

Reaction of sodium cyanide with 5-bromo-1-benzosuberone: a reappraisal

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The reaction of 5-bromo-1-benzosuberone with KCN or NaCN in hot DMSO leads, not to the formation of 5-cyano-1-benzosuberone as previously reported, but to the 4-cyano isomer *via* elimination to benzo-4-suberen-1-one and subsequent conjugate addition.

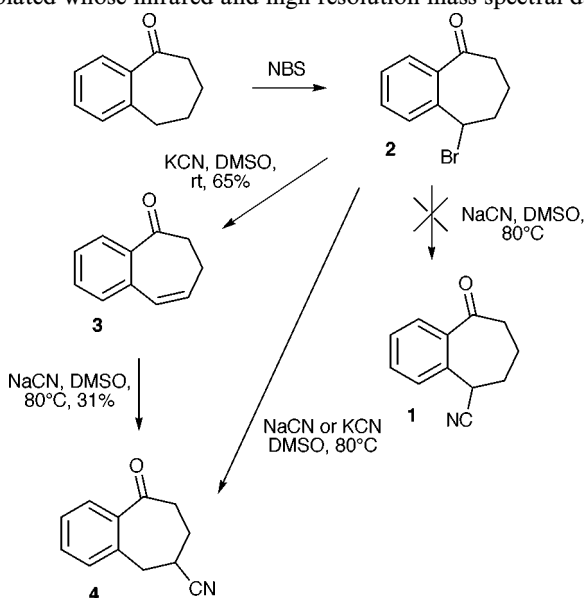
In the context of an ongoing investigation we required 5-cyano-1-benzosuberone **1**. A search of the literature revealed that this substance had been previously prepared once, by Sedgeworth and Proctor,¹ and not subsequently reported. These authors reportedly obtained **1** by the logical sequence of NBS bromination of benzosuberone, giving the bromide **2**, followed by displacement with NaCN in hot DMSO (see Scheme 1). The isolated yield was 60% and the mass, infrared spectral and microanalytical data were in accord with the assigned structure, as was the poorly detailed ¹H-NMR spectrum, which consisted of a 4H aromatic multiplet (δ 7.8–7.1), a 5H aliphatic multiplet (δ 3.3–2.7) and a second 2H aliphatic multiplet (δ 2.5–2.0).

Results and discussion

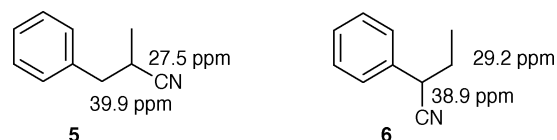
We repeated the preparation of bromide **2**, whose structure was confirmed by NMR analysis: the ¹H- and ¹³C-NMR spectrum showed, respectively, a 1H double-doublet (δ 5.52) and the benzylic methine (δ 54.1). When **2** was treated with NaCN, as described by Sedgeworth and Proctor, a nitrile was isolated whose infrared and high resolution mass spectral data

agreed with structure **1**. The ¹H-NMR spectrum (300 MHz) was also in agreement with the literature and consisted of two poorly resolved multiplets in the aliphatic region at δ 3.19–2.90 (5H) and 2.29 (2H). Habit, however, prompted us to record the ¹³C-NMR spectrum and assign multiplicities, by a DEPT (Distortionless Enhancement by Polarization Transfer) experiment, leading to the realization that the assigned structure (**1**) must be incorrect. This realization arose from the chemical shift of the methine carbon (δ 24.2), which was incompatible with the benzylic nature of the methine in **1**, and the presence of an equally incompatible and obvious benzylic methylene (δ 42.8).

Various other conditions were tried including NaCN, AgCN or KCN, all in DMSO; none of these provided a substance fully compatible with structure **1**. Lowering the temperature to ambient resulted in the isolation, not of a nitrile, but of the olefin **3** in yields up to 65%, and so provided the essential clue. Resubmission of **3** to the original conditions (NaCN in DMSO at 80 °C) resulted in the isolation of the identical nitrile to which we now assign the structure **4** (see Scheme 1). Evidently, the overall reaction involves initial elimination to give the styrene **3**, which then undergoes conjugate addition, perhaps assisted by the influence of the carbonyl group, leading to the formation of the isomeric nitrile **4**. This structure is in full agreement with the ¹³C-NMR spectrum as well as with the poorly resolved ¹H-NMR spectrum. Furthermore, the above mentioned ¹³C spectral data for **4** are in better agreement with those of the simple analog **5**,² than of its isomer **6**.³



Scheme 1



Although we have not followed up this avenue of research, this interesting observation opens up the possibility that other 4-substituted benzosuberones may be readily accessible through conjugate addition to olefin **3**.

Experimental

5-Bromo-1-benzosuberone (2). This compound was prepared exactly as described by Sedgeworth and Proctor.¹ δ_{H}

(300 MHz, CDCl₃): 1.97 (m, 1H); 2.23 (m, 2H); 2.43 (m, 1H); 2.68 (m, 1H); 3.16 (ddd, *J* = 13.9, 9.6 and 4.9 Hz, 1H); 5.52 (dd, *J* = 5.8 and 2.3 Hz, 1H); 7.43–7.20 (m, 3H); 7.55 (dd, *J* = 7.0 and 1.0 Hz, 1H). δ_{C} (75 MHz, CDCl₃): 21.5 (CH₂), 34.2 (CH₂), 42.0 (CH₂), 54.1 (CH), 128.7 (CH), 128.8 (CH), 129.5 (CH), 131.5 (CH), 139.6 (C), 139.7 (C), 204.7 (C=O).

Benzo-4-suberen-1-one (3). Bromide **2** (104 mg, 0.43 mmol), potassium cyanide (113 mg, 1.7 mmol) and DMSO (2 ml) were stirred at room temperature for 4 h. The reaction mixture was then diluted with water (50 ml) and extracted with Et₂O (3 × 5 ml). The combined organic extracts were washed with water and brine, dried (MgSO₄), and concentrated *in vacuo*. Purification by flash chromatography (gradient elution 0 : 100 hexane–EtOAc to 2 : 98 hexane–EtOAc) gave 44 mg (65%) of the title compound. δ_{H} (300 MHz, CDCl₃): 2.50 (m, 2H); 2.91 (m, 2H); 6.15 (dt, *J* = 11.5 and 5.6 Hz, 1H); 6.44 (d, *J* = 11.5 Hz, 1H); 7.12–7.49 (m, 3H); 7.89 (dd, *J* = 7.8 and 1.3 Hz, 1H); δ_{C} (75 MHz, CDCl₃): 24.2 (CH₂), 41.8 (CH₂), 126.9 (CH), 129.4 (CH), 131.1 (CH), 131.6 (CH), 132.3 (CH), 133.0 (CH), 135.7 (C), 136.5 (C), 201.9 (C=O). HR-MS: *m/z* 158.0731 (M⁺, C₁₁H₁₀O requires 158.0732).

4-Cyano-1-benzosuberone (4). A solution of **3** (40 mg, 0.25 mmol) in DMSO (0.5 ml) was added dropwise to a stirred suspension of sodium cyanide (37 mg, 0.75 mmol) in 1 ml of DMSO at 80 °C. The resulting mixture was heated for 4 h,

then cooled and poured onto water and extracted with Et₂O. The combined organic extracts were washed with water and brine, dried (MgSO₄), and concentrated *in vacuo*. Purification by flash chromatography (gradient elution 0 : 100 hexane–EtOAc to 2 : 98 hexane–EtOAc) gave 14 mg (31%) of the title compound. δ_{H} (300 MHz, CDCl₃): 2.29 (m, 2H); 2.90–3.19 (m, 5H); 7.21 (d, *J* = 7.4 Hz, 1H); 7.33 (t, *J* = 7.4 Hz, 1H); 7.47 (t, *J* = 7.4 Hz, 1H); 7.70 (d, *J* = 7.4 Hz, 1H); δ_{C} (75 MHz, CDCl₃): 24.2 (CH), 29.5 (CH₂), 30.6 (CH₂), 42.8 (CH₂), 121.0 (C), 127.5 (CH), 128.9 (CH), 129.8 (CH), 133.0 (CH), 137.8 (C), 139.3 (C), 199.9 (C=O). HR-MS: *m/z* 185.0843 (M⁺, C₁₂H₁₁NO requires 185.0841).

Acknowledgement

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References

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