SHORT PAPER

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Sodium bismuthate mediated oxidation study of hydrofluorenes†

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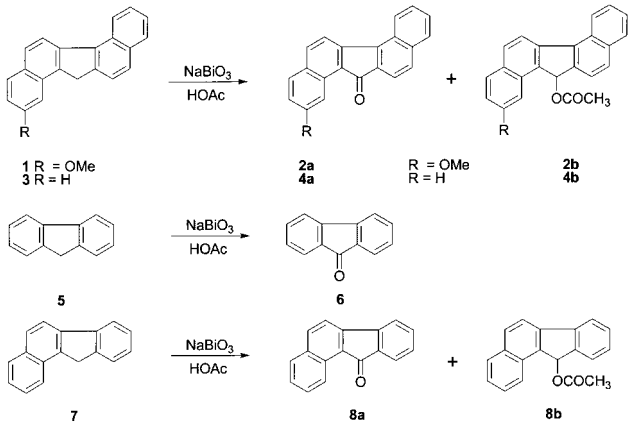
The product distribution of sodium bismuthate mediated oxidation of several hydrofluorenes was found to depend on the structure of the starting materials and reaction conditions.

In our earlier publication,[1] we demonstrated a simple method for the oxidation of benzylic methylenes to the benzylic ketones by sodium bismuthate in acetic acid. We also showed[2] that this reagent may be used for the oxidation of benzylic and allylic alcohols to the carbonyl compounds. In continuation of our examination of sodium bismuthate mediated oxidation, we wish to report a study of this reaction applied to hydrofluorenes.

We[3] have been engaged in the development of polyaromatic compounds as anticancer agents, which requires several methoxy substituted dibenzofluorenols for structure-activity relationship comparison. Synthesis of these alcohols is difficult and the method in the literature for this purpose is cumbersome, since oxidation by molecular oxygen in the presence of *n*-BuLi is a complicated process.[4] Oxidation by sodium bismuthate[5] and subsequent reduction by sodium borohydride is another alternative which works well in certain cases.

The methoxy hydrocarbon **1**[6] (Scheme 1) on refluxing with sodium bismuthate in the presence of acetic acid produced the ketone **2a** and acetoxy derivative **2b** in a ratio of 2:1.



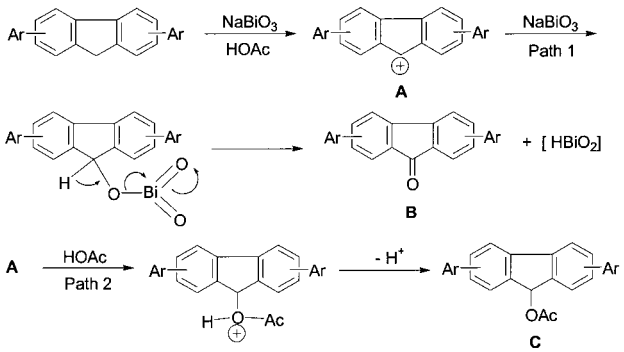
Scheme 1

When the reaction was conducted at room temperature, the ratio of the ketone **2a** and the acetoxy compound **2b** was found to be 1:2.8. Reaction of the unsubstituted hydrocarbon **3**[1,7] at room temperature under identical condition gave a 1:2.5 mixture of ketone **4a** and the acetate **4b**. However, the ketone **4a** was the only product isolated from the oxidation of the unsubstituted hydrocarbon **3** at reflux temperature. These results indicated that the oxidation by sodium bismuthate is temperature dependent, and that the structure of the starting hydrofluorenes **1** and **3** have a significant impact on the product distribution. Additional examples (**5** and **7**[7]) were selected to investigate benzylic oxidation by this reagent system. The tricyclic hydrofluorene **5** produced ketone **6** at reflux temperature, but at room temperature the reaction did not proceed to completion. The isolated product was found to be the ketone **6** in only 30% yield and no acetoxy compound was detected. The tetracyclic hydrocarbon **7** produced a mixture of ketone **8a** and acetoxy compound **8b** (1:2.5) at room temperature while at high temperature, ketone **8a** was the only product.

From these results, one can speculate that the acetoxy compounds **2b**, **4b** and **8b** represent an intermediate which is transformed to the ketones **2a**, **4a** and **8a** by the excess oxidizing agent present in the medium. However, treatment of the acetoxy compound **4b** with sodium bismuthate in the presence of acetic acid did not produce the ketone **4a** suggesting that acetate is not an intermediate.

The time required for the completion of the oxidation under identical conditions deserves some comments. The order of the reactivity was found to be **1**>**3**>**7**>**5**. This is interesting as one could expect a slower reaction with larger ring systems because of steric hindrance. The formation of a significant amount of acetoxy compound with the tetracyclic and pentacyclic ring systems suggests different mechanisms.

The mechanism of sodium bismuthate mediated oxidation reaction has never been studied. The formation of the ketones and acetates can be explained by assuming the generation of a carbocation by the direct attack of the bismuthate (Scheme 2). The carbocation (**A**) formed by the attack of bismuthate anion can produce the ketone (**B**) or by a nucleophilic attack by acetic acid it can give the acetate (**C**). The ketone **6** from the tricyclic hydrocarbon **5** is exclusively formed through the direct attack by the bismuthate anion to the carbocation (**A**) because of lower steric hindrance (path 1). On the other hand, because of the steric hindrance due to the additional aromatic moiety (as in **1**, **3** and **7**), a competitive path can be followed (path 1 and 2) and this can produce a mixture of the ketone and the acetate. It appears that because of the higher stability



Scheme 2

* To receive any correspondence.
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Oxidation of hydrofluorenes

Entry	Hydrofluorene	Method	Product (yield %) [ratio]	Time (h)
1	**1**	A[a]	**2a** (34.3) + **2b** (16.7) [2] [1]	8
		B[b]	**2a** (17.1) + **2b** (47.6) [1] [2.8]	16
2	**3**	A	**4a** (56)	10
		B	**4a** (17.3) + **4b** (43.3) [1] [2.5]	16
3	**5**	A	**6** (61)	36
		B	**6** (30.7)	72
4	**7**	A	**8a** (56.6)	4
		B	**8a** (17) + **8b** (42.4) [1] [2.5]	40

[a]Reaction carried out under refluxing condition. [b]Reaction carried out at room temperature

of the carbonium ion in tetracyclic and pentacyclic systems (**1**, **3** and **7**) compared to the tricyclic system (**5**), a dual path[8]-direct attack by the bismuthate anion or the nucleophilic attack by the solvent (combination of path 1 and 2) are equally possible. At higher temperature, it appears that path 1 is favored and thus ketone is the major or exclusive product.

Experimental

Melting points are uncorrected. IR spectra were recorded as films. ^{1}H NMR were recorded at 300 MHz and ^{13}C NMR were recorded at 75 MHz.

Method A: Oxidation of 2-methoxy-13H-dibenzo[a, g]fluorene **(1):** A mixture of **1** (0.1 g, 0.34 mmol) and $NaBiO_3$ (0.38 g, 1.36 mmol) in AcOH (4 ml), water (4 ml) and acetone (2 ml) was refluxed under argon for 8 h. It was diluted with CH_2Cl_2, filtered through a pad of celite and washed with water and saturated $NaHCO_3$ solution. Drying (Na_2SO_4) and concentration afforded a solid residue, which was subjected to chromatography on silica gel to produce **2a** (0.036 g, 34.3 %) and **2b** (0.02 g, 16.7 %).

Method B: Oxidation of 2-methoxy-13H-dibenzo[a, g]fluorene **(1):** A mixture of **1** (0.1 g, 0.34 mmol) and $NaBiO_3$ (0.38 g, 1.36 mmol) in AcOH (6 ml) was stirred in a stoppered flask for 16 h. It was diluted with CH_2Cl_2 and filtered through a pad of celite. Similar workup and purification as *Method A* provided **2a** (0.018 g, 17.1 %) and **2b** (0.057 g, 47.6 %).

2a: m.p. 168–170° C (acetone : hexane). IR (cm^{-1}): 3053, 2938, 1699, 1624, 1588. NMR ^{1}H: δ 3.98 (s, 3H), 7.02 (dd, 1H, *J* = 9 and 2.4 Hz), 7.48–7.66 (m, 4H), 7.72 (d, 1H, *J* = 8.1 Hz), 7.81–7.87 (m, 2H). 7.98 (dd, 1H, *J* = 8.1 and 1.8 Hz), 8.29 (d not properly resolved, 1H), 8.47 (d, 1H, *J* = 8.1 Hz). ^{13}C: δ 55.91 (O*C*H$_3$), 101.79 (Ar-*C*H), 119.3 (Ar-*C*H), 119.88 (Ar-*C*H), 120.58 (Ar-*C*H), 124.99 (Ar-*C*H), 125.85, 128.02 (Ar-*C*H), 128.14 (Ar-*C*H), 129.13, 130.07 (Ar-*C*H), 130.12 (Ar-*C*H), 130.21 (Ar-*C*H), 130.48, 132.19, 132.65, 135.38 (Ar-*C*H), 138.40, 142.1, 147.61, 161.18, 196.81 (*C*O).

2b: m.p. 182 – 184° C (CH_2Cl_2 : hexane). IR (cm^{-1}): 3056, 2936, 2831, 2360, 1731, 1628, 1595. NMR ^{1}H: δ 2.26 (s, 3H), 3.92 (s, 3H), 7.13–7.16 (m, 2H), 7.32 (s, 1H), 7.51 – 7.57 (m, 1H), 7.61–7.67 (m, 1H), 7.70 (d, 1H, *J* = 8.2 Hz), 7.81 (d, 1H, *J* = 9.7 Hz), 7.82 (d, 1H, *J* = 8.2 Hz), 7.94 (d, 2H, *J* = 8.4 Hz), 8.29 (d, 1H, *J* = 8.5 Hz), 8.74 (d, 1H, *J* = 8.5 Hz). ^{13}C: δ 21.2 (CO*C*H$_3$), 55.28 (O*C*H$_3$), 74.2 (*C*H), 101.45 (Ar-*C*H), 118.93 (Ar-*C*H), 119.17 (Ar-*C*H), 122.61 (Ar-*C*H), 123.97 (Ar-*C*H), 126.0 (Ar-*C*H), 126.88 (Ar-*C*H), 128.34, 128.6 (Ar-*C*H), 129.19, 129.32 (Ar-*C*H), 130.2 (Ar-*C*H), 130.35 (Ar-*C*H), 131.11, 134.91, 136.68, 136.97, 141.01, 141.3, 158.55, 172.0 (*C*O).

The compounds **4a**, **4b**, **6**, **8a** and **8b** were prepared by similar procedure.

4a: m.p. 162–164° C (acetone : hexane) (lit.[7] 164–165° C).

4b: m.p. 176–178° C (CH_2Cl_2 : hexane). IR (cm^{-1}): 3056, 2928, 1728, 1626, 1590. NMR ^{1}H: δ 2.27 (s, 3H), 7.35 (s, 1H), 7.47–7.57 (m, 3H), 7.58–7.65 (m, 1H), 7.66 – 7.96 (m, 5H), 8.03 (d, 1H, *J* = 8.6 Hz), 8.46 (d, 1H, *J* = 8.6 Hz), 8.77 (d, 1H, *J* = 8.4 Hz).

6: m.p. 81–83° C (acetone : hexane) (lit.[9] 82 – 85° C).

8a: m.p. 96–98° C (acetone : hexane). IR (cm^{-1}): 3046, 2926, 2360, 2342, 1698, 1625, 1605, 1581. NMR ^{1}H: δ 7.23 (dt, 1H, *J* = 1.5 and 7.1 Hz), 7.37–7.45 (m, 3H), 7.53–7.6 (m, 3H), 7.74 (d, 1H, *J* = 8.2 Hz), 7.93 (d, 1H, *J* = 8.2 Hz), 8.92 (d, 1H, *J* = 8.4 Hz). ^{13}C: δ 118.46 (Ar-*C*H), 120.32 (Ar-*C*H), 124.18 (Ar-*C*H), 124.66 (Ar-*C*H), 126.78 (Ar-*C*H), 127.22, 128.9 (Ar-*C*H), 129.62 (Ar-*C*H), 129.79 (Ar-*C*H), 130.54, 134.56 (Ar-*C*H), 134.79, 134.95, 136.24 (Ar-*C*H), 144.24, 146.5, 195.75 (*C*O).

8b: IR (cm^{-1}): 3056, 2932, 2361, 2342, 1732, 1625, 1593. NMR ^{1}H: δ 2.21 (s, 3H), 7.21 (s, 1H), 7.27 (dt, 1H, J = 0.9 and 7.4 Hz), 7.38–7.55 (m, 3H), 7.61 (d, 1H, *J* = 7.4 Hz), 7.67 (d, 1H, *J* = 7.4 Hz), 7.76–7.83 (m, 2H), 7.86 – 7.92 (m, 2H). ^{13}C: δ 21.69 (CO*C*H$_3$), 74.71 (*C*H), 118.81 (Ar-*C*H), 120.3 (Ar-*C*H), 124.03 (Ar-*C*H), 126.11 (Ar-*C*H), 126.31 (Ar-*C*H), 127.69 (Ar-*C*H), 128.06 (Ar-*C*H), 129.52 (Ar-*C*H), 129.92 (Ar-*C*H), 130.61, 131.13 (Ar-*C*H), 133.99, 137.16, 139.82, 142.02, 143.32, 172.19 *C*O).

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