SYNTHESIS OF δ-TETRAHYDROFURYLALKANOLS AND HOMOLOGS OF TETRAHYDROPYRAN

I. F. Bel'skii and I. E. Grushko

Khimiya Geterotsiklicheskikh Soedinenii, Vol. 5, No. 1, pp. 6–8, 1969

UDC 547.722.3.723:542.941.7'952.1+547.811

A method for converting γ-tetrahydrofurylalkanols into δ-tetrahydrofurylalkanols has been developed. The latter are converted on Pt/C, as a result of isomerization of the tetrahydrofuran ring, intramolecular cyclization, and hydrogenation, into homologs of tetrahydropyran or dihydropyran with a yield of 80%.

In a number of our previous investigations [1–4], new methods have been found for the catalytic synthesis of heterocyclic compounds by the vapor-phase hydrogenation of furan ketones, alcohols, and amines, and of β-furyl carboxylic acids. The dimensions of the heterocycles formed and the positions of the substituents are determined by the structure of the initial furan compounds—primarily by the relative position of the furan ring and the functional groups in the side chains. The most accessible in relation to synthesis are the 2-alkyl-5-acylfurans and the γ-furylalkanols which, as is well known, can be obtained by the catalytic hydrogenation of furylacroleins and furylidene ketones [5]. Their hydrogenation by the continuous-flow method on a platinum catalyst leads to the formation of homologs of tetrahydrofuran [1] and tetrahydropyran.

Since the tetrahydropyran ring is formed from the carbon atoms which, in the initial compound (a 2-alkyl-5-acylfuran) form part of the furan ring, 2,4,6-trialkyltetrahydropyrans can be obtained from furan ketones with alkyl substituents in the β-position of the furan ring [6].

At the present time an important problem in synthesis is the production of furan or tetrahydrofuran alcohols containing the hydroxy group in position 4 in the side chain, since in this case the primary bifunctional aliphatic compounds are compounds of the δ-series.

We have studied the possibility of a simple passage from γ-tetrahydrofurylalkanols to δ-tetrahydrofurylalkanols. γ-Tetrahydrofurylalkanols were converted by the action of phosphorus tribromide into the corresponding bromides, which were then subjected to the Grignard reaction with aliphatic aldehydes and ketones. These reactions yielded δ-tetrahydrofurylalkanols with various alkyl substituents in the side chain, depending on the structure of the γ-tetrahydrofurylalkanols and the aliphatic oxo compounds.

As is well known, the tetrahydrofuran ring readily isomerizes on platinum with the formation of a propylcarbonyl group. The isomerization can be carried out in a current of hydrogen so as to obtain fully hydrogenated products. Under these conditions the δ-tetrahydrofurylalkanols are converted into homologs of tetrahydropyran which isomerize to a slight extent with formation of aliphatic ketones [7].

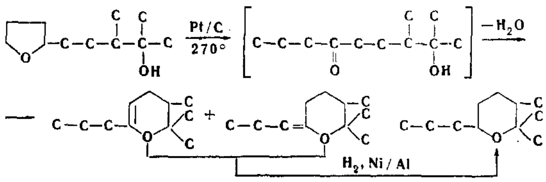
In some cases, on fractionation through an efficient column, fractions were isolated corresponding to tetrahydropyrans with different physical properties (see table). It is possible that these are the cis and trans forms of the polysubstituted tetrahydropyran homologs. Interesting results were obtained if the isomerization of the δ-tetrahydrofurylalkanols was carried out in the absence of hydrogen. In this case the reaction of the carbonyl group formed by the isomerization of the tetrahydrofuran ring with the hydroxy group in the side chain led to the formation of the dihydropyran ring.

Properties of Homologs of Tetrahydropyran and Dihydropyran

Compound	Bp, °C (pressure, mm)	n_D^{20}	d_4^{20}	MR_D		Empirical formula	Found, %		Calculated, %	
				found	calculated		C	H	C	H
2,2,3-Trimethyl-6-propyltetrahydropyran	71 (5)	1.4308	0.8303	53.06	52.81	$C_{11}H_{22}O$	77.66	13.07	77.58	13.02
3-Methyl-2,6-dipropyltetrahydropyran	88 (8)	1.4377	0.8321	58.11	58.22	$C_{12}H_{24}O$	78.63	13.27	78.19	13.12
cis-	89—92 (8)	1.4377	0.8356	57.86	58.22					
trans-	92—94 (8)	1.4382	0.8330	57.80	58.22					
2,2,3-Trimethyl-6-propyl-5,6-dihydropyran	85—87 (7)	1.4483	0.8543	52.43	51.97	$C_{11}H_{20}O$	78.00	11.88	78.51	11.98
2,2,3-Trimethyl-6-propylidenetetrahydropyran	66—68 (3)	1.4499	0.8607	52.43	52.52					
2,3-Dimethyl-6-nonanone	86—87 (4)	1.4263	0.8233	53.02	53.01	$C_{11}H_{22}O$*	77.76	13.06	77.58	13.02

---

*Mp of the semicarbazone 129.5 °C.



The dihydropyran homolog obtained was hydrogenated in an autoclave in tetrahydrofuran in the presence of a Raney Ni-Al catalyst at 100° C. A tetrahydropyran homolog was obtained in quantitative yield.

EXPERIMENTAL

The γ-tetrahydrofurylalkanols were obtained by the hydrogenation in an autoclave on a Raney nickel-aluminum catalyst at 100–130° C of, respectively, furfurylidene acetone, and α-ethyl-β-furylacrolein [5]. After vacuum distillation through a column they possessed the following properties: 1) 1-tetrahydrofuryl-3-butanol; bp 109–111° C (12 mm); n_D^{20} 1,4580; d_4^{20} 0.9771; 2) 2-ethyl-1-tetrahydrofuryl-3-propanol: bp, 98–99° C (5 mm); n_D^{20} 1.4670; d_4^{20} 0.9694.

Bromination. The γ-tetrahydrofurylalcohols were converted into the corresponding bromides under the action of phosphorus tribromide by a published method [8]. To obtain purer products, after the end of the reaction the reaction mixture was treated with a mixture of water and ether, and the ethereal layer was separated from aqueous. The reaction products were extracted from the aqueous layer with ether, and the ethereal extracts were washed with sodium carbonate solution, dried with potassium carbonate and distilled. The following compounds were obtained: 1) 3-bromo-1-tetrahydrofurylbutane: bp 76° C (5 mm); n_D^{20} 1.4779; d_4^{20} 1.2474. Yield 46%. Found: MR_D 46.76. Calculated for $C_8H_{15}BrO$: MR_D 46.35; 2) 3-bromo-2-ethyl-1-tetrahydrofurylpropane: bp 126° C (18 mm); n_D^{20} 1.4796; d_4^{20} 1.2109. Yield 49%. Found: MR_D 51.84. Calculated for $C_9H_{17}BrO$: MR_D 50.97.

The following compounds were obtained by the Grignard reaction: 1) 3-methyl-1-tetrahydrofuryl-4-heptanol (from 3-bromo-1-tetrahydrofurylbutane and butyraldehyde): bp 108° C (5 mm); n_D^{20} 1.4562; d_4^{20} 0.9248. Yield 52%; found: MR_D 58.90. Calculated for $C_{12}H_{24}O_2$: MR_D 58.58; 2) 2-ethyl-1-tetrahydrofuryl-4-heptanol (from 3-bromo-2-ethyl-1-tetrahydrofurylpropane and butyraldehyde): bp 155° C (9 mm); n_D^{20} 1.4595; d_4^{20} 0.9252. Found: MR_D 63.39. Calculated for $C_{13}H_{26}O_2$: MR_D 63.20; 3) 3,4-dimethyl-1-tetrahydrofuryl-4-pentanol (from 3-bromo-1-tetrahydrofurylbutane and acetone): bp 93° C (5 mm); n_D^{20} 1.4578; d_4^{20} 0.9273. Yield 43%. Found: MR_D 54.79. Calculated for $C_{11}H_{22}O_2$: MR_D 53.96.

The Pt catalysts were prepared in two ways. In the first case, activated carbon was impregnated with a solution of chloroplatinic acid, after which it was reduced with hydrogen in the reaction tube. In the second case the reduction was carried out with formalin in an alkaline medium [9]. The catalyst prepared in this way contained practically no adsorbed hydrogen.

Reduction. The δ-tetrahydrofurylalkanols were passed into the catalyst tube over Pt/C in a current of hydrogen or without it at 250–270° C. The catalyzate was separated from the water, dried with calcium chloride, and distilled in vacuum through a column. The properties of the tetrahydropyran and dihydropyran homologs are given in the table.

The presence of the dihydropyran compounds of endo- and exocyclic double bonds was shown by the IR spectra of the products (bands at 1650 and 1680 cm^{-1}) [10–12].

REFERENCES

1. I. F. Bel'skii and N. I. Shuikan, DAN, **128**, 945, 1959.
2. I. F. Bel'skii, N. I. Shuikin, G. K. Vasilevskaya, and G. K. Gaivoronskaya, Izv. AN SSSR, OKhN, 1650, 1962.
3. I. F. Bel'skii, ZhOKh, **32**, 2905, 1962.
4. I. F. Bel'skii, Izv. AN SSSR, OKhN, 1077, 1962.
5. A. Hinz, G. Meyer, and G. Schüking, Ber., **76**, 676, 1943.
6. N. I. Shuikin, I. F. Bel'skii, A. B. Balaban, and K. D. Nenitsesku, Izv. AN SSSR, OKhN, 138, 1962.
7. I. F. Bel'skii, and N. I. Shukin, DAN, **127**, 91, 1959.
8. A. A. Ponomarev, Syntheses and Reactions of Furan Compounds [in Russian], Izd-vo SGU, Saratov, p. 205, 1960.
9. N. I. Shuikin, I. F. Bel'skii, and V. M. Shostakovskii, ZhOKh, **34**, 2118, 1964.
10. M. Stoll and M. Hinder, Helv. Chim. Acta, **36**, 1984, 1953.
11. F. E. Bader, Helv. Chim. Acta, **36**, 215, 1953.
12. R. C. Lord and F. A. Miller, Appl. Spectrosc., **10**, 115, 1956.

20 September 1966

Zelinskii Institute of Organic
Chemistry AS USSR, Moscow