Reactions of α,β-Enones with Diazo Compounds

Part 4[1])

Reaction Pathways from (*Z*)- and (*E*)-α,β-Enones with Dimethyl Diazomalonate

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In this study, (*E*)- and (*Z*)-enones carrying only a phenyl substituent at their C(β) atom were treaced with dimethyl diazomalonate in the presence of (acetylacetonato)copper(II). According to the configuration of the starting enones, the products were dioxole or dihydrofuran derivatives, significant heterocycles in natural products.

Introduction. – Dioxole and dihydrofuran derivatives are among the most-significant heterocycles in natural products, and consequently a wide range of methods for their syntheses has been developed [2–8]. We previously reported the reactions of several α,β-enones and -enals with ethyl acetodiazoacetate and dimethyl diazomalonate (DMDM) in the presence of (acetylacetonato)copper(II) ([$Cu(acac)_2$]) [1][9][10]. In these reports, we noted that under mild conditions, dihydrofuran derivatives such as **3**–**5** should be formed predominantly, by a 1,5-electrocyclic ring-closing reaction of the related carbonyl ylides derived from properly chosen (*E*)-enones existing mainly as s-*cis* conformers. Substituents at both the enone **1** or **2** and the diazocarbonyl compound that can stabilize the concerted transition state of the initially formed enone ylide by conjugation had a beneficial influence on the reaction rate. On the other hand, while steric inhibitions at the C(β) atom (as in 1-(2-methylcyclopent-1-en-1-yl)ethanone (**6**)) retarded the reactions, steric crowdings at the remaining part, *i.e.*, at C(α) and at the carbonyl C-atom of the enone, such as in 2-methyl-1-phenylpent-1-en-3-one (**2**), provided a beneficial effect of preventing possible follow-up reactions (*Scheme 1*).

Furthermore, the corresponding ylides arising from (*E*)-enals (with a preference of s-*trans* conformation) yielded dioxole derivatives by following a different reaction route than those reported by *Huisgen* and *March* [8] (*Scheme 1*).

In this study, as a part of our continuous interest in this particular field, we worked on similar competing reactions of enones to yield dihydrofurans *vs.* furofurans. Furthermore, we also tried to find out what product patterns would give (*Z*)-enones and (*E*)-enones with s-*trans* conformation under similar conditions.

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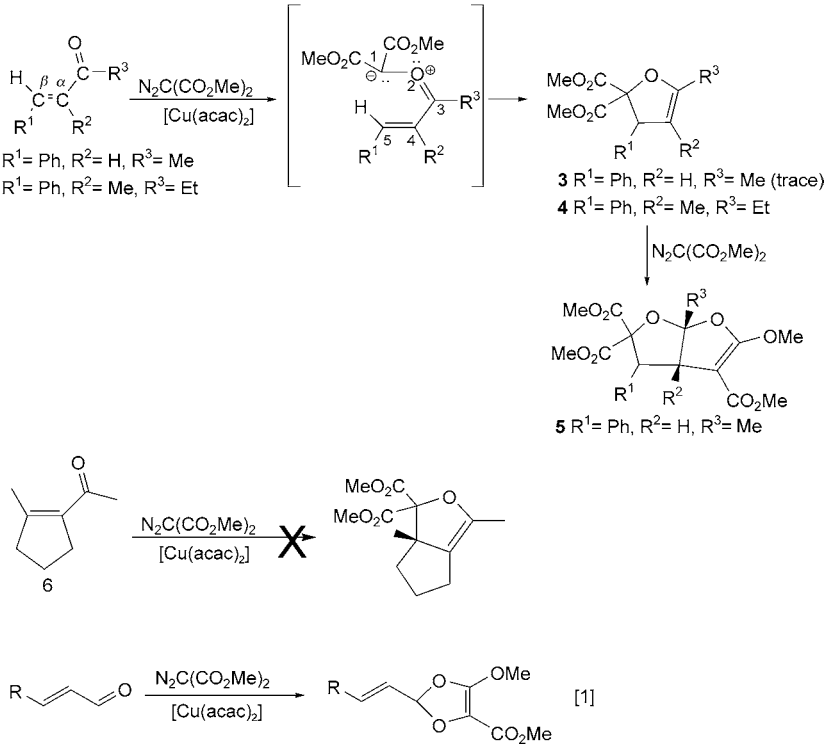
[1]) Part 3: [1].

Scheme 1. *Reactions of α,β-Enones with Dimethyl Diazomalonate* [1][9][10]



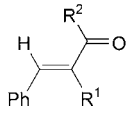
Results and Discussion. – In this study, all enones that were synthesized by traditional aldol condensation reaction had a phenyl substituent at their C(β) atom to stabilize the possible concerted transition state of the initially formed enone ylide by conjugation (see compounds **2**, **7**, and **8**; *Table 1*).

As the main feature of an aromatic-like transition state must be securing a close proximity between the two termini especially with respect to dihydrofuran formation, the synthesized enones were chosen to contain H-substituents at their C(β) atoms.

Thus, 2-methyl-1-phenylpent-1-en-3-one (**2**) was obtained in 94% yield with a different method but with similar yields as those reported by *Bartoli et al.* [12][13]; the (E)/(Z)-isomer mixture (76:24) was separated by column chromatography. The 5-methyl-1-phenylhex-1-en-3-one (**8**) was synthesized by an aldol condensation according to an old procedure reported by *Metayer* [15]; we now established the (E)/(Z) isomer ratio (98:2) and recorded the spectral data.

The 5,7-dimethyl-1-phenyloct-1-en-3-one (**7**) was also obtained as an (E)/(Z)-isomer mixture (95:5), the isomers could be enriched by column chromatography and were identified by spectral analyses.

Both isomers (E)- and (Z)-**7** gave the same mass spectra. The ^{1}H-NMR spectrum of (E)-**7** ($CDCl_3$) showed an *AB* pattern at δ 7.50 and 6.72 with $^3J_{(AB)} = 16.2$ Hz for the olefinic H-atoms. The four H-atoms at C(4) and



(*E*)-**2** R^1=Me, R^2= Et
(*E*)-**7** R^1=H, R^2=$Me_2CHCH_2CH(Me)CH_2$
(*E*)-**8** R^1=H, R^2 = Me_2CHCH_2

Table 1. *α,β-Conjugated Enones Synthesized by Aldol Condensation Reactions with Benzaldehyde*

Starting material[a])	Products	(*E*) [%]	(*Z*) [%]	Yield [%][b])
$MeCH_2COCH_2Me$	**2**, (2*E*)/(2*Z*)-PhCH=C(Me)COEt	76 [1][13]	24 [1]	94
$Me_2CHCH_2CH(Me)CH_2COMe$ [14]	**7**, (7*E*)/(7*Z*)-PhCH=CHCOCH$_2$CH(Me)-$CH_2CH(Me)_2$	95	5	85
$(Me)_2CHCH_2COMe$	**8**, (8*E*)/(8*Z*)-PhCH=CHCOCH$_2$CH$(Me)_2$ [15]	98	2	75

[a]) All starting materials were commercially available or were prepared by conventional methods. [b]) Yields of products isolated by column chromatography.

C(6) are all diastereotopic due to the stereogenic center C(5). One H-atom signal at δ 2.60 (H_a–C(4)) is a *dd* with ^2J = 15.1 and ^3J = 5.7 Hz and another one at δ 2.40 (H_b–C(4)) is also a *dd* with ^2J = 15.1 and ^3J = 8.1 Hz. Similarly H_a–C(6) is a *ddd* (^2J = 12.5, ^3J = 6.3, 6.0 Hz) at δ 1.17 and H_b–C(6) is also a *ddd* (^2J = 12.5, ^3J = 6.1, 5.9 Hz) at δ 1.08. There are 2 *m* at δ 2.17 (1 H) and 1.65 (1 H).

We compared the relative stabilities of s-*cis*/s-*trans* conformations of both (*E*)- and (*Z*)-enones **1**, **2**, **7**, and **8** as well as of **6** using geometry-optimization studies which yielded E_{total} values. The latter were calculated by molecular mechanics with the program Desktop Molecular Modeller on a PC-windows platform (*Table 2*) and furnished a tool to rationalize the product distribution of the catalytic reaction of these enones with DMDM.

Table 2. *Calculated Relative Stabilities of Conformers of the Available and Synthesized Enones*

Enone	Relative stabilities[a])
1	(*E*)-**1**; s-*cis* > (*E*)-**1**; s-*trans*
2	(*E*)-**2**; s-*cis* > (*E*)-**2**; s-*trans* > (*Z*)-**2**[b])
6	**6**; s-*cis* > **6**; s-*trans*
7	(*E*)-**7**; s-*cis* > (*E*)-**7**; s-*trans* > (*Z*)-**7**[b])
8	(*E*)-**8**; s-*cis* > (*E*)-**8**; s-*trans* > (*Z*)-**8**[b])

[a]) Based on the calculated ΔH° values. [b]) The calculated enone torsion angles (Θ (C(β)–C(α)–O) are close to 90° in these cases.

The enones (*Z*)-**2**, **6**, (*E*)-**7**, (*Z*)-**7**, and (*E*)-**8**) were treated with DMDM in the presence of [Cu(acac)$_2$] as catalyst (*Scheme 2*).

The (*Z*)-enones (*Z*)-**2** and (*Z*)-**7**, and enone **6** (with an additional Me substituent at C(2) = C(β)) did not give any dihydrofuran derivatives, as expected from the prerequisite of both termini being closest to each other (C(1) and C(5) in the transition state of *Scheme 1*) for an electrocyclic 1,5-ring closure reaction [1]; instead

dioxole derivatives **9**–**11**, respectively, were formed (*Scheme 2*,*a*) under mild conditions.

To the contrary and in accordance with our rationalization from *Table 2*, the enones (*E*)-**7** and (*E*)-**8**, being mainly present as s-*cis* conformers, yielded dihydrofuran derivatives **12** and **14**, respectively, *via* conjugated-carbonyl ylides, besides some furofuran derivatives **13** and **15**/**16**, respectively (*Scheme 2*,*b*). Thus, these two enones (*E*)-**7** and (*E*)-**8** having only one alkyl group of long to medium length could also prevent to some extent the subsequent reaction step as compared to the behavior of benzalacetone, *i.e.*, furofuran formation is also very sensitive to steric effects. This [3 + 2] cycloaddition reaction might also progress *via* an *endo*-approach mechanism (*Figure*).

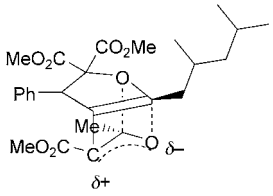
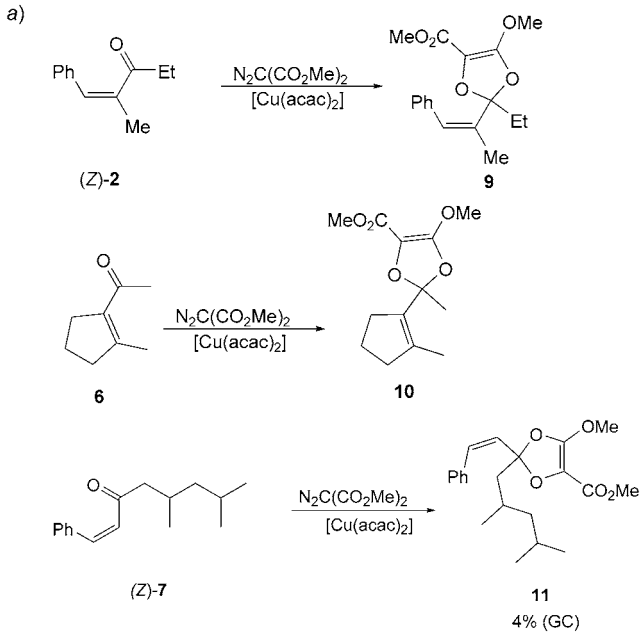


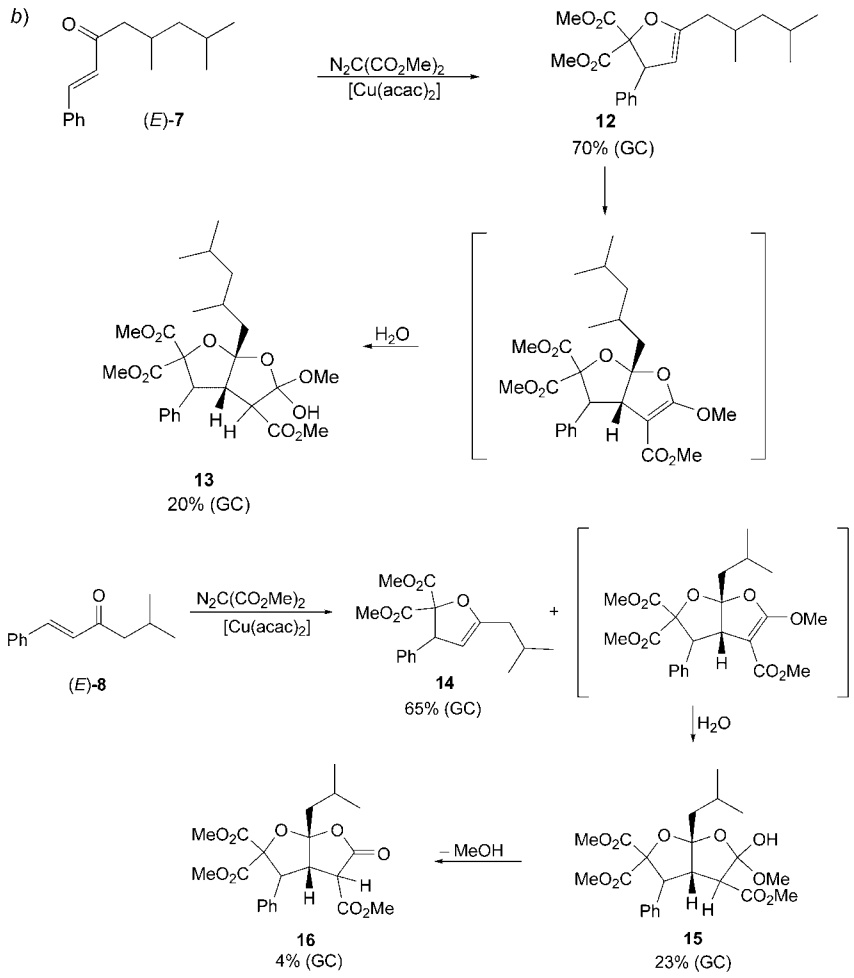
Figure. endo *Approach*

Conclusions. – A recent report [16] describes a high-pressure-promoted [4 + 2] cycloaddition of enol ethers with 3-aryl-2-cyanoprop-2-enoates. Under our conditions

Scheme 2. *Reactions of* (Z)-**2**, **6**, (E)-**7**, (Z)-**7**, *and* (E)-**8** *with Dimethyl Diazomalonate*



Scheme 2 (cont.)



and with the proper choice of the starting enones analog, the [3+2] cycloaddition reaction to yield furofurans can easily be achieved without the need of pressure [17].

The obtained furofuran derivatives are promising starting compounds for further syntheses. This ring structure is an important motif in several compounds acting on the central nervous system. They may be easily hydrolyzed or alcoholyzed under acidic conditions to yield corresponding open acetals or carbonyl compounds. Even under our chromatographic conditions, these furofuran derivatives may easily add water to the enol C=C bond (**12** → **13** or **14** → **15**) and then may loose MeOH to give corresponding γ-lactone (**15** → **16**, see *Scheme 2*, *b*).

Experimental Part

General. Dimethyl diazomalonate (DMDM) was prepared according to literature procedures. CC = column chromatography. IR Spectra: *Jasco FT-IR-5300* apparatus. NMR Spectra: *Bruker* apparatus; at 250 (^{1}H) or 60 MHz (^{13}C); Me_4Si as internal standard, δ in ppm, J in Hz; at 25°. GC/MS: *Hewlett-Packard* instrument with *HP-1* capillary column (24 m, packed with cross-linked (phenylmethyl)siloxane); column conditions: isothermal at 150° for 7 min, then heating to 280° with 5°/min; 0.54 bar He; EI detector; t_R in min. MS: *VG-Zapspec* double-focusing spectrometer; EI at 70 eV; CI in isobutane.

Enones: General Procedure. Enones **2**, **7**, and **8** were prepared by aldol condensation reactions [18] between benzaldehyde and pentano-3-one, 4,6-dimethylheptan-2-one, and 4-methylpentan-2-one, respectively, with pyrrolidine as an amine catalyst. Results: *Table 1*.

Reaction of Enones with DMDM: General Procedure. A soln. of 1 equiv. of DMDM in benzene (4 mmol/1 ml) was added very slowly to a refluxing benzene soln. of 1.5 equiv. of the substrate (2 mmol/1 ml) and 0.007 equiv. of [Cu(acac)$_2$] under N_2. Consumption of DMDM was monitored by IR. After the complete disappearance of the band at 2130 cm^{-1}, the mixture was filtered (gravity), and the soln. was passes rapidly through a short column of neutral aluminium oxide to remove the highly colored impurities and the catalyst.

*(*E*)-2-Methyl-1-phenylpent-1-en-3-one* ((*E*)-**2**) [1][13]. GC/MS: (*E*)-**2** as the major product (76%). The oily compound was purified by CC (neutral aluminium oxide, hexane/AcOEt 5:1); 65% of (*E*)-**2**. ^{1}H-NMR ($CDCl_3$): 7.52 (br. *s*, PhC*H*); 7.40–7.14 (*m*, Ph); 2.83 (*q*, *J* = 7.2, CH_2(4)); 2.06 (*s*, Me–C(2)); 1.14 (*t*, *J* = 7.2, Me). ^{13}C-NMR ($CDCl_3$): 198.5 (C=O); 136.2; 135.1; 134.4; 126–128 (Ph); 32.6; 12.1; 18.6. CI-MS: 175 (38, $[M+1]^+$), 174 (93, M^+), 159 (7), 145 (93), 117 (100), 91 (93), 77 (26), 51 (35). HR-MS: 174.2378 (M^+, $C_{12}H_{15}O^+$; calc.174.2390).

*(*Z*)-2-Methyl-1-phenylpent-1-en-3-one* ((*Z*)-**2**). GC/MS: (*Z*)-**2** as the minor product (24%). The oily compound was purified by CC (neutral aluminium oxide, hexane/AcOEt 5:1): 15% of (*Z*)-**2**. ^{1}H-NMR ($CDCl_3$): 8.08 (br. *s*, PhC*H*); 7.40–7.14 (*m*, Ph); 2.79 (*q*, *J* = 7.2, CH_2(4)); 2.02 (*s*, Me–C(2)); 1.12 (*t*, *J* = 7.2, Me). ^{13}C-NMR ($CDCl_3$): 198.5 (C=O); 136.2; 135.1; 134.4; 126–128 (Ph); 32.6; 12.1; 18.6. CI-MS: 175 (38, $[M+1]^+$), 174 (93, M^+), 159 (7), 145 (93), 117 (100), 91 (93), 77 (26), 51 (35). HR-MS: 174.2378 (M^+, $C_{12}H_{15}O^+$; calc.174.2390).

*(*E*)-5,7-Dimethyl-1-phenyloct-1-en-3-one* ((*E*)-**7**). Yield of (*E*)-**7**/(*Z*)-**7** 85%. GC/MS: (*Z*)-**7** as the major product (95%); not isolated in pure form. Data from crude fraction. ^{1}H-NMR ($CDCl_3$): 7.60–7.30 (*m*, Ph); 7.50 (*d*, *J* = 16.2, PhC*H*); 6.72 (*d*, *J* = 16.2, H–C(2)); 2.60 (*dd*, *J* = 15.1, 5.7, CH_2(4)); 2.40 (*dd*, *J* = 15.1, 8.1, CH_2(4)); 2.17 (*m*, H–C(5)); 1.17 (*ddd*, *J* = 12.5, 6.3, 6.0, CH_2(6)); 1.08 (*ddd*, *J* = 12.5, 6.1, 5.9, CH_2(6)); 1.65 (*m*, H–C(7)); 0.90 (*d*, *J* = 6.7, 2 Me); 0.87 (*d*, *J* = 6.54, Me(8)). ^{13}C-NMR ($CDCl_3$): 198.2 (C=O); 142.4 (C(1)); 135.0–126.0 (Ph, C(2)); 48.6; 45.5; 25.8; 22.9; 22.6; 19.2. GC/MS: t_R 14.47. EI-MS: 230 (4, M^+), 173 (14), 146 (98), 131 (100), 171 (11), 103 (41), 91 (3), 77 (21). HR-MS: 230.3441 (M^+, $C_{16}H_{22}O^+$; calc. 230.3453).

*(*Z*)-5,7-Dimethyl-1-phenyloct-1-en-3-one* ((*Z*)-**7**). GC/MS: (*Z*)-**7** as the minor product (5%); not isolated in pure form. Data from crude fraction. ^{1}H-NMR ($CDCl_3$): 7.60–7.30 (*m*, Ph); 6.80 (*d*, *J* = 12.8, PhC*H*); 6.16 (*d*, *J* = 12.8, H–C(2)); 2.40 (*dd*, *J* = 15.2, 6.6, CH_2(4)); 2.20 (*dd*, *J* = 15.2, 8.2, CH_2(4)); 2.10 (*m*, H–C(5)); 1.60 (*m*, H–C(7)); 0.97 (*m*, CH_2(6)); 0.96–0.77 (*m*, 3 Me). GC/MS: t_R 11.25. EI-MS: 230 (9, M^+), 173 (13), 146 (74), 131 (100), 117 (8), 103 (40), 91 (3), 77 (20).

*(*E*)-5-Methyl-1-phenylhex-1-en-3-one* ((*E*)-**8**). GC/MS: (*E*)-**8** as the major product (98%); not isolated in pure form. Data from crude fraction. ^{1}H-NMR ($CDCl_3$): 7.56 (*d*, *J* = 16.1, H–C(1)); 7.40–7.30 (*m*, Ph); 6.76 (*d*, *J* = 16.3, H–C(2)); 2.55 (*d*, *J* = 7, CH_2); 2.27 (*m*, CH); 1 (*d*, *J* = 6.7, 2 Me). ^{13}C-NMR ($CDCl_3$): 199.1 (C=O); 143.2; (C(1)); 135.0–126.0 (Ph, C(2)); 50.4; 22.4; 21.8. GC/MS: t_R 13.3. EI-MS: 188 (39, M^+), 146 (36), 131 (100), 103 (56), 77 (27). HR-MS: 188.2628 (M^+, $C_{13}H_{16}O^+$; calc. 188.2655).

*(*Z*)-5-Methyl-1-phenylhex-1-en-3-one* ((*Z*)-**8**). GC/MS: (*Z*)-**8** as the minor product (2%); not isolated in pure form. Data from crude fraction. GC/MS: t_R 11.6 min. EI-MS: 188 (27, M^+), 173 (2), 146 (13), 131 (100), 103 (37), 91 (2), 77 (16), 51 (4).

Methyl 2-Ethyl-5-methoxy-2-(1′-methyl-2′-phenylethenyl)-1,3-dioxole-4-carboxylate (**9**). GC/MS: **9** as the main product (85%). The compound was purified by CC (neutral aluminium oxide, hexane/AcOEt 5:1): 68% of **9**. ^{1}H-NMR ($CDCl_3$): 7.25–6.99 (*m*, Ph); 6.43 (br. *s*, H–C(1)); 3.80 (*s*, COOMe); 3.79 (*s*, MeO); 2.16 (*d*, *J* = 1.8, Me–C(2′)); 1.74–1.65 (*m*, MeCH_2); 0.91 (*t*, *J* = 7.3, MeCH_2). ^{13}C-NMR ($CDCl_3$): 160 (CO_2Me); 142.1 (C(5)); 137.2 (Ph–C(2′)); 129.2, 128.5, 126.8, 126.5 (Ph); 129.0 (C(2′)); 106.2 (C(2)); 95.1 (C(4)); 53.2 (CO_2Me); 52.8 (MeO); 26.1 (MeCH_2); 20.7 (*Me*–C(1′)); 9.9 (*Me*CH_2). GC/MS: t_R 18.5. EI-MS: 304 (2, M^+), 275 (32), 243 (25), 185 (100), 171 (22), 157 (27), 141 (26), 128 (85), 115 (60), 91 (10), 77 (10), 59 (60). HR-MS: 304.3362 (M^+, $C_{17}H_{20}O_5^+$; calc. 304.3377).

Methyl 5-Methoxy-2-methyl-2-(2′-methylcyclopent-1-en-1-yl)-1,3-dioxole-4-carboxylate (**10**). GC/MS: **10** as the main product (86%). The oily compound was purified by CC (neutral aluminium oxide, CCl_4/AcOEt 10:1): 72% of **10**. ^{1}H-NMR ($CDCl_3$): 3.69 (*s*, COOMe); 3.42 (*s*, MeO); 2.18 (*s*, Me–C(2)); 2.45–2.61 (*m*, other H);

1.73 (*s*, Me–C(2′)). ^{13}C-NMR ($CDCl_3$): 161 (*C*OOMe); 158.2 (C(5)); 144.5 (C(1′)); 127 (C(2′)); 85.6 (C(2)); 82.3 (C(4)); 51.1 (COO*Me*); 43.4 (MeO); 32.4 (C(3′)); 25.5 (Me–C(2)); 21.7 (C(5′)); 12.9 (*Me*–C(2′)); 7.67 (C(4′)). GC/MS: t_R 13.96. CI-MS: 255 (5, $[M+1]^+$), 224 (5), 195 (17), 108 (75), 145 (100), 81 (56), 59 (15). HR-MS: 254.2772 (M^+, $C_{13}H_{15}O_5^+$; calc. 254.2790).

Methyl-2-(2,4-Dimethylpentyl)-5-methoxy-2-(2′-phenylethenyl)-1,3-dioxole-4-carboxylate (**11**). GC/MS: **11** present to 4% in the reaction mixture; not isolated in pure form. Data from crude fraction. GC/MS: t_R 18.5. EI-MS: 360 (6, M^+), 300 (3), 276 (33), 232 (35), 189 (80), 161 (100), 115 (31), 102 (64), 91 (14), 76 (8), 59 (28).

Dimethyl 5-(2,4-Dimethylpentyl)-2,3-dihydro-3-phenylfuran-2,2-dicarboxylate (**12**). GC/MS: **12** as the main product (70%). The compound was purified by CC (silica gel; hexane/AcOEt 10:1): 52% of **12**. ^{1}H-NMR ($CDCl_3$): 7.27–7.20 (*m*, Ph); 5.30 (*d*, *J* = 3, H–C(3)); 4.70 (*dd*, *J* = 3, H–C(4)); 3.14 (*s*, 2 MeO); 2.20 (*d*, *J* = 7.2, CH_2–C(5)); 1.90 (*m*, H–C(4′)); 1.70 (*m*, H–C(2′)); 1.20 (*m*, CH_2); 1.10 (*d*, *J* = 6.7, Me–C(2′)); 1.00 (*d*, *J* = 6.6, 2 Me). ^{13}C-NMR ($CDCl_3$): 168.5; 168.1; 161.7; 142.5; 127.6; 126.2; 124.5; 96.2; 91.3; 45.8; 45.2; 27.3; 23.3; 22.7; 20.3. GC/MS: t_R 21.27. EI-MS: 360 (9, M^+), 302 (26), 269 (32), 229 (100), 214 (51), 212 (85), 184 (33), 157 (31), 128 (39), 115 (18). HR-MS: 360.4427 (M^+, $C_{21}H_{28}O_5^+$; calc. 360.4440).

*6aβ-(2′,4′-Dimethylpentyl-2,3,3aβ,4,5,6a-hexahydro-5-hydroxy-5-methoxy-3-phenylfuro[2,3-*b*]furan-2,2,4-tricarboxylate* (**13**). GC/MS: **13** as the minor product (20%). This compound was purified by CC (silica gel; hexane/AcOEt 10:1): 12% of **13**. ^{1}H-NMR ($CDCl_3$): 7.39–7.27 (*m*, Ph); 4.52 (br. *s*, H–C(3)); 4.42 (D_2O exchange); 3.85 (*s*, COOMe); 3.75 (*s*, COOMe); 3.83 (*s*, COOMe); 3.18–3.10 (*m*, other H); 3.10 (*s*, MeO); 1.39 (*d*, *J* = 7.2, CH_2–C(6a)); 1.23 (*m*, CH_2); 1.08 (*m*, 2 CH); 1.09 (*s*, 3 Me). ^{13}C-NMR ($CDCl_3$): 175.3; 172.1; 130.8; 128.7; 127.9; 125.2; 107.5; 93.2; 90.1; 51.2; 50.8; 49.9; 47.2; 44.9; 43.9; 42.0; 34.0; 29.3; 26.2; 22.6; 21.0. GC/MS: t_R 26.7. EI-MS: 508 (5, M^+), 433 (13), 385 (100), 341 (13), 305 (31), 274 (20), 242 (28), 231 (20), 204 (15), 157 (26), 121 (13), 59 (8). HR-MS: 508.548 (M^+, $C_{26}H_{36}O_{10}^+$; calc. 508.558).

Dimethyl 2,3-Dihydro-5-(2-methylpropyl)-3-phenylfuran-2,2-dicarboxylate (**14**). GC/MS: **14** as the major product (65%). The compound was purified by CC (silica gel, CCl_4/acetone 10:1): 55% of **14**. ^{1}H-NMR ($CDCl_3$): 7.40–7.30 (*m*, Ph); 5.02 (*d*, *J* = 2.6, H–C(3)); 4.80 (*dt*, *J* = 2.6, 1.1, H–C(4)); 3.84 (*s*, COOMe); 3.80 (*s*, COOMe); 2.08–2.03 (*m*, CH_2CH); 0.94 (*d*, *J* = 6.57, 2 Me). ^{13}C-NMR: 173.2; 171.4; 159.3; 145.1; 129.2; 127.5; 123.7; 96.5; 91.8; 52.1; 50.7; 42.5; 23.0; 18.3. GC/MS: t_R 13.7. EI-MS: 318 (31, M^+), 303 (100), 259 (10), 243 (14), 221 (9), 189 (13), 155 (6), 129 (10), 115 (15), 83 (9), 69 (60), 59 (6). HR-MS: 318.3632 (M^+, $C_{26}H_{36}O_{10}^+$; calc. 318.3643).

*Trimethyl 2,3,3aβ,4,5,6a-Hexahydro-5-hydroxy-5-methoxy-6aβ-(2′-methylpropyl)-3-phenylfuro[2,3-*b*]furan-2,2,4-tricarboxylate* (**15**) *and Trimethyl 2,3,3aβ,4,5,6a-Hexahydro-6aβ-(2′-methylpropyl)-5-oxo-3-phenyl furo[2,3-*b*]furan-2,2,4-tricarboxylate* (**16**). GC/MS: 23% of **15** and 4% of **16**. These compounds were purified by CC (silica gel, CCl_4/acetone 10:1). 17% of **15** and a minor amount of **16**.

Data of **15**: ^{1}H-NMR ($CDCl_3$): 7.50–7.26 (*m*, Ph); 5.70 (*d*, *J* = 9.3, H–C(4)); 4.88 (*d*, *J* = 9.3, H–C(3)); 4.18 (distorted *t*, *J* = 9.4, H–C(3a)); 3.86 (*s*, COOMe); 2.20 (D_2O exchange, OH–C(5)); 1.57 (*m*, CH_2CH); 0.60 (*d*, *J* = 6.2, Me); 0.34 (*d*, *J* = 6.2, Me). ^{13}C-NMR ($CDCl_3$): 174.0; 173.2; 172.5; 150.3; 128.4; 125.6; 106.3; 93.7; 89.1; 50.5; 50.3; 49.9; 47.2; 44.4; 41.8; 34.0; 29.2; 22.9; 18.5. GC/MS: t_R 20.5. EI-MS: 466 (2, M^+), 365 (2), 339 (2), 318 (7), 275 (9), 5.3 (26), 221 (73), 204 (98), 189 (100), 162(88), 147 (39), 115 (36), 85 (40), 59 (5).

Data of **16**: ^{1}H-NMR ($CDCl_3$): 7.40–7.25 (*m*, Ph); 5.29 (br. *s*, H–C(3)); 4.56 (*m*, H–C(3)); 3.95 (*m*, H–C(3a)); 3.82 (*s*, COOMe); 3.80 (*s*, COOMe); 3.56 (*s*, COOMe); 1.24 (*m*, CH_2CH); 0.75 (*d*, *J* = 0.68, Me); 0.22 (*d*, *J* = 6.7, Me). GC/MS: t_R 19.2. EI-MS: 434 (1, M^+), 376 (1), 356 (3), 319 (2), 279 (16), 167 (37), 149 (100), 113 (8), 85 (5), 57 (17).

REFERENCES

[1] O. Anaç, A. D. Özdemir, Ö. Sezer, *Helv. Chim. Acta* **2003**, *86*, 290.
[2] T. L. B. Boivin, *Tetrahedron* **1987**, *43*, 3309.
[3] D. L. Storm, T. A. Spencer, *Tetrahedron Lett.* **1967**, *20*, 1865.
[4] T. A. Spencer, R. M. Villarica, D. L. Storm, T. D. Weaver, R. J. Friary, J. Posler, P. R. Shafer, *J. Am. Chem. Soc.* **1967**, *89*, 5497.
[5] S. T. Murayama, T. A Spencer, *Tetrahedron Lett.* **1969**, *51*, 4479.
[6] M. Alt, G. Maas, *Tetrahedron* **1994**, *50*, 7435.
[7] M. Alt, G. Maas, *Chem. Ber.* **1994**, *127*, 1537.
[8] R. Huisgen, R. March, *J. Am. Chem. Soc.* **1982**, *104*, 4952.
[9] O. Anaç, A. Daut, *Liebigs Ann. Recl.* **1997**, 1249.

[10] O. Anaç, A. D. Özdemir, H. Bormann, M. Somer, *Z. Kristallogr.* **2002**, *217*, 607.
[11] R. Huisgen, *Angew. Chem., Int. Ed*. **1980**, *19*, 947.
[12] T. Mukaiyama, *Org. React*. **1992**, *28*, 203.
[13] G. Bartoli, M. C. Bellucci, M. Petrini, E. Marcantoni, *Org. Lett*. **2000**, *2*, 1791.
[14] Guerbet, C.r, C. R. Acad. Sci., Ser. II **1909**, 1537.
[15] M. Metayer, *Recl. Trav. Chim. Pays-Bas* **1952**, *71*, 153.
[16] R. W. M. Aben, R.Gelder, H. W. Scheeren, *Eur. J. Org. Chem.* **2002**, 3126.
[17] R. W. M. Aben, J. Goudriaan, J. M. M. Smits, J. W. Scheeren, *Synthesis* **1993**, 37.
[18] C. F. H. Allen, H. B. Rosener, *J. Am. Chem. Soc.* **1927**, *49*, 2110.

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