SYNTHESIS AND STEREOCHEMISTRY OF CHIRAL 1,3-DIOXANIC COMPOUNDS OBTAINED FROM α-ALKYLATED β-KETOESTERS

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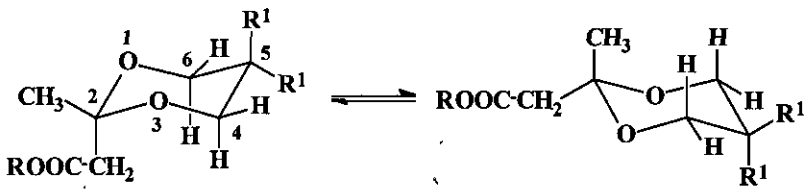
Abstract-1,3-Dioxanic compounds were obtained by the ketalisation reaction of some α -alkylated β-ketoesters. The conformational analysis by means of ^{1}H- and ^{13}C-nmr investigations showed the anancomeric structure of the compounds. The axial or the equatorial position of the groups was inferred by N.O.E. experiments. The influence of the chiral carbon atom of the esteric group located at C^2 was studied using the diastereotopicity of the protons and of the carbon atoms recorded in high field nmr spectra.

INTRODUCTION

In a previous work[1] we have reported on the stereochemistry of some 1,3-dioxanic compounds obtained by the ketalisation reaction of some esters of the acetylacetic acid with symmetrically 2,2-disubstituted 1,3-propanediols. The conformational analysis of these compounds, bearing different groups in the ketalic part of the heterocycle, revealed flipping structures. The differences between the conformational free enthalpies of a methyl group and of an alkyloxycarbonylmethyl group (ROOC-CH_2-) in the position 2 of the heterocycle were too small to induce the anancomericity of the ring (Scheme 1).



Scheme 1

The ^{1}H-nmr spectra of these compounds display unique signals, with mean values of the chemical shifts, for the axial and equatorial positions of the protons of the ring (positions 4 and 6) and of the protons of the identical groups located in the position 5 of the heterocycle .

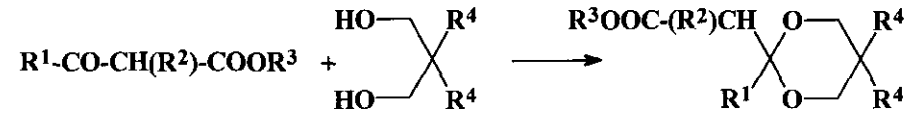
On the other hand, the nmr investigations[2-7] of some chiral 2, 5-substituted 1,3-dioxanic compounds showed the diastereotopicity of the protons and of the carbon atoms of the heterocycle (positions 4 and 6) or of the formally identical fragments [e.g., -CH(*H*)Br, -CCH$_3$(*CH$_3$*)Br, -COOCH(*H*)CH$_3$] of the axial or of the equatorial groups located on it (positions 2 and 5). The values of the diastereotopicity ($\Delta\delta$) were correlated with the type of chirality (chiral center for monocyclic, or axial and helical chirality for spiranic 1,3-dioxanes), with the position of the chiral center and with the position of the diastereotopic protons or carbon atoms.

In this context it was considered of interest to develop a stereochemical investigation of some 1,3-dioxanic compounds bearing in the position 2 more bulky chiral alkyloxycarbonylalkyl groups and having as geminal substituent alkyl groups (methyl or ethyl). The nmr investigations of this kind of compounds allow the observation both of the anancomericity or the flipping of the rings and of the influence of the chirality (by means of the diastereotopicity of the protons and carbon atoms).

RESULTS AND DISCUSSION

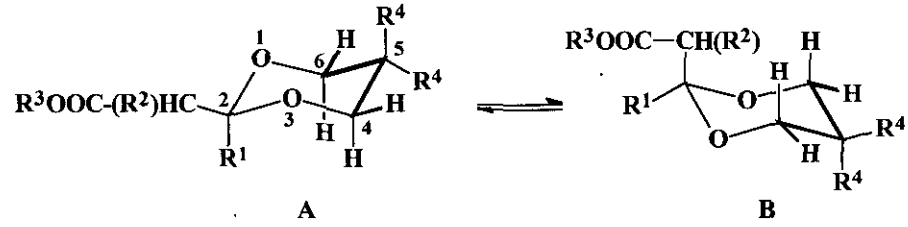
1,3-Dioxanic compounds (**5-10**) were obtained (Scheme 2) by the ketalisation reaction of some α-alkylated β-keto esters (**1-4**).

Compound (**5-10**) exhibit anancomeric structure, the characteristic conformational equilibrium for the 1,3-dioxanic ring (Scheme 3) being shifted to one of the conformation A or B. If the substituent R^1 is methyl, the alkyloxycarbonylalkyl group [R^{3}OOC-(R^2)CH-] prefers an equatorial position (conformation A) and if R^1 is ethyl, the conformational equilibrium is shifted to the conformation B with the esteric group in an axial orientation.



β-Ketoester	R^1	R^2	R^3	,	R^4	1,3-Dioxane
1	CH_3	CH_3	CH_3	,	$COOC_2H_5$	**5**
2	CH_3	C_2H_5	C_2H_5	,	$COOC_2H_5$	**6**
3	CH_3	iC_3H_7	CH_3	,	$COOC_2H_5$	**7**
2	CH_3	C_2H_5	C_2H_5	,	CH_3	**8**
4	C_2H_5	CH_3	CH_3	,	CH_3	**9**
4	C_2H_5	CH_3	CH_3	,	$COOCH_3$	**10**

Scheme 2



Scheme 3

These results were inferred by the nmr investigation of the compounds.

The anancomericity of the structures has as a consequence the recording in the nmr spectra of different signals for the axial and for the equatorial protons of the heterocycle and for the protons and for the carbon atoms of the axial and of the equatorial identical groups located in the position 5 of the 1,3-dioxanic ring, respectively.

The presence of a chiral carbon atom in the alkylesteric group at C^2 entails the diastereotopicity of the positions 4 and 6 of the 1,3-dioxanic ring. The nmr spectra exhibit different signals for the protons and for the carbon atoms of these positions.

The ^{1}H-nmr pattern for the protons of the ring shows two doublets of doublets with a further splitting of the signals corresponding to the equatorial protons due to the long range coupling ($^4J_{4e,6e}$), possible as a consequence of the W (M) disposal of the bonds $H_{eq.}$-C^4-C^5-C^6-$H_{eq.}$

As an example (Figure 1) the spectrum of compound (**9**) displays an AB system for the protons of the position 4 ($\delta_{4ax.}$=3.67, $\delta_{4eq.}$=3.28 ppm) and another one for those of position 6 ($\delta_{6ax.}$=3.23, $\delta_{6eq.}$=3.18 ppm) The magnitude of the long range coupling constant observed by the further splitting of the signals

corresponding to the equatorial protons (^4J=1.7 Hz) is somewhat smaller than the usual values reported for this type of coupling constants ($^4J_{4e,6e}$=2,5 Hz).[8] The smaller values (0.70 Hz < $^4J_{4e,6e}$ < 1.70 Hz) for this type of coupling constants recorded in all the spectra of the investigated compounds result probably as a consequence of the flattering of the 1,3-dioxanic ring in its aliphatic part. The axial protons are in an unusual way more deshielded than the equatorial ones. This deshielding is due to the "steric compression" exerted by the axial group located at C^2.

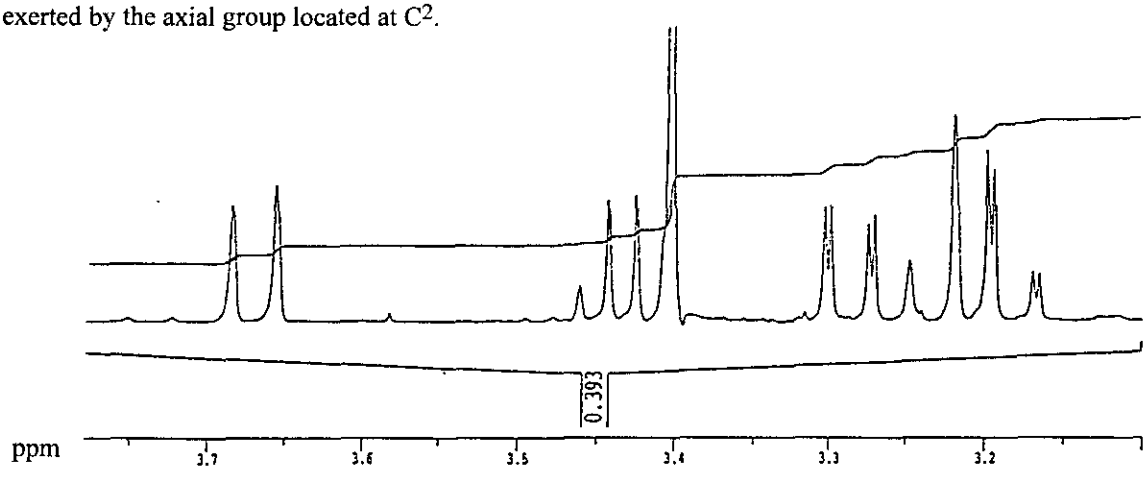


Figure 1 ^{1}H-Nmr spectrum (fragment) of compound (**9**)

This phenomenon was reported previously for other anancomeric 2,2-disubstituted 1,3-dioxanes.[9,10] The diastereotopicities recorded for the equatorial and for the axial protons of compound (**9**) are $\Delta\delta_{4eq.-6eq.}$= 0.10 ppm and $\Delta\delta_{4ax.-6ax.}$=0.44 ppm, respectively. These values are usual, as well as the values recorded (Table 1, 0.06 < $\Delta\delta_{4eq.-6eq.}$ < 0.29 ppm; 0.07 < $\Delta\delta_{4ax.-6ax.}$ < 0.44 ppm) for compounds (**5-8**) and (**10**).

Table 1. ^{1}H-Nmr data (δ ppm) for the 1,3-dioxanic ring in compounds (**5-10**)

Compound	Protons					
	4eq.	6eq.	Δδ	4ax.	6ax.	Δδ
5	4.67	4.46	0.21	4.45	4.35	0.10
6	4.76	4.49	0.27	4.51	4.43	0.08
7	4.51	4.45	0.06	4.69	4.50	0.19
8	3.55	3.26	0.29	3.33	3.26	0.07
9	3.28	3.18	0.10	3.67	3.23	0.44
10	4.52	4.42	0.10	4.59	4.18	0.31

The ^{13}C-nmr spectra of compounds (**5-10**) also display different signals for the carbon atoms of the positions 4 and 6 (Table 2). The diastereotopicity of the carbon atoms is about $0.16 < \Delta\delta_{4\text{-}6} < 0.37$ ppm.

Table 2. ^{13}C-Nmr data (δ ppm) for the diastereotopic positions of the 1,3-dioxanic ring in compounds (**5-10**)

Compound	Carbon atoms		
	4	6	Δδ
5	62.55	62.34	0.21
6	62.58	62.38	0.20
7	62.40	62.03	0.37
8	70.30	70.12	0.18
9	70.04	69.85	0.19
10	63.22	63.06	0.16

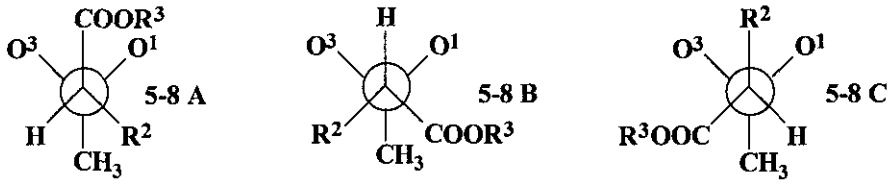
The different values of the diastereotopicities recorded for the protons of the positions 4 and 6 of the 1,3-dioxanic ring of the compounds (**5-10**) can be correlated with the rotameric arrangement of the chiral groups located in the ketal part of the heterocycle.

The conformational analysis of the possible staggered conformations [Scheme 4; it is considered the rotation around the bond C^2-C^{α}(eq.)] of the equatorial chiral group (e.g., R configuration of the chiral center) in compounds (**5-8**) shows the lowest stability for the conformation B [three bulky groups (R^2, CH_3 and $COOR^3$) in "gauche" disposal]. The ratio of the conformational free energies, as well as of the populations, of the other two conformers (A and C) can be estimated by the values of the diastereotopicities recorded for the equatorial protons of the 1,3-dioxanic ring and depends of the volume of the R^2 group.

The differences between the magnetic environments of the two diastereotopic protons (4-eq., 6-eq.) are higher in conformation C as in conformation A (different influences of the esteric group).

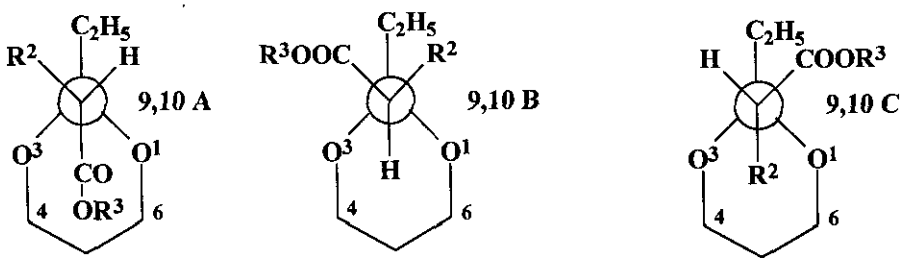
The higher values of the diastereotopicities recorded for the equatorial protons of the heterocycle in the case of compounds (**5**, **6** and **8**; $\Delta\delta_{4eq.\text{-}6eq.}$=0.21-0.29 ppm) as for compound (**7**; $\Delta\delta_{4eq.\text{-}6eq.}$=0.06 ppm) show a higher preference of the chiral group for conformation C when R^2 is CH_3 or C_2H_5 (compounds

5, **6** and **8**) than when this group (R^2) is *i*-C_3H_7 (compound **7**). The lower preference of the chiral group of compound (**7**) for conformation C is suggested also by the analysis of the rotameric disposal of the isopropyl group. The preferred rotamer of this group in conformation C has the hydrogen atom oriented through the 1,3-dioxanic ring. In this rotamer the interactions of the isopropyl group with the geminal ester group are higher than in conformation A.



Scheme 4

The analysis in compounds (**9** and **10**) of the relation between the diastereotopicity of the protons of the heterocycle and the preferred conformations of the chiral group revealed some interesting aspects. These compounds display the chiral group in an axial orientation. The rotation of the chiral group (e.g., configuration R) around the bond C^2-C^{α}(ax.) generates the conformations A, B and C (Scheme 5). In the analysis of the stability (populations) of these conformers the intensity of the interactions of the axial chiral group with the axial protons of the positions 4 and 6 of the 1,3-dioxanic was considered to be the most important.[8] The chiral group prefers conformation B (this can be named "H in side"). The high population of this conformer determines an enlargement of the diastereotopicity for the axial protons of the 1,3-dioxanic ring $\Delta\delta_{4ax.-6ax.}$=0.31-0.41 ppm [the diastereotopicities of the axial protons of compounds (**5-8**) are about $\Delta\delta_{4ax.-6ax}$=0.07-0.19 ppm]. The axial position of the chiral group (compounds **9** and **10**) has as result also the recording of smaller values for the diastereotopicity of the equatorial protons ($\Delta\delta_{4eq.-6eq.}$=0.10 ppm).



Scheme 5

The chirality of the molecules also influences the magnetic resonance of the protons and of the carbon atoms of the formally identical groups located on the 1,3-dioxanic ring. Thus, the diastereotopicity of the

protons or of the protons and carbon atoms of the R^2 groups (compounds **6-8**) or of the protons of the equatorial ethyl group located at C^2 (compounds **9** and **10**) could also be measured.

The diastereotopicity of the protons H^a and H^b of the groups 2-CH(COOR^3)-CH^a(H^b)-CH$_3$ is $\Delta\delta_{a-b}$(**6**) =0.21 ppm and $\Delta\delta_{a-b}$(**8**) =0.20 ppm. These values are higher than those observed for the diastereotopic protons of the equatorial ethyl group (2-CH^{a}H^b-CH$_3$); $\Delta\delta_{a-b}$(**9**) =0.14 ppm and $\Delta\delta_{a-b}$(**10**) =0.13 ppm, respectively. The diastereotopic methyl groups of the substituent -CH(COOCH$_3$)-CH(CH$_3{}^a$)CH$_3{}^b$ located at C^2 (compound **7**) display different signals in both ^{1}H ($\Delta\delta_{a-b}$=0.12 ppm) and ^{13}C-nmr ($\Delta\delta_{a-b}$ =0.53 ppm) spectra.

The axial or the equatorial position of the substituents at C^2 was established using N.O.E. experiments. The investigation of compound (**5**), bearing the substituents -CH(CH$_3$)-COOCH$_3$ and -CH$_3$ in the position 2 of the 1,3-dioxanic ring, was made using the irradiation of the protons of the methyl group (2-CH$_3$, singlet, δ=1.48 ppm) and of the methynic proton of the geminal alkylesteric group [2-CH(COOCH$_3$)CH$_3$, quartet, δ=3.18 ppm). The N.O.E. Diff. spectrum recorded in the first case shows an influence on the signals corresponding to both axial and equatorial protons of the 1,3-dioxanic ring, with a significant higher magnitude in the case of the axial ones. The N.O.E. Diff. spectrum recorded when the methynic proton was irradiated shows only a small influence on the signals of the equatorial protons of the positions 4 and 6. The results of the N.O.E. experiments permit to consider the preference of the methyl group for the axial position and the preference of the alkylesteric group for the equatorial one.

The N.O.E. experiments run for compound (**9**) were made by irradiating the methynic proton of the alkylesteric group (quartet at δ=3.43 ppm) and the methylenic protons of the ethyl group (doublets of quartets at δ=1.88 and at δ=2.02 ppm). The N.O.E. Diff. spectra show in the first case a significant influence for the signal corresponding to one of the axial protons of the ring and a smaller influence for the signals belonging to the other axial proton and to the two equatorial ones. In the second case (when the methylenic protons were irradiated) only a small influence on the signals of the equatorial protons of the rings was recorded. It can be inferred that the ethyl group prefers the equatorial position and the alkylesteric group prefers the axial one. The N.O.E. experiment made with compound (**10**) involving the irradiation of the same type of methylenic protons (doublets of quartets δ=1.79 and δ=1.92 ppm) of the ethyl group (position 2) shows in the N.O.E. Diff. spectrum only an small influence on the signals corresponding to the equatorial protons of the 1,3-dioxanic ring confirming the equatorial position of the ethyl group in this compound, too.

The changes in the preference for an axial and for an equatorial position in the ketal part of the 1,3-dioxanic ring for an alkyl and an alkyl ester group, respectively when the methyl group is replaced with an ethyl one are remarkable. That suggests a higher difference of the conformational energies for a methyl and an ethyl group in this part of the 1,3-dioxanic ring as expected from thermodynamically data.[8]

The nmr investigations of compounds (**5-10**) revealed some other interesting peculiar aspects. The ^{1}H-nmr spectrum (Figure 2) of compound (**8**) exhibits a unique signal (singlet, δ= 3.26 ppm) for the equatorial and for the axial protons of the position 6 as a consequence of a fortuitously identical magnetic environment of the two protons. In contrast, the equatorial and the axial protons of the position 4 display a well-separated AB system ($\Delta\delta_{4eq.-4ax.}$=0.22 ppm).

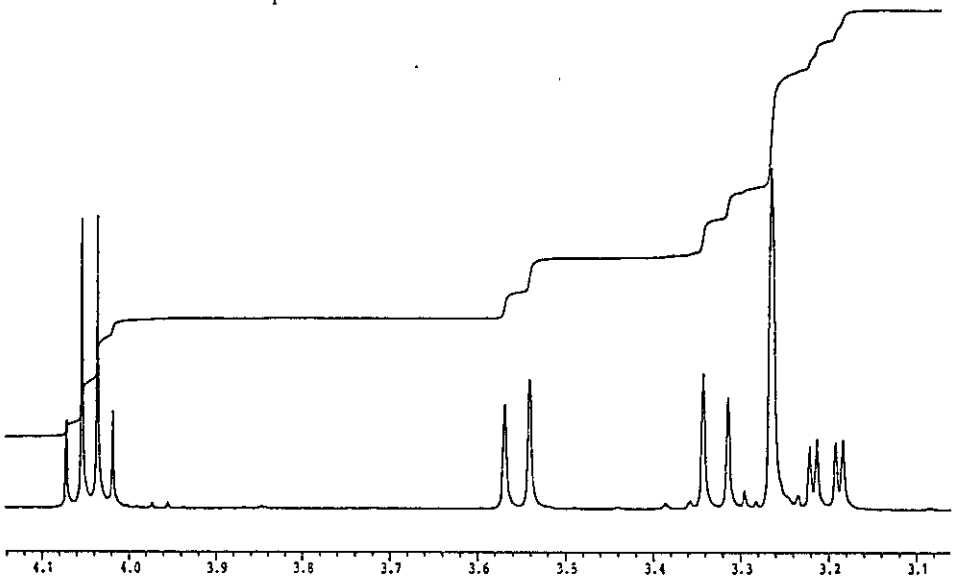


Figure 2. ^{1}H-Nmr spectrum (fragment) of compound (**8**)

An unusual influence of a chiral carbon atom was recorded in the ^{1}H-nmr spectrum of compound (**7**). Two different signals (doublets of quartets δ_a=3.894; δ_b=3.897 ppm) for the methylenic protons of the axial esteric group located in the position 5 [5-COOCH^a(H^b)CH$_3$] were recorded. The influence of the chiral carbon atom is filled at 8 atoms distance from this one. Probably, the influence is transmitted through space and not by bonds. This option is supported by the missing of the same influence in the case of the similar equatorial geminal esteric group. Situations as those observed for compounds (**7**) and (**8**) were also reported for some brominated chiral 1,3-dioxanic compounds.[6]

EXPERIMENTAL

General. - Nmr spectra were obtained on a Bruker AM 400 spectrometer (with an Aspect 3000 calculator) operating at 400 MHz for protons and 100 MHz for carbon atoms. No TMS was added; the chemical shifts were measured against the solvent peak (in all the cases C_6D_6).

The α-alkylated β-keto esters (**1-3**) were obtained under usual conditions using the alkylation reaction of the corresponding esters of the acetylacetic acid with alkyl iodide. Compound (**4**) was obtained by the classic Claisen condensation reaction of the methyl ester of the propionic acid.

New *compounds (5-10), general procedure.* - Equimolecular (0.1 mol) amounts of 1,3-diol and β-keto ester with catalytic quantities of *p*-toluenesulphonic acid (0.1 g) were solved in 200 ml of benzene. The mixture was refluxed and the water was removed using a Dean-Stark trap. When 80 % of the theoretical quantity of water was separated, after cooling at room temperature, the reaction mixture was neutralized (under stirring 0.5 h) with CH_3-COONa powder in excess (0.2 g). The mixture was washed twice with 100 ml of water. After drying (with Na_2SO_4) the benzene was removed and the 1,3-dioxanic compound was purified by vacuum distillation (1-2 mmHg). These conditions are similar to those used in the synthesis of other 2,5-substituted 1,3-dioxanic compounds obtained from β-keto esters.[1,11-13]

5,5-Bis(ethyloxycarbonyl)-2-[1-methyloxycarbonylethyl]-2-methyl-1,3-dioxane (**5**).

Liquid, bp 166-168 °C (1 mmHg). Yield 64%. Anal. Calcd for $C_{15}H_{24}O_8$: C, 54.21, H, 7.28. Found: C, 54.38; H, 7.21. ^{1}H-Nmr (C_6D_6, δ, ppm) 0.82[3H, t, J=7.1 Hz, 5-COOCH$_2$C*H*$_3$(eq.)], 0.87[3H, t, J=7.1 Hz, 5-COOCH$_2$C*H*$_3$(ax.)], 1.16[3H, d, J=7.0 Hz, 2-CH(COOCH$_3$)-C*H*$_3$], 1.48(3H, s, 2-CH$_3$), 3.18[1H, q, J=7.0 Hz, 2-C*H*(COOCH$_3$)-CH$_3$], 3.32[3H, s, 2-CH(CH$_3$)-COOC*H*$_3$], 4.26[2H, q, J=7.1 Hz, 5-COOC*H*$_2$CH$_3$(eq.)], 4.33[2H, q, J=7.1 Hz, 5-COOC*H*$_2$CH$_3$(ax.)], 4.35(1H, d, J=11.8 Hz, 6-H$_{ax.}$), 4.45 (1H, d, J= 11.8 Hz, 4-H$_{ax.}$), 4.46(1H, dd, J=11.8, 1.1 Hz, 6-H$_{eq.}$), 4.67(1H, dd, J=11.8, 1.1 Hz, 4-H$_{eq.}$); ^{13}C-nmr (C_6D_6, δ, ppm) 12.59[2-CH(COOCH$_3$)-*C*H$_3$], 13.83[5-COOCH$_2$*C*H$_3$(eq.)], 13.84[5-COO-CH$_2$*C*H$_3$(ax.)], 17.43(2-CH$_3$), 41.63(C^5), 45.56[2-CH(CH$_3$)-COO*C*H$_3$], 51.26[2-*C*H(COOCH$_3$)CH$_3$], 61.73[5-COO*C*H$_2$CH$_3$(eq.)], 61.76 [5-COO*C*H$_2$CH$_3$ (ax.)], 62.34 (C^6), 62.55(C^4), 100.36(C^2), 167.72[5-*C*OOCH$_2$CH$_3$ (eq.)], 167.84[5-*C*OOCH$_2$CH$_3$ (ax.)], 173.09[2-CH(CH$_3$)-*C*OOCH$_3$].

5,5-Bis(ethyloxycarbonyl)-2-[1-ethyloxycarbonylpropyl]-2-methyl-1,3-dioxane (**6**)

Liquid, bp 172-174 °C (1 mmHg). Yield 68. Anal. Calcd for $C_{17}H_{28}O_8$: C, 56.65, H, 7.83. Found: C, 56.47; H, 7.61. ^{1}H-Nmr (C_6D_6, δ, ppm) 0.83[6H, (overlapped triplets), J=7.1 Hz, 5-COOCH$_2$C*H*$_3$(eq.), 2-CH(C$_2$H$_5$)-COOCH$_2$-C*H*$_3$], 0.85[3H, t, J=7.1 Hz, 5-COOCH$_2$C*H*$_3$(ax.)], 0.93[3H, t, J=7.1 Hz, 2-CH(COOC$_2$H$_5$)-CH$_2$-C*H*$_3$], 1.56(3H, s, 2-CH$_3$), 1.65[1H, ddq, J=13.3, 7.1, 3.3 Hz, 2-CH(COOC$_2$H$_5$)-C(H)*H*-CH$_3$], 1.86[1H, ddq, *J=13.3, 11.6, 7.1 Hz*, 2-C*H*(COOC$_2$H$_5$)-C(H)*H*-CH$_3$], 3.17(1H, dd, J=11.6, 3.3 Hz, 2-C*H*(COOC$_2$H$_5$)-CH$_2$-CH$_3$], 3.88[2H, q, J=7.1 Hz, 5-COOC*H*$_2$CH$_3$(eq.),], 3.91 [2H, q, J=7.1 Hz, 5-COOC*H*$_2$CH$_3$(ax.)], 3.98[1H, q, J=7.1 Hz, 2-CH(C$_2$H$_5$)-COOC(H)*H*-CH$_3$], 3.99 [1H, q, J=7.1 Hz, 2-CH(C$_2$H$_5$)-COOC(*H*)H-CH$_3$], 4.43 (1H, d, J=11.8 Hz, 6-H$_{ax.}$), 4.49(1H, dd, J=11.8, 0.9 Hz, 6-H$_{eq.}$), 4.51(1H, d, J=11.8 Hz, 4-H$_{ax.}$), 4.76 (1H, dd, J=11.8, 0.9 Hz, 4-H$_{eq.}$); ^{13}C-nmr (C_6D_6, δ, ppm) 12.48[2-CH(COOC$_2$H$_5$)-CH$_2$-*C*H$_3$], 13.83 [5-COOCH$_2$*C*H$_3$(eq.)], 13.84[5-COOCH$_2$*C*H$_3$(ax.)], 14.19[2-CH(C$_2$H$_5$)-COOCH$_2$-*C*H$_3$], 18.30(2-CH$_3$), 21.25[2-CH(COOC$_2$H$_5$)-*C*H$_2$-CH$_3$], 41.53 (C^5), 53.46[2-*C*H(COOC$_2$H$_5$)-CH$_2$-CH$_3$], 60.25[2-CH(C$_2$H$_5$)-COO*C*H$_2$-CH$_3$], 61.70[5-COO*C*H$_2$-CH$_3$(eq.)], 61.74[5-COO*C*H$_2$CH$_3$ (ax.)], 62.38(C^6), 62.58(C^4), 100.50(C^2), 167.83[5-*C*OOCH$_2$CH$_3$(eq.)], 167.89[5-*C*OOCH$_2$CH$_3$(ax.)], 172.17[2-CH(C$_2$H$_5$)-*C*OOCH$_2$CH$_3$].

5,5-Bis(ethyloxycarbonyl)-2-[1-ethyloxycarbonyl-2-methylpropyl]-2-methyl-1,3-dioxane (**7**)

Liquid, bp 180-182 °C (1 mmHg). Yield 59%. Anal. Calcd for $C_{17}H_{28}O_8$: C, 56.65, H, 7.83. Found: C, 56.82; H, 8.01. ^{1}H-Nmr (C_6D_6, δ, ppm) 0.87[3H, d, J=6.6 Hz, 2-CH(COOCH$_3$)CH(CH$_3$)C*H*$_3$], 0.96[3H, t, J=7.1 Hz, 5-COOCH$_2$C*H*$_3$(eq.)], 0.97[3H, t, J=7.1 Hz, 5-COOCH$_2$C*H*$_3$(ax.)], 0.98[3H, d, J=6.6 Hz, 2-*C*H(COOCH$_3$)-CH(*C*H$_3$)CH$_3$], 1.59(3H, s, 2-CH$_3$), 2.12[1H, dqq, J=9.7, 6.6, 6.6 Hz, 2-CH(COOCH$_3$)-C*H*(CH$_3$)CH$_3$], 3.04[1H, d, J=9.7 Hz, 2-C*H*(COOCH$_3$)-CH(CH$_3$)CH$_3$], 3.42(3H, s, 2-CH(COOC*H*$_3$)-CH(CH$_3$)CH$_3$], 3.88[2H, q, J=7.1 Hz, 5-COOC*H*$_2$CH$_3$(eq.)], 3.894[1H, dq, J=12.9, *7.1 Hz*, 5-COO-C(*H*)H-CH$_3$(ax.)], 3.897[1H, dq, J=12.9, 7.1 Hz, 5-COOC(H)*H*-CH$_3$(ax.)], 4.45(1H, dd, J=11.8, 0.70 Hz, 6-H$_{eq}$), 4.50(1H, d, J=11.8 Hz, 6-H$_{ax.}$), 4.51(1H, dd, J=11.9, 0.7 Hz, 4-H$_{eq.}$), 4.69(1H, d, J=11.9, 4-H$_{ax.}$); ^{13}C-nmr (C_6D_6, δ, ppm) 13.86 [5-COOCH$_2$*C*H$_3$(eq.)], 13.88[5-COOCH$_2$CH$_3$(ax.)], 18.70(2-CH$_3$), 21.40[2-CH(COOCH$_3$)-CH(*C*H$_3$)CH$_3$], 21.93[2-CH(COOCH$_3$)-CH(CH$_3$)*C*H$_3$], 28.12[2-CH(COOCH$_3$)-*C*H(CH$_3$)CH$_3$], 41.53(C^5), 50.90[2-CH(*COOC*H$_3$)-CH(CH$_3$)CH$_3$], 57.54[2-*C*H(COOCH$_3$)-CH(CH$_3$)

CH_3], 61.71[5-$COOCH_2CH_3$(eq.)], 61.74[5-$COOCH_2CH_3$ (ax.)], 62.03(C^6), 62.40(C^4), 100.85(C^2), 167.86[5-$COOCH_2CH_3$(eq.)], 167.91[5-$COOCH_2CH_3$(ax.)], 172.24[2-CH($COOCH_3$)-CH(CH_3)CH_3].

2-[1-Ethyloxycarbonylpropyl]-2,5,5-trimethyl-1,3-dioxane (**8**).

Liquid, bp 130-132 °C. Yield 71%. Anal. Calcd for $C_{13}H_{24}O_4$: C, 63.91, H, 9.90. Found: C, 63.72; H, 9.80. ^{1}H-Nmr (C_6D_6, δ, ppm) 0.68[3H, s, 5-CH_3(eq.)], 0.76[3H, s, 5-CH_3(ax.)], 0.92[3H, t, J=7.6 Hz, 2-CH($COOC_2H_5$)-CH_2-CH_3], 0.98[3H, t, J=7.1 Hz, 2-CH(C_2H_5)-$COOCH_2$-CH_3], 1.60(3H, s, 2-CH3), 1.76[1H, ddq, J= 13.3, 7.6, 3.3 Hz, 2-CH($COOC_2H_5$)-C(H)*H*-CH_3], 1.95[1H, ddq, J=13.3, 11.6, 7.6 Hz, 2-CH($COOC_2H_5$)-C(*H*)H-CH_3], 3.20[1H, dd, J=11.6, 3.3 Hz, 2-C*H*($COOC_2H_5$)-CH_2-CH_3], 3.26[2H, s (overlapped AB system), 6-$H_{ax.}$, 6-$H_{eq.}$], 3.33(1H, d, J=11.4 Hz, 4-$H_{ax.}$), 3.55(1H, d, J=11.4 Hz, 4-$H_{eq.}$), 4.04[2H, q, J=7.1 Hz, 2-CH(C_2H_5)-$COOCH_2$-CH_3]; ^{13}C-nmr (C_6D_6, δ, ppm) 12.70(2-CH_2-CH_3), 14.30 [2-CH(C_2H_5)-$COOCH_2$-CH_3], 18.52(2-CH_3), 21.40[2-CH($COOC_2H_5$)-CH_2-CH_3], 22.54[5-CH_3 (eq.)], 22.61[5-CH_3(ax.)], 29.82(C^5), 53.64[2-CH($COOC_2H_5$)-CH_2-CH_3], 60.08[2-CH(C_2H_5)-$COOCH_2$-CH_3], 70.12(C^6), 70.30(C^4), 99.68(C^2), 172.62[2-CH(C_2H_5)-$COOCH_2$-CH_3].

2-Ethyl-5,5-dimethyl-2-[1-methyloxycarbonylethyl]-1,3-dioxane (**9**).

Liquid, bp 124-126 °C. Yield 69%. Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.57, H, 9.63. Found: C, 62.41; H, 9.75. ^{1}H-Nmr (C_6D_6, δ, ppm) 0.60[3H, s, 5-CH_3(eq.)], 0.86[3H, s, 5-CH_3(ax.)], 1.12[3H, t, J=7.4 Hz, 2-CH_2-CH_3], 1.24[3H, d, J=7.1 Hz, 2-CH($COOCH_3$)-CH_3], 1.88[1H, dq, J=14.6, 7.4 Hz, 2-C(H)*H*-CH_3], 2.02[1H, dq, J=14.6, 7.4 Hz, 2-C(*H*)H-CH_3], 3.18(1H, dd, J=11.4, 1.7 Hz, 6-eq.), 3.23(1H, d, J=11.4 Hz, 6-ax.), 3.28[1H, dd, J=11.4, 1.7 Hz, 4-$H_{eq.}$], 3.40(3H, s, 2-CH($COOCH_3$)CH_3), 3.43(1H, q, J=7.1 Hz, 2-C*H*($COOCH_3$)CH_3), 3.67[1H, d, J=11.4 Hz, 4-ax.]; ^{13}C-nmr (C_6D_6, δ, ppm) 7.17(2-CH_2-CH_3), 12.18[2-CH($COOCH_3$)-CH_3], 22.41[5-CH_3(eq.)], 22.81[5-CH_3(ax.)], 25.27(2-CH_2-CH_3) 29.24(C^5), 40.79[2-CH($COOCH_3$)-CH_3], 51.94[2-CH(CH_3)-$COOCH_3$], 69.85(C^6), 70.04(C^4), 100.36(C^2), 173.34[2-CH(CH_3)-$COOCH_3$].

2-Ethyl-5,5-bis(methyloxycarbonyl)-2-[1-methyloxycarbonylethyl]-1,3-dioxane (**10**).

Liquid, bp 158-160 °C (1 mmHg). Yield 65%. Anal. Calcd for $C_{14}H_{22}O_8$: C, 52.81, H, 6.97. Found: C, 52.60; H, 7.10. ^{1}H-Nmr (C_6D_6, δ, ppm) 0.95(3H, t, J=7.4 Hz, 2-CH_2CH_3), 1.12[3H, d, J=7.0 Hz, 2-

$CH(COOCH_3)C\mathit{H}_3$], 1.79[1H, dq, J= 14.5, 7.4 Hz, 2-C(H)*H*-CH_3], 1.92[1H, dq, J=14.5, 7.4 Hz, 2-C(*H*)H-CH_3], 3.25[3H, s, 2-$CH(COOC\mathit{H}_3)$-CH_3], 3.32[3H, s, 5-$COOC\mathit{H}_3$(eq.)], 3.33[1H, q, J=7.4 Hz, 2-$CH(CH_3)$-$COOCH_3$], 3.36[3H, s, 5-$COOC\mathit{H}_3$(ax.)], 4.18(1H, d, J=11.7 Hz, 6-$H_{ax.}$), 4.42(1H, dd, J=11.7, 1.6 Hz, 6-$H_{eq.}$), 4.52(1H, dd, J=11.8, 1.6 Hz, 4-$H_{eq.}$), 4.59 (1H, d, J=11.8 Hz, 4-$H_{ax.}$); ^{13}C-nmr (C_6D_6, δ, ppm) 7.30(2-CH_2-$\mathit{C}H_3$), 12.59[2-CH($\mathit{C}H_3$)-$COOCH_3$], 25.67(2-$\mathit{C}H_2$-CH_3), 41.67[2-$CH(CH_3)$-$COOCH_3$], 51.98[2-$\mathit{C}H(COOCH_3)CH_3$], 52.85[5-$COOCH_3$(eq.)], 53.07[5-$COOCH_3$ (ax.)], 54.01(C^5), 63.06(C^6), 63.22(C^4), 101.57(C^2), 168.47[5-$\mathit{C}OOCH_3$(eq.)], 168.77[5-$\mathit{C}OOCH_3$(ax.)], 173.53[2-$CH(CH_3)$-$\mathit{C}OOCH_3$].

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