff, and R.E. Ratych, *Tetrahedron Lett.*, 763 (1975).
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13. For example, from 3-homoadamantanol a 2 : 3 mixture of 4-homoprotoadamantan-4-one (tricyclo[5.3.1.$0^{3,9}$]undecan-4-one) and 4-homoadamantanone was obtained in 78% total yield: Z. Hameršak, D. Škare, and Z. Majerski, *Chem. Commun.*, 478 (1977).