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Reaction of Some Alkenols with Tetrachloromethane

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Summary. The reaction of some alkenols with tetrachloromethane in the presence of a radical initiator was investigated. Regarding the effects of structural features of the starting alkenol (number and position of methyl substituents at the double bond and at the carbinol carbon atom, constitutional relationship between the double bond and the hydroxyl group) there are two possible competing reactions: addition and cyclization. In the case of the simplest alkenols (without substituents and with a more remote double bond) addition occurs; mono- and disubstituted secondary and tertiary Δ^4- and Δ^5-alkenols cyclize in high yields to give the corresponding cyclic ethers.

Keywords. Addition; Alkenols; Cyclization; Tetrachloromethane; Radical initiator.

Introduction

Substituted tetrahydrofuran and tetrahydropyran rings are common in many naturally occuring products, and thus play an important role as building blocks for the syntheses of various biologically active organic molecules [1]. Intramolecular cyclization of unsaturated alcohols has become a convenient route for the construction of these oxacyclic compounds [2]. In continuation of our studies on electrophile-assisted intramolecular cyclization of alkenols [3–6] we have investigated the reaction of olefinic alcohols with tetrachloromethane in the presence of a radical initiator.

Tetrachloromethane adds to a double bond in the presence of radical initiators (acyl peroxides) as a result of a radical chain reaction [7]. Reactions can be complicated by rearrangement and/or elimination of hydrogen chloride. Such rearrangements involving a halogen shift have been reviewed by *Friedlina* [8]. A common complication of these reactions is polymerization which often becomes the prevailing process. On the other hand, it has recently been reported that tetrachloromethane in the presence of dibenzoyl peroxide (*DBP*) is an efficient reagent for the oxidation of some secondary alcohols to ketones [9].

In connection with these results, the oxidation of some alkenols with tetrachloromethane in the presence of *DBP* was investigated with respect to the

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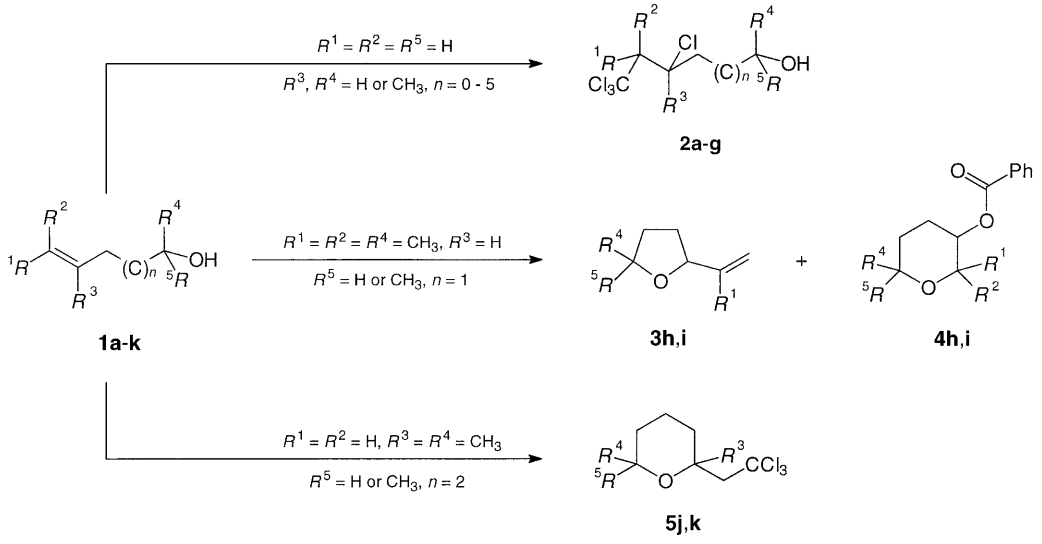
effect of methyl substitution at the unsaturated (trigonal) carbon atoms and at the carbinol carbon atom as well as a function of the constitutional relationship (distance) between the double bond and the hydroxyl group.

Results and Discussion

The reactions with CCl_4 were performed by addition of the alkenols dissolved in CCl_4 to a stirred solution of dibenzoyl peroxide (*DBP*) as a radical initiator and $NaHCO_3$ in the same solvent at room temperature. The ratio of substrate to *DBP* was 2:1, and tetrachloromethane served at the same time as reagent and solvent. The reaction mixture was stirred under reflux for 24 h. After work-up and separation of the reaction products the isolated products were analyzed and characterized chromatographically and spectroscopically. The results are given in Scheme 1 and in Table 1.

Regarding the effects of structural features in the starting alkenols in general, two possible competing reactions may occur, one giving addition and the other one leading to cyclization, which are illustrated in Scheme 1. The most simple alkenols (without substituents at the double bond and at the carbinol carbon atom) do not undergo cyclization upon treatment with tetrachloromethane. Some Δ^3- and Δ^4-alkenols, such as 3-buten-1-ol (**1a**), 4-penten-1-ol (**1b**), and some primary and secondary alkenols with a more remote double bond (**1e**–**g**), yield addition products only (**2a**–**g**, Scheme 1). In contrast, the secondary and tertiary Δ^4- and Δ^5-alkenols mono- and disubstituted at the double bond cyclize in good yield to give the corresponding cyclic ethers **3h**,**i**, **4h**,**i**, and **5j**,**k** (Scheme 1). The ring size of the heterocyclic products was found to be in accordance with *Baldwin*'s rules [10]. In the case of Δ^4-alkenols with a terminally disubstituted double bond (**1h** and **1f**) the reaction was mostly dominated by the ring size and stability of the products (favoured according to *Baldwin*'s terminology). Two cyclic products were



Scheme 1

Table 1. Reaction of alkenols with tetrachloromethane

	R^1	R^2	R^3	R^4	R^5	n	Products	Yield/%[a]
1a	H	H	H	H	H	0	**2a**	80
1b	H	H	H	H	H	1	**2b**	86
1c	H	H	H	H	H	2	**2c**	85
1d	H	H	CH_3	H	H	3	**2d**	80
1e	H	H	H	CH_3	H	3	**2e**	60
1f	H	H	H	H	H	4	**2f**	88
1g	H	H	H	H	H	5	**2g**	84
1h	CH_3	CH_3	H	CH_3	H	1	**3h**+**4h**	80[b] (45:55)[c]
1i	CH_3	CH_3	H	CH_3	CH_3	1	**3i**+**4i**	86[b] (45:55)[c]
1j	H	H	CH_3	CH_3	H	2	**5j**	89
1k	H	H	CH_3	CH_3	CH_3	2	**5k**	95

[a] Isolated yields; [b]combined yields; [c]relative distribution of the *THF*- and *THP*-type products as evaluated by capillary GLC and ^{1}H NMR analysis

likely to be formed in about equal amounts. The unsaturated tetrahydrofuran derivatives **3h** and **3i** resulted from elimination of trichloromethane (which was identified in the reaction mixture). As previously reported, intramolecular cyclization of alcohols **1h** and **1i** by means of *t*-butyl hypochlorite [5] and lead tetraacetate [3] also affords these products. The tetrahydropyran-type products **4h** and **4i** are formally derived from initial addition of a benzoyloxy radical. It has been noticed that acyloxylation also takes place upon reaction with lead tetraacetate and lead tetrabenzoate [3, 11]. As expected, cyclization of the Δ^5-alkenols **1j** and **1k** afforded solely the tetrahydropyran-type products **5j** and **5k** in high yields (Scheme 1 and Table 1).

All investigated secondary alkenols afforded as minor products the corresponding carbonyl compounds (10–20%). Primary alkenols usually do not afford oxidation products because of a very high activation barrier for α-hydrogen abstraction [9].

The mechanism of the above reactions has not been studied extensively, but current knowledge suggests that initial electrophilic attack of the reagent ($CCl_3^{\cdot}$ from CCl_4) on the π-system of the double bond results in the preferential formation of a more stable secondary or tertiary free radical as the favoured intermediate. The decisive factors which lead to either addition or cyclization appear to be the stability of free radicals and the activation entropy. On the one hand, in the case of unsubstituted alkenols external nucleophilic addition of $Cl^{\cdot}$ furnished the final reaction product. On the other hand, substituted alkenols gave cyclic ether products by internal nucleophilic addition of the hydroxylic oxygen to the initially generated free radical.

In conclusion, the mild conditions used, inexpensive reagents, and no necessity to use a complicated apparatus make this reaction useful for the synthesis of many organic compounds. The method described here is thus a versatile way of introducing one more carbon atom into alkenols. The trichloromethyl group can then be converted to a carboxyl group [12]. Moreover, the polychloroalkanols prepared by treatment with tetrachloromethane are suitable for the transformation

into a variety of reaction products by dehalogenation, dehydrohalogenation, and cyclization reactions [13]. It thus appears that this procedure is of value for the preparation of cyclic ethers and their functionalized derivatives.

Experimental

GLC analyses were obtained with a Deni 2000 instrument with capillary apolar columns. ^{1}H and ^{13}C NMR spectra were run in $CDCl_3$ on a Varian Gemini 200 MHz NMR spectrometer. IR spectra were obtained with Perkin-Elmer Model 137B and Nicolet 7000 FT spectrophotometers. Thin layer chromatography (TLC) was carried out on 0.25 mm (Merck) precoated silica gel plates (60F-254) using UV light for visualization. For column chromatography silica gel 60 (Merck, particle size 0.063–0.200 mm) was used. All olefinic alcohols used as substrates are known compounds which are either commercially available or were prepared according to known procedures [3, 14]. Tetrachloromethane was dried by distillation from P_2O_5. Dibenzoyl peroxide (Aldrich) was purified prior to use by precipitation from a solution in $CHCl_3$ by addition of twice its volume of methanol.

General procedure

All reactions were carried out on a 10 mmol scale. To a magnetically stirred solution of 1.21 g *DBP* (5 mmol) and 0.84 g $NaHCO_3$ (10 mmol) in 25 cm^3 dry CCl_4, 10 mmol alkenol dissolved in 5 cm^3 CCl_4 were added. Stirring was continued under reflux for 24 h. After completion of the reaction, the mixture was allowed to reach room temperature. Insoluble parts were filtered off, and the mixture was washed a few times with H_2O and dried over Na_2SO_4. After drying, the solvent was distilled off, and the residue was analyzed by gas chromatography and TLC. Reaction products were separated by column chromatography (silica gel/CH_2Cl_2:petroleum ether (b.p. 40–60°C) = 7:3) or by preparative gas chromatography (20% Carbowax column at 100°C) and identified and characterized by their spectroscopic data.

3,5,5,5-Tetrachloropentan-1-ol (**2a**; $C_5H_8OCl_4$)

Yield: 80%; IR (film): ν = 700, 790, 1070, 3400 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.52–1.94 (m, CH_2CH_2OH), 2.53 (br s, OH), 3.12 (ABX system, J_{AB} = 15.3 Hz, J_{AX} = 6.7 Hz, $CHCCl_3$), 3.26 (ABX system, J_{AB} = 15.3 Hz, J_{BX} = 6.9 Hz, $CHCCl_3$), 3.65 (t, J = 6.0 Hz, CH_2OH), 4.09 (m, CHCl) ppm.

4,6,6,6-Tetrachlorohexan-1-ol (**2b**; $C_6H_{10}OCl_4$)

Yield: 86%; IR (film): ν = 704, 790, 1060, 3400 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.62–2.17 (m, $CH_2CH_2CH_2OH$), 2.61 (br s, OH), 3.13 (ABX system, J_{AB} = 15.6 Hz, J_{AX} = 6.9 Hz, $CHCCl_3$), 3.27 (ABX system, J_{AB} = 15.6 Hz, J_{BX} = 7.0 Hz, $CHCCl_3$), 3.67 (t, J = 6.0 Hz, CH_2OH), 4.11 (m, CHCl) ppm; ^{13}C NMR ($CDCl_3$, DEPT, 50 MHz): δ = 28.83 (CH_2CHCl), 35.29 (CH_2CH_2OH), 57.32 (CHCl), 61.17 (CH_2CCl_3), 62.01 (CH_2OH), 95.93 (CCl_3) ppm.

5,7,7,7-Tetrachloroheptan-1-ol (**2c**; $C_7H_{12}OCl_4$)

Yield: 85%; IR (film): ν = 706, 790, 1064, 3420 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.53–2.05 (m, $CH_2CH_2CH_2$), 2.05 (s, OH), 3.12 (ABX system, J_{AB} = 15.7 Hz, J_{AX} = 7.9 Hz, $CHCCl_3$), 3.26 (ABX system, J_{AB} = 15.7 Hz, J_{BX} = 10.6 Hz, $CHCCl_3$), 3.67 (t, J = 6.0 Hz, CH_2OH), 4.27 (m, CHCl) ppm; ^{13}C NMR ($CDCl_3$, DEPT, 50 MHz): δ = 22.13 (CH_2CH_2), 31.44 (CH_2CHCl), 38.47 (CH_2CH_2OH), 57.22 (CHCl), 61.56 (CH_2CCl_3), 61.87 (CH_2OH), 95.82 (CCl_3) ppm.

6-Methyl-6,8,8,8-tetrachlorooctan-1-ol (**2d**; $C_9H_{16}OCl_4$)

Yield: 80%; IR (film): $\nu = 710$, 800, 1068, 3432 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 1.84$ (s, CH_3), 1.33–1.85 (m, $CH_2CH_2CH_2$), 1.95 (t, $J = 6.8$ Hz, CH_2CCl), 2.15 (s, OH), 3.22 (s, CH_2CCl_3), 3.65 (t, $J = 6.2$ Hz, CH_2OH) ppm.

7,9,9,9-Tetrachlorononan-2-ol (**2e**; $C_9H_{16}OCl_4$)

Yield: 60%; IR (film): $\nu = 709$, 810, 1062, 1411, 3416 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 1.22$ (d, $J = 6.0$ Hz, CH_3), 1.45–2.18 (m, $CH_2CH_2CH_2$), 2.16 (s, OH), 3.12 (ABX system, $J_{AB} = 16.1$ Hz, $J_{AX} = 6.9$ Hz, $CHCCl_3$), 3.26 (ABX system, $J_{AB} = 16.1$ Hz, $J_{BX} = 10.6$ Hz, $CHCCl_3$), 3.68 (t, $J = 6.0$ Hz, CHOH), 4.25 (m, CHCl) ppm.

7,9,9,9-Tetrachlorononan-1-ol (**2f**; $C_9H_{16}OCl_4$)

Yield: 88%; IR (film): $\nu = 705$, 791, 1070, 3476 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 1.25$–2.05 (m, $CH_2CH_2CH_2CH_2$), 2.31 (br s, OH), 3.12 (ABX system, $J_{AB} = 15.8$ Hz, $J_{AX} = 7.8$ Hz, $CHCCl_3$), 3.26 (ABX system, $J_{AB} = 15.8$ Hz, $J_{BX} = 10.5$ Hz, $CHCCl_3$), 3.69 (t, $J = 6.0$ Hz, CH_2OH), 4.25 (m, CHCl) ppm.

8,10,10,10-Tetrachlorodecan-1-ol (**2g**; $C_{10}H_{18}OCl_4$)

Yield: 84%; IR (film): $\nu = 704$, 790, 1069, 3456 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 1.25$–2.05 (m, $CH_2CH_2CH_2CH_2CH_2$), 2.23 (br s, OH), 3.12 (ABX system, $J_{AB} = 15.8$ Hz, $J_{AX} = 7.8$ Hz, $CHCCl_3$), 3.26 (ABX system, $J_{AB} = 15.8$ Hz, $J_{BX} = 10.5$ Hz, $CHCCl_3$), 3.68 (t, $J = 6.0$ Hz, CH_2OH), 4.25 (m, CHCl) ppm.

2-(1-Methylvinyl)-5-methyl-tetrahydrofuran (**3h**; $C_8H_{14}O$)

Yield: 36%; for spectroscopic data, see Ref. [3].

2-(1-Methylvinyl)-5,5-dimethyl-tetrahydrofuran (**3f**; $C_9H_{16}O$)

Yield: 39%; for spectroscopic data, see Ref. [3].

2,2,6-Trimethyl-3-benzoyloxy-tetrahydropyran (**4h**; $C_{15}H_{20}O_3$)

Yield: 44%; IR (film): $\nu = 715$, 780, 1178, 1260, 1715 cm^{-1}; ^1H NMR ($CDCl_3$, COSY, 200 MHz): $\delta = 1.22$ (d, $J = 6$ Hz, CH_3CHO), 1.45–1.55 (m, CH_2CHCH_3), 1.61 and 1.63 (2×s, $(CH_3)_2CO$), 1.82–1.98 (m, $CH_{ax}CHOCOPh$), 1.98–2.21 (m, $CH_{eq}CHOCOPh$), 4.05 (m, CHO), 5.28 (dd, $J = 2$ Hz and 10.1 Hz, CHOCOPh), 7.40–7.62 (m, *o*- and *p*-CH), 8.06–8.12 (m, *m*-CH) ppm; ^{13}C NMR ($CDCl_3$, DEPT, HETCOR, 50 MHz): $\delta = 24.96$ (CH_2OCOPh), 28.82 and 29.35 ($(CH_3)_2CO$), 31.12 (CH_3CO), 39.97 (CH_2CHCH_3), 70.45 (CHO), 70.64 (CO), 79.86 (CHOCOPh), 128.43 (*p*-CH), 129.64 (= CCOO), 129.76 (*o*-CH), 133.73 (*m*-CH), 166.15 (C=O) ppm.

2,2,6,6-Tetramethyl-3-benzoyloxy-tetrahydropyran (**4f**; $C_{16}H_{22}O_3$)

Yield: 47%; IR (film): $\nu = 715$, 784, 1180, 1262, 1715 cm^{-1}; ^1H NMR ($CDCl_3$, COSY, 200 MHz): $\delta = 1.20$ and 1.22 (2×s, $(CH_3)_2CCH_2$), 1.43–1.56 (m, $CH_2C(CH_3)_2$), 1.62 and 1.64 (2×s, $(CH_3)_2CCH$), 1.82–1.98 (m, $CH_{ax}CHOCOPh$), 1.98–2.21 (m, $CH_{eq}CHOCOPh$), 5.28 (dd, $J = 2$ Hz

and 10.1 Hz, CHOCOPh), 7.40–7.62 (m, *o*- and *p*-CH), 8.06–8.12 (m, *m*-CH) ppm; ^{13}C NMR ($CDCl_3$, DEPT, HETCOR, 50 MHz): $\delta = 24.90$ (CH_2OCOPh), 28.76 and 29.23 ($CH_3)_2$CCH), 28.91 and 29.59 ($CH_3)_2CCH_2$), 39.70 ($CH_2C(CH_3)_2$), 70.52 and 70.59 (*COC*), 79.89 (*C*HOCOPh), 128.41 (*p*-CH), 129.66 (= *C*COO), 129.75 (*o*-CH), 133.75 (*m*-CH), 166.13 (C=O) ppm.

2,6-Dimethyl-2-(1,1,1-trichloroethyl)-tetrahydropyran (**5i**; $C_9H_{15}OCl_3$)

Yield: 89%; IR (film): $\nu = 710$, 736, 775, 913, 1149 cm^{-1}; ^{1}H NMR ($CDCl_3$, COSY, 200 MHz): $\delta = 1.21$ (d, $J = 6.0$ Hz, CH_3CHO), 1.40–1.54 (m, CH_2CH_2), 1.55–1.72 (m, CH_2CHO), 1.86 (s, CH_3CO), 1.88–2.05 (m, CH_2CO), 3.38 (s, CH_2CCl_3), 3.83 (d, $J = 6.0$ Hz, CHO) ppm.

2,6,6-Trimethyl-2-(1,1,1-trichloroethyl)-tetrahydropyran (**5j**; $C_{10}H_{17}OCl_3$)

Yield: 95%; IR (film): $\nu = 710$, 736, 775, 913, 1149 cm^{-1}; ^{1}H NMR ($CDCl_3$, COSY, 200 MHz): $\delta = 1.25$ (s, $(CH_3)_2CO$), 1.42–1.52 (m, CH_2CH_2), 1.53–1.72 (m, $CH_2C(CH_3)_2$), 1.86 (s, CH_3CO), 1.88–2.04 (m, CH_2CCH_3), 3.39 (s, CH_2CCl_3) ppm; ^{13}C NMR ($CDCl_3$, DEPT, HETCOR, 50 MHz): $\delta = 19.25$ (CH_2CH_2), 29.05 and 29.10 ($CH_3)_2CO$), 29.93 (CH_3CO), 43.22 ($CH_2C(CH_3)_2$), 44.88 (CH_2CCH_3), 63.94 (CH_2CCl_3), 70.51 $C(CH_3)_2$), 71.43 (CCH_3), 95.63 (CCl_3) ppm.

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