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SYNTHESIS OF FURO-FURANS BY REARRANGEMENT OF 4-ACETYLPYRANS

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Abstract - The hetero-Diels-Alder reaction of 1-oxabutadienes **1a-c** bearing electron-withdrawing groups with ethyl vinyl ether and 2,3-dihydrofuran gave the functionalized 5,6-dihydro-4H-pyrans **2a-c**, **4c** and 4H-4a,5,6,6a-tetrahydrofuro[2,3-b]pyrans **5a-c** and **6c**. Cycloadducts **2a** and **4c** easily rearranged to furo[2,3-b]furans **3a**, **3c** and **9c** and cycloadducts **5a** and **6c** to difuro[2,3-b:3',4'-d]furans **7a**, **7c** and **8c**. The stereochemistry of compounds **5c** and **7a** was determined by single crystal X-ray analysis. Relative configurations of the other compounds were established by nOe data. Some aspects of the reaction mechanisms are discussed.

Introduction

The hetero Diels-Alder reaction of substituted α,β-unsaturated carbonyl compounds and electron-rich dienophiles is an attractive route to the synthesis of dihydropyran derivatives.

In earlier work by one of us[1] it was found that 3,4-diacetyl-3-hexen-2,5-dione, **1a** and ethyl vinyl ether gave the expected cycloadduct **2a** with a 4-acetylpyran structure. This compound was labile, isomerising irreversibly to the furo[2,3-b]furan **3a**. The rearrangement was stereospecific and the reaction yield was practically quantitative.

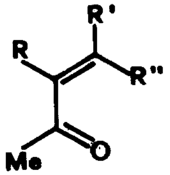
We therefore undertook a study to gain some understanding of the extent of this rearrangement in other 4-acylpyrans. We used heterodienes with one or more electron-withdrawing groups such as 1a-c[2-4] to obtain the desired 4-acylpyrans.

Results

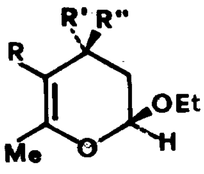
The reaction of Z-3-hexen-2,5-dione **1b** with ethyl vinyl ether or with 2,3-dihydrofuran gave only one cycloadduct in each case, the structures of which were **4b** and **5b** respectively. The trans configuration between the acetyl and ethoxy groups was tentatively attributed on the basis of the well-known endo-selectivity of Diels-Alder reactions[5,6] and confirmed by ^{1}H-NMR spectra (coupling constants and nOe experiments).

The cycloadducts **4b** and **5b** were not very stable and decomposed, the latter more easily than the former. This made their purification difficult.

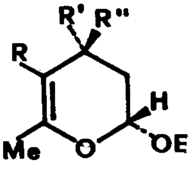
The introduction of two other electron-withdrawing groups in positions 3 and 4 of the heterodiene not only increased the rate of cycloaddition but also made the cycloadducts obtained more stable. Thus the tetraketone **1a** reacted with 2,3-dihydrofuran to give the cycloadduct **5a** in a quantitative yield. This compound gave rise to a rearrangement which was catalyzed by acidity. On the basis of spectral data the rearranged product was at-



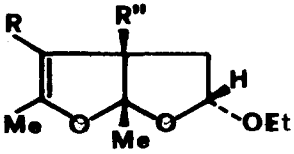
1a R = R' = R" = Ac
1b R = R' = H , R" = Ac
1c R = R" = COOEt , R' = Ac



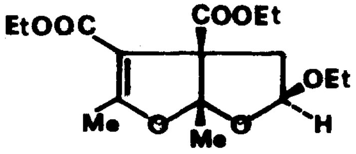
2a-c



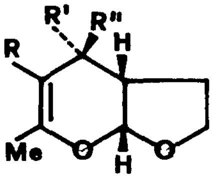
4b,c



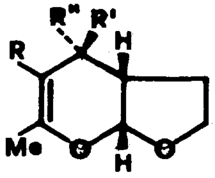
3a,c



9c



5a-c



6b,c

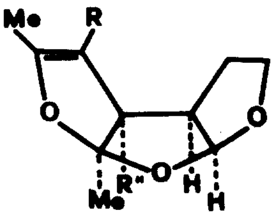
tributed the structure of 3,3a-diacetyl-2,7a-dimethyl-3b,4,5,6a-tetrahydrodifuro[2,3-b:3',4'-d]furan. The data was not sufficient to establish the configuration of this compound out of the eight possibilities.

X-ray analysis was undertaken and it was established that the rearranged compound had the cis-syn-cis configuration **7a**.

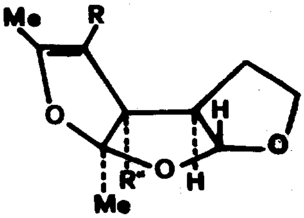
The substitution of two acetyl groups by two ethoxycarbonyl groups made the cycloaddition slower than in the case of compound **1a**, even if the reaction trend was analogous. Thus diethyl ester of E-2,3-diacetyl-3-butendioic acid **1c** with 2,3-dihydrofuran gave a mixture of products from which two cycloadducts were isolated. One was stable but the other slowly rearranged. On the basis of spectral data the stable cycloadduct was tentatively attributed structure **5c** and the other **6c**. This attribution was confirmed by X-ray analysis, which established diethyl 4α-acetyl-2-methyl-4H-4aβ,5,6,7aβ-tetrahydrofuro[2,3-b]pyran-3,4-dicarboxylate as the structure for compound **5c**.

The exo adduct **6c** rearranged easily to give a mixture of compounds **7c** and **8c** in the ratio 60:40. Spectral data, chiefly nOe data, confirmed cis-syn-cis configuration for **7c** and cis-syn-trans for compound **8c**.

The alkene **1c** also reacted with ethyl vinyl ether to yield a mixture of three compounds in the ratio 83:13:4. The main product was identified as the cycloadduct 4c. The other two had the furo[2,3-b]furan structures 3c and 9c respectively.



7a,c

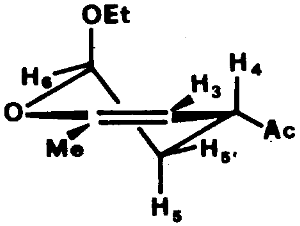


8c

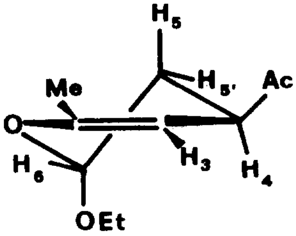
Discussion

NMR and X-ray Data

The NMR spectrum of compound 4b clearly indicates that the ethoxy group is in axial position: in fact the $^3J_{H5,H6}$ and $^3J_{H5',H6}$ coupling constant values (2.48 and 4.60 Hz) exclude the presence of the H6 axial-H5 axial coupling pathway. The trans position of the acetyl group with respect to the ethoxy group can then be deduced from the reaction mechanism and the relative configuration of C4 and C6 chiral centers can be established. Further support for this interpretation is offered by nOe experiments: on saturation of H3 we have nOes on both methylene hydrogens of the ethoxy group (2.3 % and 3.7 %) and no nOe on H6. However we cannot choose between conformation A and B:



A

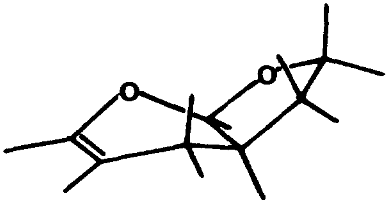


B

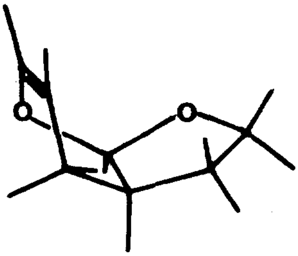
The relative configuration of compound **5b** may be deduced from the mechanism, and also fairly well from nOe results: on irradiation of protons 7a and 4 we have nOes on 4a (3.4 % and 2.1 % respectively); in this case it is possible to exploit quantitative nOe analysis and. equation [1] can be written, provided that cross-saturation terms are negligible[7]:

$$\frac{f_{4a}(7a)}{f_{4a}(4)} = \frac{r^6{}_{4a,4}}{r^6{}_{4a,7a}} \qquad [1]$$

The distance between the 4a and 7a protons ($r_{4a,7a}$) is a constant independent of conformation (C or D) and, can be estimated from the corresponding Dreiding models of compound **5b**: $r_{4a,7a}$ = 2.30 Å. Applying equation [1] we obtain $r_{4,4a}$ = 2.5 Å.



C



D

If the furan ring is in the pseudo-equatorial position with respect to the dihydropyran ring, then this distance is satisfied only if the 4 and 4a protons are cis (from the Dreiding model $r_{4,4a}$ = 2.45 Å and $r_{4,4a}$ = 3.1 Å for cis and trans configuration respectively). As a consequence the distance $r_{3,4}$ is 2.5 Å. NOe analysis reveals that on irradiation of the 3 and 7a protons, there are nOes on the 4 proton (12.5% and 1.05% respectively), thus we can write:

$$\frac{f_4(3)}{f_4(7a)} = \frac{12.5}{1.05} = \frac{r^6{}_{4,7a}}{r^6{}_{3,4}} \qquad \frac{r_{4,7a}}{r_{3,4}} \cong 1.51 \qquad [2]$$

Introducing $r_{3,4}$ = 2.50 Å, we obtain $r_{4,7a}$ = 3.8 Å. According to the Dreiding model, however, this distance should be 4.2 Å.

Now, if the furan ring is in axial position with respect to the dihydropyran ring, the distance $r_{4,4a}$ = 2.5 Å is satisfied with the H4 in either axial or equatorial position. Let us suppose that H4 is equatorial, then $r_{3,4}$ = 2.5 Å and from equation [2] $r_{4,7a}$ = 3.8 Å (whereas according to the Dreiding model $r_{4,7a}$ = 4.0 Å). If H4 is axial, then $r_{3,4}$ = 2.9 Å and, as a consequence, $r_{4,7a}$ = 4.4 Å (according to the Dreiding model $r_{4,7a}$ = 3.3 Å). So the furan ring is very probably in axial position and trans to the acetyl group.

The configurational problem of **7a** cannot be settled using coupling constants. The nOe obtained on H6a (3.4%), on saturation of the quaternary methyl hydrogens, offers evidence in favor of a cis relationship between Me-7a and H-6a but cannot be taken as conclusive. The problem was therefore solved by X-ray diffraction. The structure so determined is **7a** as shown in the ORTEP plot (Fig.1). Bond distances and angles are listed in Tables 1 and 2, respectively.

The configuration of compound **5c** was determined by X-ray study. The ORTEP plot of the molecule is shown in Fig.2. Bond distances and angles are listed in Tables 3 and 4, respectively.

The structure of the compounds derived from **6c** by rearrangement can be deduced from nOe data analysis. On irradiation of the methyl protons (Me group bonded to 7a carbon) of the more abundant compound we obtained nOes on both 3b and 6a protons (0.013), on irradiation of 6a there was a nOe on 3b (0.088) and on irradiation of 3b there was a nOe on 6a (0.143). As in the case of compound **5b**, it is possible to apply quantitative analysis:

$$\frac{f_{6a}(3b)}{f_{6a}(Me)} = \frac{r^6_{6a,Me}}{r^6_{6a,3b}} \quad [3] \qquad\qquad \frac{f_{3b}(6a)}{f_{3b}(Me)} = \frac{r^6_{3b,Me}}{r^6_{3b,6a}} \quad [4]$$

From these equations it is possible to extract $r_{3b,Me}$ and $r_{6a,Me}$ distances if $r_{3b,6a}$ is known. Let us suppose that 6a and 3b are cis: then their distance is 2.35 Å and it is independent of syn or anti structures. Thus from the equations [3] and [4] we have $r_{3b,Me}$ = 3.2 Å and $r_{6a,Me}$ = 3.5 Å.

However, from the Dreiding model, these distances are $r_{6a,Me}$ = 3.5 Å and $r_{3b,Me}$ = 3.3-3.5 Å for the cis-syn-cis structure (**7c**), while for the other structures the same distances have values in the range 4.3-4.5 Å (the values express the distances between 3b or 6a and the closest methyl proton). If 3b and 6a are trans, their distance is 3.1 Å and, from equations [3] and [4], $r_{3b,Me}$ = 4.3 Å and $r_{6a,Me}$ = 4.6 Å. These distances are not matched by any trans structure. Thus the structure **7c** can be safely attributed to the compound.

For the less abundant compound, on irradiation of the methyl protons (Me group bonded to 7a carbon) we have a nOe on 3b proton (0.026), on irradiation of 3b there are nOes on 6a (0.042) and methyl protons (Me group bonded to 7a carbon) (0.031) and on irradiation of 6a there is a nOe on 3b (0.033). We can therefore write:

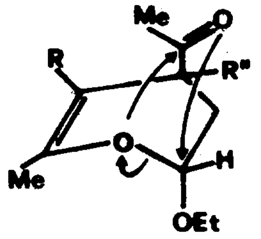
$$\frac{f_{3b}(Me)}{f_{3b}(6a)} = \frac{r^6{}_{3b,6a}}{r^6{}_{3b,Me}} \qquad [5]$$

This equation allows the calculation of $r_{3b,Me}$ if $r_{3b,6a}$ is known. Let us suppose that the 3b and 6a protons are trans, then their distance is 3.1 Å independent on syn or anti structure. Thus, from equation [5] we have $r_{3b,Me}$ = 3.2 Å. This distance is satisfied only by configuration cis-syn-trans for which $r_{3b,Me}$ = 3.4 A. If 3b and 6a are cis $r_{3b,6a}$ = 2.35 Å and then $r_{3b,Me}$ = 2.45 A which is not compatible with any structure. Thus the structure **8c** can be attributed to the compound.

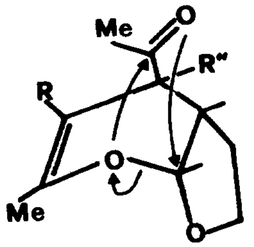
From the reaction between compound **1c** and ethyl vinyl ether, a mixture of two rearranged products was obtained in the ratio ca. 3:1 as deduced from NMR integration. Their relative configuration was established by nOe. On saturation of the protons of the methyls in position 6a, nOes were obtained on the protons of the methylenes of ethoxy groups (11% and 1.5% for the minor and major derivatives respectively). Structures **3c** and **9c** could then be attributed to the major and minor derivatives. In both the compounds **3c** and **9c**, the ethoxy group may assume a pseudo-axial position.

Mechanistic aspects

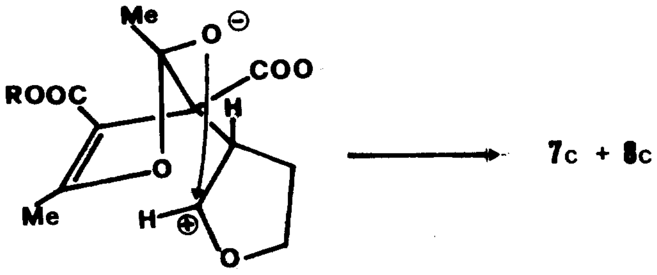
The formation of the rearranged products **3a**, **3c**, **7a**, and **7c** can be explained by nucleophilic attack of a 4-acetyl group on the 6 position of the pyran ring in compound **2a** or **2c**, or on the furo[2,3-b]pyran system **5a** or **5c** and attack by the pyran oxygen on the acyl carbon as shown below:



2 a,c



5a,c



If both the acetyl groups of the cycloadduct **2a** and **5a** partecipated in this attack, we would obtain two rearranged products.

Since the rearrangement is quite stereospecific we have to conclude that only one of the two acetyl groups is in a suitable position to attack the carbon 6 of **2a** or the carbon 7a of **5a**.

The crystal structure of **7a** as determined by X-ray analysis revealed a syn configuration, so we can deduce that only the acetyl group on the other side of the furan ring carried out the rearrangement.

A similar conclusion can be reached for the cycloadduct between **1a** and ethyl vinyl ether[1].

From the reaction between **1c** and 2,3-dihydrofuran we isolated both the endo-adduct **5c** and the exo adduct **6c**. The former showed the acetyl group cis to the tetrahydrofuran ring and did not give rise to the rearrangement. The exo-adduct **6c** slowly gave rise to a mixture of rearranged products **7c** and **8c**. The rearrangement was accelerated by traces of acidity. In this case the rearrangement was slower than in the former cases. It can be supposed that the oxygen atom of the pyran ring of **6c** first attacks the cis carbonyl group at C-4 giving the intermediate **9c**. Then, the carbonyl oxygen can attack the carbonium 7a on both sides of the tetrahydrofuran ring to give compounds **7c** and **8c**.

In the case of the reaction between **1c** and ethyl vinyl ether the rearrangement rate of the exo-adduct was so high that it was not even seen in the NMR spectrum of the raw material. The rearrangement reactions of the cycloadducts derived from **1c** are less stereospecific than in the case of **1a**. In fact two rearranged compounds, **3c** and **9c**, in the ratio 75:25, were isolated and their formation can be explained as for compounds **7c** and **8c**.

The cycloaddition of compound **1b** with ethyl vinyl ether or with 2,3-dihydrofuran was much slower, as expected, since **1b** has less electron-withdrawing groups. Moreover, in contrast with the behavior of **1c**, it was fully stereospecific, giving one cycloadduct only.

Compounds **4b** and **5b** seem to have the acetyl group in a suitable position for the rearrangement, but, possibly due to the presence of a mobile hydrogen atom in position 4, the cycloadducts prefer to follow different pathways to yield a mixture of products.

Experimental

Unless otherwise stated, IR spectra were recorded on a Perkin-Elmer 782 spectrophotometer using samples in potassium bromide pellets; ^1H NMR spectra were recorded for $CDCl_3$ solutions with a Hitachi-Perkin-Elmer instrument (60 MHz) or a Varian XL-200 FT spectrometer (200 MHz); chemical shifts (J in Hz) are reported downfield from internal tetramethylsilane. Proton-Proton nOes were measured with gated decoupling techniques using nOe difference pulse sequences.

Silica gel plates (Merck F_{254}) and silica gel 60 (Merck 70-230 mesh) were used for analytical and preparative TLC and for column chromatography, respectively. Extracts were dried over sodium sulphate and solvents were evaporated *in vacuo*.

Starting heterodienes were prepared by the literature procedures cited: **1a**[2], **1b**[3] and **1c**[4].

General Procedure for Cycloadditions

Compounds **1a-c** were heated with an excess of ethyl vinyl ether or 2,3-dihydrofuran. When the starting material had disappeared (TLC or NMR check), the excess reagent was removed under vacuum and the residue worked up (see Table 5).

Table 5 - Cycloaddition Reactions

Heterodiene	Ether x,y[a]	°C	Time (h)	Products	% Yield
1a	x	36	28	**2a**	89
1a	y	55	6	**5a** + **7a**	54:36
1b	x	60	50	**2b**	80
1b	y	85	29	**5b**	90
1c	x	60	40	**2c** + **3c** + **9c**	83:13:4
1c	y	55	8	**5c** + **6c** + **7c** + **8c**	32:49:6:4

[a] x = Ethyl vinyl ether; y = 2,3-dihydrofuran.

Compound 1a and 2,3-Dihydrofuran

The NMR spectrum of the residue showed the presence of two products **5a** and **7a**. Preparative TLC with ether/petroleum ether 3:1 as eluent revealed **5a** as the faster running band and **7a** as the slower band.

2-Methyl-3,4,4-triacetyl-4H-4aα,5,6,7aα-tetrahydrofuro[2,3-b]furan, **5a**: oil; IR (neat) 1730, 1710, 1620(vs) cm^{-1}; NMR δ: 5.56(d,1H,J=4.8,H7a), 4.4-3.8(m,2H,H6,H6'), 2.7-3.1(m,1H,H4a), 2.47(s,3H,Me), 2.29(s,6H,2xMe), 2.12(s,3H,Me), 1.7-1.9(m,2H,H5,H5') ppm. Anal.calcd for $C_{14}H_{18}O_5$: C 63.16, H 6.77; found: C 63.05, H 6.71.

3,3aa-Diacetyl-2,7aa-dimethyl-3ba,4,5,6aa-tetrahydrodifuro[2,3-b:3',4'-d] furan, **7a**: mp 145-148°C (cyclohexane); IR : 1700, 1680, 1600(vs) cm^{-1}; NMR δ: 5.95(d,1H,J=6.4,H6a), 3.87(m,1H,H5), 3.79(m,1H,H3b), 3.54(m,1H, H5'), 2.34(s,3H,MeCO), 2.36(s,3H,MeCO), 2.11(s,3H,Me-2), 1.75-1.95 (m, 1H,H4) 1.45 (m,1H,H4'), 1.42(s,3H,Me-5) ppm. Anal.calcd for $C_{14}H_{18}O_5$: C 63.16, H 6.77; found: C 63.42, H 6.88.

*Compound **1b** and ethyl vinyl ether*

The residue was purified by preparative TLC with ether/petroleum ether 1:1. The faster running band was the cycloadduct **2b** and the slower band was a mixture of E and Z starting alkene.

4a-Acetyl-4H-5,6-dihydro-6β-ethoxy-2-methylpyran, **2b**: oil; IR (neat): 1720, 1710, 1690 cm^{-1}; NMR δ: 4.84(dd,1H,J=2.48 and 4.60, H6), 4.51(brd, 1H,J=3.05,H3), 3.60-3.75(m,1H,CH_2-O), 3.34-3.49(m,1H,CH_2-O), 3.06-3.13(m, 1H,H4), 2.01(s,3H,MeCO), 1.68-1.79(m,2H,H5,H5'), 1.59(brd,3H,J=1.95,Me-2), 1.04(t,3H,J=7.08,Me) ppm.

*Compound **1b** and 2,3-dihydrofuran*

The residue was sublimed at room temperature and 0.05mm.Hg to give the cycloadduct **5b**.

4a-Acetyl-2-methyl-4H-4aa,5,6,7aa-tetrahydrofuro[2,3-b]pyran, ***5b***: oil; IR (neat): 1705, 1670 cm^{-1}; NMR δ: 5.25(d,1H,J=4.1,H7a), 4.43(brd,1H,J=5.4, H3), 3.79(dd,2H,J=8.0 and 16.9,H6+H6'), 3.02(brd,1H,J=5.7,H4), 2.45-2.57 (m,1H,H4a), 2.07(s,3H,MeCO), 1.7-1.92(m,2H,H5+H5'), 1.62(s,3H,Me-2) ppm.

*Compound **1c** and ethyl vinyl ether*

The residue was purified by preparative TLC with ether/petroleum ether 1:2. The faster running band was the rearranged compound **3c** together with the stereoisomer **9c**. The slower band was the cycloadduct **2c**.

Diethyl 2,6aa-dimethyl-5β-ethoxy-3a,4,5,6a-tetrahydrofuro[2,3-b]furo-3, 3aa-dicarboxylate, **3c**: oil; IR (neat): 1730, 1720, 1680, 1610 cm^{-1}; NMR δ:

5.17(dd,1H,J=4.2 and 7.6, H5), 4.05-4.26(m,4H,2xCH_2,CH_2 ester), 3.76-3.92 (m,1H,OCH_2 acetal), 3.52-3.66(m,1H,OCH_2 acetal), 2.79(dd,1H,J=7.5 and 14.1, H4), 2.44 (dd,1H,J=4.2 and 14.1, H4'), 2.26 (s,3H,Me-2), 1.52 (s,3H, Me6a), 1.05-1.30(m,9H,3xMe, esters + acetal) ppm.

Diethyl 2,6aa-dimethyl-5a-ethoxy-3a,4,5,6a-tetrahydrofuro[2,3-b]furo-3,3aa-dicarboxylate, **9c**, oil, NMR δ: 5.27(d,1H,J=5.3,H5), 4.05-4.25(m,4H, 2xCH_2 esters), 3.61-3.78(m,1H,OCH_2 acetal), 3.41-3.48(m,1H,OCH_2 acetal), 3.01(dd,1H,J=5.3 and 14.1,H4), 2.20(s,3H,Me-2), 1.47(s,3H,Me-6a),1.05-1.30 (m,9H,3xMe esters + acetal).

Diethyl 4a-Acetyl-4H-5,6-dihydro-6a-ethoxy-2-methylpyran-3,4-dicarboxylate, **2c**, oil (purified by sublimation at 50°C, 0.02 mmHg), IR (neat): 1740, 1720, 1690, 1620 cm^{-1}, NMR δ: 4.88(dd,1H,J=2.4 and 7.0,H6), 4.08-4.26(m,4H,2xCH_2), 3.79-3.95(m,1H,OCH_2), 3.49-3.64(m,1H,OCH_2), 2.51(dd,1H, J=2.4 and 13.3,H5), 2.27(s,3H,Me-2), 2.20(dd,1H,J=7.0 and 13.3, H5'), 2.19 (s,3H,Me-CO), 1.23(t,6H,J=7.8,2xMe esters), 1.19(t,3H,J=7.3,Me acetal).

Compound 1c and 2,3-dihydrofuran

The residue was solved by preparative TLC with ether/petroleum ether 1:3 as eluent and gave, in order of mobility, the cycloadduct **6c**, the rearranged products **7c** and **8c**, and the cycloadduct **5c**.

Compound **7c** was purified from traces of the diastereoisomer anti **8c** with repeated preparative TLC in the same mixture of solvents.

Diethyl 4a-acetyl-2-methyl-4H-4aa,5,6,7aa-tetrahydrofuro[2,3-b]furan-3,4β-dicarboxylate, **6c**: oil; IR (neat): 1735, 1720, 1680, 1610 cm^{-1}; ^{1}H NMR δ 5.87(d,1H,J=5.3,H7a), 4.14(q,2H,J=7.6,CH_2-ester), 3.65-4.09(m,6H, H4a+H6+ CH_2 ester), 2.36(s,3H,Me-2), 2.11(s,3H,MeCO), 1.78-2.0(m,1H, H5), 1.5- 1.7 (m,1H,H5'), 1.21(t,3H,J=7.6,Me ester), 1.14(t,3H,J=7.6,Me ester). Anal. calcd for $C_{16}H_{22}O_7$: C 58.89; H 6.75; found: C 58.44; H 6.76.

Diethyl 2,7aa-dimethyl-3a,3ba,4,5,6aa,7a-hexahydrodifuro[2,3-b:3',4'-d] furan-3,3aa-dicarboxylate, **7c**: oil; IR (neat): 1730, 1715, 1680, 1600 cm^{-1}; NMR δ: 5.64(d,1H,J=3.8,H6a), 4.1-4.3(m, 5H, 2xCH_2+H5), 4.01(dd,1H,J = 8.5 and 16.2,H5'), 3.16(dt,1H,J=3.8 and 9.2,H3b), 2.15-2.24(m,2H, H4+H4'), 2.24 (s,3H,Me-2), 1.60 (s,3H,Me-7a), 1.23 (t,3H,J=7.2, Me ester), 1.22 (t, 3H,J=7.2, Me ester) ppm. Anal.calcd for $C_{16}H_{22}O_7$: C 58.89; H 6.75; found:

C 58.57; H 6.79.

Diethyl 2,7aα-dimethyl-3a,3bα,4,5,6aβ,7a-hexahydrodifuro[2,3-b:3',4'-d] furan-3,3aα-dicarboxylate, **8c**: oil; IR (neat): 1725, 1710, 1665, 1610 cm^{-1}; NMR δ: 5.98(d,1H,J=5.2,H6a), 3.7-4.3(m,6H,2xCH_2,H5+H5'), 3.45-3.65 (m,1H,H3b), 2.0-2.3(m,2H,H4+H4'), 2.18(s,3H,Me-2), 1.43(s,3H,Me-7a), 1.15-1.3(m,6H, 2xMe esters).

Diethyl 4β-acetyl-2-methyl-4H-4aα,5,6,7aα-tetrahydrofuro[2,3-b]furan-3,4a-dicarboxylate, **5c**: mp 65-68°C (cyclohexane); IR 1740, 1720, 1690, 1625 cm^{-1}; NMR δ: 5.53(d,1H,J=7.3,H7a), 3.9-4.3(m,5H,H5+2xCH_2-esters), 3.96(dd, 1H,J=8.5 and 16.9,H6), 2.80(dt,1H,J=3.7 and 9.5,H4a), 2.34(s,3H,Me-2 or Me-4), 2.25(s,3H,Me-2 or Me-4), 1.69-1.85(m,2H,H5+H5'), 1.25(t,3H,J=5.9, Me ester), 1.19(t,3H,J=5.9,Me ester). Anal.calcd for $C_{16}H_{22}O_7$: C 58.89; H 6.75; found: C 58.52; H 6.69.

X-Ray Structure Analysis

Single crystals of compounds **5c** and **7a**, obtained by slow crystallization from cyclohexane, were examined with an Enraf-Nonius CAD4 X-ray diffractometer. Cell parameters were determined from the setting angle of 25 reflections. The weighting scheme used was $\omega = [\sigma^2(Fo)]^{-1}$, where σ(Fo) is the individual standard deviation for each reflection from the diffractometer counting statistics. Positional parameters and equivalent isotropic temperature factors, anisotropic temperature parameters of carbon and oxygen atoms, positional parameters and isotropic temperature parameters of hydrogen atoms, and a list of observed and calculated structure factors have been deposited with the Cambridge Crystallographic Data Centre.

Compound ***7a***

$C_{14}H_{18}O_5$ mw 266.29

Monoclinic, a = 23.53(3), b = 9.61(1), c = 12.07(2) Å, β = 106.15(10)°, V= 2622(6) $Å^3$, ϱ_c = 1.349 $g.cm^{-3}$, Z = 8, F(000) = 1136 (20°C, graphite monochromated Mo-Kα, λ= 0.71069 Å), μ(Mo-Kα) = 0.62 cm^{-1}. Space group C2/c.

1148 Unique reflections in the range $5° \leqslant 2\theta \leqslant 50°$ were collected. The intensities were corrected for Lorentz and polarization effects. The 694 reflections with $I \geqslant 3\sigma(I)$ were used for structure solution and refinement

Table 1 . Bond lengths(A)

Bond	Length	Bond	Length
O(1)-C(2)	1.36(2)	C(4)-C(5)	1.50(2)
O(1)-C(7a)	1.48(2)	C(5)-O(6)	1.48(2)
C(2)-C(3)	1.36(2)	O(6)-C(6a)	1.43(2)
C(2)-C(8)	1.48(2)	C(6a)-O(7)	1.45(2)
C(3)-C(3a)	1.56(2)	O(7)-C(7a)	1.40(2)
C(3)-C(9)	1.40(2)	C(7a)-C(15)	1.50(2)
C(3a)-C(3b)	1.51(2)	C(9)-C(10)	1.52(3)
C(3a)-C(7a)	1.56(2)	C(9)-O(11)	1.22(2)
C(3a)-C(12)	1.47(2)	C(12)-C(13)	1.55(3)
C(3b)-C(4)	1.56(2)	C(13)-O(14)	1.19(2)
C(3b)-C(6a)	1.50(2)		

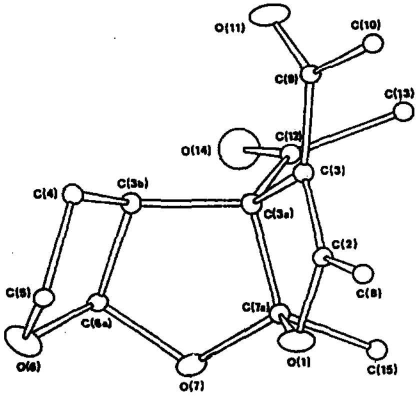


Figure 1. ORTEP plot of compound 7a.

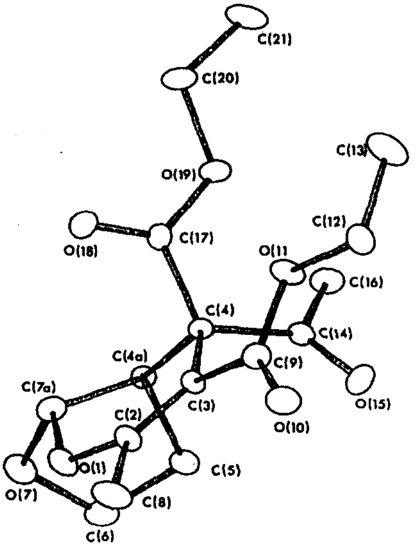


Figure 2. ORTEP plot of compound 5c.

Table 2 . Bond angles(deg)

Bonds	Angle(deg)	Bonds	Angle(deg)
C(2)-O(1)-C(7a)	116(1)	C(6a)-O(6)-C(5)	108(1)
O(1)-C(2)-C(3)	114(1)	O(6)-C(6a)-C(3b)	108(1)
O(1)-C(2)-C(8)	113(1)	O(7)-C(6a)-C(3b)	108(1)
C(3)-C(2)-C(8)	132(1)	O(7)-C(6a)-O(6)	108(1)
C(2)-C(3)-C(3a)	108(1)	C(7a)-O(7)-C(6a)	111(1)
C(2)-C(3)-C(9)	132(1)	O(1)-C(7a)-C(3a)	106(1)
C(3a)-C(3)-C(9)	119(1)	O(1)-C(7a)-C(15)	106(1)
C(3)-C(3a)-C(3b)	115(1)	C(3a)-C(7a)-C(15)	121(1)
C(3)-C(3a)-C(7a)	98(1)	O(7)-C(7a)-O(1)	108(1)
C(3)-C(3a)-C(12)	117(1)	O(7)-C(7a)-C(3a)	107(1)
C(3b)-C(3a)-C(12)	110(1)	O(7)-C(7a)-C(15)	109(1)
C(7a)-C(3a)-C(3b)	104(1)	C(3)-C(9)-C(10)	120(1)
C(7a)-C(3a)-C(12)	110(1)	O(11)-C(9)-C(3)	121(2)
C(3a)-C(3b)-C(4)	118(1)	O(11)-C(9)-C(10)	119(1)
C(3a)-C(3b)-C(6a)	106(1)	C(3a)-C(12)-C(13)	121(1)
C(6a)-C(3b)-C(4)	103(1)	O(14)-C(12)-C(3a)	122(1)
C(3b)-C(4)-C(5)	106(1)	O(14)-C(12)-C(13)	116(1)
O(6)-C(5)-C(4)	101(1)		

and were corrected once the structure had been solved[8]. The structure was solved by direct methods[9]. Successive Fourier synthesis revealed all non-hydrogen atoms. All hydrogen atoms, except those of the acetyl groups, were introduced in calculated positions; hydrogen atoms of the acetyl groups were located in the Fourier difference map; all hydrogen and carbon atoms were isotropically refined. Anisotropic temperature factors were used for all oxygen atoms. Final R = 0.096, Rw = 0.074. The maximum fluctuation of the residual electron density was 0.31 $e\text{Å}^{-3}$.

Compound 5c

$C_{16}H_{22}O_7$ mw 326.34

Triclinic, a = 8.06(1), b = 10.31(2), c = 10.77(2) A, α = 70.65(7), β = 75.99(8), γ = 83.19(8)°, V = 818(2) Å^3, ϱ_c = 1.325 gcm^{-3}, Z = 2, F(000) = 348 (20°C, grafite monochromated Mo-Kα, λ = 0.71069 Å), μ(Mo-Kα) = 0.64 cm^{-1}. Space group P1.

2495 Unique reflections in the range $5° \leqslant 2\theta \leqslant 50°$ were collected. The intensities were corrected for Lorentz and polarization effects. The 1495 reflections with $I \geqslant 3\sigma(I)$ were used for structure solution and refinement and were corrected once the structure had been solved[8]. The structure was solved by direct methods[9]. Successive Fourier synthesis revealed all non-hydrogen atoms. All hydrogen atoms were introduced in calculated positions and not refined. Anisotropic temperature factors were used for non-hydrogen atoms. Final R = 0.096, Rw = 0.070. The maximum fluctuation of the residual electron density was 0.48 eÅ^{-3}.

Table 3. Bond lengths(A)

Bond	Length	Bond	Length
O(1)-C(2)	1.34(1)	C(6)-O(7)	1.47(1)
O(1)-C(7a)	1.51(1)	O(7)-C(7a)	1.38(1)
C(2)-C(3)	1.30(1)	C(9)-O(10)	1.24(1)
C(2)-C(8)	1.52(1)	C(9)-O(11)	1.35(1)
C(3)-C(4)	1.56(1)	O(11)-C(12)	1.43(1)
C(3)-C(9)	1.45(1)	C(12)-C(13)	1.46(1)
C(4)-C(4a)	1.54(1)	C(14)-O(15)	1.20(1)
C(4)-C(14)	1.53(1)	C(14)-C(16)	1.54(1)
C(4)-C(17)	1.51(1)	C(17)-O(18)	1.19(1)
C(4a)-C(5)	1.53(1)	C(17)-O(19)	1.32(1)
C(4a)-C(7a)	1.50(1)	O(19)-C(20)	1.47(1)
C(5)-C(6)	1.51(1)	C(20)-C(21)	1.47(1)

Table 4 . Bond angles(deg)

Bonds	Angle(deg)	Bonds	Angle(deg)
C(2)-O(1)-C(7a)	118.6(7)	C(7a)-O(7)-C(6)	106.0(7)
O(1)-C(2)-C(8)	105.4(7)	O(1)-C(7a)-C(4a)	109.3(7)
C(3)-C(2)-O(1)	127.0(8)	O(1)-C(7a)-O(7)	104.5(6)
C(3)-C(2)-C(8)	127.6(8)	C(4a)-C(7a)-O(7)	107.8(8)
C(2)-C(3)-C(9)	122.5(8)	C(3)-C(9)-C(10)	128.3(9)
C(4)-C(3)-C(2)	121.6(7)	C(3)-C(9)-O(11)	112.8(7)
C(4)-C(3)-C(9)	115.6(7)	O(10)-C(9)-O(11)	118.9(8)
C(3)-C(4)-C(4a)	107.6(6)	C(9)-O(11)-C(12)	120.3(7)
C(3)-C(4)-C(14)	108.2(6)	O(11)-C(12)-C(13)	110.3(7)
C(3)-C(4)-C(17)	107.9(6)	C(4)-C(14)-O(15)	124.0(8)
C(4a)-C(4)-C(14)	106.5(6)	C(4)-C(14)-C(16)	117.3(7)
C(4a)-C(4)-C(17)	108.4(7)	O(15)-C(14)-C(16)	118.6(8)
C(14)-C(4)-C(17)	117.9(7)	C(4)-C(17)-O(18)	123.7(8)
C(4)-C(4a)-C(5)	116.3(7)	C(4)-C(17)-O(19)	112.8(8)
C(4)-C(4a)-C(7a)	115.8(7)	O(18)-C(17)-O(19)	123.4(9)
C(7a)-C(4a)-C(5)	101.9(7)	C(17)-O(19)-C(20)	115.1(7)
C(4a)-C(5)-C(6)	102.4(7)	O(19)-C(20)-C(21)	106.7(7)
C(5)-C(6)-O(7)	108.7(7)		

All calculations were performed on an IBM personal computer model Personal System 2/80 with SHELX-76 set of programs [10], which uses the analytical approximation for the atomic scattering factors and anomalous dispersion corrections for all the atoms from ref.[11]. The molecular plots were produced by the program ORTEP[12].

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