benzyl alcohols were recovered by crystallization.) The alcohol was characterized by its melting point or that of its phenylurethan.

In several cases crystalline residues remained in the flask after distillation of the product. These were recrystallized from acetic acid and characterized as dibenzalacetones by their melting points and, in the case of dibenzalacetone, by a mixed melting point with an authentic sample. The percentages of starting aldehyde accounted for in these products based on weight of the crude dibenzalacetone were: 2-chlorobenzaldehyde, 23%; 4-chlorobenzaldehyde, 29%; benzaldehyde (43-hour reduction), 28%.

Reaction of Cyclohexanone with Allyl Borate.—The product from the reaction of 29.6 g. (0.302 mole) with cyclohexanone with 62.8 g. (0.342 mole) of allyl borate at 160–170° for 32 hours was treated in the usual manner and fractionated at 35 mm. through a 100 cm. × 0.5 cm. Podbielniak column. Three main fractions were collected: (a) 2.7 g. at 83°; (b) 5.6 g. at 106–108°; (c) 2.6 g. at 136–140°. Fraction (a) was characterized as cyclohexanol by the melting point[5] of its α-naphthylurethan, 127.5–128.0° and mixed melting point with an authentic sample. Fraction (b) yielded a semicarbazone melting at 165.5–167°. A mixed melting point with cyclohexanone semicarbazone (m.p. 165–167°) showed a great depression (m.p. 140–163°). With 2,4-dinitrophenylhydrazine a derivative melting at 141–142° after several crystallizations from ethyl acetate was obtained.

Anal. Calcd. for $C_{15}H_{16}O_4N_4$: N, 17.8. Found: N, 17.7, 17.7, 17.9.

This analysis corresponds to a one to one aldol condensation product of acrolein and cyclohexanone.

Characterization of fraction (c) was not attempted.

Reaction of *n*-Heptaldehyde with Isopropyl Borate.—A mixture of 68 g. (0.306 mole) of isopropyl borate and 62 g. (0.544 mole) of *n*-heptaldehyde was heated at 150–160° for 44 hours. The product was hydrolyzed, extracted with ether and dried. Fractionation at 15 mm. yielded: (a) 11.6 g. at 82–85°; (b) 11.7 g. at 150–153°; and (c) 18.8 g. residue. Fraction (a) was shown to be 1-heptanol: 3-nitrophthalate m.p. 125–126° (lit.[6] 127°). Fraction (b), $n^{28}D$ 1.4515, had a molecular weight of 210 (benzene, cryoscopic); calcd. for $C_{14}H_{26}O$, 211. This compound is probably the aldol condensation product of two molecules of heptaldehyde, **2-*n*-amyl-2-nonenal**. Its 2,4-dinitrophenylhydrazine derivative melted at 127–128° after crystallization from ethyl acetate.

Anal. Calcd. for $C_{20}H_{18}O_4N_4$: N, 14.6. Found: N, 14.6, 13.8, 14.4.

Distillation of fraction (c) at about 1 mm. yielded further fractions: 5.5 g. at 130–175°; mol. wt., 380; 4.2 g. at 175–185°, mol. wt., 410, 398; 8.9 g. at 185–205°. The mol. wt. of the condensation product of four moles of *n*-heptaldehyde, $C_{28}H_{50}O$, would be 402.

Summary

The reactions of several aldehydes and ketones with alkyl borates have been investigated. Reduction, aldol condensation of starting material or polymerization of the product may be the main reaction depending upon the carbonyl compound and borate used.

---

[5] All melting points are uncorrected.

[6] Dickinson, Crosson and Copenhaver, THIS JOURNAL, **59**, 1095 (1937).

DURHAM, N. H. RECEIVED MAY 25, 1950

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF NORTHWESTERN UNIVERSITY AND THE UNIVERSITY OF ILLINOIS]

The Reaction of Trimethylene Oxide with Grignard Reagents and Organolithium Compounds

BY SCOTT SEARLES

The reaction of ethylene oxide with Grignard reagents and organolithium compounds is a well known method of preparing certain primary alcohols and lengthening the carbon chain by two carbon atoms. The analogous reaction of trimethylene oxide, however, appears to be but little known. This situation is no doubt largely due to the low yields previously reported for the synthesis of trimethylene oxide, but with recent improvements in the latter synthesis the reaction is of some interest as a synthetic method for adding three carbon atoms at one time.

The reaction of trimethylene oxide with the Grignard reagent was first reported by Derick and Bissell.[1] These workers obtained from the reaction of *n*-propylmagnesium bromide and trimethylene oxide a 49% yield of *n*-hexanol, which was rather incompletely characterized. The only other example of the reaction in the literature appears to be the corresponding one with ethylmagnesium bromide, which was reported to yield both *n*-pentanol and 3-bromopropanol (each in about 30% yield).[2] The present work was carried out to investigate the course of the reaction with a variety of other Grignard reagents and with organolithium compounds.

As shown in Table I, trimethylene oxide reacted with aromatic and primary aliphatic Grignard reagents and organolithium compounds to give, after hydrolysis, the expected 3-substituted propanols in generally good yields. The products were characterized with some care, so that there is no question about the course and generality of the reaction. The method represents a more convenient synthesis than has previously appeared in the literature for several of these compounds, such as 4-phenylbutanol[3] and 3-(2-naphthyl)-propanol-1.[4]

The experimental conditions and procedures are similar to those employed with the analogous reaction of ethylene oxide with Grignard reagents.[5] Further similarity to the ethylene oxide reaction[6] is observed in the formation of trimethylene halohydrin in the reaction of trimethylene oxide with secondary and tertiary Grignard reagents. This formation of halohydrin by the competing reaction (B) of trimethylene oxide with magnesium halide present in the Grignard reagent is supported by the formation of trimethylene bromohydrin upon

---

[1] Derick and Bissell, THIS JOURNAL, **38**, 2478 (1916).

[2] Bermejo and Aranda, *Anales soc. españ. fis. quim.*, **27**, 798 (1929); *Chem. Centr.*, **101**, I, 2382 (1930).

[3] von Braun, *Ber.*, **44**, 2871 (1911); Conant and Kirner, THIS JOURNAL, **46**, 241 (1924).

[4] Manske and Ledingham, *Can. J. Research*, **17B**, 19 (1939).

[5] For example, Dreger in "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 306.

[6] Huston and Agett, *J. Org. Chem.*, **6**, 123 (1941).

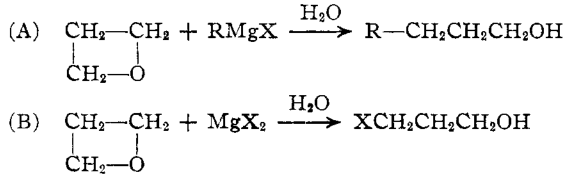
TABLE I

REACTION OF TRIMETHYLENE OXIDE WITH ORGANOMETALLIC COMPOUNDS, RM, AND WITH MAGNESIUM BROMIDE

RM	Mole of halide	Mole of $(CH_2)_3$-O	Products	Yield, %	B. p. °C.	B. p. Mm.	n^{20}D	Derivatives	M. p., °C.
Phenyl MgBr	0.2	0.18	3-Phenylpropanol-1	84	110–112	10	1.5288	*p*-Nitrophenylurethan	104[a]
								3,5-Dinitrobenzoate	96–96.3[b]
			3-Bromopropanol-1	4	65–75	10		α-Naphthylurethan	75[c]
Phenyl Li	.3	.18	3-Phenylpropanol-1	85	81–83	2	1.5293	3,5-Dinitrobenzoate	
1-Naphthyl MgBr	.3	.18	3-(1-Naphthyl)-propanol-1[d,4]	80	118–119	1	1.616	Phenylurethan[e]	75–76
								3-(1-Naphthyl)-butyric acid[f]	107–108[g]
2-Naphthyl MgBr	.18	.18	3-(2-Naphthyl)-propanol-1[h]	60[i]	120–121	7		Phenylurethan[j]	94
9-Fluorenyl Li[k]	.22	.21	3-(9-Fluorenyl)-propanol-1[l]	44[i]	141	0.2		α-Naphthylurethan[m]	124–125
Benzyl MgCl[n]	.2	.13	4-Phenylpropanol-1	83	150	24	1.5220	Phenylurethan[o]	53.5–54.5
n-Butyl Li	.2	.15	Heptanol-1	28	175–177	750	1.4243	α-Naphthylurethan	60[p]
Cyclohexyl MgBr	.3	.2	3-Cyclohexylpropanol-1	28	102–105	15	1.475	Phenylurethan	83[q]
			3-Bromopropanol-1	40	71–77	18		α-Naphthylurethan	75[c]
Isopropyl MgBr	.25	.2	2-Methylpentanol-5	28[r]	151–152	752	1.4178	3,5-Dinitrobenzoate	70[s]
			3-Bromopropanol-1	12[r]					
t-Butyl MgCl[t]	.25	.18	2,2-Dimethylpentanol-5(?)		144–145	745			
			3-Chloropropanol-1	37	57	8	1.4415	α-Naphthylurethan	76[c]
Anhydrous $MgBr_2$[u]	.5	.2	3-Bromopropanol	54	95–96	43		α-Naphthylurethan	75[c]
								Phenylurethan	46–47

[a] Hoeke, *Rec. trav. chim.*, **54**, 513 (1935). [b] Recryst. from alc. The 3,5-dinitrobenzoate of authentic 3-phenylpropanol-1 also melted at 86–86.3° and mixed m. p. showed no depression, although this m. p. is stated to be 92° by Huntress and Mulliken, "Identification of Pure Organic Compounds, Order I," John Wiley and Sons, Inc., New York, N. Y., 1941, p. 477. [c] Bickel and French, THIS JOURNAL, **48**, 747 (1926). [d] *Anal.* Calcd. for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 83.68; H, 7.64. [e] *Anal.* Calcd. for $C_{20}H_{19}O_2N$: C, 78.66; H, 6.27. Found: C, 78.73; H, 6.47. [f] 3-(1-Naphthyl)-propanol-1 was treated with hydrobromic acid and sulfuric acid in refluxing acetic acid for four hours to give the corresponding bromide, b. p. 148° (2 mm.); this was converted into a Grignard reagent, which was carbonated by pouring on solid carbon dioxide. [g] Hoch, *Bull. soc. chim.*, [5] **5**, 269 (1938); Drake and McVey, *J. Org. Chem.*, **4**, 468 (1939). [h] M. p. 33°. *Anal.* Calcd. for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 83.72; H, 7.76. [i] Based on yield of Grignard reagent (Gilman, Zoellner and Dickey, THIS JOURNAL, **51**, 1576 (1929)) or organolithium compound (Tucker and Whalley, ref. *k*). [j] *Anal.* Calcd. for $C_{20}H_{19}O_2N$: C, 78.66; H, 6.27. Found: C, 78.73; H, 6.45. [k] Prepared by method of Tucker and Whalley, *J. Chem. Soc.*, 50 (1949). [l] M. p. 61–61.5°. *Anal.* Calcd. for $C_{16}H_{16}O$: C, 85.67; H, 7.19. Found: C, 85.64; H, 7.47. [m] *Anal.* Calcd. for $C_{27}H_{23}O_2N$: C, 82.42; H, 5.89; N, 3.56. Found: C, 82.66; H, 6.00; N, 3.49. [n] Method of Gilman and Catlin, "Organic Syntheses," Coll. Vol. I, p. 471. [o] M. p. of 51–52° reported by von Braun, ref. 3. *Anal.* Calcd. for $C_{17}H_{19}O_2N$: C, 75.81; H, 7.11. Found: C, 75.93; H, 7.22. [p] Adamson and Kenner, *J. Chem. Soc.*, 842 (1934). [q] De Benneville and Connor, THIS JOURNAL, **62**, 283 (1940). [r] Similarity of boiling points of these products prevented effective separation by distillation; yields computed from the amount and bromine content (21.5% Br) of the mixed product. Treatment of the mixture with alcoholic silver nitrate, followed by filtration and distillation gave pure 2-methylpentanol-5 (22%). [s] Sutter, *Helv. Chim. Acta*, **29**, 1248 (1946). [t] Puntambeker and Zoellner, "Organic Syntheses," Coll. Vol. I, p. 525. [u] Rowley, THIS JOURNAL, **58**, 1337 (1936).

treatment of trimethylene oxide with magnesium bromide in ether solution.



$$\text{(A)}\quad \underset{CH_2-O}{\overset{CH_2-CH_2}{|\qquad|}} + RMgX \xrightarrow{H_2O} R-CH_2CH_2CH_2OH$$

$$\text{(B)}\quad \underset{CH_2-O}{\overset{CH_2-CH_2}{|\qquad|}} + MgX_2 \xrightarrow{H_2O} XCH_2CH_2CH_2OH$$

A study of the chemistry of trimethylene oxide being continued.

Experimental[7]

Trimethylene Oxide.—The procedure of Derick and Bissell[1] was modified by adding 3-chloropropyl acetate (60 g.) dropwise but rapidly (45 minutes) to a well-stirred liquid mixture of sodium hydroxide (65 g.), potassium hydroxide (65 g.) and water (5 g.) at 150–160° and conducting the gaseous product through a 40-cm. Vigreux column into a Dry Ice trap. The crude product was purified in a manner similar to that described by Noller[8] to give 10.7–11.4 g. (42–45%) of trimethylene oxide, b. p. 48° (750 mm.), n^{25}D 1.3895.[9] On this reaction scale Noller's procedure gave 35–38% yields in these laboratories.

Reaction of Trimethylene Oxide with Organometallic Compounds.—The general procedure was to add with stirring a solution of trimethylene oxide in three volumes of anhydrous ether to a cold ethereal solution of the Grignard reagent or organolithium compound. After an initial, mildly exothermic reaction, during which a white precipitate generally separated, the mixture was refluxed for one hour. Benzene (150–200 ml.) was then added; the ether was removed by distillation through a Vigreux column; and the mixture was refluxed four hours, after which it was cooled and hydrolyzed with saturated ammonium chloride solution. Following separation of the benzene layer the aqueous layer was extracted with ether (or carbon tetrachloride in the case of 3-(9-fluorenyl)-propanol), and the non-aqueous solution were dried over sodium sulfate and distilled.

The procedure was modified for the reactions with the cyclohexyl, isopropyl and *t*-butyl Grignard reagents and with anhydrous magnesium bromide, in that the reaction mixture was allowed to stand at room temperature 24 hours (nitrogen atmosphere) before benzene was added, and the benzene mixture was refluxed only two hours after removal of the ether.

Summary

In a study of trimethylene oxide with ten Grignard reagents and organolithium compounds marked similarity to the analogous reaction of ethylene oxide was observed. Primary Grignard reagents and organolithium compounds cleave the trimethylene oxide ring to form the expected 3-substituted propan-1-ols in generally good yields, but considerable amounts of trimethylene halohydrin are formed in the reaction of trimethylene oxide with secondary and tertiary Grignard reagents. An improvement in the preparation of trimethylene oxide is described.

EVANSTON, ILL. RECEIVED JUNE 3, 1950

---

[7] Microanalyses by Misses E. Davis, R. Kopel, J. Sorenson and V. Hobbs.

[8] Noller, *Org. Syntheses*, **29**, 92 (1949).

[9] The assistance of Messrs. Joseph Velardi and Harold Wanger in studying optimum conditions for this synthesis is gratefully acknowledged.