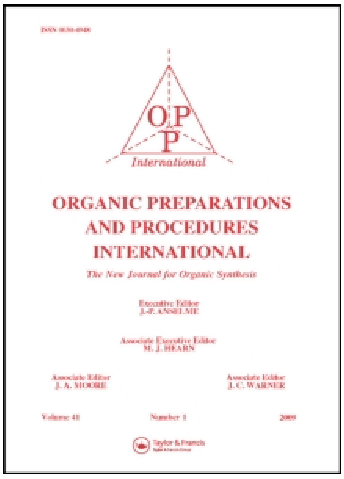

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THE UTILITY OF BENZYLSODIUM AS A REAGENT IN ALCOHOL SYNTHESIS

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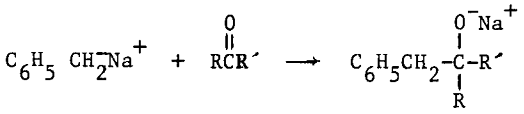
The use of benzylsodium in the synthesis of representative secondary and tertiary alcohols from selected aldehydes and ketones, such as benzaldehyde, p-anisaldehyde, acetophenone, benzophenone and cyclohexanone was investigated. In order to obtain maximum yields, it was at times necessary to use 2-4 fold excess of benzylsodium. The method appears general and provides an alternative route in alcohol synthesis. The preparation of benzylsodium is a two-step process as shown below.

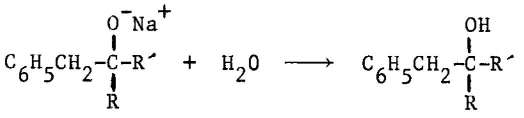
$$C_6H_5Cl + 2Na \longrightarrow C_6H_5Na + NaCl \qquad (1)$$

$$C_6H_5Na + C_6H_5CH_3 \longrightarrow C_6H_5CH_2Na + C_6H_6 \qquad (2)$$

After the benzylsodium is formed, the aldehyde or ketone is added to it and the resulting product is hydrolyzed to yield the alcohol. These reactions are shown in equations 3 and 4.



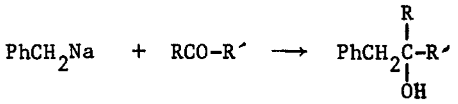
$$C_6H_5\ CH_2^-Na^+ + R\overset{\overset{\displaystyle O}{\|}}{C}R' \longrightarrow C_6H_5CH_2\text{-}\underset{\underset{\displaystyle R}{|}}{\overset{\overset{\displaystyle O^-Na^+}{|}}{C}}\text{-}R' \qquad (3)$$



$$C_6H_5CH_2\text{-}\underset{\underset{\displaystyle R}{|}}{\overset{\overset{\displaystyle O^-Na^+}{|}}{C}}\text{-}R' + H_2O \longrightarrow C_6H_5CH_2\text{-}\underset{\underset{\displaystyle R}{|}}{\overset{\overset{\displaystyle OH}{|}}{C}}\text{-}R' \qquad (4)$$

R = aryl, alkyl or H.

Addition of Benzylsodium to Carbonyl Compounds



$$PhCH_2Na + RCO{-}R' \longrightarrow PhCH_2\overset{\overset{\large R}{|}}{\underset{\underset{\large OH}{|}}{C}}{-}R'$$

R	R′	$\frac{PhCH_2Na}{R-CO-R'}$	% Yield	
			Crude, mp.	Recrystallized, mp.
Phe	H	1:1	41, 54-56°	19, 64-65°[a]
		2:1	64, 55-57°	42, 66-67°
		4:1	64, 55-57°	40, 66-67°
p-MeOPhe	H	1:1	-, 49-51°	6, 66-67°
		2:1	23, 49-51°	19, 50-51°
		4:1	26, 49-51°	19, 50-51°
		4:1	26, 49-51°	23, 52-53°
Phe	Me	1:1	15, 41-43°	8, 45-46°[c]
		2:1	96, 43-45°	69, 49-51°
Phe	Phe	1:1	59, 82-84°	45, 86.5-87.5°[d]
		2:1	95, 86-88°	91, 88-89°
$-(CH_2)_5-$		1:1	20, 47-49°	4, 54-55°[e]
		2:1	66, 46-49°	38, 55-56°
		4:1	93, 53-55°	71, 55-56°

a) Lit.[5] mp. 59-62°; b) lit.[6] mp. 57-58°; c) lit.[4] mp. 49°;
d) lit.[2] mp. 87-88°; e) lit.[3] mp. 57-58°

Analysis of results (see Table) shows that benzophenone gave the highest yield (91% recrystallized) when a 2-fold excess of benzylsodium was used. Acetophenone (69% recrystallized, 2-fold excess) and cyclohexanone (71% recrystallized, 4-fold excess) also gave good yields. The lowest yields were obtained with benzaldehyde (42% recrystallized, 2-fold excess) and p-anisaldehyde (23% recrystallized, 4-fold excess). The yields with ketones are comparable to those expected using Grignard reagents, while the yields with aromatic aldehydes are lower than can be obtained from Grignard reagents.[1]

EXPERIMENTAL

Freshly distilled chlorobenzene and toluene were kept over molecular sieves in a tightly-sealed container for at least 24 hrs before use. All melting points were taken on a Fisher-Johns Melting Point Apparatus and are corrected. Infrared spectra were determined on a Beckman IR-8 Spectrophotometer.

Benzylsodium.- This reagent was prepared according to the procedure of Gilman, Pacevitz and Baine,[2] using a 40% dispersion of sodium in mineral oil (Ventron Corporation) in place of sodium sand. The precautions given[2] should be carefully observed in handling sodium and sodium reagents. For each of the following preparations, 20.6 ml (22.7 g, 0.2 mole) of chlorobenzene, 31.6 g (12.7 g sodium, 0.54 mole) of sodium dispersion and 500 ml of toluene were used.

Carbonation of Benzylsodium. - The procedure of Gilman, Pacevitz and Baine[2] was used for the carbonation and gave 26.5 g (97%) of crude material, mp. 73-76°. Recrystallization from an ether-pentane mixture gave 19.9 g. (73%) of phenylacetic acid, mp. 77-78°.

1,1,2-Triphenylethanol. - To the benzylsodium solution, a solution of benzophenone (18.2 g., 0.1 mole) in 50 ml toluene was added dropwise over a 0.5-hr period. Stirring was continued for an additional 2 hrs while the temperature was kept below 40° at all times. Absolute ethanol

(150 ml) was then added over a 1-hr period to destroy any excess sodium, followed by 250 ml of water over a 1-hr period; the mixture was allowed to stir for an additional 2 hrs. The temperature was maintained below 40° during the addition of the ethanol and water. The organic layer was extracted with 200 ml of ether and the ethereal layer was dried overnight over sodium sulfate. The solvent was removed on a rotary evaporator and the residue was further evaporated using a vacuum pump at 0.1 mm to remove volatile impurities. The crude product (26.1 g, 95%, mp. 86-8°) was recrystallized from hexane to give 25.0 g, (91%) of 1,1,2-triphenylethanol, mp. 88-89°, lit.[2] mp. 87-88°.

This same procedure was used in each of the following reactions with exceptions as noted. All alcohols prepared by this method were free of contamination by carbonyl compounds, as evidenced by negative tests with 2,4-dinitrophenylhydrazine and Tollens' reagent and by absence of an infrared absorption in the 1600-1800 cm^{-1} region.

1-Benzylcyclohexanol. - To the benzylsodium solution was added 4.9 g (0.05 mole) of cyclohexanone. The crude product (8.8 g, 92%) was recrystallized from pentane to give 6.8 g (71%), mp. 55-6°, lit.[3] mp. 57-58°.

1,2-Diphenyl-2-propanol. - To the benzylsodium solution was added 12.0 g (0.1 mole) of acetophenone. The crude product (20.3 g, 96%) mp. 43-45°, was recrystallized from pentane to give 14.6 g (69%), mp. 49-51°, lit.[4] mp. 49°.

1,2-Diphenylethanol. - To the benzylsodium solution was added 12.6 g (0.1 mole) of benzaldehyde. Problems with isolation, purification and yield were encountered in this reaction. High pressure liquid chromatography (UV detector, 254 nm, Chromasep -RPV 4 ft x 2.1 mm column, #1135) showed that several impurities were present. The semisolid mass was dissolved in ether and placed on a column of activated alumina (80 - 200 mesh) and eluted successively with pentane, pentane-ether (1:1), ether and absolute alcohol. All fractions were evaporated under reduced pressure and the crude product (12.7 g, 64%), mp. 55-57°, was recrystallized from an ether-pentane mixture to give 8.2 g (42%), mp. 66-67°, lit.[5] mp. 59-62°.

<u>1-p-Anisyl-2-phenylethanol</u>. - To the benzylsodium solution was added 6.8 g (0.05 mole) of anisaldehyde. Problems similar to those encountered with benzaldehyde, occurred in this reaction. The semisolid mass was dissolved in ether and placed on a column of activated alumina (80-200 mesh) and eluted successively with pentane, pentane-chloroform (1:1), chloroform and absolute alcohol. All fractions were evaporated and the alcohol was recovered from the chloroform fraction. The crude product (3.0 g, 26%) mp. 49-51°, was recrystallized from ether-pentane to give 2.7 g (23%) mp. 52-53°, lit.[6] 57-58°.

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