JOURNAL OF THE CHEMICAL SOCIETY

Chemical Communications

Number 4
1987

Synthesis of 2-Cumyladamantan-2-ol by the Catalytic Use of 4,4′-Di-t-butylbiphenyl as an Electron-transfer Agent with Lithium in a Barbier-type Reaction of Adamantanone and Cumyl Chloride

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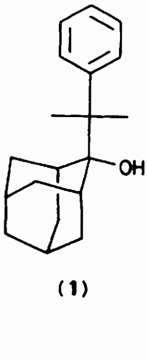
A Barbier-type condensation between adamantanone and cumyl chloride to produce the strained product 2-cumyladamantan-2-ol (**1**) has been effected using lithium metal in tetrahydrofuran (THF) with a catalytic amount of 4,4′-di-t-butylbiphenyl as an electron-transfer reagent; (**1**) is characterised by *X*-ray analysis.

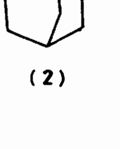
Our continuing interest in the chemical behaviour of highly strained systems[1] led us to synthesize 2-cumyladamantan-2-ol (**1**). We report here a novel method promising general utility which overcomes the inherent limitations of commonly used synthetic approaches to this compound.

The formation of highly reactive, sterically strained tertiary alcohols by the condensation of organometallic reagents and ketones is a formidable synthetic challenge. Organolithium compounds are generally much more effective in such syntheses than are the corresponding organomagnesium compounds,[2] yet some organolithium compounds such as benzyl-lithiums[3] are not available by simple, direct metallation routes. In fact, the 'Grignard-like' method successfully used previously for the synthesis of a number of 2-alkyladamantan-2-ols, *viz.*, the reaction of an alkyl chloride with metallic lithium in tetrahydrofuran (THF) or ether followed by addition of adamantan-2-one (**2**),[1] gave only recovered ketone and some unidentified by-products when cumyl chloride was used in an attempt to prepare (**1**). The same results were obtained through use of the Barbier reaction where the alkyl halide and ketone were co-added to a suspension of lithium metal in tetrahydrofuran (THF)[4] or ether.[5]

In the face of these failures, the Barbier-type approach was combined with the use of an aromatic hydrocarbon to function as an electron-transfer agent.[4,6] In anticipation of the expected extreme acid sensitivity of the product, it seemed likely that the problem of removal of the aromatic hydrocarbon during work-up could not be solved by using Cohen's 1-dimethylaminonaphthalene technique;[7] therefore, 4,4′-di-t-butylbiphenyl (DBB) was selected as the superior electron-transfer agent.[6]



(**1**)



(**2**)

When the reaction was run in THF at 0 °C using near stoicheiometric amounts of DBB, (**2**), and cumyl chloride with an excess of lithium sand containing *ca.* 3.3% Na,[8] the reaction proceeded nicely to give good conversion into (**1**). However, it proved impossible to separate the alcohol product from the large amount of DBB present. The reaction was therefore run using only a catalytic amount (1—3 mol%) of the electron-transfer agent, as suggested by previous work.[4,6,7] This technique proved successful. Separation of the crude product mixture by flash column chromatography[9] gave pure samples of alcohol (**1**) in good yield.†

The *X*-ray structure of compound (**1**) is shown in Figure 1.‡

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† In a typical experiment conducted under an argon atmosphere in oven-dried glassware, a solution of cumyl chloride (11.0 mmol) and adamantan-2-one (9.93 mmol) in THF (40 ml) was added dropwise at 0 °C with vigorous stirring to a mixture of lithium sand (75.4 mmol; 3.3% Na) and DBB (0.30 mmol) in THF (10 ml) at a rate to maintain the dark-green colour of the radical anion. Following overnight stirring at room temperature, the excess of lithium was destroyed by careful addition of sat. aq. ammonium chloride solution and the mixture was extracted with pentane. The pentane extract was then washed with conc. brine, dried (Na_2SO_4), and concentrated *in vacuo* to give 67% of crude product. Purification by elution from a silica gel column (hexane–ether, 60:10) followed by recrystallization from pentane–ether (90:10) gave pure alcohol; m.p. 80—81 °C. All microanalytical and spectral properties were consistent with the assigned structure.

‡ *Crystal data* for (**1**): $C_{19}H_{26}O$, $M = 270.42$, monoclinic, space group $P2_1/n$, $a = 10.864(5)$, $b = 6.601(1)$, $c = 20.908(6)$ Å, $\beta = 92.82(3)°$, $Z = 4$, $D_c = 1.20$ g cm^{-3}, Mo-K_α ($\lambda = 0.71073$ Å), $T = 294$ K. Data were collected on an Enraf–Nonius CAD 4 diffractometer, 1727 'observed' reflections [$I > 3\sigma(I)$], $2\theta_{max.} = 52.0°$, $R = 0.041$, $R_w = 0.054$. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

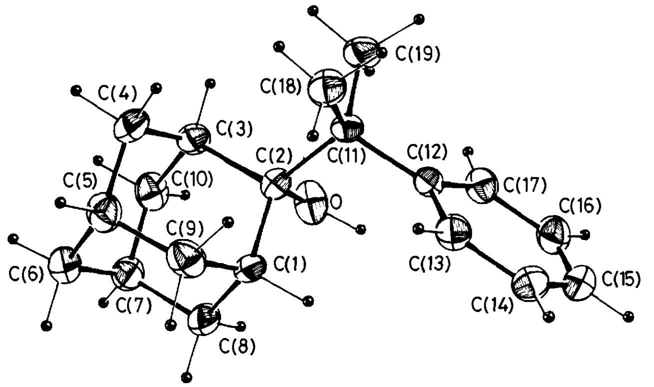

Figure 1. An ORTEP plot showing the *X*-ray structure of alcohol (**1**) and the atom numbering scheme. Important distances (Å) and angles (°) are as follows: O–C(2) 1.444(2), C(1)–C(2) 1.542(3), C(2)–C(3) 1.562(3), C(2)–C(11) 1.607(3), C(11)–C(18) 1.537(3), C(11)–C(19) 1.544(3); C(1)–C(2)–C(3) 106.5(1), C(1)–C(2)–C(11) 116.8(2), C(3)–C(2)–C(11) 116.4(2), C(2)–C(11)–C(12) 108.0(1), C(2)–C(11)–C(18) 117.3(2), C(2)–C(11)–C(19) 108.2(2), C(18)–C(11)–C(19) 104.7(2).

Noteworthy features include the elongated C(2)–C(11) bond and the abnormally large C(2)–C(11)–C(18) bond angle. Both are indicative of steric strain in the molecule. Preliminary studies attest to the high chemical reactivity of this system.

We thank The University of Toledo Faculty Research Awards and Fellowships Program for support of this work (J. L. F.) and the College of Arts and Sciences of The University of Toledo for providing resources for the *X*-Ray Diffraction Center.

Received, 15th September 1986; Com. 1323

References

1 R. C. Badger and J. L. Fry, *J. Am. Chem. Soc.*, 1979, **101**, 1680; J. A. Saba and J. L. Fry, *ibid.*, 1983, **105**, 533.
2 B. J. Wakefield, 'The Chemistry of Organolithium Compounds,' Pergamon Press, Oxford, 1974.
3 M. Clarembeau and A. Krief, *Tetrahedron Lett.*, 1985, **26**, 1093.
4 P. J. Pearce, D. H. Richards, and N. F. Scilly, *Chem. Commun.*, 1970, 1160; *J. Chem. Soc., Perkin Trans. 1*, 1972, 1655.
5 P. Bauer and G. Molle, *Tetrahedron Lett.*, 1978, 4853; G. Molle and P. Bauer, *J. Am. Chem. Soc.*, 1982, **104**, 3481.
6 P. K. Freeman and L. L. Hutchinson, *Tetrahedron Lett.*, 1976, 1849; *J. Org. Chem.*, 1980, **45**, 1924.
7 T. Cohen, J. P. Sherbine, J. R. Matz, R. R. Hutchins, B. M. McHenry, and P. R. Willey, *J. Am. Chem. Soc.*, 1984, **106**, 3245.
8 P. D. Bartlett and E. B. Lefferts, *J. Am. Chem. Soc.*, 1955, **77**, 2804.
9 W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.