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FIVE-MEMBERED RING FORMATION OF 2-HYDROXYALKYL MALONATE AND ACETOACETATE DERIVATIVES. THE PROBLEM OF O- VERSUS C-ALKYLATION.

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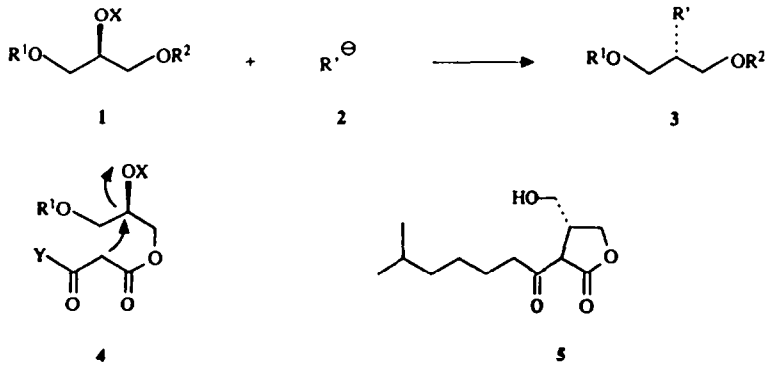
Abstract - The cyclization reactions of type **32**, **34**, **36**, **37/38** compounds have been studied with the aim of achieving a carbon-carbon bond forming reaction at C-2 of optically active glycerol derivatives as indicated in Scheme 1. In all cases O-alkylation at the proximal CO group has been observed.

The achievement of a stereospecific carbon-carbon bond formation as depicted in Scheme 1 (**1** + **2** --> **3**) would provide access to a wide array of useful starting materials for the syntheses of complex natural products and biologically active materials. Our interest in this sort of reactions arose from research on optically active glycerol derivatives of both enantiomeric series, in which the secondary and one of the primary alcoholic functions are readily amenable to manipulation.[1] We thought that an intramolecular substitution process as indicated in **4** (OX = leaving group, Y=R or OR) would diminish the danger of side reactions such as elimination. Furthermore, introduction of a ß-dicarbonyl grouping allows the generation



1 **2** **3**

4 **5**

Scheme 1.

Dedicated with appreciation to Professor Wolfgang Kirmse on the occasion of his 60th birthday.

of the carbanionic reaction centre by deprotonation under mild conditions. Obvious synthetic targets[2] employing this type of chemistry are the Khokhlof A-factor (**5**) and related compounds that act as autoregulators of differentiation and antibiotic biosynthesis in a variety of Streptomyces species.[3]

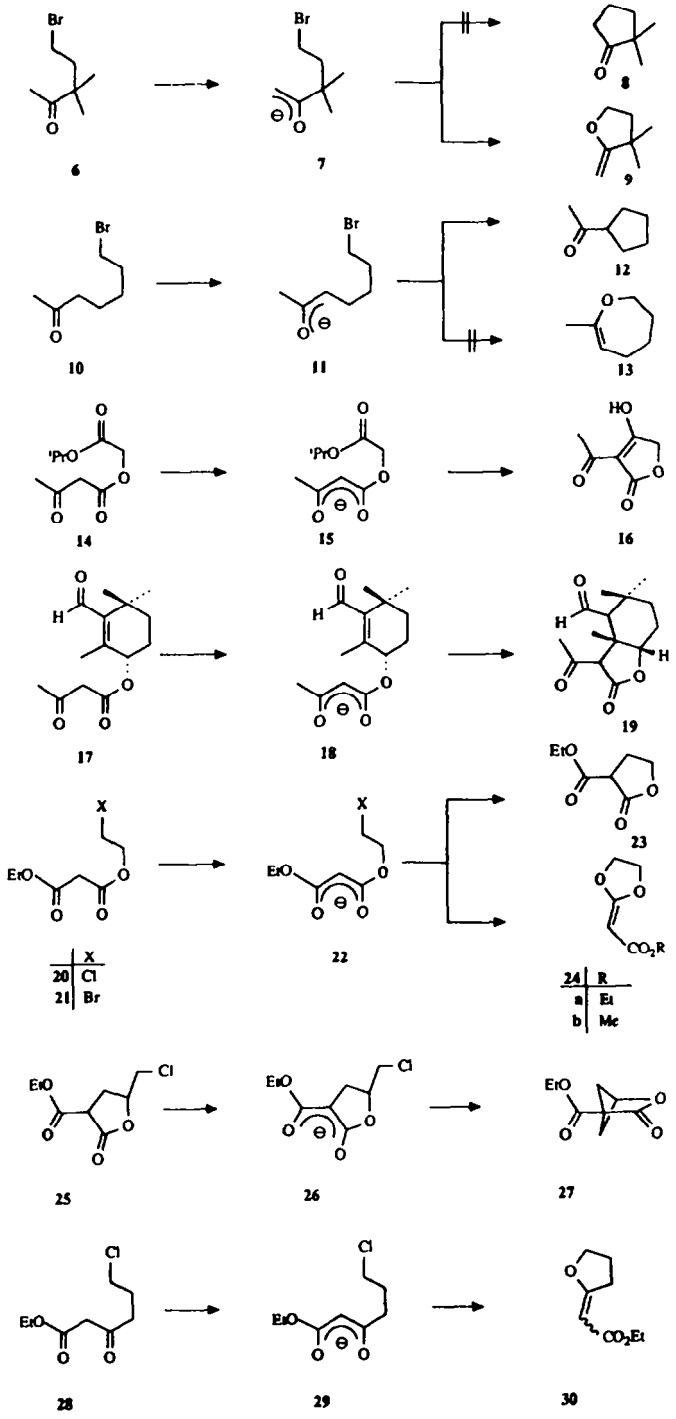
A difficulty frequently encountered in intermolecular alkylations of ß-dicarbonyl compounds is the concurrent formation of both C- and O-alkylated products. It is, however, normally possible to direct the alkylation toward carbon[4] by proper selection of (i) the solvent,[5] (ii) the enolate counter ion,[5,6,7] and (iii) the leaving group of the alkylating agent (customarily correlated with reference to the HSAB principle[8]). On the other hand, for many intramolecular nucleophilic substitution processes,[9] the ratio of O- vs. C-alkylation has been shown to be subject to stereoelectronic control.[10,11] Thus, the potassium or lithium enolate generated from bromoketone **6** (Scheme 2) gives only enol ether **9** with no detectable formation of cyclopentanone **8**. In contrast, bromoketone **10**, under the same conditions, yields acylcyclopentane **12** rather than enol ether **13**.[12] Using the nomenclature of the Baldwin rules for ring closure,[13] the process **7**-->**8** is an example of an (enolendo)-exo-tet cyclization (6- and 7-membered ring formation being favoured and 3- to 5-membered ring formation, e.g. **7**-->**8**, being disfavoured). On the other hand, the reaction **11**-->**12** corresponds to an (enolexo)-exo-tet closure, all 3- to 7-membered processes being favoured. This difference in behaviour has been rationalized by consideration of the transition states for C-and O-alkylation. Carbon alkylation occurs through attack on the enolate carbon perpendicular to the C-C-O plane, while oxygen alkylation takes place by reaction at an oxygen lone pair within that plane. At the electrophilic carbon the geometry associated with an S_N2 transition state is required. It is assumed that the combination of both stereoelectronic requirements precludes the formation of **8** from **7** (because of substantial ring strain in the transition state).[10,13]

What is to be expected for the cyclization of the anion generated from **4** in which, in principle, anions **7** and **11** are combined?

When the electrophilic site is an sp^2 centre, 5-ring (C-C bond) formation has been observed. For example, 3-acetyl-tetronic acid (**16**) was available via cyclisation of **15**.[14,15,16] Similarly, intramolecular Michael additions such as **18**-->**19** have been used to construct five-membered rings.[17]

However, in cases, where the electrophilic site is an sp^3 centre, conflicting results have been reported. Thus, Michael and Weiner have claimed that the enolate anion obtained from **20** closes to give five-membered ring C-alkylation product **23**.[18,19] They also reported the formation of **27** from

Formation of 2-hydroxyalkyl malonate



Scheme 2.

25.[18] In contrast to this, Parker (without referring to Michael's publication) described that **21** cyclizes on base treatment to give ketene acetal **24** by O-alkylation at the proximal ester CO group.[20] In ß-keto esters such as **28**, O-alkylation at the keto CO takes place (**28**-->**29**-->**30**) as found by Boll[21] and others.[22]

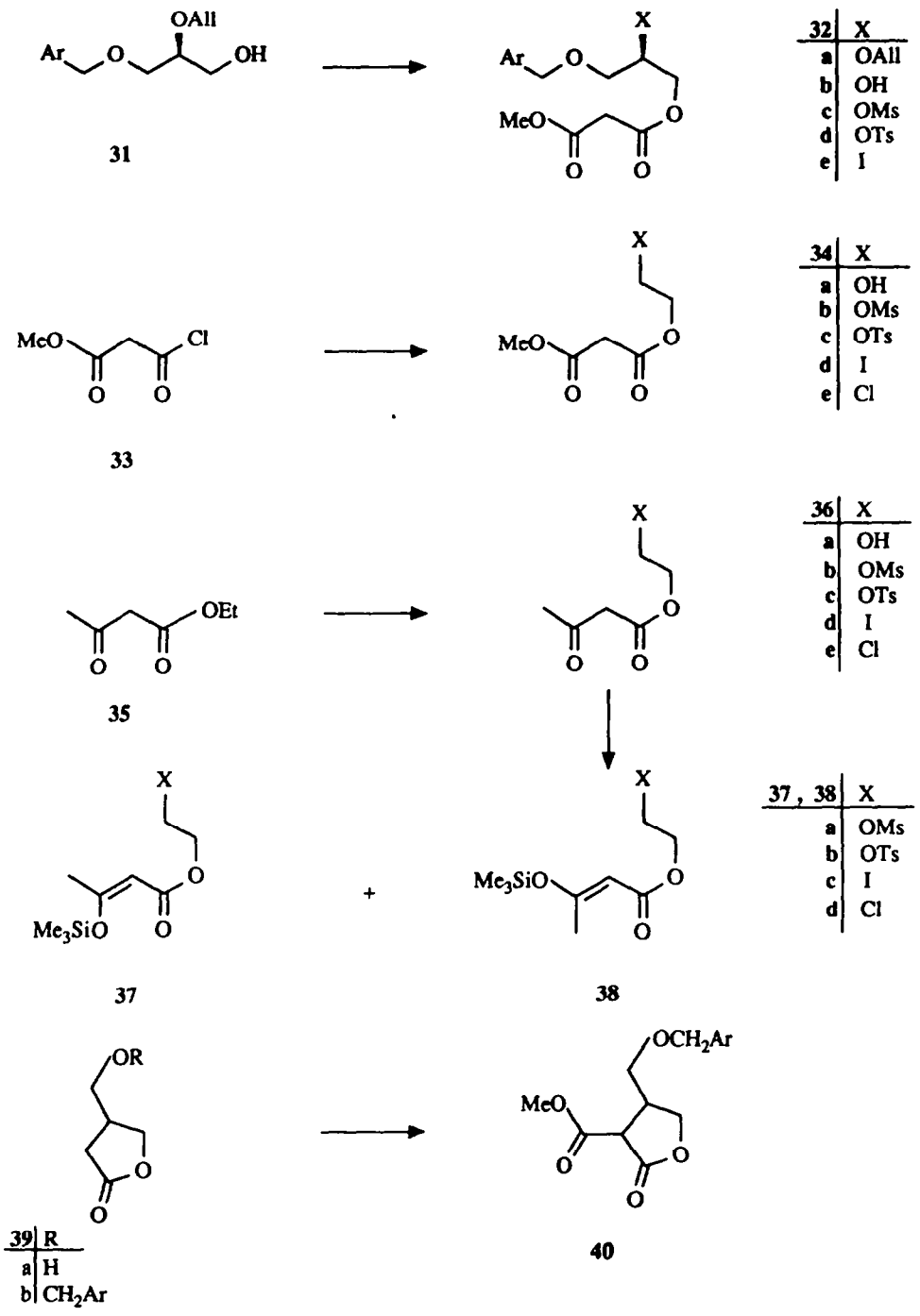
The purpose of this publication is to outline the reactions of type **4** compounds under cyclization conditions. Different leaving groups were tested and a variety of bases and solvents. Furthermore, **25**, **20**, and malonates of type **34** are included in order to probe the effect of a primary substitution site on the outcome of the cyclization reaction and to remove the inconsistencies between the results of Michael and Parker. In addition, acetoacetates **36** and especially their silyl enol ethers **37/38** with the enol form suitably fixed for cyclization were investigated.

Synthesis of malonates **32**, **34**, and **20**, of acetoacetates **36**, of silyl enol ethers **37/38**, and of reference compound **40**.

D-mannitol was converted to the optically active glycerol derivative **31** as recently described.[1b] Reaction of **31** with methyl (chloroformyl)acetate (**33**) provided **32a** which was deallylated with $PdCl_2$ in acetic acid - water[23] to give **32b**. **32c** and **32d** were prepared from **32b** and the respective sulfonyl chloride. For conversion of **32b** into the iodo derivative **32e** the Garegg-Samuelsson protocol[24] was followed. **32e** was optically active but probably partly racemic.

Compounds **34a-34e** and **20** were also available straightforwardly (see Scheme 3 and Experimental). Acetoacetates **36a** and **36e** were prepared from **35** by trans-esterification.[25] **36a** was converted to **36b-36d** as described above. From **36b-36e** the corresponding trimethylsilyl enol ethers were formed on reaction with trimethylsilyl chloride - triethylamine in ether solution.[26,27] The ^1H NMR spectrum of the reaction product obtained from **36e** showed the presence of two stereomeric enol silyl ethers in the ratio of 1:3 (from integration of the olefinic proton signals at δ = 5.12 and 5.41). The minor compound was shown by an NOE experiment[28] (NOE between the olefinic proton and the CH_3 group) to have the Z-configuration (**37d**). In all other cases, too, mixtures of **37** and **38** were obtained, **38** being the main component.

39a was obtained as described by Ishida et al.[29] and converted into p-methoxybenzyl ether **39b** using the trichloroacetimidate procedure.[30] On reaction with dimethyl carbonate[29,31] the sodium enolate of **39b** furnished racemic **40**, the compound that in it's optically active form is the desired cyclization product of compounds **32b-32e**. In $CDCl_3$ solution **40** obviously exists exclusively in the non-enolized form. Addition of D_2O did not cause


OAll
Ar
O
OH
31
X
Ar
O
MeO
O
O
O
O
32 X
a OAll
b OH
c OMs
d OTs
e I
MeO
Cl
O
O
33
34 X
a OH
b OMs
c OTs
d I
e Cl
OEt
35
36 X
a OH
b OMs
c OTs
d I
e Cl
Me3SiO
37
+
38
37, 38 X
a OMs
b OTs
c I
d Cl
OR
39 R
a H
b CH2Ar
OCH2Ar
40

Scheme 3.

exchange of the proton at C-3, even after two weeks, in agreement with Campbell's results.[31b,32]

Cyclization of malonates 32b - 32e.

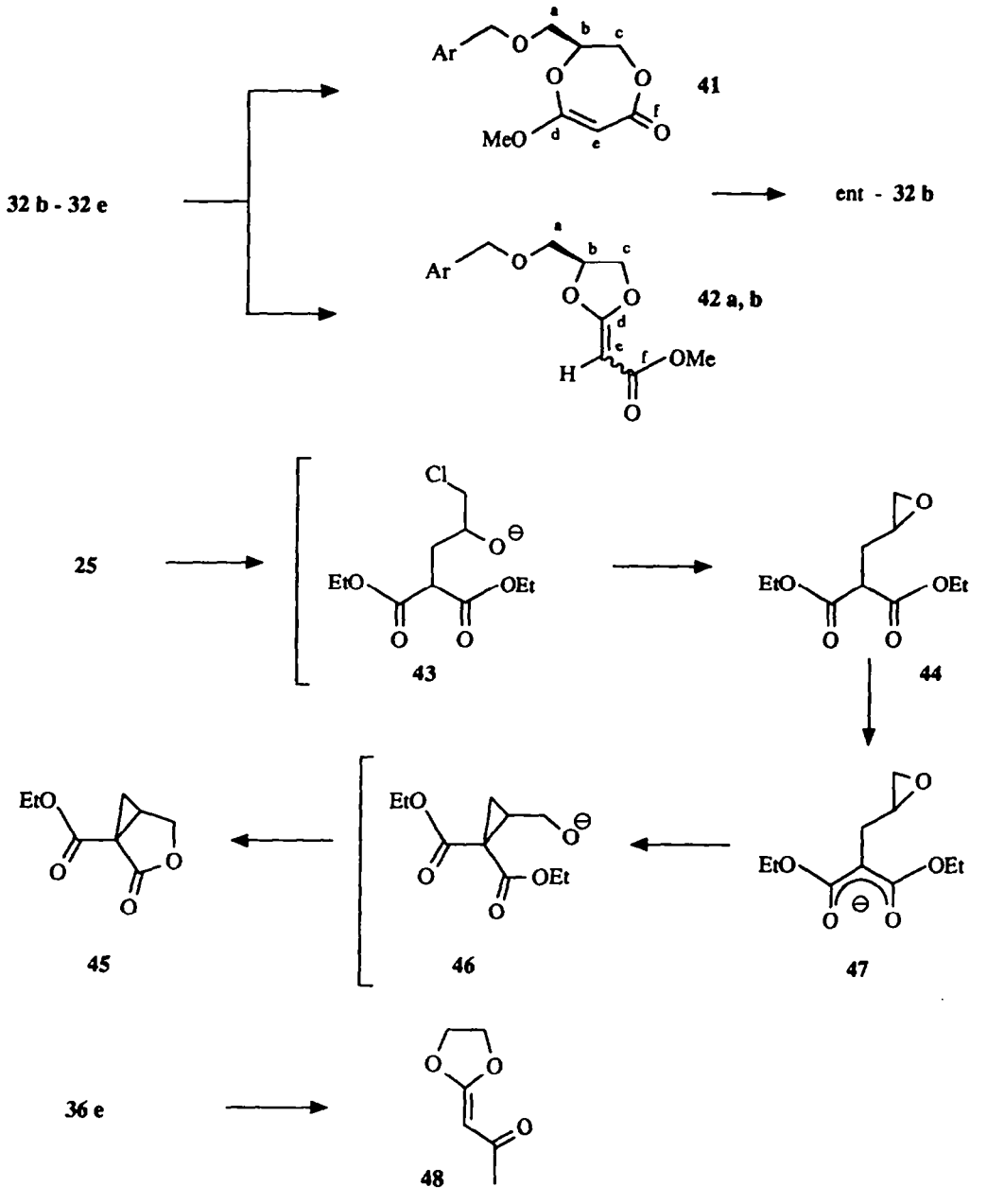
Treatment of **32c** in benzene solution with DBU[12a] led to the formation of two very sensitive reaction products which decomposed if no special precautions to form the single hydrolysis product ent-**32b**. From this observation it became immediately clear that an O- rather than the desired C-alkylation had taken place. Under carefully selected conditions (see Experimental) the two O-alkylation products could be separated. Prominent in their NMR spectra were the signals of the ring protons (b and c, see Scheme 4) and the adjacent CH_2 group (protons a) which formed a 5-spin system at δ =

isomer 1	isomer 2	
2.96-3.05 and 3.15-3.22	2.78-2.90	CH_2(a)
3.44-3.49 and 3.61-3.67	3.48-3.56 and 3.63-3.68	CH_2(c)
4.13-4.27	3.72-3.78	H(b)

and the signals of the unsaturated carbons at δ =

isomer 1	isomer 2	
166.6, 169.3	167.7, 169.5	C(d) and C(f)
67.0	67.3	C(e)

On the basis of ordinary ^1H, ^{13}C (DEPT) and H,C COSY spectra it was impossible to decide which of the structures **41** or **42** had to be attributed to the cyclization products. Finally recourse was made to two selective INEPT experiments[33] seeking to exploit the three-bond coupling between ^{13}C and ^1H. The coupling constant depends on the angle between the two planes defined by three atoms and on the nature of the four atoms in the pathway (Karplus equation).[34] For structure **41** polarization transfer from H(c) to C(f) and from H(b) to C(d) is expected, whereas polarization transfer both from H(b) and H(c) to C(d) would prove structure **42**. The results for isomer 1 are described here in detail. ^3J values of 5 and 7 Hz were selected giving the same results. Polarization transfer via irradiation at δ = 3.65 (one of the H(c) protons) resulted in enhancement at δ = 169.3. Similarly irradiation at δ = 4.20 (H(b)) enhanced the δ = 169.3 signal. These results strongly favour structure **42** and would have been unambiguous were there not the appearance of a small signal at δ = 166.7 (C(f)), 15% of the



Scheme 4.

intensity of the δ = 169.3 signal) in the first experiment (irradiation at δ = 3.65). Practically identical results have been obtained for isomer 2 (see Experimental). Therefore, we assume that the two cyclization products of **32c** are stereoisomers **42a** and **42b**. The configuration around the double bond was not determined.

In addition to DBU (benzene) the following base (solvent) systems have been examined: NaH[35] (CH_2Cl_2, THF, DMF, DMPU), K_2CO_3[36] (acetone, DMSO), and tetrabutylammonium fluoride[37] (THF). In all cases ketene acetals **42a/42b** were formed. Since we had a reference sample of the C-alkylation product **40** at our disposal, we could specifically search for it in the reaction mixtures by TLC; however, it was never detected. In control experiments **40** was found to be stable at least under the DBU and tetrabutylammonium fluoride cyclization conditions.- Treatment of **32c-32e** with LDA (THF) yielded mixtures of (unidentified) products, and neither **40** nor **42a/42b** were found.[38,39] Finally it should be mentioned that even **32b** yielded **42a/42b** in an intramolecular Mitsunobu reaction.[40]

Cyclization of malonates **34b - 34e** and **20**.

DBU, NaH, K_2CO_3, and tetrabutylammonium fluoride mediated reaction of malonates **34b - 34d** carrying the leaving group at a primary position gave exclusively O-alkylation product **24b**. In many instances the IR spectra of the reaction mixtures were analyzed to identify a C-alkylation product by its lactone band. A test series confirmed that 5% of a lactone component would have been possible to detect. Even such a small lactone content was absent in all cyclization mixtures investigated. Structural assignment of **24b** rests on ^1H and ^{13}C NMR spectra which were very similar to those of **42a** and **42b** discussed above.

24b was also formed from chloro compound **34e** on treatment with NaH in benzene, and reaction of **20** with Na in benzene provided ketene acetal **24a** rather than the C-alkylation product **23** as assumed by Michael and Weiner.[18] These results prove the correctness of Parker's report.[20]

Cyclization of **25**.

As mentioned above, formation of **27** by C-alkylative ring closure of **25** has been claimed by Michael and Weiner.[18] When this experiment was repeated (with sodium ethoxide in ethanol), a reaction product was isolated that was easily shown by ^1H and ^{13}C NMR spectroscopy to have structure **45**. It may be formed as indicated in Scheme 4.

Cyclization of acetoacetate **36e**.

Treatment of **36e** with NaH in THF gave ketene acetal **48** in agreement with the result reported by Parker.[20] The structure of the reaction product

followed from an ^1H NMR spectrum and a hydrolysis experiment which furnished **36a**.

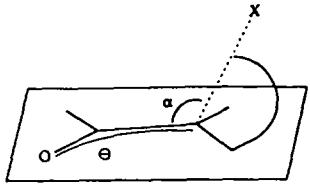
Cyclization of silyl enol ethers 37/38 (a - d).

Tetrabutylammonium fluoride was used to induce cyclization. Formation of **48** was observed in all cases (isolated after hydrolysis to give **36a**).

Summary.

Cyclization of β-dicarbonyl compounds, both malonates and acetoacetates, of type **4** has been studied. Regardless of a) the base, b) the solvent, c) the leaving group, and d) the substitution degree at the electrophilic reaction site (primary versus secondary) only O-alkylation at the proximal CO group has been observed giving ketene acetals **42a/42b** and **24**, respectively. Even the tetrabutylammonium enolates derived from enol silyl ethers **37/38** (**a-d**) cyclized by O-alkylation to give **48**. It may be recalled that tetraalkylammonium enolates of β-ketoesters have been specially recommended for C-alkylation in intermolecular alkylations.[41]

The anions generated from β-dicarbonyl compounds form a very complex system both with regard to their structures (conformation,[42] aggregation state[43]) and their reactivity. It is tempting to compare the behaviour of the enolates from type **4** compounds with that of the anion generated from **10** which reacts in the desired manner to C-alkylation product **12** (see Scheme 5). If it is assumed that the transition state geometry resembles that calculated by Houk[44] for the C-alkylation of the acetaldehyde enolate with methyl fluoride, the electrophilic carbon must be positioned in a plane perpendicular to the enolate plane with an angle α of 106°.



Scheme 5.

Inspection of models shows that this transition state geometry can readily be reached from **11** (in contrast to **7**) and also seems to be accessible from an anion such as **22**. Possibly the desired C-alkylation in the 5-(enolexo)-exo-tet sense (see **4**) is therefore not generally prevented by a stereo-

electronic barrier. Work is in progress aimed at overcoming the difficulties associated with the unwanted O-alkylation reaction.
Formation of the two isomers **42a** and **42b** from **32b - 32e** indicates that in the transition states for O-alkylation, the anions adopt an E,Z conformation in addition to the U-shaped Z,Z geometry (depicted in formulae **15**, **18**, **22**).

Experimental[45]

Methyl [((R)-2-allyloxy-3-(4-methoxy-benzyloxy)-propyl] malonate (**32a**).
A solution of methyl (chloroformyl)acetate (**33**, 3.51 ml, 32.73 mmol) and triethylamine (4.54 ml) in CH_2Cl_2 (15 ml) was added to a solution of **31** (4.13 g, 16.37 mmol) in CH_2Cl_2 (155 ml). The mixture was left at 20°C for 15 min. Work-up (H_2O - CH_2Cl_2) and LC (150 g SiO_2, hexanes - ethyl acetate 2:1) gave **32a** (3.92 g, 68%).- $[\alpha]_D^{20}$ = - 8 (c 0.97, $CHCl_3$).- ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.38 (s, 2H, $COCH_2CO$), 3.47-3.54 (m, 2H, CH_2-3), 3.69-3.75 (m, 1H, 2-**H**), 3.72 (s, 3H, $COOCH_3$), 3.79 (s, 3H, OCH_3), 4.08 (m, 2H, CH_2-CH=CH_2, ^3J = 5.5 Hz, ^4J(cis) = ^4J(trans) = 1.5 Hz), 4.18-4.32 (m, 2H, CH_2-1), 4.45 (s, 2H, $ArCH_2O$), 5.16 (m, 1H, CH=CH**H'**, cis, ^3J(cis) = 10.3 Hz), 5.27 (m, 1H, CH=C**H**H', trans, ^3J(trans) = 17 Hz), 5.89 (m, 1H, CH=CH_2), 6.83-6.88 and 7.20-7.26 (4H, aromat. **H**).- IR ($CHCl_3$): 1750, 1730, 1610, 1510, 1435 cm^{-1}.- MS: m/z (%) = 352 (0.1) [M^+], 311 (2), 137 (14), 121 (100), 101 (23), 41 (45). (Found: C, 61.25; H, 6.60. $C_{18}H_{24}O_7$ (352.4) requires C, 61.35; H, 6.87).

Methyl [(R)-2-hydroxy-3-(4-methoxy-benzyloxy)-propyl] malonate (**32b**).
To a solution of **32a** (22.2 mg, 0.063 mmmol) in 1 M NaOAc in 20:1 acetic acid - water (0.7 ml) were added $PdCl_2$ (24 mg, 0.143 mmol) and after 80 min 20:1 acetic acid - water (6.3 ml). The mixture was stirred at 20°C for 19.5 h. Work-up (ethyl acetate - water) followed by MPLC (hexanes - ethyl acetate 2:1) gave **32b** (17.8 mg, 90%).- $[\alpha]_D^{20}$ = - 5 (c 1.00, $CHCl_3$).- ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.79-2.84 (d br., 1H, **OH**), 3.39 (s, 2H, $COCH_2CO$), 3.40-3.50 (m, 2H, CH_2-3), 3.70 (s, 3H, $COOCH_3$), 3.78 (s, 3H, OCH_3), 3.95-4.03 (m, 1H, 2-**H**), 4.14-4.26 (m, 2H, CH_2-1), 4.45 (s, 2H, $ArCH_2O$), 6.82-6.88 and 7.18-7.24 (m, 4H, aromat. **H**).- ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 41.0 ($COCH_2CO$), 52.5 ($COOCH_3$), 55.2 (OCH_3), 66.4 (CH_2-1), 68.4 (CH-2), 70.2 (CH_2-3), 73.0 ($ArCH_2O$), 113.8, 129.4, 129.6, 159.2 (Ar-C's), 166.2 and 167.0 (CO's).- IR ($CHCl_3$): 3415-3720, 1755 (shoulder), 1735, 1509, 1509, 1438 cm^{-1}.- MS: m/z (%) = 312 (4) [M^+], 137 (25), 121 (100).- (Found: C, 57.51; H, 6.51. $C_{15}H_{20}O_7$ (312.3) requires C, 57.69; H, 6.45).

Methyl [(R)-2-methanesulfonyloxy-3-(4-methoxy-benzyloxy)-propyl] malonate (**32c**).
A solution of **32b** (272 mg, 0.87 mmol), methanesulfonyl chloride (102 µl, 1.31 mmol), and triethylamine (183 µl, 1.31 mmol) in CH_2Cl_2 (15 ml) was left at 40°C for 2 h. Work-up (CH_2Cl_2 - water) and LC (hexanes - ethyl acetate 2:1) gave **32c** (277 mg, 81%).- $[\alpha]_D^{20}$ = - 12 (c 0.96, $CHCl_3$).- ^{1}H NMR (80 MHz, $CDCl_3$): δ = 3.02 (s, 3H, SO_2CH_3), 3.40 (s, 2H, $COCH_2CO$), 3.49-3.88 (m, 2H, CH_2-3), 3.73 (s, 3H, $COOCH_3$), 3.80 (s, 3H, OCH_3), 4.24-4.47 (m, 2H, CH_2-1), 4.47 (s, 2H, $ArCH_2O$), 4.77-5.10 (m, 1H, 2-**H**), 6.75-7.35 (4H, aromat. **H**).- IR ($CHCl_3$): 1750 (shoulder), 1737, 1605, 1505, 1435, 1355, 1245, 1173, 1030 cm^{-1}.- $C_{16}H_{22}O_9S$ (390.1), MS: mz (%) = 390.0985 (3, Calc 390.0997), 121 (100), 101 (71), 59 (69).

Methyl [(R)-3-(4-methoxy-benzyloxy)-2-(4-toluenesulfonyloxy)-propyl] malonate (**32d**).
A solution of **32b** (19 mg, 0.06 mmol), 4-toluenesulfonic acid (23 mg, 0.12 mmol), and triethylamine (18 µl, 0.12 mmol) in CH_2Cl_2 (0.5 ml) was stirred

at 20°C for 2.25 h and at 50°C for 3.75 h. Work-up (CH_2Cl_2 - water) and LC (3 g SiO_2, hexanes - ethyl acetate 2:1) gave **32d** (12 mg, 44%), 5 mg of **32b** were recovered.- $[\alpha]_D^{20}$ = - 10 (c 0.75, $CHCl_3$).- ^1H NMR (80 MHz, $CDCl_3$): δ = 2.42 (s, 3H, Ts-CH_3), 3.15-3.92 (m, 4H, CH_2-3 and $COCH_2CO$), 3.72 (s, 3H, $COOCH_3$), 3.80 (s, 3H, OCH_3), 3.97-4.52 (m, 4H, CH_2-1 and $ArCH_2O$), 4.95-5.32 (m, 1H, 2-H), 6.72-7.95 (8H, aromat. H).- IR ($CHCl_3$): 1750-1730, 1610, 1508, 1363, 1170 cm^{-1}.- MS: m/z (%) = 466 (0.25) [M^+], 136 (35), 121 (100), 59 (54).- (Found: C, 56.48; H, 5.71. $C_{22}H_{26}O_9S$ (466.5) requires C, 56.64; H, 5.62).

Methyl [2-iodo-3-(4-methoxy-benzyloxy)-propyl] malonate (**32e**).
A solution of **32b** (150 mg, 0.48 mmol), triphenylphosphine (189 mg, 0.72 mmol), imidazole (98 mg, 1.44 mmol), and iodine (183 mg, 0.72 mmol) in THF (3.5 ml) was stirred at 0°C for 15 min and at 20°C for 6 h. Work-up (diethylether - 10% aq. $Na_2S_2O_3$) and LC (16 g SiO_2, hexanes - ethyl acetate 5:2) gave **32e** (120 mg, 72%, based on consumed **32b**). 26 mg **32b** were recovered.- $[\alpha]_D^{20}$ = + 3 (c 1.00, $CHCl_3$).- ^1H NMR (80 MHz, $CDCl_3$): δ = 3.30-3,84 (m, 6H, $COCH_2CO$, CH_2-1 and CH_2-3), 3.73 (s, 3H, $COOCH_3$), 3.80 (s, 3H, OCH_3), 4.37-4.52 (m, 2H, $ArCH_2O$), 4.78-5.12 (m, 1H, 2-H), 6.72-6.98 and 7.14-7.35 (4H, aromat. H).- MS: m/z (%) = 422 (2) [M^+], 121 (100).- (Found: C, 42.58; H, 4.61. $C_{15}H_{19}IO_6$ (422.2) requires C, 42.67; H, 4.54).

Methyl (2-hydroxy-ethyl) malonate (**34a**).
34a was prepared from ethylene glycol and **33** as described for **32a**.- ^1H NMR (80 MHz, $CDCl_3$): δ = 1.84-2.46 (s br., 1H, OH), 3.41 (s, 2H, $COCH_2CO$), 3.74 (s, 3H, $COOCH_3$), 3.76-3.90 (m, 2H, CH_2OH), 4.18-4.39 (m, 2H, $COOCH_2$).- IR ($CHCl_3$): 3640-3240, 1735 cm^{-1}.- MS: m/z (%) = 145 (10) [M-OH^+], 101 (100), 59 (36).- (Found: C, 44.41; H, 6.17. $C_6H_{10}O_5$ (162.1) requires C, 44.44; H, 6.21).

Methyl (2-methanesulfonyloxy-ethyl) malonate (**34b**).
34b was prepared from **34a** as described for **32c**.- ^1H NMR (80 MHz, $CDCl_3$): δ = 3.02 (s, 3H, SO_2CH_3), 3.40 (s, 2H, $COCH_2CO$), 3.72 (s, 3H, $COOCH_3$), 4.40 (s, 4H, OCH_2CH_2O).- IR ($CHCl_3$): 1760, 1740, 1360, 1340, 1170 cm^{-1}.- MS: m/z (%) = 240 (0.2) [M^+], 209 (1), 101 (100), 59 (45).- (Found: C, 34.96; H, 5.00. $C_7H_{12}O_7S$ (240.2) requires C, 35.00; H, 5.03).

Methyl [2-(4-toluenesulfonyloxy)-ethyl] malonate (**34c**).
34c was prepared from **34a** as described for **32d**.- ^1H NMR (60 MHz, $CDCl_3$): δ = 2.53 (s, 3H, $PhCH_3$), 3.39 (s, 2H, $COCH_2CO$), 3.75 (s, 3H, $COOCH_3$), 4.18-4.44 (m, 4H, OCH_2CH_2O), 7.13-7.44 and 7.60-7.87 (4H, aromat. H).- IR (CCl_4): 1762, 1748, 1376, 1178 cm^{-1}.- MS: m/z (%) = 316 (0.6) [M^+], 145 (22), 101 (100), 91 (34), 59 (74).- (Found: C, 49.35; H, 5.03. $C_{13}H_{16}O_7S$ (316.3) requires C, 49.36; H, 5.10).

Methyl (2-iodo-ethyl) malonate (**34d**).
34d was prepared from **34a** as described for **32e**.- ^1H NMR (80 MHz, $CDCl_3$): δ = 3.28 (t, J = 6 Hz, 2H, CH_2I), 3.39 (s, 2H, $COCH_2CO$), 3.74 (s, 3H, $COOCH_3$), 4.38 (t, 2H, $COOCH_2$).- IR (CCl_4): 1764, 1749, 1145 cm^{-1}.- MS: m/z (%) = 272 (1.6) [M^+], 241 (6), 155 (54), 145 (100), 127 (7), 103 (31), 101 (32), 59 (53).- (Found: C, 26.78; H, 3.35. $C_6H_9IO_4$ (272.0) requires C, 26.49; H, 3.34).

Methyl (2-chloro-ethyl) malonate (**34e**).
34e was prepared from 2-chloroethanol and **33**[48] as described for **32a**.- ^1H NMR (60 MHz, $CDCl_3$): δ = 3.46 (s, 2H, $COCH_2CO$), 3.71 (t, J = 6 Hz, 2H, CH_2Cl), 3.80 (s, 3H, $COOCH_3$), 4.42 (t, 2H, $COOCH_2$).- IR (CCl_4): 1762, 1745, 1190 cm^{-1}.- MS: m/z (%) = 145 (14) [M-Cl^+], 131 (15), 119 (17), 101 (100), 59 (38).- (Found: C, 39.86; H, 5.18. $C_6H_9ClO_4$ (180.6) requires C, 39.91; H, 5.02).

Ethyl (2-chloro-ethyl) malonate (20).[18]
20 was prepared from 2-chloroethanol and ethyl (chloroformyl)acetate as described for **32a**.- ^{1}H NMR (60 MHz, $CDCl_3$): δ = 1.36 (t, J = 7 Hz, 3H, CH_2CH_3), 3.41 (s, 2H, $COCH_2CO$), 3.51-3.93 (m, 2H, CH_2Cl), 3.93-4.58 (m, 4H, $COOCH_2$).

2-Hydroxy-ethyl acetoacetate (36a).[46]
36a (obtained as a mixture of keto and enol form) was prepared from ethyl acetoacetate and ethylene glycol as described by Jones et al.[25] - ^{1}H NMR (80 MHz, $CDCl_3$): δ = 1.94 (s, 0.27H, C=CCH_3, cis), 2.10-2.50 (s br., 1H, OH), 2.25 (s, 2.73H, $COCH_3$), 3.49 (s, 1.82H, $COCH_2CO$), 3.65-3.93 (m, 2H, CH_2OH), 4.16-4.37 (m, 2H, $COOCH_2$), 5.00 (s, 0.09H, C=CH).- IR (CCl_4): 3655-3480, 1750, 1724, 1656, 1630, 1157 cm^{-1}.- $C_6H_{10}O_4$ (146.1), MS: m/z (%) = 146 (1.7) [M$^+$], 116 (15), 103 (13), 85 (58), 43 (100).

2-Methanesulfonyloxy-ethyl acetoacetate (36b).
36b (obtained as a mixture of keto and enol form) was prepared from **36a** as described for **32c**.- ^{1}H NMR (80 MHz, $CDCl_3$): δ = 1.95 (s, 0.3H, C=CCH_3, cis), 2.24 (s, 2.7H, $COCH_3$), 3.02 (s, 3H, SO_2CH_3), 3.49 (s, 1.8H, $COCH_2CO$), 4.39 (s, 4H, OCH_2CH_2O), 5.00 (s, 0.1H, C=CH), 11.78 (s, 0.1H, C=COH).- IR ($CHCl_3$): 1750, 1720, 1177 cm^{-1}.- MS: m/z (%) = 224 (3) [M$^+$], 85 (16), 79 (7), 43 (100).- (Found: C, 37.50; H, 5.36. $C_7H_{12}O_6S$ (224.2) requires C, 37.50; H, 5.39).

2-(4-Toluenesulfonyloxy)-ethyl acetoacetate (36c).
36c (obtained as a mixture of keto and enol form) was prepared from **36a** as described for **32d**.- ^{1}H NMR (80 MHz, $CDCl_3$): δ = 1.94 (s, 0.3H, C=CCH_3, cis), 2.21 (s, 2.7H, $COCH_3$), 2.41 (s, 3H, $PhCH_3$), 3.40 (s, 1.8H, $COCH_2CO$), 4.10-4.45 (m, 4H, OCH_2CH_2O), 4.90 (s, 0.1H, C=CH), 7.20-7.45 and 7.67-7.90 (4H, aromat. H), 11.73 (s, 0.1H, C=COH).- IR ($CHCl_3$): 1753, 1725, 1604, 1178 cm^{-1}.- MS: m/z (%) = 300 (0.6) [M$^+$], 129 (28), 91 (32), 85 (31), 43 (100).- (Found: C, 51.97; H, 5.47. $C_{13}H_{16}O_6S$ (300.3) requires C, 51.99; H, 5.37).

2-Iodo-ethyl acetoacetate (36d).
36d (obtained as a mixture of keto and enol form) was prepared from **36a** as described for **32e**.- ^{1}H NMR (80 MHz, $CDCl_3$): δ = 1.94 (s, 0.33H, C=CCH_3, cis), 2.27 (s, 2.67H, $COCH_3$), 3.29 (t, J = 7 Hz, 2H, CH_2I), 3.46 (s, 1.78H, $COCH_2CO$), 4.39 (t, 2H, $COOCH_2$), 5.00 (s, 0.22H, C=CH).- MS: m/z (%) = 256 (4) [M$^+$], 155 (97), 129 (100), 87 (29), 85 (23), 43 (76).- (Found: C, 28.29; H, 3.60. $C_6H_9IO_3$ (256.0) requires C, 28.15; H, 3.54).

2-Chloro-ethyl acetoacetate (36e)
36e was prepared from ethyl acetoacetate and 2-chloroethanol using the procedure described by Jones et al.[25] - ^{1}H NMR (60 MHz, $CDCl_3$): δ = 2.37 (s, 3H, $COCH_3$), 3.55 (s, 2H, $COCH_2CO$), 3.73 (t, J = 8 Hz, 2H, CH_2Cl), 4.45 (t, 2H, $COOCH_2$).- IR ($CHCl_3$): 1750, 1725, 1661, 1635, 1155 cm^{-1}.- $C_6H_9ClO_3$ (164.4), MS: m/z (%) = 166, 164 (0.2, 0.7) [M$^+$], 85 (10), 63 (8), 43 (100).

Formation of silyl enol ethers 37/38 (a-d).[26]
Trimethylsilyl chloride (38 µl, 0.27 mmol) and triethylamine (42 µl, 0.3 mmol) were added to a solution of **36e** (25 mg, 0.15 mmol) in ether (450 µl) and the mixture was left at 20°C for 1 h. After filtration and solvent evaporation (by passing argon over the surface) the product was analyzed by NMR.- **36b-d** were converted into the corresponding silyl enol ethers using the same procedure.

2-Methanesulfonyloxy-ethyl (≡)-3-trimethylsilyloxy-but-2-enoate (37a/38a).
^{1}H NMR (400 MHz, NOE, benzene d_6): Ratio **37a/38a** 1:5.0 (from integration of the olefinic proton signals in the spectrum of the mixture).- **37a**: δ =

0.21 (s, 9H, $Si(CH_3)_3$), 1.46 (s br., 3H, $C=CCH_3$), 2.19 (s, 3H, SO_2CH_3), 3.86-4.00 (m, 4H, OCH_2CH_2O), 5.10 (m, 1H, C=CH). NOE: Irradiation at δ = 5.10: signal at δ = 1.46.- **38a**: δ = 0.01 (s, 9H, $Si(CH_3)_3$), 2.19 (s, 3H, SO_2CH_3), 2.34 (m, 3H, $C=CCH_3$), 3.86-4.00 (m, 4H, OCH_2CH_2O), 5.35 (s, 1H, C=CH).

2-(4-Toluenesulfonyloxy)-ethyl (≡)-3-trimethylsilyloxy-but-2-enoate (37b/38b).
^1H NMR (400 MHz, NOE, benzene d_6): Ratio **37b/38b** 1:10.6 (from integration of the olefinic proton signals in the spectrum of the mixture).- **37b**: δ = 0.21 (s, 9H, $Si(CH_3)_3$), 1.44 (s br., 3H, $C=CCH_3$), 1.82 (s br., 3H, $PhCH_3$), 3.82-3.98 (m, 4H, OCH_2CH_2O), 5.01 (s br., 1H, C=CH), 6.61-6.75 and 7.62-7.72 (4H, aromat. H).- **38b**: δ = 0.01 (s, 9H, $Si(CH_3)_3$), 1.82 (s br., 3H, $PhCH_3$), 2.30 (s, 3H, $C=CCH_3$), 3.82-3.98 (m, 4H, OCH_2CH_2O), 5.29 (s br., 1H, C=CH), 6.61-6-75 and 7.62-7.72 (4H, aromat. H). NOE: Irradiation at δ = 0.01: signal at δ = 5.29.

2-Iodo-ethyl (≡)-3-trimethylsilyloxy-but-2-enoate (37c/38c).
^1H NMR (400 MHz, NOE, benzene d_6): Ratio **37c/38c** 1:6.6 (from integration of the olefinic proton signals in the spectrum of the mixture).- **37c**: δ = 0.22 (s, 9H, $Si(CH_3)_3$), 1.45 (d, LRC J < 1 Hz, 3H, $C=CCH_3$), 2.77 (t, J = 6.5 Hz, 2H, CH_2I), 4.03 (t, 2H, $COOCH_2$), 5.12 (m, LRC J < 1 Hz, 1H, C=CH). NOE: irradiation at δ = 5.12: signal at δ = 1.45.- **38c**: δ = 0.01 (s, 9H, $Si(CH_3)_3$), 2.35 (d, LRC J < 1 Hz, 3H, $C=CCH_3$), 2.78 (t, J = 6.7 Hz, 2H, CH_2I), 4.07 (t, 2H, $COOCH_2$), 5.39 (m, LRC J < 1 Hz, 1H, C=CH).

2-Chloro-ethyl (≡)-3-trimethylsilyloxy-but-2-enoate (37d/38d).
^1H NMR (400 MHz, NOE, benzene d_6): Ratio **37d/38d** = 1:3.2 (from integration of the olefinic proton signals in the spectrum of the mixture).- **37d**: δ = 0.22 (s, 9H, $Si(CH_3)_3$), 1.45 (d, LRC J < 1 Hz, 3H, $C=CCH_3$), 3.09-3.15 (m, 2H, CH_2Cl), 3.98-4.02 (m, 2H $COOCH_2$), 5.12 (m, LRC J < 1 Hz, 1H, C=CH). NOE: irradiation at δ = 5.12: signal at δ = 1.45. **38d**: δ = 0.01 (s, 9H, $Si(CH_3)_3$), 2.36 (d, LRC J < 1 Hz, 3H, $C=CCH_3$), 3.12-3.17 (m, 2H, CH_2Cl), 4.02-4.07 (m, 2H, $COOCH_2$), 5.41 (m, LRC J < 1 Hz, 1H, C=CH).

p-Methoxybenzyl trichloroacetimidate.

At 0°C NaH (55% suspension in oil, 4 mg, 0.100 mmol) was added to a solution of p-methoxybenzyl alcohol (68 mg, 0.495 mmol) in ether (2 ml). After 5 min trichloroacetonitrile (50 µl, 0.495 mmol) was added, and the mixture was stirred at 0°C for 50 min, at 0°C --> 20°C for 2h, and at 20°C for 1 h. Solvent evaporation and LC (10 g SiO_2, hexanes - ethyl acetate 5:1) gave the trichloroactimidate (57 mg, 41%) .- ^1H NMR (60 MHz, $CDCl_3$): δ = 3.31 (s, 3H, OCH_3), 4.76 (s, 2H, CH_2O), 6.18-6.51 and 6.63-6.99 (4H, aromat. H), 7.60-8.03 (s br., 1H, C=NH).- IR (CCl_4): 3340, 1655, 1605, 1502 cm^{-1}.- $C_{10}H_{10}Cl_3NO_2$ (282.6).

4-(4-Methoxy-benzyloxy-methyl)-tetrahydrofuran-2-one (39b).
A solution of p-methoxybenzyl trichloroacetimidate (380 mg, 1.34 mmol), crude **39a** (prepared from diethyl 2-formyl succinate as described by Ishida,[29] 139 mg), and p-toluenesulfonic acid (38 mg, 0.22 mmol) in CH_2Cl_2 (20 ml) was stirred at 20°C for 23.5 h. Work-up (CH_2Cl_2 - saturated aq. $NaHCO_3$) and LC (44 g SiO_2, hexanes - ethyl acetate 3:1) gave **39b** (121 mg, 26%, based on diethyl 2-formylsuccinate).- ^1H NMR (80 MHz, $CDCl_3$): δ = 2.30-2.58 (m, 2H, CH_2-3), 2.65-3.00 (m, 1H, CH-4), 3.34-3.49 (m, 2H, OCH_2CH), 3.78 (s, 3H, OCH_3), 3.98-4.50 (m, 2H, CH_2-5), 4.43 (s, 2H, $ArCH_2O$), 6.74-6.98 and 7.10-7.32 (4H, aromat. H).- IR (CCl_4): 1775, 1610, 1510 cm^{-1}.- $C_{13}H_{16}O_4$ (236.1), MS: m/z (%) = 236.1050 (10, Calc 236.1049) [M^+], 235 (5), 121 (100), 44 (38).

Methyl 4-(4-methoxy-benzyloxy-methyl)-2-oxo-tetrahydrofuran-3-carboxylate (**40**).
A mixture of dimethyl carbonate (215 µl, 2.54 mmol), NaH (55% suspension in oil, 28 mg, 0.64 mmol) and **39b** (75 mg, 0.317 mmol) in benzene (400 µl) was stirred at 80°C for 5 h. 1:3 acetic acid - water (2 ml) was added at 0°C. Work-up (benzene - brine) and LC (9 g SiO_2, hexanes - ethyl acetate 3:1) gave **40** (34 mg, 37%).- ^{1}H NMR (400 MHz, benzene d_6 - $CDCl_3$ 1:1): δ = 2.79-2.89 (m, 1H, CH-4), 2.99 and 3.02 (AB part of an ABX system, OCH_2CH-4, J_{AB} = 9.6 Hz, $J_{4,A}$ = 6.7 Hz, $J_{4,B}$ = 7.6 Hz), 3.23 (d, 1H, CH-3, $J_{3,4}$ = 8 Hz), 3.42 (s, 3H, $COOCH_3$), 3.45 (s, 3H, OCH_3), 3.62 (5-H), 3.98 (5-H', $J_{5,5'}$ = 8.9 Hz, $J_{4,5}$ = 7.4 Hz, $J_{4,5'}$ = 8.5 Hz), 4.11 (s, 2H, $ArCH_2O$), 6.68-6.74 and 6.97-7.01 (4H, aromat. H).- ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 39.9 and 48.7 (CH-3 and CH-4), 53.1 ($COOCH_3$), 55.2 (OCH_3), 67.9 (CH_2-5), 69.3 (OCH_2CH), 72.9 ($ArCH_2O$), 113.8, 129.3, 129.4, 159.4 (Ar-C's), 167.8 and 171.6 (CO's).- IR (CCl_4): 1790, 1740, 1609, 1505 cm^{-1}. $C_{15}H_{18}O_6$ (294.1), MS: m/z (%) = 294.1104 (6, Calc 294.1104) [M$^+$], 143 (30), 121 (100).

Reaction of **32c-32d** with DBU.
A: A solution of **32c** (58 mg, 0.149 mmol) and DBU (22 µl, 0.159 mmol) in benzene (5.8 ml) was stirred at 60°C for 9 h, at 20°C for 14 h and at 60°C for 3.75 h. Filtration through Florisil, solvent evaporation and HPLC (hexanes - tert-butyl methyl ether (^{t}BuOMe) - 2-propanol - NEt_3 10:20:2:0.03) gave **32c** (9 mg, 16%), **42a** (16 mg, 36%), and **42b** (10 mg, 23%).
B: A mixture of the malonate (**32c-32d**, 4.3 µmol), DBU (4.3 µmol) in benzene (0.5 ml) was stirred at 20°C for 3 d and at 55°C for 1 h. TLC (hexanes - ^{t}BuOMe - 2-propanol - NEt_3 10:20:2:0.03) demonstrated the formation of **42a** (R_f = 0.20) and **42b** (R_f = 0.17).

ent-**32b** from **32c**.
32c was treated with DBU as described above. After slow LC (SiO_2, hexanes - ethyl acetate 2:1) only ent-**32b** was isolated. $[\alpha]_D^{20}$ = + 4 (c 0.45, $CHCl_3$).

Reaction of **32c-32e** with NaH.
A solution of **32c** (2 mg, 5.1 µmol) in a) DMPU, b) DMF, c) THF, d) CH_2Cl_2 (50 µl) was added to a suspension of NaH (1 mg, ca. 20 µmol) in the same solvent (150 µl). The reaction mixture was stirred at 20°C for 5.5 h. **32d-32e** were cyclized using the same procedure. In all cases TLC (hexanes - ethylacetate 2:3) showed only the ketene acetals **42a** und **42b** (R_f 0.18) and the educts (R_f(**32c**) 0.42, R_f(**32d**) 0.58, R_f(**32e**) 0.68).

Reaction of **32c-32e** with Bu_4NF.
A solution of **32c** (1 mg, 2.6 µmol) and Bu_4NF (2.6 µmol) in 100 µl THF was stirred at 20°C for 6 h. TLC (hexanes - ^{t}BuOMe- 2-propanol - NEt_3 10:20:2:0.03) showed **32c** (R_f 0.49), **42a** (R_f 0.20), **42b** (R_f 0.17), (ent-) **32b** (R_f 0.47). **32d-32e** were cyclized using the same procedure. TLC (hexanes - ethylacetate 2:3) showed **32d** (R_f 0.58) and **32e** (R_f 0.68), respectively, **42a/b** (R_f 0.18), and (ent-) **32b** (R_f 0.24).

Reaction of **32c-32e** with K_2CO_3.
A solution of K_2CO_3 (30 mg, 20.4 mmol) in a) DMSO, b) acetone (200 µl) was added to a solution of **32c-32e** (5.1 µmol) in the solvents indicated above (100 µl). The reaction mixture was stirred at 20°C (for 5.5 h in DMSO, and 20 h in the acetone experiments). After solvent evaporation (stream of argon) the residue was hydrolyzed with SiO_2 (short SiO_2 column). Hydrolysis product (ent-) **32b** was identified besides the educts by analytical HPLC (hexanes - ^{t}BuOMe - 2-propanol 5:10:0.6, 1ml/min). Retention times [min]: **32b**: 7.74, **32c**: 6.27, **32d**: 4.75, **32e**: 4.55.

Mitsunobu reaction of **32c**.
A solution of diethyl azodicarboxylate (17 µl, 0.111 mmol), triphenylphosphine (30 mg, 0.111 mmol) and **32c** (23 mg, 0.074 mmol) in THF (0.7 ml) was stirred at 20°C for 130 min. After solvent removal HPLC (hexanes - ^{t}BuOMe - 2-propanol - NEt_3 10:20:2:0.03) indicated the presence of **42a** and **42b** and of two unidentified products (TLC (hexanes - ^{t}BuOMe - 2-propanol - NEt_3 10:20:2:0.03, 2x), R_f values 0.16 and 0.13).

Methyl [(4S)-4-(4-methoxy-benzyloxy-methyl)-[1,3]dioxolan-2-yliden]-acetate, isomers **42a** und **42b**.
42a: ^{1}H NMR (400 MHz, C,H COSY, benzene d_6): δ = 3.01 and 3.19 (AB part of a five-spin system, OCH_2CH-4, J_{AB} = 11.1 Hz, $J_{4,A}$ = 4.0 Hz, $J_{4,B}$ = 4.0 Hz), 3.33 (s, 3H, OCH_3), 3.53 (s, 3H, $COOCH_3$), 3.46 (5-H), 3.64 (5-H', $J_{5,5'}$ = 8.1 Hz, $J_{4,5}$ = 7.8 Hz, $J_{4,5'}$ = 6.2 Hz), 4.13-4.27 (m, 3H, CH-4 and $ArCH_2O$), 4.87 (s, 1H, C=CH), 6.75-6.80 and 7.09-7.14 (4H, aromat. H).- ^{13}C NMR (100.6 MHz, benzene d_6): δ = 50.0 ($COOCH_3$), 54.5 (OCH_3), 66.6 (CH_2-5), 67.0 (C=CH), 67.5 (OCH_2CH), 72.9 ($ArCH_2O$), 78.6 (CH-4), 113.8, 129.4, 129.5, 159.6 (Ar-C's), 166.6 (CO), 169.3 (C-2).- INEPT (400 MHz, benzene d_6): irradiation at δ = 4.20 (4-H): 169.3 (C-2), other signals: 67.7, 72.8, 78.9, 129.4, 129.7; irradiation at δ = 3.64 (5-H'): 169.3 (C-2), other signals: 66.7, 67.7, 78.9, 166.7.- IR (CCl_4): 1710, 1640, 1510, 1435, 1120 cm^{-1}.- $C_{15}H_{18}O_6$ (294.1).
42b: ^{1}H NMR (400MHz, C,H COSY, benzene d_6): δ = 2.82 and 2.88 (AB part of a five-spin system, OCH_2CH-4, J_{AB} = 9.8 Hz), 3.29 (s, 3H, OCH_3), 3.56 (s, 3H, $COOCH_3$), 3.52 (5-H), 3.66 (5-H', $J_{5,5'}$ = 8.3 Hz, $J_{4,5}$ = 8.1 Hz, $J_{4,5'}$ = 6.4 Hz), 3.72-3.80 (m, 1H, 4-H), 4.08 and 4.10 ($ArCH_2O$, AB system, J_{AB} = 13 Hz), 4.95 (s, 1H, 6-H), 6.74-6.79 and 7.00-7.07 (4H, aromat. H).- ^{13}C NMR (100.6 MHz, benzene d_6 - $CDCl_3$): δ = 50.4 ($COOCH_3$), 54.9 (OCH_3), 67.3 (C=CH), 68.0 (OCH_2CH), 69.4 (CH_2-5), 73.2 ($ArCH_2O$), 76.5 (CH-4), 114.1, 129.6, 159.9 (Ar-C's), 167.6 (CO), 169.4 (C-2).- INEPT (100.6 MHz, benzene d_6): irradiation at δ = 3.78 (4-H): 169.5 (C-2), additional signals: 54.8, 69.1, 166.9; irradiation at δ = 3.65 (5-H'): 169.5 (C-2) additional signals: 50.2, 69.1, 73.1, 129.8.- IR (CCl_4): 1710, 1642, 1610, 1510, 1438, 1120 cm^{-1}.- $C_{15}H_{18}O_6$ (294.1).

Reaction of **34b-34d** with DBU.
Conditions as described above (20°C, 7 h). **24b** was isolated by HPLC (hexanes - ^{t}BuOMe - 2-propanol 5:10:1.5, 10 ml/min). Yields: 96% (from **34b**), 81% (from **34c**), and 78% (from **34d**).

Methyl ([1,3]-dioxolan-2-yliden)-acetate (**24b**).
^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.63 (s, 3H, $COOCH_3$), 4.32-4.38 and 4.52-4.58 (m, 4H, OCH_2CH_2O), 4.50 (s, 1H, C=CH).- ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 50.6 ($COOCH_3$), 65.6 and 67.9 (CH_2-4 and CH_2-5), 67.2 (C=CH), 167.6 (CO), 169.0 (C-2).- IR (CCl_4): 1715, 1660 cm^{-1}.- $C_6H_8O_4$ (144.1).

Reaction of **34b-d** with Bu_4NF.
Conditions as described above (20°C, 4 h). TLC ($CHCl_3$ - 2-propanol 20:1) showed the presence of the respective educt **34b** (R_f 0.46), **34c** (R_f 0.67), **34d** (R_f 0.49), and of **24b** (R_f 0.40), and a small amount of a UV-active compound (R_f 0.32).

Reaction of **34b-34c** with NaH.
Conditions as described above (0°C, 3h; 20°C 3 h). TLC ($CHCl_3$ - 2-propanol 20:1) showed the presence of **24b**, a UV-active compound and in the case of **34b** also the educt. In the IR spectra of the reaction mixtures ($CHCl_3$) no lactone band was present.

Reaction of **34b-d** with K_2CO_3.
Conditions as described above (solvents a) DMSO, b) acetone, 20°C, 3 h). In all experiments TLC ($CHCl_3$ - 2-propanol 20:1) showed only the presence

of ketene acetal **24a** (R_f 0.40) and of hydrolysis product **34a** (R_f 0.24). In the IR spectra ($CHCl_3$) no lactone band was found.

Reaction of **20** with NaH.
20 (194 mg, 1.0 mmol) was added to a suspension of NaH (24 mg, 1.0 mmol) in benzene (5 ml). After being left at 20°C for 25 min the reaction mixture was refluxed for 24 h. The salts were removed by filtration through Florisil. HPLC (hexanes - ^{t}BuOMe - 2-propanol - NEt_3 10:20:3:0.03, 10 ml/min) gave **24a** (131 mg, 83%).

Ethyl ([1,3]-dioxolan-2-yliden)-acetate (**24a**).[20]
^{1}H NMR (400 MHz, C,H COSY, $CDCl_3$): δ = 1.12 (t, J = 7 Hz, 3H, CH_3), 3.99 (q, 2H, CH_2CH_3), 4.25-4.33 and 4.43-4.51 (m, 4H, CH_2-4 and CH_2-5), 4.40 (s, 1H, C=CH).- ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 14.2 (CH_3), 58.8 (CH_2CH_3), 65.5 and 67.8 (CH_2-4 and CH_2-5), 67.1 (C=CH), 167.0 (CO), 168.8 (C-2).- IR (CCl_4): 1710, 1645 cm^{-1}.- $C_7H_{10}O_4$ (158.2).

Reaction of **20** and **34e** with Na.[18]
Conditions as described by Michael and Weiner.[18] TLC (hexanes - ethyl acetate 2:3) of the cyclization mixture of **20** showed only the presence of ketene acetal **24a** (R_f 0.13) and educt **20** (R_f 0.54). In the case of **34e** TLC (hexanes - ethyl acetate 2:3) of the cyclization mixture indicated **24b** (R_f 0.10) and **34e** (R_f 0.50).

[1,3]-Dioxolan-2-yliden-acetone (**48**).[20]
A reference sample was prepared from **36e** with NaH in THF (20°C, 23 h) showing the following properties: TLC (hexanes - ethyl acetate 1:2, R_f 0.03), ^{1}H NMR (80 MHz, benzene d_6): δ = 2.25 (s, 3H, $COCH_3$), 2.90-3.23 (m, 4H, OCH_2CH_2O), 5.14 (s, 1H, C=CH). The spectrum showed also the signals of **36a**.- IR ($CHCl_3$): 1715, 1649, 1621, 1582, 1161 cm^{-1}.

Reaction of **37/38** (a-d) with Bu_4NF.
37a/38a (27 mg, 0.11 mmol), 1 M Bu_4NF-THF solution (258 µl, 0.26 mmol), and 100 µl THF were stirred 20°C for 1.5 h. TLC (hexanes - ethyl acetate 1:2) showed only the presence of ketene acetal **48** (R_f 0.03). 10 ml $CHCl_3$ and 400 mg SiO_2 were added to the reaction mixture. After solvent evaporation the residue was placed on top of an SiO_2 column (4 g). Elution with hexanes - ethyl acetate 1:1) gave **36b** (7 mg) and **36a** (14 mg, 94% corrected for recovered **36b**).
37b/38b, **37c/38c**, and **37d/38d** were treated in the same way and furnished **36a** in 81%, 89%, and 85% yield.

Ethyl 5-chlormethyl-2-oxo-tetrahydrofuran-3-carboxylate (**25**).[18,47]
25 was prepared as described by Traube and Lehmann[47] from diethyl malonate and epichlorohydrin. A 1.1:0.9 mixture of stereoisomers (configuration not determined) was isolated.- ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26-1.32 (2 t, J = 7 Hz and 7.2 Hz, 6H, 2 CH_3 groups), 2.35-2.45 (m, 1.1H, CHH'-4), 2.49-2.68 (m, 1.8H, CH_2-4), 2.72-2.82 (m, 1.1H, CHH'-4), 3.60-3.80 (m, 6H, 3-H and CH_2Cl), 4.232 (q, 2H, OCH_2-8, J_{AB} = 7.0 Hz), 4.242 (q, J = 7.2 Hz, 1H, CHH'-CH_3), 4.245 (q, J = 7.2 Hz, 1H, CHH'-CH_3), 4.61-4.70 (m, 0.9H, 5-H), 4.87-4.95 (m, 1.1H, 5-H).- ^{13}C NMR (100.6 MHz, DEPT, $CDCl_3$): δ = 13.8 (CH_2-CH_3), 28.7 and 29.1 (CH_2Cl), 44.7 and 46.0 (CH_2-4), 46.4 and 46.5 (CH-3), 62.18 and 62.24 (CH_2CH_3), 77.1 (CH-5), 167.2 and 167.4 (CO, ester), 170.8 and 171.1 (C-2).- IR (CCl_4): 1790, 1735 cm^{-1}.- MS: m/z (%) = 208, 206 (0.6, 1.6) [M$^+$], 157 (45), 129 (49), 111 (27), 99 (75), 85 (32), 55 (100).

Ethyl 2-oxo-3-oxa-bicyclo[3.1.0]hexan-1-carboxylate (**45**).
25 was treated with NaOEt as described at Michael and Weiner.[18]- ^{1}H NMR (400 MHz, H,H COSY, $CDCl_3$):[48] δ = 1.28 (t, J = 7.3 Hz, 3H, CH_3), 1.34 and 2.04 (AB part of an ABX system, CH_2-6, $J_{6,6'}$ = 5.1 Hz, $J_{5,6}$ = 5.2 Hz,

$J_{5,6'}$ = 8.0 Hz), 2.65-2.73 (m, 1H, 5-H), 4.16 and 4.33 (AB part of an ABX system, CH_2-4, $J_{4,4'}$ = 9.5 Hz, $J_{5,4}$ < 1Hz, $J_{5,4'}$ = 4.9 Hz), 4.22 (q, 1H, CHH'-CH_3), 4.23 (q, 1H, CHH'-CH_3).- ^{13}C NMR (100.6 MHz, C,H COSY, DEPT, $CDCl_3$): δ = 14.0 (CH_3), 20.7 (CH_2Cl), 27.9 (CH-5), 29.3 (C-1), 61.9 (CH_2CH_3), 66.9 (CH_2-4), 166.6 (CO, ester), 170.5 (C-2).- IR ($CHCl_3$): 1780, 1721 cm^{-1}.- MS: m/z (%) = 170 (5) [M^+], 143 (100), 125 (76), 83 (50), 53 (60).- $C_8H_{10}O_4$ (170.2).

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