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The Reductions of Carbonyl Compounds with Sodium 1-Benzyl-3-carbamoyl-1,4-dihydropyridine-4-sulfinate

Hiroo Inoue,* Ichiro Sonoda, and Eiji Imoto

Department of Applied Chemistry, College of Engineering, University of Osaka Prefecture, Sakai, Osaka 591

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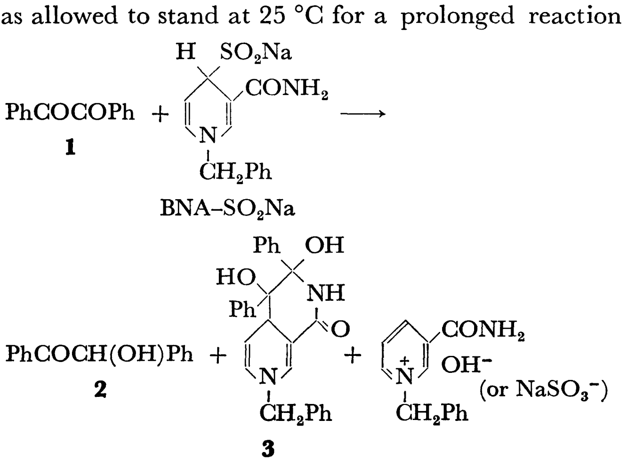
Synopsis. It is found that sodium 1-benzyl-3-carbamoyl-1,4-dihydropyridine-4-sulfinate reduces α-keto carbonyl compounds to α-hydroxy carbonyl compounds with the assistance of $MgCl_2$ and reacts with 9-fluorenone to give an adduct.

Although sodium 1-benzyl-3-carbamoyl-1,4-dihydropyridine-4-sulfinate (BNA-SO_2Na) is of interest as a reducing agent, not a great deal is yet known about the chemical reactivity of BNA-SO_2Na. Recently we reported that BNA-SO_2Na can undergo reductions of α-halo ketones to the parent ketones[1] and that of acridine to 9,9′-bi(9,10-dihydroacridine)[2] in a protic solvent. In analogy with sodium hydroxymethanesulfinate[3] and thiourea dioxide,[4] the carbon-sulfur bond of BNA-SO_2Na is cleaved in the reduction process. Our interest in the reactivity of BNA-SO_2Na prompted us to examine the capability of BNA-SO_2Na for the reductions of the carbonyl compounds. We now wish to report several results giving information on the reactivity of BNA-SO_2Na caused by its unique structure.

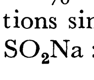
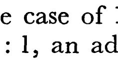
Results and Discussion

Reactions of BNA-SO_2Na with α-Keto Carbonyl Compounds. BNA-SO_2Na reacted under nitrogen with benzil (**1**) in 80 vol % aqueous methanol at 25 °C for 12 min to give α-hydroxydeoxybenzoin (**2**) and a thermally unstable adduct (**3**) in isolated yields of 80 and 19% respectively. In this reaction, BNA-SO_2Na was converted to 1-benzyl-3-carbamoylpyridinium salt[5] in a 92% yield, based on **1**. The amount of the salt produced indicates that BNA-SO_2Na undergoes a two-electron reduction of **1**. When the reaction mixture was allowed to stand at 25 °C for a prolonged reaction time (20 h), the yield of **2** (88%) increased with a decrease in that of **3** (5%). On the other hand, the reaction of **1** with BNA-SO_2Na in a 0.6 M sodium hydroxide solution (80 vol % aqueous methanol) gave **3** as the only product in a 92% yield.



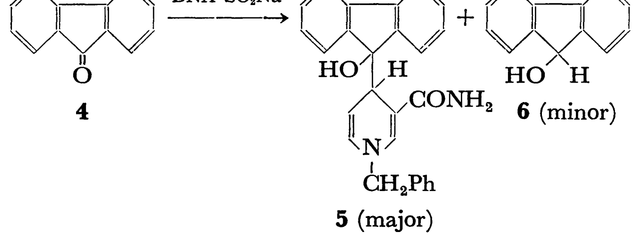
The addition of $MgCl_2$ to the reaction system containing **1** and BNA-SO_2Na (the molar ratio of $MgCl_2$: BNA-SO_2Na: **1**=5: 2: 1) resulted in the selective formation of **2** in a high yield, as Table 1 shows. Furthermore, **3** reacted with $MgCl_2$ to give **2** in a high yield (87% at 25 °C for 17 h). These facts indicate that **3** is converted to **2** with the assistance of $MgCl_2$. The results of the reductions of the other α-keto carbonyl compounds by the BNA-SO_2Na–$MgCl_2$ system are summarized in Table 1. In the absence of $MgCl_2$, the yields of the α-hydroxy carbonyl compounds became much lower because of the formation of adducts and unproved by-products. Thus, the BNA-SO_2Na–$MgCl_2$ system is effective as a reducing system for the conversion of α-keto carbonyl compounds to α-hydroxy carbonyl compounds.

TABLE 1. THE YIELDS OF α-HYDROXY CARBONYL COMPOUNDS IN THE REDUCTION OF α-KETO CARBONYL COMPOUNDS WITH THE BNA-SO_2Na–$MgCl_2$ SYSTEM[a)]

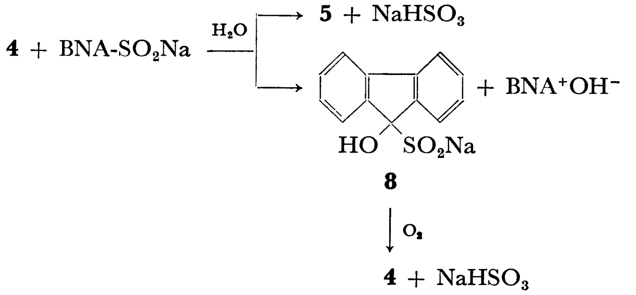
Substance	Time, h	Product (%)[b)]
PhCOCOPh	1	PhCOCH(OH)Ph (92)
PhCOCOOEt	17	PhCH(OH)COOEt (70)
PhCOCHO	18	$PhCOCH_2OH$ (55)
$C_3H_7COCOC_3H_7$	1	$C_3H_7COCH(OH)C_3H_7$ (61)
	2	 (49)

a) Molar ratio of $MgCl_2$: BNA-SO_2Na: substance= 5: 2: 1. Concentration of the substance: 0.06 mol/l. 80 vol % aqueous methanol. 25 °C. b) Isolated yield.

Reactions of BNA-SO_2Na with Diaryl Ketones. The reaction of BNA-SO_2Na with 9-fluorenone (**4**) in 80 vol % aqueous methanol was carried out under conditions similar to those in the case of **1**. With a BNA-SO_2Na : **4** molar ratio of 2: 1, an adduct (**5**) and 9-fluorenol (**6**) were obtained in 30 and 1% yields respectively, with a 62% recovery of **4**. [9,9′-Bi-9*H*-fluorene]-9,9′-diol (**7**) was not obtained at all. BNA-SO_2Na was converted to 1-benzyl-3-carbamoylpyridinium salt in a 72% yield, based on **4**. The yield of the salt was approximately comparable to the recovery



% of **4**. Even with a BNA-SO_2Na:**4** molar ratio of 5:1, the yields of **5** and **6** did not increase, as Table 2 shows. These facts suggest that the reaction proceeds through the cleavage of the carbon-sulfur bond of BNA-SO_2Na to give an unstable SO_2Na-adduct (**8**) in addition to **5**. The **8** must be converted to **4** and $NaHSO_3$ by hydrolysis, accompanied by oxidation with air on the separation of the products.



In an alkaline medium, the yield of **5** became better. Furthermore, $MgCl_2$ was ineffective in the reduction of **4** to **6** and **7** by BNA-SO_2Na. When $Mg(OCH_3)_2$ was used with BNA-SO_2Na, **5** was obtained in a good yield (Table 2).

TABLE 2. THE REACTION OF **4** WITH BNA-SO_2Na[a)]

Additive	Molar ratio Additive/**4**	Yield, %[b)]			Recovered **4**, %[b)]
		5	**6**	**7**	
None[c)]	0	30	1	0	62
NaOH	10	53	0	0	27
$MgCl_2$[d)]	5	3	0	4	85
$Mg(OCH_3)_2$[e)]	1	75	0	0	21

a) Concentration of **4**: 0.06 mol/l. BNA-SO_2Na:**4** molar ratio=2:1. 80 vol % aqueous methanol. 1 h. 25 °C. b) Isolated yield. c) In the BNA-SO_2Na:**4** molar ratio of 5:1, **5** was obtained in a 35% yield, with a 62% recovery of **4**. d) 20 h. e) MeOH solvent.

Benzophenone did not react with BNA-SO_2Na, even in an alkaline medium at 25 °C, and was recovered unreacted. When the temperature was raised to 90 °C, however, benzhydrol was found to be obtained in a 16% yield.[6)] Thus, BNA-SO_2Na was not effective as a reducing agent for the reductions of monoketones to alcohols.

$$\mathrm{PhCOPh} \xrightarrow[90\,^{\circ}\mathrm{C}]{\text{BNA-SO}_2\text{Na}} \mathrm{Ph_2CHOH}$$

Experimental

Material. The BNA-SO_2Na was prepared according to the procedures described in our preceding paper.[1)]

Reaction of 1 with BNA-SO_2Na. A typical experiment was as follows: to a solution of 3 mmol of **1** in 50 cm^3 of 80 vol % aqueous methanol we added 5.9 mmol of BNA-SO_2Na. The solution was stirred under nitrogen at 25 °C for 12 min. A pale yellow precipitate of **3** was removed by filtration, washed under nitrogen with 80 vol % aqueous methanol, and dried *in vacuo*. The yield of **3** (mp 132—134 °C), was 19%. **3** exhibited NMR (DMSO-d_6) signals at δ=3.9 (d, 1H, H_4), 4.4 (s, 2H, CH_2), 4.7 (d, 1H, H_5), 5.95 (d, 1H, H_6), 7.02 (s, 5H, aromatic protons), 7.23 (s, 10H, aromatic protons), and 7.5 ppm (d, 1H, H_2), and an IR (KBr) peaks at 3450 (OH), 3200—3250 (NH), and 1680 cm^{-1} (CO).

Found: C, 74.51; H, 5.84; N, 6.56%. Calcd for $C_{27}H_{24}N_2O_3 1/2\,H_2O$: C, 74.78; H, 5.81; N, 6.47 %.

The removal of the methanol from the filtrate gave 80% of **2** (mp 131—132 °C), which was identified by comparing its IR and NMR spectra with those of authentic specimens. After the removal of the methanol, the residual solution was developed on an anion-exchange resin (Amberlite IRA-400) to yield 92% of BNA^+Cl^-, based on **1**. Similar procedures were used for the reaction of **1** with BNA-SO_2Na in an alkaline medium and the reactions of **1** and the other α-keto carbonyl compounds with the BNA-SO_2Na–$MgCl_2$ system.

Reaction of 4 with BNA-SO_2Na. To a solution of 3 mmol of **4** in 50 cm^3 of 80 vol % aqueous methanol we added 5.7 mmol of BNA-SO_2Na. After the solution had been stirred under nitrogen at 25 °C for 1 h, the mixture was neutralized by dilute hydrochloric acid, the methanol was removed *in vacuo*, and the resinous material was extracted with benzene. After the removal of the benzene *in vacuo*, the residue was chromatographed on silica gel. Elution with benzene and then chloroform gave **4**, **5**, and **6** in 62, 30, and 1% yields respectively. The purification of **5** was carried out as follows: a solution of **5** in chloroform was placed on the silica gel column and eluted with 15 % acetone in chloroform to give the purified **5** (mp 88 °C (dec)); **5** exhibited NMR ($CDCl_3$) signals at δ=2.2 (s, 1H, OH), 3.85 (s, 2H, CH_2), 4.2 (d, 1H, H_4), 5.2 (d, 1H, H_5), 6.35 (d, 1H, H_6), 6.5—6.7 (m, 2H, NH_2), and 7.0—7.5 (m, 14H, aromatic protons and H_2), and IR (KBr) peaks at 3300—3350 and 3170—3200 (NH_2) and 1680 cm^{-1} (CO).

Found: C, 78.99; H, 5.75; N, 7.14%. Calcd for $C_{25}H_{22}N_2O_2$: C, 79.14; H, 5.62; N, 7.10 %.

In the reactions of **4** with BNA-SO_2Na in the presence of NaOH, $MgCl_2$, and $Mg(OCH_3)_2$, the procedures of the reactions and the isolation of the products were carried out in a manner similar to that described above.

Reaction of Benzophenone with BNA-SO_2Na. To a solution containing 6 mmol of sodium hydroxide in 100 cm^3 of 80 vol % aqueous methanol we added 2 mmol of benzophenone and then 10 mmol of BNA-SO_2Na. The solution was heated under nitrogen at 90 °C for 2 h. The white precipitate was then removed by filtration, and the methanol was evaporated *in vacuo*. The residual solution, containing a solid, was extracted with benzene. After the removal of the benzene, the residue was placed on the silica gel column and eluted with benzene and then chloroform to give benzophenone (81%) and benzhydrol (16%).

References

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4) K. Nakagawa and K. Minami, *Tetrahedron Lett.*, **1972**, 343; J. E. Herz and L. A. Marquez, *J. Chem. Soc., Perkin Trans. 1*, **1973**, 2633.

5) This salt was isolated as 1-benzyl-3-carbamoylpyridinium chloride.

6) It has been reported recently that benzophenone is reduced to benzhydrol by sodium dithionite in an alkaline medium at 90 °C: J. G. de Vries, T. J. van Bergen, and R. M. Kellogg, *Synthesis*, **1977**, 246.