

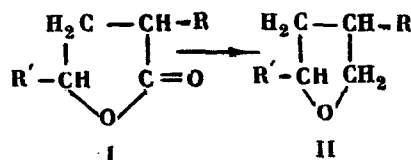
SUBSTITUTED LACTONES AND THEIR TRANSFORMATIONS;
 IV*. HYDROGENATION OF SUBSTITUTED LACTONES TO
 ALKYL TETRAHYDROFURANS

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To make a comparative study of the connection between odor and structure in the alkyl- γ -butyrolactone and alkyltetrahydrofuran series, α -, γ -, and α , γ -dialkylbutyrolactones are hydrogenated over copper-chromium catalyst to give the corresponding tetrahydrofurans. Most of the compounds obtained retain a fruity odor, reminiscent of that of the starting lactones.

In connection with previously undertaken searches [1, 2] for new perfumes, among α -substituted butyrolactones, a series of new compounds of that type were synthesized, enabling certain conclusions to be drawn regarding the connection between structure and odor. In pursuing the research, our interest was directed toward the role of the lactone carbonyl group in relation to the characteristic fruity odor of the lactone. It would have been possible to determine its role by comparing the odors of the substituted lactone with those of the products of reduction of the lactone carbonyl to a methylene group, i. e., to tetrahydrofuran derivatives with alkyl substituents in the 2 and 3 positions II:



Ia, IIa R = *cis*-C₆H₁₁, R' = H; Ib, IIb R = *cis*-C₆H₁₁CH₂, R' = H; Ic, IIc R = H, R' = *n*-C₇H₁₅; Id, II d R = *cis*-C₆H₁₁, R' = *n*-C₇H₁₅; Ie, IIe R = *cis*-C₆H₁₁CH₂, R' = *n*-C₇H₁₅.

Synthesis of 3-alkyltetrahydrofurans is a more difficult problem.

The basic methods for synthesizing 3-alkyl-substituted tetrahydrofurans are: preparation of 3-tetrahydrofuryllithium from 3-bromotetrahydrofuran with subsequent reaction with an alkyl bromide [3]; reaction of 3-ketotetrahydrofuran with an alkyl magnesium halide, followed by dehydration of the resultant 3-alkyl-3-hydroxytetrahydrofuran and hydrogenation of the unsaturated compound formed [4]; hydrogenation of 3-alkylfurans, synthesized, in particular, from furan-3-carboxylic acids [5]; Stobbe condensation of aldehydes with succinic ester, followed by hydrogenation of the resultant alkylideneformic esters involving reduction of the ester groups to hydroxymethylene groups and dehydration of the resultant 2-alkylbutan-1,4-diols to 3-alkyl-tetrahydrofurans [6].

It was desired to obtain the compounds II directly from lactones I, while avoiding the difficulties attending synthesis of such compounds II with R \neq H by the above methods. Accordingly, a study was made of the hydrogenation of lactone carbonyl over Raney nickel and copper-chromium catalyst. Here consideration was given primarily to results [7], which show that hydrogenation of butyrolactone and γ -valerolactone over Raney nickel give, respectively, tetrahydrofuran (9% yield) and 2-methyltetrahydrofuran (17% yield). Paper [8] deals with the possible formation of tetrahydrofuran derivatives when lactones are hydrogenated over copper-chromium catalyst. Butan-1,4-diols can be prepared by such hydrogenation [9] and converted into tetrahydrofurans by dehydration. It is known [10] that hydrogenation of γ -butyl- γ -methylbutyrolactone gives, along with substituted alcohols or glycols, 2-methyl-2-*n*-butyltetrahydrofuran in small yield. The present interest in alkyltetrahydrofurans as perfumery compounds is also due to a recent brief communication dealing with the use of heptyltetrahydrofuran in perfumery. The precise structure of this substance and how it is made are not stated. However, as far back as 1912 [12], information was published about the pleasant odor of 2-*n*-heptyltetrahydrofuran (IIc) (prepared by cyclizing undecylenic alcohol with zinc chloride or sulfuric acid).

It was shown that hydrogenation of α -alkylbutyrolactones Ia, b, d, e over copper-chromium catalyst at 260-300° actually gives the substituted tetrahydrofurans II. Unreacted lactones and side products were removed by treating with aqueous or aqueous-alcoholic alkali, followed by distillation over sodium metal. Evidently the ease of formation of II is to some extent connected with the presence of a substituent in the α position in the lactone ring, since hydrogenation of γ -heptylbutyrolactone (Ic) takes place at much lower temperature, though giving 2-*n*-heptyltetrahydrofuran (IIc) in lower yield (see Table). Along with compounds II, alcohols, products of the hydrogenolysis of II, and glycols are sometimes formed.

* For Part III see [1].

Properties of alkyltetrahydrofurans

Compound	bp, °C (pressure, mm)	d_4^{20}	n_D^{20}	MR _D		Molecular formula	C, %		H, %		Odor**
				Found	Calculated		Found	Calculated	Found	Calculated	
3-cyclohexyltetrahydrofuran (IIa)	62.5—66 (1.5)	0.9399	1.4710	45.85	45.62	C ₁₀ H ₁₈ O	77.84 78.13	77.86	11.91 11.99	11.76	Unlike Ia; recalls the odor of isoamyl alcohol
3-cyclohexylmethyltetrahydrofuran (IIb)	86.5—90 (4)	0.9292	1.4730	50.82	50.24	C ₁₁ H ₂₀ O	78.51	78.49	11.73	11.98	Fruity odor with leafy tone
2-n-heptyltetrahydrofuran (IIc)	79—83 (4)*	0.8547	1.4403	52.53	52.44	C ₁₁ H ₂₂ O	77.39 77.49	77.58	13.39 13.23	13.02	Flowery smell with characteristic leafy tone
2-n-heptyl-4-cyclohexyltetrahydrofuran (IIId)	147—149 (3)	0.8993	1.4710	78.45	77.95	C ₁₇ H ₃₂ O	81.03	80.88	13.02	12.78	Fruity smell with fatty tone
2-n-heptyl-4-cyclohexylmethyltetrahydrofuran (IIe)	172—176 (3—4)	0.9016	1.4710	82.62	82.56	C ₁₈ H ₃₄ O	81.01 81.06	81.13	12.77 12.82	12.86	Same

* The literature [12] gives bp 216—226°, d_4^{18} 0.8538. ** Perfumery evaluation by E. S. Kaboshina and A. G. Livschitz

At the same time, hydrogenation of α -substituted lactones I over Raney nickel only begins at about 300°, and results in the complete removal of the oxygen. Judging by the physical constants and analytical data for the resultant hydrocarbon fraction, there is practically no carbon-carbon bond hydrogenolysis.

Apart from the analytical data, the structure of the compounds II is supported by ir spectrum data, showing that these molecules contain C—O—C ether linkage, and the absence of oxygen functional groups. Thus, tetrahydrofurans are characterized by absorption in the range 1075—1100 cm⁻¹ due to C—O—bond vibration [13]; a sample of 2-n-heptyl-4-cyclohexyltetrahydrofuran (IIId) gives a spectrum with a band at 1073 cm⁻¹.*

On hydrogenation of α -cyclohexylmethyl- γ -heptylbutyrolactone (Ie) and α -cyclohexylmethylbutyrolactone (Ib), the small amount of aromatic isolog present is not hydrogenated into the ring, and the resultant tetrahydrofurans IIe and IIb contain small amounts of the corresponding aromatic derivatives. This is confirmed by the low intensity of absorption of a lactone in the region 240—270 μ , the character of which is reminiscent of the fine structure of the aromatic nucleus [14], while for the nearest homolog, compound IIId, where the presence of an aromatic ring is excluded by the method used for preparing the starting lactone Id, the absorption in this region is even less, and in no wise recalls the fine structure.

In the case of IIa the structure of compounds II is confirmed by reaction with acetic anhydride in the presence of zinc chloride. This reaction gives an ester, whose analytical data show that it corresponds to the expected 2-cyclohexylbutan-1,4-diol diacetate. Ring opening takes place under rather more drastic conditions and gives a lower yield than the corresponding reaction for tetrahydrofuran itself. This is most probably connected with the effect of the substituent.

Replacement of the carbonyl group in lactones I by a methylene group did not always lead to a sharp change in odor. Thus, it was only on passing from Ia to IIa that the odor changed completely. With compounds IIId and IIe it remained fruity, like the starting compounds Id and Ie, though the tone changed considerably. With IIb the odor was leafy, compared with that of Ib, while compared with Ic (γ -heptylbutyrolactone which can be used in perfumery to give a fruity odor) IIc has a flowery fragrance, differing considerably in character from the odor of Ic.

EXPERIMENTAL

Hydrogenation of alkylbutyrolactones to substituted tetrahydrofurans. A 150 ml rotating stainless steel autoclave was charged with 10—15 g alkylbutyrolactone and 2—3 g copper-chromium catalyst, and hydrogen was admitted to 100—110 atm. Hydrogenation of the α -alkylbutyrolactone was carried out for 3—4 hr at 230—240° and 150—170 atm; hydrogenation of Ic was carried out for 2 hr at 190—215° and 150—170 atm. Usually about 2 moles of hydrogen were absorbed per mole of lactone. The autoclave was emptied, the catalyst separated off, the residue dissolved in 30 ml alcohol, 4—5 g caustic soda added, and the mixture boiled for about 2 hr. The resulting solution was diluted to 150 ml and extracted with ether. The ether solution was dried and the ether distilled off. II was isolated by distilling the residue over a small amount of sodium metal. Yield about 60%.

* The ir spectrum was obtained with a UR-10 spectrophotometer and interpreted by T. A. Rudol'fi, the uv spectrum with an SF-4 spectrophotometer and interpreted by R. I. Sharapova and G. D. Kayukova.

After extracting II the aqueous solution was acidified and extracted with ether. After drying, the ether was distilled off, and vacuum distillation of the residue gave 10-15% of the starting lactone.

Hydrogenolysis of α -cyclohexyl- γ -heptylbutyrolactone over Raney nickel. A 230 ml rotating stainless steel autoclave was charged with 40 g Id and about 15 g Raney nickel, and hydrogen was admitted. Absorption began at about 310°, and finished at about 330° (160 atm). In all about 3 moles hydrogen were absorbed. The autoclave was emptied, the catalyst separated off, washed with alcohol, the filtrate and wash waters evaporated, and the residue vacuum-distilled. This gave a considerable amount of polymer and 14 g (40%) of a colorless liquid, odor like that of kerosene, bp 128-136° (5 mm), d_4^{20} 0.8310, n_D^{21} 1.4612. Found: C 86.49; 86.28; H 13.81; 14.01%, calculated for $C_{17}H_{34}$: C 85.63; H 14.37%.

Fractionation of 3-cyclohexyltetrahydrofuran. A thick-walled ampul holding about 100 ml was charged with 8.5 g IIa, 20 ml acetic anhydride, and 0.75 g anhydrous zinc chloride, sealed, and after wrapping in asbestos, heated at 220-240° in a furnace for 2 hr 30 min. After cooling, the ampul was carefully opened, the contents shaken with thrice their volume of water, and the whole carefully neutralized to pH 7-8 with dry bicarbonate. The solution was repeatedly extracted with ether, the ether solution dried, and after distilling off the ether the residue was vacuum-distilled, and the fractions boiling at 71-108° (3 mm) (4.2 g) and 120-133° (4 mm) (3.2 g) were collected. From its ester number, the second fraction contains 72% 2-cyclohexylbutan-1,4-dioldiacetate, equivalent to a 16.5% yield.

The first fraction has a strong odor of 3-cyclohexyltetrahydrofuran. The second fraction was subjected to thin layer chromatography, using Brockman grade 2 alumina and benzene-petrol ether (1:1), and gave two spots, one, $R_f \approx 0.25$, corresponding to the cyclohexylbutan-1,4-diol diacetate, the other, $R_f \approx 0.8$, corresponding to an unsaponified impurity. Chromatographing 2.2 g of the second fraction on a column of 80 g alumina of the same activity, using the same solvent, gave 0.95 g of 2-cyclohexylbutan-1,4-diol diacetate, a light yellow liquid bp 130-134° (4 mm), n_D^{20} 1.4638, ester number corresponding to 97% diester $C_{14}H_{24}O_4$. Found: C 65.59; 65.66; H 9.67; 9.69%, calculated for $C_{14}H_{24}O_4$: C 65.59; H 9.44%.

REFERENCES

1. V. M. Dashunin, R. V. Maeva, G. A. Samotuga, and V. N. Belov, ZhOKh, 34, 3096, 1964.
2. V. M. Dashunin, R. V. Maeva, and V. N. Belov, ZhOKh, 31, 3118, 1961; 32, 422, 1962.
3. Yu. K. Yurev and I. P. Gragerov, ZhOKh, 18, 1811, 1948.
4. Yu. K. Yurev, E. M. Lukina, and I. K. Korobitsyna, ZhOKh, 24, 1238, 1954.
5. P. Grünanger and A. Mantegani, Gazz., 89, 913, 1959.
6. P. Grünanger and F. Piozzi, Gazz., 89, 897, 1959.
7. H. Adkins and B. Wojcik, J. Am. Chem. Soc., 56, 2424, 1934.
8. H. Adkins, Reactions of Hydrogen with Organic Compounds over Copper-Chromium Oxide and Nickel Catalyst, The University of Wisconsin Press, Madison, 107, 1937.
9. H. Adkins and K. Folkers, J. Am. Chem. Soc., 54, 1145, 1932.
10. J. Cason, P. Brewer, and E. Pippen, J. Org. Chem., 13, 239, 1948.
11. Parfümerie und Kosmetik, 1, 21, 1963.
12. N. A. Logginov, ZhRFKhO, 45, 139, 1913.
13. L. Bellami, The Infrared Spectra of Complex Molecules [Russian translation], IL, Moscow, 143, 1957.
14. A. E. Gillam and E. B. Stern, Introduction to Electronic Absorption Spectroscopy in Organic Chemistry [Russian translation], IL, Moscow, 169, 1957.

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