LITERATURE CITED

1. G. Z. Stasevich, O. N. Bubel', I. G. Tishchenko, and M. V. Kudrevatikh, Khim. Geterotsikl. Soedin., No. 8, 1028 (1987).
2. A. S. Martin, J. Rovirosa, O. Munoz, M. H. M. Chen, R. D. Gunerathe, and J. Clardy, Tetrahedron Lett., 24, 4063 (1983).
3. R. M. Carman, F. N. Lahey, and J. K. MacLeod, Aust. J. Chem., 20, 1957 (1967).
4. S. M. Kupchan, C. W. Sigel, M. J. Matz, C. J. Gilmore, and R. F. Bryan, J. Am. Chem. Soc., 98, 2295 (1976).
5. P. W. Le Quesne, M. D. Menachery, M. P. Pastore, C. J. Kelly, T. F. Brennan, K. D. Onan, R. F. Raffauf, and C. M. Weeks, J. Org. Chem., 47, 1519 (1982).
6. W. Parker, R. A. Raphael, and D. I. Wilkinson, J. Chem. Soc., No. 11, 3871 (1958).
7. F. N. Lahey and J. K. MacLeod, Aust. J. Chem., 26, 1943 (1967).
8. P. G. Baraldi, A. Barco, S. Benetti, M. Guarneri, S. Manfredini, G. P. Pollini, and D. Simoni, Tetrahedron Lett., 26, 5319 (1985).
9. R. F. W. Jackson and R. A. Raphael, J. Chem. Soc., Perkin Trans. 1, No. 3, 535 (1984).
10. G. Casnatti and A. Ricca, Tetrahedron Lett., No. 4, 327 (1967).
11. D. P. Curran and D. H. Singleton, Tetrahedron Lett., 24, 2079 (1983).
12. I. G. Tishchenko, V. M. Yazychenko, N. M. Pasechnik, and P. M. Malashko, Izv. Akad. Nauk Beloruss. SSR, Ser. Khim., No. 6, 103 (1969).
13. E. S. Balenkova and M. A. Gorokhova, Zh. Org. Khim., 13, 1625 (1977).
14. I. G. Tishchenko, I. F. Revinskii, V. G. Grinkevich, and V. P. Suboch, Vest. Beloruss. Gos. Univ., Ser. 2, No. 1, 28 (1978).

SYNTHESIS OF 2-SUBSTITUTED TETRAHYDROFURANS

N. P. Volynskii and L. I. Perepelitchenko

UDC 547.722.3'32.322'281.04

We have developed a three-stage scheme for the preparative synthesis of 2-substituted tetrahydrofurans from allyl halides and aldehydes to give the first stage – a Grignard reaction – mixed alkoxides, which on treatment with acetic anhydride are converted to 4-acetoxy-1-alkenes. Addition of hydrogen bromide to the latter contrary to Markownikoff's rule gives 4-acetoxy-1-bromoalkanes, which as a result of hydrolysis form 2-R-tetrahydrofurans.

2-Substituted tetrahydrofurans (THF) are important starting materials for the preparation of 2-substituted thiolanes and other five-membered saturated heterocycles. The main methods for the synthesis of compounds of type IIIa-c are based on the use of furfural, which gives secondary alcohols in a Grignard reaction, and these are then dehydrated and hydrogenated [1]. With symmetrical aldehydes or ketones furfural forms furfurylidenealdehydes or ketones, which are reduced and hydrogenated to the required furans [2]. The use of ketones with an asymmetrical structure gives mixtures of isomers. It should be noted in this case that [3-5] are inaccurate concerning the condensation of furfural with methyl alkyl ketones exclusively on the methyl group since a similar reaction of aldehydes occurs mainly on the α-methylene group of the ketone [6]. 2-Phenyl-THF is obtained by reduction of ethyl β-benzoylpropionate followed by dehydration of the 1-phenyl-1,4-butanediol formed [7]. Other synthetic methods, namely, alkylation of THF with olefins in the presence of tert-butyl peroxide [8], acylation of furan followed by reduction and hydrogenation [9], or the use of 3-bromo-1-(1,1-dimethylpropoxy)propane as an initial compound [10] are multistage processes that are complicated to carry out or lead to the formation of mixtures.

A. V. Topchiev Institute of Petrochemical Synthesis, Academy of Sciences of the USSR, Moscow 117912. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1604-1607, December, 1988. Original article submitted March 2, 1987; revision submitted March 9, 1988.

TABLE 1. Properties of Compounds Synthesized

Compound	bp, °C (mm Hg)	d_4^{20}	n_D^{20}	MR_D		Yield, %
				found	calculated	
Ia*	79 (60)	0,8931	1,4160	39,95	40,29	48
[14] Ib	72 (23)	0,8761	1,4210	45,22	44,95	70
Ic	[12, 15] 91 (6)	0,8696	1,4318	59,12	58,90	76
IIa†	[12, 16] 68 (2)	1,2567	1,4570	48,35	48,41	97
IIb‡	—	—	—	—	—	95
IIc‡	—	—	—	—	—	95
IIIa	106 (760)	0,8559	1,4177	29,47	29,42	52
IIIb	60 (60)	0,8529	1,4228	34,09	34,08	53
IIIc	57 (2,5)	0,8540	1,4370	47,93	47,97	47
IX [17, 18]	73 (2,5)	1,0246	1,5310	44,75	44,48	80

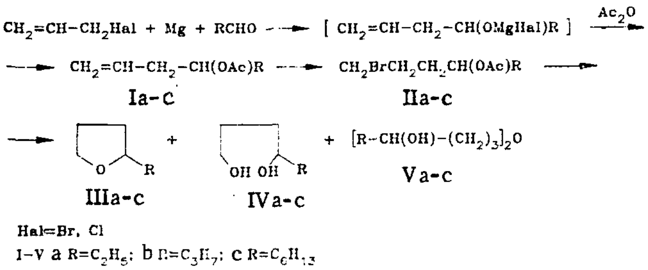
---

*Found, %: C 66.9; H 9.8. $C_8H_{14}O_2$. Calculated, %: C 67.6; H 9.9.

†Found, %: Br 36.4. $C_8H_{15}BrO_2$. Calculated, %: Br 35.8.

‡Compound was not purified.

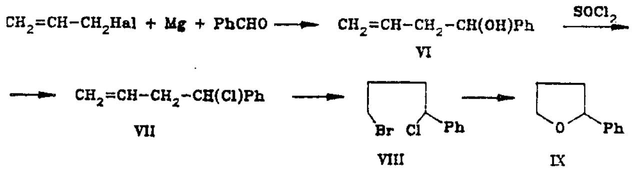
We have developed a convenient scheme for the preparative synthesis of pure tetrahydrofurans IIIa-c.



Acetates Ia-c obtained in one stage are hydrobrominated in the presence of benzoyl peroxide and the 4-acetoxy-1-bromoalkanes IIa-c formed by this are hydrolyzed with an aqueous solution of KOH. The necessity for obtaining esters Ia-c and not alcohols arises because addition of hydrogen bromide to unsaturated alcohols even in the presence of peroxides follows Markownikoff's rule to give secondary bromides [11]. 4-Acetoxy-1-alkenes Ia-c were previously obtained by acetylation of unsaturated alcohols with acetyl chloride in the presence of pyridine or by boiling them for many hours with acetic anhydride [12]. The decomposition with acetic anhydride used by us for the products of the Grignard reaction — halomagnesium alkoxides — has considerably simplified the process and has resulted in an increased yield of acetates.

Hydrobromination of compounds Ia-c in the presence of benzoyl peroxide contrary to Markownikoff's rule only takes place effectively when there is a sufficient quantity of solvent present. When there is insufficient dilution there is virtually no addition of HBr. The presence of PBr_3 in the reaction mixture also slows down the reaction considerably. The 4-acetoxy-1-bromoalkanes IIa-c that we obtained had not been reported in the literature. The lowest-boiling 4-acetoxy-1-bromohexane IIa was purified by distillation and analyzed, while acetoxybromides IIb and IIc were treated with an aqueous solution of KOH without preliminary purification. The main products of this reaction were 2-substituted THFs IIIa-c, which were readily separated by distillation on a fractionating column. As a result of side reactions occurring when acetates IIa-c were cyclized in alkaline medium, 1,4-diols IVa-c and di(4-hydroxyalkyl) ethers Va-c were formed. When the reaction took place under heterophase conditions the time required for complete elimination of bromine was 30-60 h. When the temperature is increased in order to accelerate cyclization, the effect of side reactions increases and at 160°C the main products are diols IVa-c.

We obtained 2-phenyltetrahydrofuran by a somewhat different route, having taken into consideration the instability of benzyl acetates in an acidic medium. Elimination of acetic acid in the hydrobromination of α-allylbenzyl acetate would have led unavoidably to addition of hydrogen bromide according to Markownikoff's rule.



The hydroxyl group in benzyl alcohol VI was replaced under mild conditions by a chlorine atom, and the chloride VII formed added on HBr contrary to Markownikoff's rule [13]. The reaction product — 4-bromo-1-phenyl-1-chlorobutane (VIII) — when treated with alkali was converted to 2-phenyl-THF (IX).

The purity of the 2-substituted THF compounds obtained was confirmed by GLC.

EXPERIMENTAL

Chromatographic analysis of compounds IIIa-c and IX was conducted on Tsvet (50-80 m, PEGA and OV-17, 90-171°C, hydrogen carrier gas) and PAKhV-05 (designed at the Institute of Petrochemical Synthesis, Academy of Sciences of the USSR; 9 m × 4 mm, PEGA on INZ-600, 122°C, helium carrier gas) chromatographs.

The properties of compounds I-III and IX are given in Table 1.

4-Acetoxy-1-decene (Ic). A mixture of 36 g (1.5 mole) of Mg and 150 ml of absolute ether was added to a flask of volume 2 liters fitted with stirrer, dropping funnel, and reflux condenser, 8 ml of allyl chloride was added and the mixture was carefully heated until the reaction had started. Then a solution of 134 ml (1 mole) of freshly distilled enanthal and 98 ml (1.2 mole) of allyl chloride in 250 ml of absolute ether was added over a period of 30 min. To prevent the boiling of ether becoming too vigorous the flask was cooled with a mixture of ice and salt. After the addition was complete spontaneous boiling continued for ~10 min, then the mixture was heated to boiling for a further 30 min, cooled with a mixture of ice and salt, and 134 ml (1.38 mole) of acetic anhydride was added over a period of 15-20 min. Agitation was continued for 1.5 h, the mixture was heated for 15 min to complete the reaction, it was then cooled and decomposed with 250 ml of ice-cold water. The ether layer was separated and the aqueous layer extracted once with 50 ml of ether. The ether extracts were combined, the ether distilled off, and the residue distilled under vacuum on a fractionating column of efficiency 10 theoretical plates. Compound Ic (150 g) was obtained.

4-Acetoxy-1-bromodecane (IIc). Pure, dry hydrogen bromide was passed through a mixture of 150 g (0.76 mole) of 4-acetoxy-1-decene IIc, 400 ml of benzene, and a solution of 14 g (0.06 mole) of benzoyl peroxide in 100 ml of benzene added to a flask of volume 1 liter fitted with a reflux condenser, thermometer, and tube reaching the bottom of the flask; the temperature was kept at ~20°C (exothermic reaction). After ~30 min saturation was reached, which was evident from the fixation of HBr in a water trap attached to the upper section of the reflux condenser. The passage of HBr was stopped 5 min after saturation was recorded, the reaction mixture was poured into ice-cold water, the organic layer was separated and washed with water and a solution of sodium carbonate, and the benzene was distilled off. Impure 4-acetoxy-1-bromodecane IIc was obtained in the residue.

2-Hexyltetrahydrofuran (IIIc). A. A mixture of 212 g (0.76 mole) of impure 4-acetoxy-1-bromodecane IIc, 700 ml of 20% aqueous KOH, 150 ml of dioxane, and 4 g of dioctadecyldiethylammonium chloride was boiled for 60 h. After cooling the mixture, the dioxane layer was separated and the aqueous alkaline layer extracted once with 50 ml of pentane. The pentane extract was combined with the dioxane layer and washed once with 50 ml of water, the pentane was distilled off, and the residue was distilled on a fractionating column of efficiency 10 theoretical plates. 2-Hexyl-THF IIIc (59.3 g) and 1,4-decanediol IVc (28.7 g, 21%) were obtained. Compound IIIc was purified by heating with metallic sodium and by distillation. 1,4-Decanediol IVc was purified by heating with a solution of 1 g of KOH in 50 ml of methanol at 150°C over a period of 1 h in an autoclave. Subsequent distillation gave compound IVc as a viscous liquid: bp 126°C (1.5 mm Hg), d_4^{20} 0.9222, n_D^{20} 1.4570 [19].

B. A mixture of 118 g (0.42 mole) of impure compound IIc, 600 ml of a 20% aqueous solution of KOH, 100 ml of dioxane, and 5 g of dioctadecyldiethylammonium chloride was heated for 8 h at 160°C in a rotating autoclave. As a result of treatment similar to that described in method A, 17.1 g (26%) of 2-hexyl-THF IIIc and 40 g (55%) of 1,5-decanediol IVc were obtained.

2-Propyltetrahydrofuran (IIIb). This was obtained in a similar manner to A. 1,4-Heptanediol IVb with a yield of 20% was isolated as a by-product: bp 115°C (3 mm Hg), d_4^{20} 0.9514, n_D^{20} 1.4525 [19]. The high-boiling residue was not analyzed.

2-Ethyltetrahydrofuran (IIIa). This was obtained in a similar manner to A. 1,4-Hexanediol IVa (8.5% yield), bp 93°C (1.5 mm Hg), d_4^{20} 0.9686, n_D^{20} 1.4525 [19], and di(4-hydroxylhexyl)ether Va (6.3% yield), bp 135°C (1.5 mm Hg), d_4^{20} 0.9553, n_D^{20} 1.4590, were isolated as by-products. Found, %: C 66.3; H 12.2. MR_D 62.48. $C_{12}H_{26}O_3$. Calculated, %: C 66.0; H 12.0. MR_D 62.50.

LITERATURE CITED

1. Yu. K. Yur'ev and I. P. Gragerov, Zh. Obshch. Khim., 19, 724 (1949).
2. R. Onesta and A. Ferretti, Gazz. Chim. Ital., 85, 288 (1955).
3. I. F. Bel'skii and N. I. Shuikin, Dokl. Akad. Nauk SSSR, 128, 945 (1959).
4. I. F. Bel'skii and N. I. Shuikin, The Chemistry of Organosulfur Compounds Contained in Oils and Petroleum Products [in Russian], Vol. 4, GNTI Neftyanoi i Gorno-toplivnoi Lit., Moscow (1961), p. 17.
5. E. N. Karaulova, The Chemistry of Petroleum Sulfides [in Russian], Nauka, Moscow (1970), p. 61.
6. Organicum [Russian translation], Vol. 2, Mir, Moscow (1979), pp. 140, 141.
7. J. Cousseau and M. Lamant, Bull. Soc. Chim. France, No. 12, 4702 (1967).
8. N. I. Shuikin and B. A. Lebedev, Izv. Akad. Nauk SSSR, Ser. Khim., No. 3, 639 (1967).
9. Yu. K. Yur'ev, V. I. Gusev, V. A. Tronova, and P. P. Yurilin, Zh. Obshch. Khim., 11, 344 (1941).
10. B. W. Renfrow, D. Oakes, C. Lauer, and T. A. Walter, J. Org. Chem., 26, 935 (1961).
11. K. Weigand and G. Hilgetag, Experimental Methods in Organic Chemistry [Russian translation], Khimiya, Moscow (1968), p. 117.
12. S. Doležal, Chem. Comm., 2638 (1965).
13. N. P. Volynskii and L. I. Perepelitchenko, Neftekhimiya, 27, No. 2, 266 (1987).
14. J. Colonge and M. Reymermier, Compt. Rend., 237, 266 (1953).
15. R. Consden, D. Duveen, and J. Kenyon, J. Chem. Soc., 2106 (1938).
16. G. Wagner, Berichte, 27, 2434 (1894).
17. N. A. Ryabinin, I. P. Kolenko, and B. N. Lundin, Tr. Inst. Khim. Ural'sk. Fil. Akad. Nauk SSSR, No. 16, 80 (1968).
18. N. A. Ryabinin and I. P. Kolenko, Khim. Geterotsikl. Soedin., No. 1, 8 (1968).
19. V. G. Bukharov and T. E. Pozdnyakova, Izv. Akad. Nauk SSSR, Ser. Khim., No. 1, 135 (1961).