

ALUMINIUMCHLORIDE-INDUCED ADDITIONS OF FORMALDEHYDE TO ALKENES

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Dedicated to Professor H.G. Viehe on the occasion of his 65th birthday

ABSTRACT

The addition of formaldehyde to alkenes induced by AlCl_3 is a simple route to alkylsubstituted tetrahydropyrans. Additions of two equivalents of formaldehyde to 1-alkenes and 1,2-dialkylsubstituted alkenes give 3-alkyl-4-chlorotetrahydropyrans and 3,5-dialkyl-4-chlorotetrahydropyrans, respectively. The products are obtained as a mixture of diastereomers. 2,5-dialkyl-4-chlorotetrahydropyrans are obtained in AlCl_3 -induced additions of one equivalent of formaldehyde to homoallylic alcohols. Reductive dechlorination gives the corresponding 3-, 3,5- and 2,5-alkylsubstituted tetrahydropyrans, respectively.

INTRODUCTION

The acid-catalyzed addition of aldehydes to olefines is usually called the Prins reaction (1-3). Generally the reaction gives a complex mixture of products consisting of 1,3-dioxanes, 1,3-glycols and unsaturated alcohols as main products. Cyclic ethers such as tetrahydropyrans and tetrahydrofurans were identified occasionally as minor products. It should be of interest to find reaction conditions giving with high selectivity only one of the formaldehyde-alkene addition products.

There are known Lewis acid induced reactions - e.g. SnCl_4 and $\text{BF}_3 \cdot \text{Et}_2\text{O}$ - giving as main products the corresponding unsaturated alcohols (4-6). Primary homoallylic alcohols are obtained in good yields and with high selectivity in alkylaluminium halide induced ene reactions (7-9). We reported recently the alkylaluminium halide induced ene addition of formaldehyde to readily available unsaturated fatty compounds (10,11), for example oleic acid and 10-undecenoic acid which are of interest as renewable raw materials (12) and obtained in good yields the corresponding primary homoallylic alcohols.

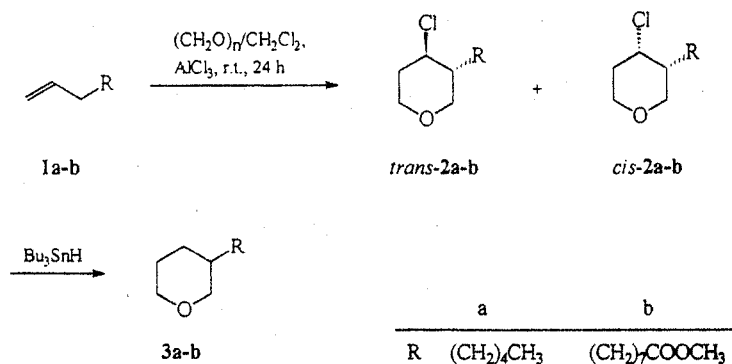
3-Alkyl-4-halotetrahydropyrans are obtained in reactions of paraformaldehyde and α -olefines in the presence of hydrogen halides (13a). Using hydrogen chloride at -60° to -70°C the products were obtained in yields of 70-80% as mixtures of diastereomers. The condensation of *cis*- and *trans*-butene with formaldehyde and hydrogen chloride affords the diastereomeric chloroalcohols and their formals as main products while the corresponding alkylsubstituted chlorotetrahydropyrans were formed only in small amounts (14). The reaction of formaldehyde and cyclohexene in the presence of hydrogen chloride gives a mixture of two chlorinated bicyclic ethers along with a small amount of the corresponding formaldehyde acetal (15). Addition of

formaldehyde to 3-buten-1-ol catalyzed by hydrochloric acid gives 4-chlorotetrahydropyran (16). 2-Alkyl-4-chlorotetrahydropyrans are obtained in analogous reactions with aldehydes such as acetaldehyde, propionaldehyde and butyric aldehyde. The corresponding reactions catalyzed by sulphuric acid afford the substituted tetrahydropyran-4-ols as major products. Additions of aldehydes and ketones to the substituted alcohol 4-methyl-4-penten-2-ol in the presence of *p*-toluenesulphuric acid give 3,6-dihydro-2*H*-pyrans (17).

In the present paper we describe the addition of formaldehyde to olefines induced by AlCl_3 to give with high selectivity alkylsubstituted tetrahydropyrans.

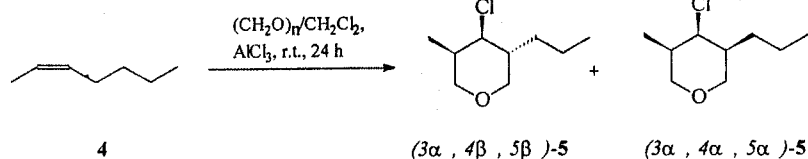
RESULTS AND DISCUSSION

The AlCl_3 -induced reaction of formaldehyde and 1-octene (1a) or methyl 10-undecenoate (1b) gave the corresponding 3-alkyl-4-chlorotetrahydropyrans *trans*-2a/*cis*-2a and *trans*-2b/*cis*-2b, respectively. The diastereomers were obtained in a ratio of [*cis*]:[*trans*] = 1:2.5. The isomers could be assigned by their ^{13}C NMR data. The chemical shifts of the ring carbons were identical to those of *cis*- and *trans*-4-chloro-3-propyltetrahydropyran (13b). The reaction takes place by addition of two equivalents of formaldehyde to the double bond of the alkene. In the first step one equivalent of formaldehyde should be added to give the ene adduct, the homoallylic alcohol. It is known that homoallylic alcohols cyclize to give 4-chlorotetrahydropyrans on reaction with formaldehyde and hydrogen chloride (18). This reaction sequence was confirmed by the following experiment: Methyl 12-hydroxydodec-9-enoate obtained by ethylaluminiumdichloride-induced addition of formaldehyde to methyl 10-undecenoate (10), reacted with formaldehyde induced by AlCl_3 to give 3-alkyl-4-chlorotetrahydropyran



trans-2b/cis-2b. Reductive dechlorination of *trans-2a/cis-2a* and *trans-2b/cis-2b* for example with Bu₃SnH afforded the 3-alkyl-tetrahydropyrans **3a** and **3b**, respectively.

column chromatography and obtained as (**3 α** , **4 β** , **5 β**)-**7a**/**(3 α** , **4 β** , **5 β**)-**8a** and (**3 α** , **4 α** , **5 α**)-**7b**/**(3 α** , **4 α** , **5 α**)-**8b** in a ratio of 3:1.

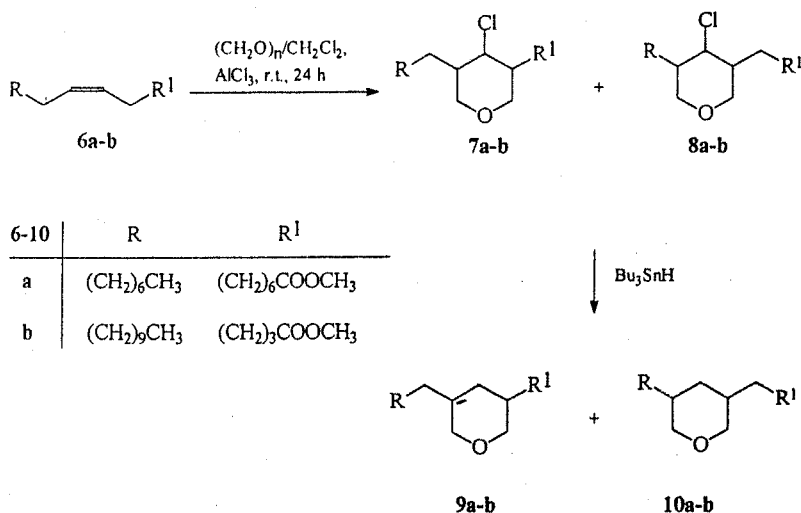


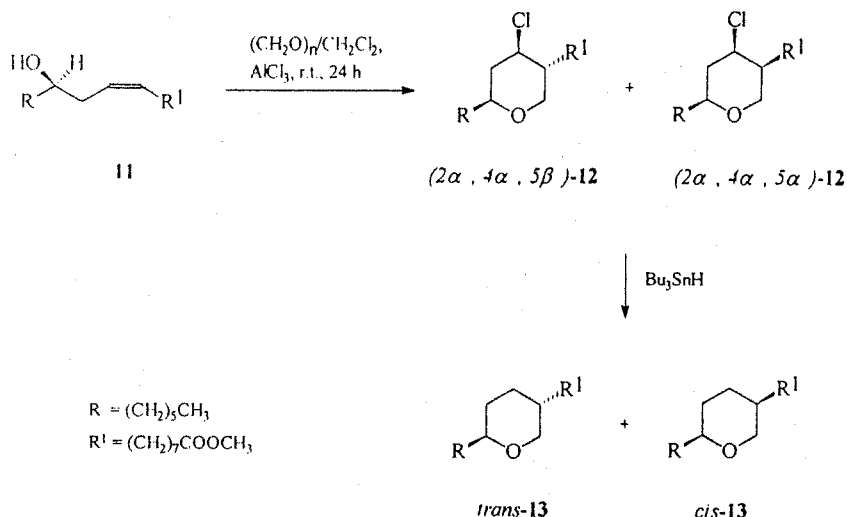
The addition of formaldehyde to 1,2-dialkylsubstituted alkenes **4**, **6a** and **6b** gave the corresponding 3,5-dialkyl-4-chlorotetrahydropyrans **5**, **7a/8a** and **7b/8b** in good yields. The reaction of *cis*-2-heptene (**4**) afforded regioselectively 4-chloro-5-methyl-3-propyltetrahydropyran (**5**) as a diastereomeric mixture of (**3 α** , **4 β** , **4 β**)-**5** and (**3 α** , **4 α** , **5 α**)-**5** in a ratio of 4:1. The addition products with methyl oleate (**6a**) and methyl petroselinate (**6b**) were obtained as regioisomers (1:1 mixture) and as diastereomers. Reductive dechlorination of **7a/8a** and **7b/8b** with Bu₃SnH gave the corresponding 3,5-dialkyltetrahydropyrans **9a/10a** and **9b/10b**.

The diastereomeric mixture of **7a/8a** was separated by

The addition of formaldehyde to methyl ricinoleate (**11**), an alkene with β -hydroxy functionality took place regioselectively to position C-9 of the olefine. Cyclization and elimination of H₂O afforded 2,5-dialkyl-4-chlorotetrahydropyran **12** as a mixture of diastereomers. (**2 α** , **4 α** , **5 β**)-**12** was obtained by recrystallization of **12** from petrolether. Reductive dechlorination of **12** gave a mixture of the 2,5-dialkyltetrahydropyrans *trans*-**13** and *cis*-**13** in a ratio of 3.8:1.

The stereochemistry of the main products can be explained by anti-attack of the formaldehyde-AlCl₃-complex to the homoallylic alcohol existent in the preferred conformation avoiding allylic strain (**19**). The minor products are formed by syn-attack.





The AlCl_3 -induced addition to formaldehyde to alkenes gives with high selectivity the corresponding alkylsubstituted 4-chlorotetrahydropyrans. In this study the synthesis of 3-, 3,5- and 2,5-alkylsubstituted tetrahydropyrans is described. By variation of the alkene on the one hand and of the carbonyl compound on the other hand it should be possible to synthesize the complete set of alkylsubstituted tetrahydropyrans.

EXPERIMENTAL

Melting points (uncorrected) : Leitz Laborlux 12. - Refractive indices n_D : Zeiss-Abbé-Refraktometer. - ^1H and ^{13}C NMR : Bruker AM 300 (**2a**, **2b**, **3a**, **3b**, **9a/10a** and **9b/10b**), Bruker AMX R 500 (**(3α, 4β, 5β)-7a/(3α, 4β, 5β)-8a**, **(3α, 4α, 5α)-7a/(3α, 4α, 5α)-8a**, **7b/8b**, **(2α, 4α, 5β)-12** and **13**). TMS as internal standard; selected data are given. Full ^1H - and ^{13}C -NMR data are available from the authors on request. The signals of the regioisomers **7b** and **8b** were distinguishable in the ^1H - and ^{13}C -NMR spectra but they could not be assigned unambiguously to the respective products. NMR-data of the minor products *cis*-**2a**, *cis*-**2b**, **(3α, 4α, 5α)-5** and **(3α, 4α, 5α)-7b/(3α, 4α, 5α)-8b** are signed by ^a. - Analytical GC : Carlo Erba GC 6000 Vega Series 2 with a FID (DB1 - column, 28 m). - Mass spectra : Finnegan MAT 212 mass spectrometer. -

Methyl oleate (new sun flower, 82.8% methyl oleate, 3.6% methyl stearate, 3.5% methyl palmitate, 8.4% $\text{C}_{18:2}$), petroselinic acid (81.3% petroselinic acid, 3.3% palmitic acid, 0.4% stearic acid, 13.5% $\text{C}_{18:2}$) and ricinoleic acid (80 - 85% purity) were obtained from Henkel KGaA. - The amounts of the starting olefines used in the reactions were calculated based on 100% purity. The free fatty acids were converted to their methyl esters by usual esterification. - Methyl 10-undecenoate (Atochem), *cis*-2-heptene and 1-octene (Merck), paraformaldehyde (Janssen), Bu_3SnH , AIBN, AlCl_3 , KF (Fluka), 18-crown-6 (Aldrich) were used without further purification. - All reactions were run under N_2 .

Synthesis of alkylsubstituted chloro-tetrahydropyrans; general procedure :

A mixture of the appropriate alkene **1a** or **4** or of the methyl alkenoate **1b**, **6a**, **6b** or **11** (5 mmol) and paraformaldehyde

(0.3 g, 10 mmol; 0.21 g, 7 mmol was used for **11**) in CH_2Cl_2 (10 mL) was stirred magnetically in N_2 atmosphere for 5 min at -15°C . After addition of AlCl_3 (0.33 g, 2.5 mmol) the sample was stirred for additional 24 h at r.t. The reaction was quenched by addition for Et_2O (100 mL) and H_2O (40 mL). 10% HCl was added until the precipitated aluminium salts dissolved. The organic layer was separated and the aqueous layer extracted with Et_2O (3x40 mL). The combined organic layers were dried (Na_2SO_4) and evaporated. The product was purified by "Kugelrohr" distillation (**2b**, **5**, **7a/8a**, **7b/8b**) or by column chromatography (28 cm x 2 cm) on silica gel (Merck, 70-230 mesh) with petrolether/ EtOAc (95:5) as eluent (**2a**, **12**). Fractions containing the tetrahydropyranderivative were collected, the solvent evaporated and the residue dried at $20^\circ\text{C}/0.01$ mbar. - Reductive dechlorination of the alkylsubstituted 4-chlorotetrahydropyrans with Bu_3SnH : A solution of the tetrahydropyran **2a**, **2b**, **7a/8a**, **7b/8b** and **12** (1-2 mmol), Bu_3SnH (1 mL, 4 mmol) and AIBN (15 mg) in benzene (30 mL) was heated at 80°C for 20 h. The solvent was evaporated and the residue dissolved in Et_2O (10 mL). KF (10% in H_2O , 10 mL) and 18-Crown-6 were added. The organic layer was separated and the precipitate washed with Et_2O (80 mL). The combined organic layers were dried (Na_2SO_4) and evaporated.

trans-4-Chloro-3-pentyltetrahydropyran (*trans*-**2a**) and *cis*-4-Chloro-3-pentyltetrahydropyran (*cis*-**2a**) (2:1 mixture) : yield 0.71 g (75%), colorless liquid, $n_D^{22} = 1.4635$. - ^1H NMR (CDCl_3) : $\delta = 4.42$ (m, 1H, 4-H)^a, 4.02 (dd, $J = 11.8, 4.9$ Hz, 1H, 2-H), 3.94 (m, 1H, 6-H), 3.78 (m, 1H, 4-H), 3.78 (m, 2H, 6-H, 6-H')^a, 3.59 (dd, $J = 11.5, 4.4$ Hz, 1H, 2-H)^a, 3.51 (dd, $J = 11.5, 9.9$ Hz, 1H, 2-H')^a, 3.41 (ddd, $J = 11.5, 11.0, 2.6$ Hz, 1H, 6-H'), 3.11 (dd, $J = 11.8, 9.4$ Hz, 1H, 2-H'), 2.16 (m, 1H, 3-H)^a, 2.11 (m, 1H, 3-H), 1.94 (m, 2H, 5-H), 1.94 (m, 2H, 5-H)^a. - ^{13}C NMR (CDCl_3) : $\delta = 70.9$ (C-2), 67.1 (C-2)^a, 66.9 (C-6), 62.5 (C-6)^a, 61.9 (C-4), 60.8 (C-4)^a, 44.9 (C-3), 40.0 (C-3)^a, 36.5 (C-5), 34.5 (C-5)^a. - MS/CI (isobutane) : m/z (%) = 191(100)/193(32) [MH^+], 155(56) [$\text{MH}^+ - \text{HCl}$]. - $\text{C}_{10}\text{H}_{20}\text{OCl}$: calcd. 191.1224, found 191.1323 (MS/CI). -

3-Pentyltetrahydropyran (**3a**) : Dechlorination of **2a** (0.45 g) gave 0.35 g (95%) of **3a**, colorless liquid, $n_D^{22} = 1.4591$. - ^1H NMR (CDCl_3) : $\delta = 3.85$ (m, 2H, 2-H and 6-H), 3.33 (ddd, $J = 11.2, 9.7, 4.4$ Hz, 1H, 6-H'), 3.02 (dd, $J = 11.0, 10.2$ Hz, 1H, 2-H'), 1.84 (m, 1H, 3-H), 1.56 (m, 4H, 4-H and 5-H). -

^{13}C NMR (CDCl_3) : δ = 73.6 (C-2), 68.5 (C-6), 36.0 (C-3), 32.5 (C-4), 30.1 (C-5). - MS/CI (isobutane) : m/z (%) = 157(100) [MH^+]. - $\text{C}_{10}\text{H}_{26}\text{O}$: calcd. 156.1514, found 156.1501 (MS/EI).

trans-4-Chloro-3-(7-methoxycarbonylheptyl)-tetrahydropyran (**trans-2b**) and *cis*-4-Chloro-3-(7-methoxycarbonylheptyl)-tetrahydropyran (**cis-2b**) (2.4:1 mixture) : yield 1.01 g (73%), colorless liquid, $n_D^{22} = 1.4701$. - ^1H NMR (CDCl_3) : δ = 4.20 (m, 1H, 4-H)^a, 3.94 (m, 2H, 2-H, 6-H), 3.75 (m, 1H, 4-H), 3.75 (m, 2H, 6-H, 6-H')^a, 3.52 (m, 2H, 2-H, 2-H')^a, 3.38 (ddd, $J = 11.5, 11.3, 2.5$ Hz, 1H, 6-H'), 3.08 (dd, $J = 11.6, 11.6$ Hz, 1H, 2-H'), 2.11 (m, 1H, 3-H)^a, 2.07 (m, 1H, 3-H), 1.91 (m, 2H, 5-H). - ^{13}C NMR (CDCl_3) : δ = 174.0 (C=O), 70.8 (C-2), 67.0 (C-2)^a, 66.8 (C-6), 62.4 (C-6)^a, 61.8 (C-4), 60.7 (C-4)^a, 44.8 (C-3), 40.9 (C-3)^a, 36.4 (C-5), 34.5 (C-5)^a. - MS/CI (isobutane) : m/z (%) = 277(100)/279(34) [MH^+], 241(56) [$\text{MH}^+ - \text{HCl}$]. - $\text{C}_{14}\text{H}_{26}\text{O}_3\text{Cl}$: calcd. 277.1591, found 277.1581 (MS/CI). -

3-(7-Methoxycarbonylheptyl)-tetrahydropyran (**3b**) : Dechlorination of **2b** (0.5 g) gave 0.43 g (97%) of **3b**, colorless liquid, $n_D^{22} = 1.4572$. - ^1H NMR (CDCl_3) : δ = 3.83 (m, 2H, 2-H and 6-H), 3.31 (ddd, $J = 10.8, 10.0, 4.3$ Hz, 1H, 6-H'), 2.99 (dd, $J = 10.6, 10.6$ Hz, 1H, 2-H'), 2.28 (t, $J = 7.5$ Hz, 2H, $\text{CH}_2\text{COOCH}_3$), 1.82 (m, 1H, 3-H), 1.56 (m, 6H, 4-H, 5-H, $\text{CH}_2\text{CH}_2\text{COOCH}_3$). - ^{13}C NMR (CDCl_3) : δ = 174.0 (C=O), 73.5 (C-2), 68.4 (C-6), 51.3 (OCH₃), 36.0 (C-3), 32.4 (C-4), 30.1 (C-5). - MS/CI (isobutane) : m/z (%) = 243(100) [MH^+]. - $\text{C}_{14}\text{H}_{26}\text{O}_3$: calcd. 242.1882, found 242.1881 (MS/EI).

4-Chloro-5-methyl-3-propyltetrahydropyran (($3\alpha, 4\beta, 5\beta$)-**5** and ($3\alpha, 4\alpha, 5\alpha$)-**5**) (4:1 mixture) : yield 0.53 g (60%), colorless liquid, $n_D^{22} = 1.4662$. - ^1H NMR (CDCl_3) : δ = 4.08 (dd, $J = 5.8, 3.7$ Hz, 1H, 4-H)^a, 4.01 (ddd, $J = 11.5, 4.5, 0.9$ Hz, 1H, 2-H), 3.97 (dd, $J = 11.6, 3.4$ Hz, 1H, 4-H, 4-H), 3.88 (ddd, $J = 11.5, 4.5, 1.0$ Hz, 1H, 6-H), 3.55 (m, 2H, 2-H, 6-H)^a, 3.32 (dd, $J = 10.6, 10.5$ Hz, 2H, 2-H', 6-H')^a, 3.04 (dd, $J = 11.5, 11.5$ Hz, 1H, 6-H'), 3.00 (dd, $J = 11.5, 11.4$ Hz, 1H, 2-H'). - ^{13}C NMR (CDCl_3) : δ = 73.6 (C-2), 72.2 (C-6), 71.0 (C-2)^a, 67.4 (C-6)^a, 70.3 (C-4), 66.2 (C-4)^a, 44.9 (C-6), 41.7 (C-3)^a, 41.4 (C-5). -

4-Chloro-3-(6-methoxycarbonylhexyl)-5-octyltetrahydropyran (**7a**) and 4-Chloro-5-heptyl-3-(7-methoxycarbonylheptyl)-tetrahydropyran (**8a**) (1:1 mixture) : yield 1.61 g (86%), colorless liquid, $n_D^{22} = 1.4723$. - MS/CI (isobutane) : m/z (%) = 375(100)/377(34) [MH^+], 339(66) [$\text{MH}^+ - \text{HCl}$]. - $\text{C}_{21}\text{H}_{39}\text{O}_3\text{Cl}$ (374.2) : calcd. C 67.39, H 10.42, found C 67.02, H 11.03. - The diastereomeric mixture of the regioisomers **7a/8a** (1:1) was separated by column chromatography on silica gel 60 (Merck, 70-230 mesh) with petroleum ether (9:1) and gave ($3\alpha, 4\beta, 5\beta$)-**7a**/($3\alpha, 4\beta, 5\beta$)-**8a** and ($3\alpha, 4\alpha, 5\alpha$)-**7a**/($3\alpha, 4\alpha, 5\alpha$)-**8a** (ratio 3:1). - ($3\alpha, 4\beta, 5\beta$)-**7a**/($3\alpha, 4\beta, 5\beta$)-**8a** : ^1H NMR (CDCl_3) : δ = 3.99 (dd, $J = 11.6, 3.8$ Hz, 1H, 2-H), 3.94 (dd, $J = 11.6, 2.8$ Hz, 1H, 4-H), 3.53 (m, 1H, 6-H), 3.39 (dd, $J = 10.8, 10.2$ Hz, 1H, 6-H'), 3.0 (dd, $J = 11.6, 11.5$ Hz, 1H, 2-H'), 1.83 (m, 2H, 3-H, 5-H). - ^{13}C NMR (CDCl_3) : δ = 174.2 (C=O), 72.2 (C-2, C-6), 69.1 (C-4), 51.4 (O-CH₃), 45.2 (C-3, C-5). - ($3\alpha, 4\alpha, 5\alpha$)-**7a**/($3\alpha, 4\alpha, 5\alpha$)-**8a** : ^1H NMR (CDCl_3) : δ = 3.90 (m, 1H, 4-H), 3.59 and 3.58 (2x dd, $J = 11.5, 3.5$ Hz, 2H, 2-H and 6-H), 3.45 (dd, $J = 11.5, 10.8$ Hz, 2H, 2-H', 6-H'), 1.90 (m, 2H, 3-H, 5-H). - ^{13}C NMR

(CDCl_3) : δ = 174.2 (C=O), 66.7 (C-2, C-6), 65.6 (C-4), 51.4 (O-CH₃), 41.8 (C-3, C-5). -

3-(6-Methoxycarbonylhexyl)-5-octyltetrahydropyran (*trans*-**9a** and *cis*-**9a**) and 5-Heptyl-3-(7-methoxycarbonylheptyl)-tetrahydropyran (*trans*-**10a** and *cis*-**10a**) (1:1 mixture) : Dechlorination of **7a/8a** (1:1 mixture, 0.5 g) gave 0.42 g (93%) of **9a/10a**, colorless liquid, $n_D^{22} = 1.4602$. - ^1H NMR (CDCl_3) : δ = 3.82 (m, 2H, 2-H, 6-H, *trans*-**9a/10a**), 3.27 (m, 4H, 2-H, 2-H', 6-H, 6-H', *cis*-**9a/10a**), 2.79 (dd, $J = 11.1, 11.0$ Hz, 2H, 2-H', 6-H', *trans*-**9a/10a**), 2.23 (t, $J = 7.5$ Hz, 2H, $\text{CH}_2\text{COOCH}_3$), 1.55 (m, 4H, 3-H, 5-H, $\text{CH}_2\text{-CH}_2\text{COOCH}_3$). - ^{13}C NMR (CDCl_3) : δ = 174.1 (C=O), 73.6 (C-2, C-6, *trans*-**9a/10a**), 72.8 (C-2, C-6, *cis*-**9a/10a**), 51.4 (O-CH₃), 45.6 (C-4, *cis*-**9a/10a**), 37.4 (C-4, *trans*-**9a/10a**), 36.1 (C-3, C-5). - $\text{C}_{21}\text{H}_{40}\text{O}_3$: calcd. 340.2977, found 340.2980 (MS/EI). -

4-Chloro-3-(3-methoxycarbonylpropyl)-5-undecyltetrahydropyran (**7b**) and 4-Chloro-5-decyl-3-(4-methoxycarbonylbutyl)-tetrahydropyran (**8b**) (1:1 mixture) : yield 0.91 g (58%), colorless liquid, $n_D^{22} = 1.4730$. - The main product is the 1:1 mixture of ($3\alpha, 4\beta, 5\beta$)-**7b** and ($3\alpha, 4\beta, 5\beta$)-**8b**. - ^1H NMR (CDCl_3) : δ = 3.97 and 3.96 (dd, $J = 11.4, 5.6$ Hz, 1H, 2-H, **7b** and **8b**), 3.92 (m, 1H, 4-H), 3.57 (m, 2H, 2-H, 6-H)^a, 3.50 (m, 2H, 2-H', 6-H')^a, 3.42 (dd, $J = 11.1, 11.1$ Hz, 1H, 6-H), 3.36 (dd, $J = 11.1, 11.1$ Hz, 1H, 6-H'), 2.99 (dd, $J = 11.4, 11.5$ Hz, 1H, 2-H'), 2.28 and 2.27 (t, $J = 7.4$ Hz, 2H, $\text{CH}_2\text{COOCH}_3$), 1.78 (m, 2H, 3-H, 5-H). - ^{13}C NMR (CDCl_3) : δ = 173.8 (C=O), 72.1 (C-2, C-6), 68.9 (C-4), 66.6 (C-2, C-6)^a, 65.3 (C-4)^a, 51.3 (O-CH₃), 45.1 and 45.0 (C-3, C-5, **7b** and **8b**), 41.8 and 41.6 (C-3, C-5, **7b** and **8b**)^a. - MS/CI (isobutane) : m/z (%) = 375(100)/377(34) [MH^+], 339(100) [$\text{MH}^+ - \text{HCl}$]. - $\text{C}_{21}\text{H}_{39}\text{O}_3\text{Cl}$ (374.2) : calcd. C 67.39, H 10.42, found C 67.47, H 10.23. -

3-(3-Methoxycarbonylpropyl)-5-undecyltetrahydropyran (*trans*-**9b** and *cis*-**9b**) and 5-Decyl-3-(4-methoxycarbonylbutyl)-tetrahydropyran (*trans*-**10b** and *cis*-**10b**) (1:1 mixture) : Dechlorination of **7b/8b** (1:1 mixture, 0.5 g) gave 0.4 g (89%) of **9b/10b**, colorless liquid, $n_D^{22} = 1.4618$. - ^1H NMR (CDCl_3) : δ = 3.90 (m, 2H, 2-H, 6-H, *trans*-**9b/10b**), 3.39 (m, 4H, 2-H, 2-H', 6-H, 6-H', *cis*-**9b/10b**), 2.87 (dd, $J = 11.0, 11.0$ Hz, 2H, 2-H', 6-H', *trans*-**9b/10b**), 2.31 and 2.30 (t, $J = 7.6$ Hz, 2H, $\text{CH}_2\text{COOCH}_3$, **9b** and **10b**). 1.62 (m, 4H, 3-H, 5-H, $\text{CH}_2\text{CH}_2\text{COOCH}_3$). - ^{13}C NMR (CDCl_3) : δ = 73.5 (C-2, C-6), 51.3 (O-CH₃), 45.5 (C-4, *cis*-**9b/10b**), 37.2 (C-4, *trans*-**9b/10b**), 36.0 (C-3, C-5). - $\text{C}_{21}\text{H}_{40}\text{O}_3$: calcd. 340.2977, found 340.2977 (MS/EI). -

4-Chloro-2-hexyl-5-(7-methoxycarbonylheptyl)-tetrahydropyran (($2\alpha, 4\alpha, 5\beta$)-**12** and ($2\alpha, 4\alpha, 5\alpha$)-**12**) (3.8:1 mixture) : yield 0.88 g (61%). Recrystallization of **12** from petroleum ether gave pure ($2\alpha, 4\alpha, 5\beta$)-**12**, solid, m.p. 29-30°C. - ^1H NMR (CDCl_3) : δ = 4.02 (dd, $J = 11.5, 4.6$ Hz, 1H, 6-H), 3.71 (ddd, $J = 11.4, 11.2, 4.5$ Hz, 1H, 4-H), 3.24 (m, 1H, 2-H), 3.05 (dd, $J = 11.5, 11.3$ Hz, 1H, 6-H'), 2.30 (t, $J = 7.5$ Hz, 2H, $\text{CH}_2\text{COOCH}_3$), 2.16 (ddd, $J = 12.8, 4.5, 1.5$ Hz, 1H, 3-H), 1.85-1.49 (m, 5H, 3-H', 5-H, $\text{CH}_2\text{CH}_2\text{COOCH}_3$, HCHCHO). - ^{13}C NMR (CDCl_3) : δ = 174.2 (C=O), 77.8 (C-2), 71.5 (C-6), 62.7 (C-4), 45.1 (C-5), 43.1 (C-3). - MS/CI (isobutane) : m/z (%) = 361(100)/363(34) [MH^+], 325(66) [$\text{MH}^+ - \text{HCl}$]. - $\text{C}_{20}\text{H}_{38}\text{O}_3\text{Cl}$: calcd. 361.2531, found 361.2505 (MS/CI). -

2-Hexyl-5-(7-methoxycarbonylheptyl)-tetrahydropyran (*trans*-**13** and *cis*-**13**) : Dechlorination of **12** (0.5 g) gave 0.41

g (91%) of **13**, solid, m.p. 34-35°C : ^1H NMR (CDCl_3) : $\delta = 3.89$ (m, 1H, 6-H, *trans*-**13**), 3.25 (m, 1H, 2-H, *cis*-**13**), 3.15 (m, 1H, 2-H, *trans*-**13**) 2.98 (dd, $J = 11.1, 11.1$ Hz, 1H, 6-H', *trans*-**13**), 1.84 (m, 1H, 3-H *trans*-**13**). -

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