Hypoiodite Thermolysis–Cyclization Reaction. Convenient Synthesis of 4-Homoprotoadamantan-4-one (Tricyclo[5.3.1.0^{3,9}]undecan-4-one) from 3-Homoadamantanol

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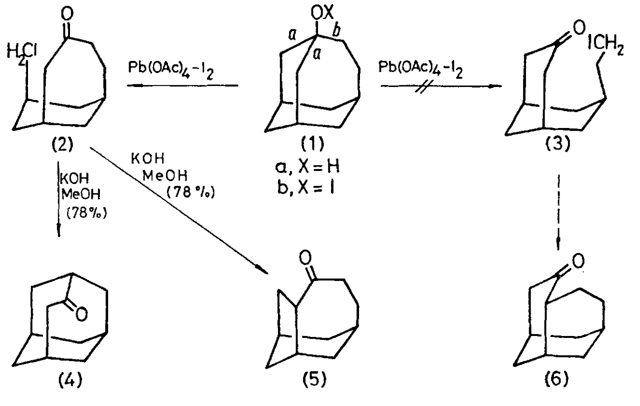
Summary Thermolysis of 3-homoadamantyl hypoiodite followed by base-promoted intramolecular cyclization yields 78% of a 3 : 2 mixture of 4-homoadamantanone and the hitherto unknown 4-homoprotoadamantan-4-one (tricyclo[5.3.1.0^{3,9}]undecan-4-one).

Recently we reported[1] the synthesis of 10-homoprotoadamantan-4-one (tricyclo[4.3.2.0^{3,8}]undecan-4-one) from 1-homoadamantanol by the hypoiodite thermolysis–cyclization reaction. This reaction appears to be an excellent method for the preparation of a variety of adamantanoid ketones.

We now report the thermolysis of 3-homoadamantyl hypoiodite (**1b**) and the intramolecular cyclization of the resulting iodoketone. Thermolysis of tertiary polycyclic hypohalites generally proceeds by scission of a β-C–C bond leading to the corresponding halogenoketone.[1–4] Since only two of the three β-bonds in (**1**) are equivalent ($a \neq b$) two isomeric iodoketones, (**2**) and (**3**), could be formed. Intramolecular, base-promoted, *C*-alkylation of the iodoketones (**2**) and (**3**) can be expected[1,3] to yield three ketones: (**4**) plus (**5**), and (**6**), respectively.



3-Homoadamantyl hypoiodite (**1b**) was prepared and thermolysed in a single operation from 3-homoadamantanol[5] (**1a**, 5 mmol) by the action of dry lead tetra-acetate (10 mmol) and iodine (11 mmol) in a dilute, dry benzene solution (70 ml). The temperature was kept at 80 °C for 5 min and at 60 °C for additional 2 h. The lead compounds were filtered off, and the filtrate was washed successively with aqueous $NaHSO_3$ and $NaHCO_3$ and dried. The solvent was evaporated off producing a single iodoketone; ν_{max} (film) 1690 cm^{-1} (C=O); ^{1}H n.m.r. ($CDCl_3$) δ 3·1 (d, *J* 6 Hz, CH_2I) and 0·6—2·7 (m, 15H). The crude iodoketone was cyclized by KOH (12 mmol) in methanol (25 ml; reflux, 3 h) to give a 3 : 2 mixture of two products.† The product mixture was purified by column chromatography on alumina (neutral, activity III/IV) using 0 → 100% ether-pentane as eluent. The overall total yield of the pure products (⩾ 97%)† was 78%, based on (**1a**). The products were separated on a 1 : 5 charcoal–silica gel column with a 3 → 5% ethyl acetate in cyclohexane solution as eluent.‡ The major product was identified as 4-homoadamantanone (**4**) by ^{1}H n.m.r. and i.r. spectroscopy, mass spectrometry, and g.l.c. in comparison with an authentic sample. The minor product had a longer g.l.c. retention time than (**4**)† and had the following spectral and physical properties: ^{13}C n.m.r. ($CDCl_3$) δ 27·7, 31·3, 35·0, 35·3, 35·5, 36·1, 36·9, 37·5, 40·5, 53·0, and 216·3 p.p.m.; ^{1}H n.m.r. ($CDCl_3$) δ 1·1—3·4 (m); ν_{max}(KBr) 2900, 2860, 1690, 1460, 1260, 1210, and 1130 cm^{-1}; mass spectra *m/e* 164 (74%), 135 (32), 108 (39), 95 (100), and 78(98); m.p. 180—182 °C. To distinguish between structures (**5**) and (**6**) the product was reduced to the corresponding hydrocarbon by the Wolff–Kishner reaction. The ^{13}C n.m.r. spectrum of the hydrocarbon showed **11** signals indicating that structure (**5**) (tricyclo[5.3.1.0^{3,9}]undecane) was correct [^{13}C n.m.r. ($CDCl_3$) δ 20·9, 27·2, 29·2, 32·7, 34·0, 34·6, 35·8, 37·1, 37·4, 37·7, and 40·7 p.p.m.; ^{1}H n.m.r. ($CDCl_3$) δ 1·1—2·3 (m); ν_{max} (KBr) 2920, 2860, 2850, 1465, and 1445 cm^{-1}; mass spectra *m/e* 150 (100%), 135 (36), 121 (34), 108 (36), 93 (48), and 79 (72); m.p. 186—189 °C.

The hypoiodite thermolysis–cyclization reaction appears to be a convenient entry to the 4-homoprotoadamantane§ system as well as to a number of other adamantanoid systems which are otherwise difficultly accessible.

Thermolysis of 3-homoadamantyl hypoiodite (**1b**), as well as that of 1-homoadamantyl hypoiodite,[1] is a highly selective process: bond *a* is exclusively cleaved and, consequently, only the iodoketone (**2**) is formed. This may be explained by the higher stability of a $>CHCH_2\cdot$ free radical over that of a $>CHCH_2CH_2\cdot$ free radical. Base-promoted cyclization of (**2**) is, however, a quite unselective process. Ketones (**4**) and (**5**) are formed in almost equal amounts although structure (**4**) is at least 7 kcal mol^{-1} more stable than structure (**5**).[6]

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† G.l.c. analysis (20% DEGS, 160 °C).

‡ The separation on silica gel alone and alumina as well as by preparative g.l.c. (DEGS, FFAP, Carbowax 20M, OV-210, QF-1) was less satisfactory.

§ Recently, N. Takaishi, Y. Inamoto, K. Aigami, Y. Fujikura, E. Osawa, M. Kawanisi, and T. Katsushima (*J. Org. Chem.*, in the press) obtained 4-homoprotoadamantane in a different manner and G. Fráter (*Helv. Chim. Acta*, 1976, **59**, 164) prepared derivatives of 3,6-dimethyltricyclo[5.3.1.0^{3,9}]undec-5-en-2-one by the cyclization of 2-substituted 2,5,7-trimethylbicyclo[4.3.1]deca-4,7-dienes.

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