

The Synthesis of the Benzyltetrahydropyrans

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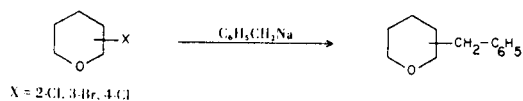
The 2-benzyl-, 3-benzyl- and 4-benzyltetrahydropyrans have been prepared *via* the reaction of benzylosodium with 2-chloro-, 3-bromo- and 4-chlorotetrahydropyran in 49, 29 and 27% yields, respectively. The structures of these compounds were substantiated from their nmr, mass spectra and analytical data.

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In connection with our studies on certain bicyclic derivatives of dihydropyran, we required authentic samples of the 3-benzyl- and 4-benzyltetrahydropyran, **1** and **2** respectively. This paper reports the synthesis of the 2-benzyl-, 3-benzyl- and 4-benzyltetrahydropyrans *via* the reaction of benzylosodium (**1**) with 2-chloro-, 3-bromo- and 4-chlorotetrahydropyran.

2-Benzyltetrahydropyran **3** has been prepared by the coupling reaction of benzylmagnesium chloride with 2-chlorotetrahydropyran (**2**) furnishing a 35% yield of the desired product (**3**). However, we found the reaction of the 3-halo- and 4-halotetrahydropyrans with the Grignard reagent resulted in poorer yields due to their diminished reactivity. Similar observations have been reported concerning the reduced reactivity of secondary halides as compared to that of α -haloethers (**4**).

Moderately good yields of the three benzyl ethers were obtained by reacting the appropriate halides with benzylosodium.



Compounds **1**, **2** and **3** each furnished correct elemental analyses for $C_{12}H_{16}O$ and exhibited molecular ions in their mass spectra at m/e 176. The nmr spectra were in agreement with the assigned structures.

EXPERIMENTAL

An F&M gas chromatograph Model 810 equipped with a 6-ft, $\frac{1}{4}$ in. copper column packed with 20% DC lubricant on Diatoport S, operated at 180° , was employed for all analytical and preparative gas chromatography. The ir spectra were recorded on a Beckman IR10 spectrophotometer. Nuclear magnetic resonance spectra were obtained using a Varian A-60 spectrometer employing tetramethylsilane as an internal standard.

All liquids were flushed with nitrogen before use, and the reactions were carried out under a nitrogen atmosphere. In each case, 2-3% of diphenyl was formed in the initial formation of benzylosodium which prompted the trapping of all analytical samples.

3-Benzyltetrahydropyran (**1**).

Into a 500 ml. four-necked flask equipped with a mechanical stirrer, a reflux condenser fitted with a calcium chloride drying tube, a thermometer, and a dropping funnel fitted with a gas inlet tube, were placed 75 ml. of dry toluene and 0.3 mole (6.87 g.) of

Table I

Compound Number	g.-atom sodium	Mole C_6H_5Cl	Mole $C_6H_5CH_3$	Mole Haloether	Reaction Temperature	B.p./10 mm	Yield %
1	0.3	0.15	0.70	0.10 3-Bromo-THP	103-105	123-127	29
2	0.4	0.20	0.70	0.125 4-Chloro-THP	30-35	122-127	27
3	0.3	0.15	0.70	0.10 2-Chloro-THP	30-35	119-124	49

sodium metal (5). Chlorobenzene, 16.87 g. (0.15 mole), was added dropwise over a period of 4.5 hours at 30-35° with vigorous stirring. The reaction mixture was heated at 100° in an oil bath for 50 minutes with stirring (brick red color was noted). Freshly prepared 3-bromotetrahydropyran (6), 16.5 g. (0.10 mole), was added dropwise during 20 minutes at 103-105°, and the resulting mixture was allowed to cool to room temperature. The excess sodium was destroyed with ethanol. The mixture was extracted with ether, washed with water until neutral, and dried over magnesium sulfate. The ether was removed *in vacuo*, and the residue was distilled furnishing 5.13 g. (29%) of **1**, 95% pure, b.p. 123-127°/10 mm; N_D^{20} 1.5269; nmr (carbon tetrachloride): δ 0.92-2.15 (5H, multiplet); 2.19-2.50 (2H, 2 doublets); 2.80-3.42 (2H, multiplet); 3.58-3.90 (2H, multiplet); 6.93-7.27 (5H, multiplet).

Anal. Calcd. for C₁₂H₁₆O: C, 81.77; H, 9.15; O, 9.08. Found: C, 81.86; H, 9.18; O, 9.23.

4-Benzyltetrahydropyran (**2**).

The previous procedure for the preparation of benzylna-
sodium, using 0.4 g.-atom of sodium and 0.2 mole of chlorobenzene, was followed. 4-Chlorotetrahydropyran (15.06 g., 0.125 mole) (7) was added in 20 minutes at 30-35°. The reaction mixture was allowed to cool to room temperature while stirring and worked up as before. Distillation of the residue *in vacuo*, gave 6.0 g. (27%) of **2**, 98% pure (8), b.p. 122-127°/10 mm; N_D^{20} 1.5236; nmr (carbon tetrachloride): δ 0.82-2.04 (5H, multiplet); 2.30-2.56 (2H, multiplet); 2.96-3.42 (2H, multiplet); 3.61-4.0 (2H, multiplet); 6.95-7.27 (5H, multiplet).

Anal. Calcd. for C₁₂H₁₆O: C, 81.77; H, 9.15; O, 9.08. Found: C, 82.00; H, 9.02; O, 9.30.

2-Benzyltetrahydropyran (**3**).

Benzylna-
sodium was prepared as before using 0.3 g.-atom of so-

dium and 0.15 mole of chlorobenzene. Freshly prepared and distilled 2-chlorotetrahydropyran (**2**), 12.05 g. (0.10 mole), was then added dropwise over a period of 20 minutes at 30-35° and the resulting mixture, being worked up as before, was distilled *in vacuo* yielding 8.62 g. (49%) of **3**, 97% pure, b.p. 119-124°/10 mm; N_D^{20} 1.5260; nmr (carbon tetrachloride): δ 0.95-1.90 (6H, multiplet); 2.30-2.80 (2H, multiplet); 2.87-3.58 (2H, multiplet); 3.70-4.05 (1H, multiplet); 7.03-7.25 (5H, singlet).

Anal. Calcd. for C₁₂H₁₆O: C, 81.77; H, 9.15; O, 9.08. Found: C, 82.03; H, 8.91; O, 8.88.

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