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Ozonolysis of Enol Ethers, Part 10[1]: A Mechanistic Study of the Regioselectivity of Ozone Oxygen Distribution During Ozonolysis of Exocyclic 2-Alkoxy-alkylidene 1-Mono- and 1,3-Dicarbonyl Compounds

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Abstract

Enol Ethers bearing one or two *ester* carbonyl groups as acceptor substituent(s) at β–carbon yield ozonides during ozonations in inert solvents whereas those bearing one or two *ketone* carbonyl groups suffer Baeyer-Villiger related rearrangements with formation of carboxylic acid derivatives. It is assumed that in both cases enol ether C,C double bonds are cleaved in a way that ether substituted α-carbon accepts one ozone oxygen and acceptor substituted β-carbon accepts two ozone oxygens. An alternative mechanistic proposal attempts to avoid permanent contradictory statements on the regioselectivety of peroxidised olefinic enol ether carbons.

Introduction

After application of enol ether ozonolysis as a synthetic method in preparing α-oxo sulfonyl compounds[2] or unsolvated *vic*. tricarbonyl compound oxo Meldrum's Acid[3] by us, also other groups recognised the value of this method and applied it in manifold variations[4]. However, it is very unsactisfactory from a mechanistic point of view that regioselectivity of oxygen distribution of three ozone oxygens to the two olefinic carbons is explained by arranging the -I effect of the ether substituent over its +M effect[5], because otherwise the preparative results would not accord to the predictions of classical alkene ozonolysis scheme[6] (Scheme 1).

Scheme 1: General prediction of the direction of carbonyl oxide generation depending on substitution of unsymmetric C,C-double bonds
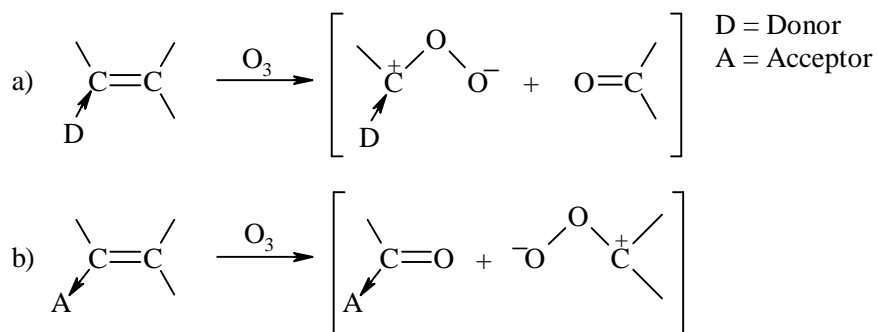
D = Donor
A = Acceptor

Classification of an ether substituent at sp^3 carbon as an acceptor instead of a donor contradicts to known reactivity of α-halogen ethers vs. alkyl halides and of acetals vs. ethers. Beyond that W.H. Bunnelle[7] reported on a generation of ester oxides in the ozonolysis of β-acyl vinyl ethers. Our earlier ozonation of 2-methoxymethylene Meldrum's Acid (**1a**)[3a] yielding ozonide **6a** in 69 percent yield did not allow a prediction whether the reaction would follow path A or path B provided the classical alkene ozonolysis Scheme was considered (Scheme 2).

Scheme 2: Ozonation of Alkoxyalkylidene Meldrum's Acids under classical aspects

a: R^1 = H; R^2 = CH_3
b: R^1 = CH_3; R^2 = CH_3
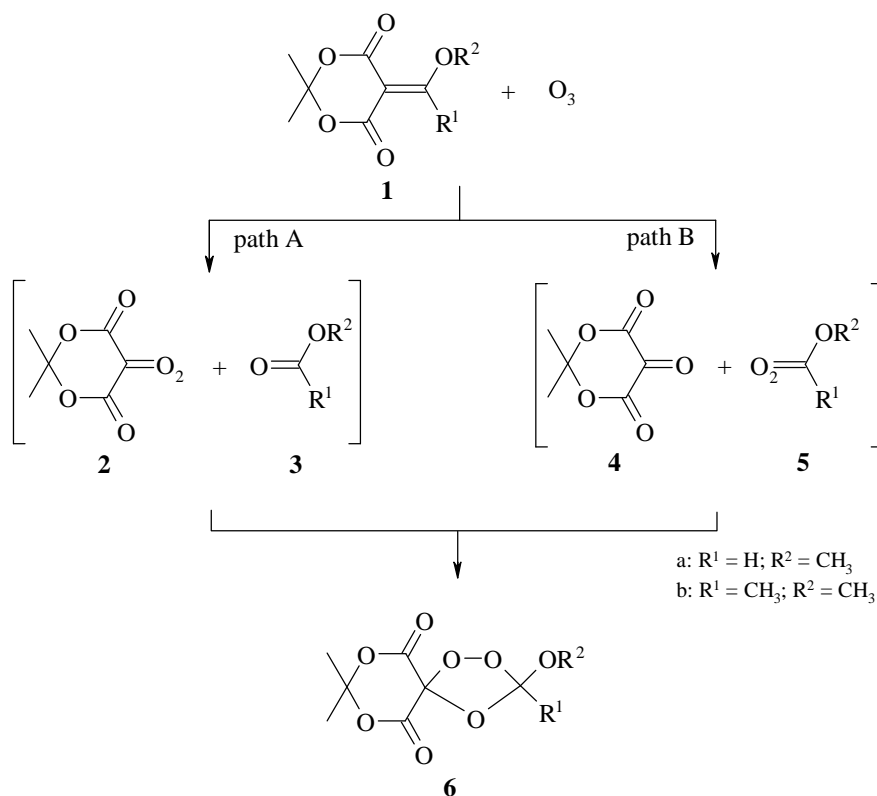
Unequivocal generation of **2** from electron poor olefin **7** must be ruled out because independently prepared **7**[8] is as insoluble in common solvents that even its NMR spectra could not be recorded. Beyond that, even tetraethyl ethylenetetracarboxylate did not react with ozone.

On the other hand it has been shown that 1,2-dimethoxy ethylene (**8a**) is very easily cleaved by ozone[3a,10]. Kuczkowski et al.[10c] described cross ozonide formations of **5a** during ozonolysis of **8a** in *pentane* in the presence of aldehydes or of acetone as cosolvents. However, a corresponding reaction in *dichloromethane* in the presence of an equimolar amount of oxo Meldrum's Acid **4** did not yield known ozonide **6**[3a] though **4** possess a much more reactive carbonyl group[3b] than the mentioned carbonyl compounds[10c] (Scheme 3) and ozonolysis of **1** yielding ozonide **6a** had been equally carried out in dichloromethane.

Scheme 3: Consideration of unequivocal generations of carbonyl oxides from symmetric C,C-double bonds
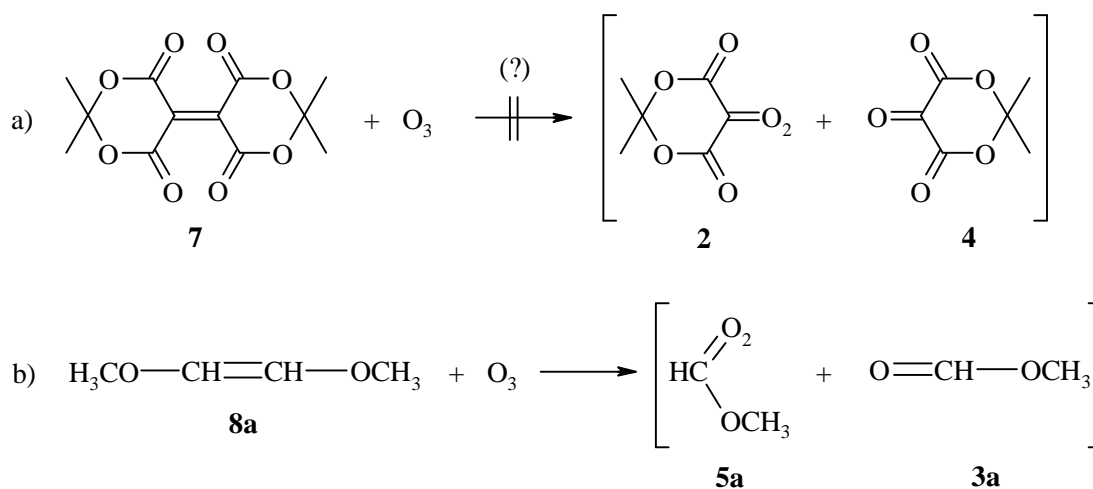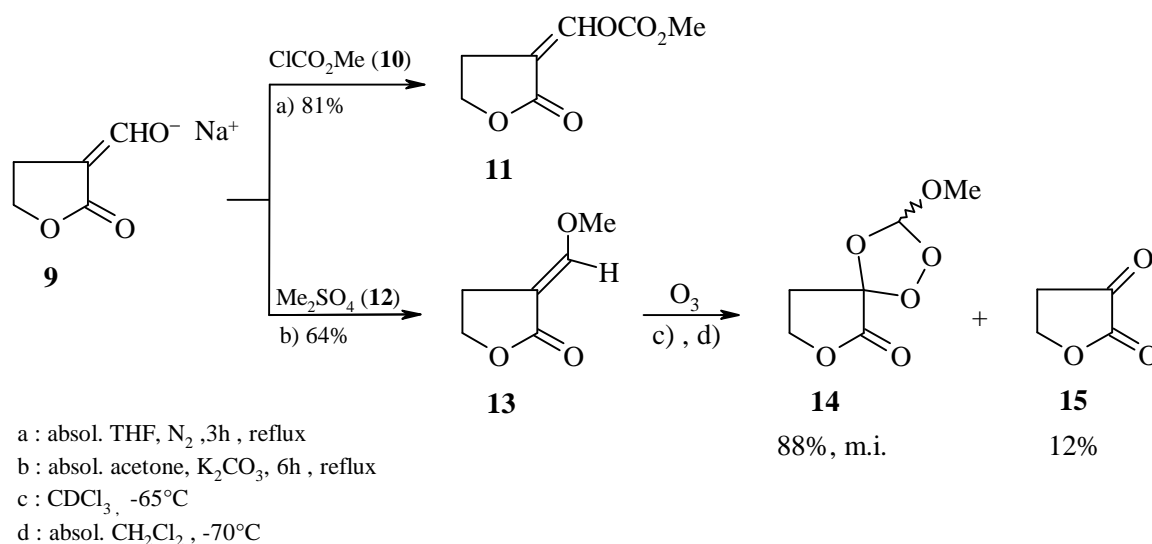

Excluding **5a** as an intermediate, consequently **2** should be the peroxidic intermediate according to path A (Scheme 2) which should add to simultaneously formed formate **3a**. Kuczkowski et al.[11] have outlined that acetate esters are unsuitable trapping agents for carbonyl oxides. In this paper preparation and ozonolysis of **1b** are described expecting that no ozonide would be formed. In order to gain more insight in the course of these enol ether ozonations, further enol ethers with one β-*ester* carbonyl substituent or with one and two β-*ketone* carbonyl substituents are additionally applied for ozonolytic studies.

Results

Ozonolysis of **1b**: Enol ether **1b** was prepared according to a known procedure[12]. Its ozonolysis under same conditions as with **1a** afforded surprisingly a *quantitative* yield of ozonide **6b** (Scheme 2) thus indicating that an intermediate carbonyl oxide to methyl acetate cycloaddition should be less probable.

Ozonolysis of 2-methoxymethylene 4-butyrolactone (**13** (E)): Conversion of sodium salt **9** of 2-formyl 4-butyrolactone with methyl chloroformate (**10)** according to literature[13] did not yield described enol ether **13** in our hands, instead enol carbonate **11** was obtained in 81% yield. Enol ether **13** was obtained by methylation of **9** with dimethyl sulfate (**12)** (Scheme 4).

Scheme 4: Preparation and ozonolysis of **13**

a : absol. THF, N_2 ,3h , reflux
b : absol. acetone, K_2CO_3, 6h , reflux
c : $CDCl_3$, -65°C
d : absol. CH_2Cl_2 , -70°C

Mp and NMR data differed markedly from those mentioned by Murray and Murray[13]: „*Configurational assignment was established by ^1H-NMR spectroscopy, the (E)-configuration being supported by the abnormal downfield shift of the vinylic proton to 7 ppm.*" The authors reported **13** to be crystalline (mp 117-118°C) and to display a vinylic proton at δ_H 6.95 ppm, **13** obtained according to scheme 4 was a colorless liquid (bp$_{13\ Torr}$ 143°C, crystalline < -10°C, liquid at RT) displaying a vinylic proton at δ_H 7.27 ppm (cf. experimental part). Consequently, it is concluded that methylation of **9** with **12** generated the real (E) isomer whereas the former compound possibly was the (Z) isomer. **13** was ozonised in CDCl$_3$ at -65ºC yielding a mixture of stereoisomeric ozonides **14** (88%, 65:23), tetrahydrofuran-2,3-dione (12%) (**15**) and methyl formate; reduction of crude ozonolysis mixture with triphenylphosphine afforded a quantitative yield of **15** as its enol **15a**. *Ozonolyses of 2-methoxymethylene-1-tetralone* (**16a**)

*and 2-methoxymethylene-1-indanone (**16b**)*: Ozonations of dichloromethane solutions of enol ethers **16** at -70°C did not lead to peroxides after quantitative conversion. Ozone uptake by **16b** was rather sluggish and a 10 percent excess was applied for complete conversion although only equimolar amounts were consumed. Removal of solvent yielded anhydrides **17**, **17b** as known monomer, **17a** as a gum-like polymer. For additional characterisation, excess methanol was added to ozonised solutions and stirred for 24h at RT. Mono esters **18** were formed quantitatively, **18b** regioselectively as one isomer, whereas **17a** formed both isomers in a ration of 6-7 : 1 (Scheme 5).

Scheme 5: Ozonolysis of monoacylated enol ethers **16**
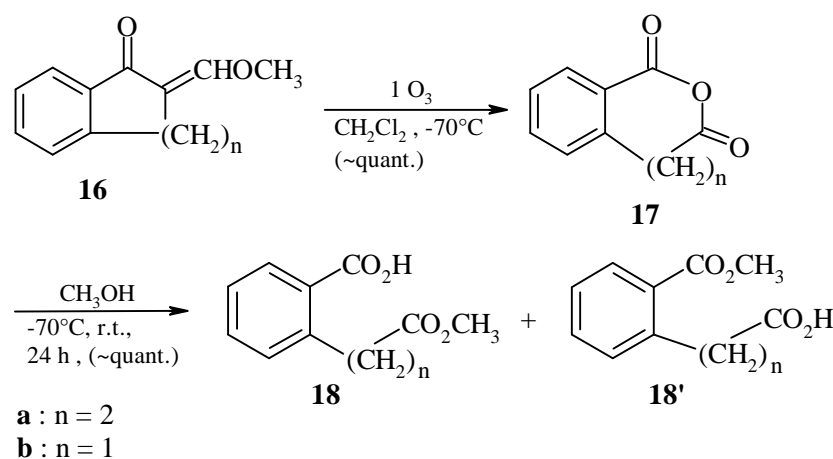
Reaction products **17** and **18** (**18'**) were compared with independently prepared substances and spectroscopic data were recorded. This regioselectivity of ozone oxygen distribution to the cleaved double bond contradicts definitely to the claims of W.H. Bunnelle for vinylogous carboxylic esters[7b] and is in complete agreement with that of vinylogous sulfonic esters[2e]. In order to gain more insight in the direction of ozonolytic cleavages of 2-alkoxyalkylidene substituted cyclic 1,3-dicarbonyl compounds, indane-1,3-diones **19** related to **1** but containing a 1,3-diketone moiety instead of two ester groups should be cleaved by ozone accordingly. However, although free enol **19a** is easily accessible from indane-1,3-dione[14] neither immediate methoxymethylenation of indane-1,3- dione with trimethyl orthoformate (according to the preparation of **1**) nor methylation of **19a** by means of methyl tosylate in the presence of different bases led to enol methyl ether **19c**, in all cases an undesired oxonol dye was formed. Finally, **19c** could be obtained by direct methylation of **19a** with diazomethane in poor yield or via preceding ethylation of **19a** with triethyloxonium fluoroborate. Enol ethyl ether **19b**

exchanged its ethoxy group quantitatively on heating with methanol. Preparation of **19d** starting from indane-1,3-dione and triethyl orthoacetate[15] was carried out as described without any difficulties. Subsequent ozonolysis of **19c,d** in *dichloromethane* afforded phthalonic acid anhydride (**20**) and esters **3a** or **3b** as sole ozonolysis products; no peroxide could be proved (Scheme 6).

Scheme 6: Ozonolyses of 2-Alkoxyalkylidene indane-1,3-diones **19**

19
a : R^1, R^2 = H   b : R^1 = H; R^2 = Et
c : R^1 = H; R^2 = Me   d : R^1 = Me; R^2 = Et

20
(~ quant.)

21
(quant.)
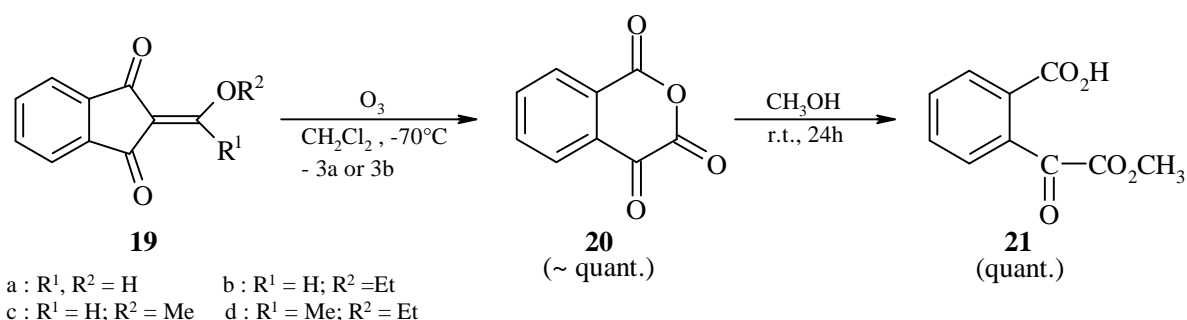
When these ozonolyses were repeated using *dichloromethane-methyl formate (1:1) mixture* as solvent under same conditions in order to obtain eventually an ozonide corresponding to *6*, surprisingly no cross-ozonide formation was observed but in the case of **19c** indane-1,2,3-trione (**22**) was formed in 18 percent yield, in the case of **19d** only 4 percent **22** were determined. Formation of this triketone as a by-product was due to the presence of methyl formate but its ET(30)-value (45.0)[16] cannot be of importance because replacement of methyl formate by DMSO (ET (30)=45.1)[16] did not cause triketone formation under comparable *(dichloromethane-DMSO (1:1) mixture)* conditions. Quantitative ^{1}H-NMR- determination of formed amounts of **20** and triketone in their mixture could be carried out after conversion of **20** to its hemiester **21** (δ OCH$_3$ 3.78 ppm) and of **22** to its hemiacetal **23** (δ OCH$_3$ 3.60 ppm) at the same time by stirring with methanol.

In order to check whether the portion of **22** would result from decomposition of a preceding carbonyl oxide, attempts were started to generate such a species from 2-diazoindane-1,3-dione via the singlet-pathway according to Scaiano[17]. However, the diazo diketone resisted a conversion with singlet oxygen generated either from triphenyl phosphite ozonide or via sensitised (sensitisers: a) methylene blue; b) rose bengale) irradiations in the presence of dioxygen.

In an earlier communication[18] of our group exclusive formation of **22** has been described during ozonolysis of 2-dimethylsulfonio indane-1,3-dione; **20** was not formed. In that case an

intermediate formation of indane-1,2,3-trione carbonyl oxide with loss of oxygen, as outlined later by Scaiano[17] in a related case, was assumed. This conversion[18] was checked, **20** could not be proved. Interestingly, open-chain 3-ethoxymethylene pentane-2,4-dione (**24**) (2-ethoxy-methylene acetylacetone) displayed a nearly 1:1-formation of its ozonide **25** (54%) and Baeyer-Villiger-like acetic acid pyruvic acid mixed anhydride **26** (45%) together with ethyl-formate. Ozonide **25** and mixed anhydride **26** are quite unstable compounds and must be characterised in solution. Apart from spectroscopic characterisation, ozonide **25** was deoxy-genated quantitatively by triphenylphosphine yielding deep red pentane-2,3,4-trione **27** and ethylformate, mixed anhydride was independently generated from anhydrous sodium acetate and pyruvic acid chloride.

Conclusion

Primary ozonide formation during enol ether ozonolyses has never been proved. The following observations made during discussed ozonations are of mechanistic importance: a) Compounds **1, 13, 16**, **19** and **24** are considered to be alkenes in which substituent effects according to scheme 2 should lead to formation of bisoxygenated α-enolether carbon fragments following the classical conception provided that substituent effects are reasonably applied. However, observed C,C-cleavages occured in the opposite sense, as already mentioned by Bunnelle[7].

b) Attempts in order to prove any type of carbonyl oxide either by cross-ozonide formation or by oxygen transfer to TCNE were unsuccessful[3]. Thus, it is concluded that carbonyl oxides are not participating in these reactions.

c) It was evident that these ozonolyses were much slower than those of enol ethers bearing no acceptor substituents. Although ozone was consumed in 1:1-stoichiometric amounts an excess must be introduced for quantitative conversions. If ozone would be a zwitterion in reality as can be learned from nearly every text book of chemistry, a substance like donor-acceptor sub-stituted methoxymethylene malodinitrile **(28)** should be an ideal trapping partner (Scheme 7).

Scheme 7: Fruitless attempt of methoxymethylene malodinitrile ozonolysis
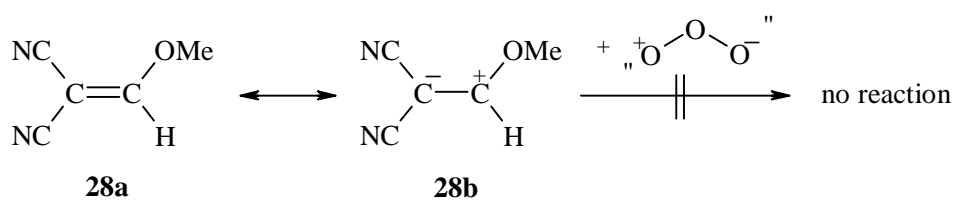
However, **28** does not react with ozone (similar to TCNE or tetraethyl ethylenetetracarb-oxylate) under usual ozonolysis conditions.

d) An *alternative mechanistic proposal* for the ozonolysis of above-mentioned donor-acceptor substituted alkenes coordinates subsequent known details not considered hitherto in connection with alkene ozonolyses: 1) If carbanionic centers of these zwitterionic alkenes are nucleophilic enough (Scheme 8) to be attacked by electrophilic ozone (opposite to scheme 7), one electron should be transferred to ozone releasing a carbon radical at β-carbon, in these cases consequently a mesomerism stabilised radical cation would result (for ESR-investigations of such species cf. ref.[19]).

Scheme 8: Direct relation between ^{13}C-NMR-δ-values and negative charge density of ß-carbons of substituted enol ethers
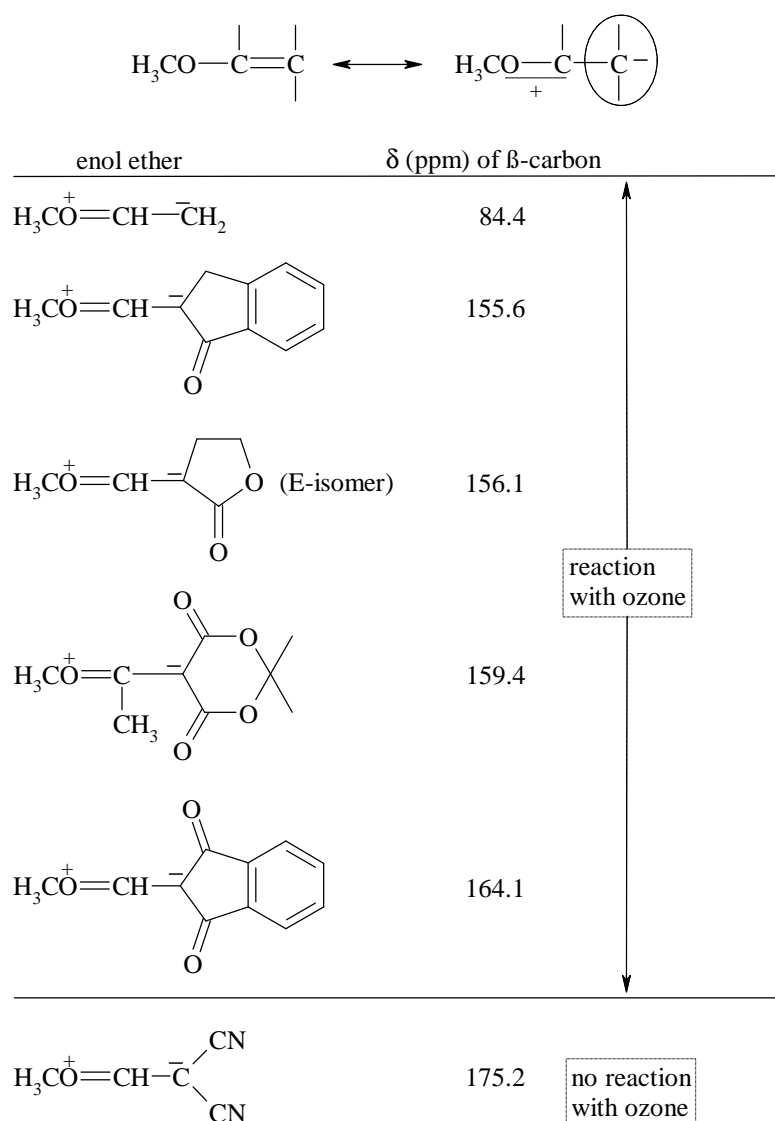
A corresponding electron transfer is generally observed with simple carbanions towards molecular oxygen[20]. 2) Fore-mentioned radical cations should be monooxygenated at β-carbon by ozone (or its radical anion) with splitting off dioxygen (or its radical anion) together with evolution of a considerable amount of bond energy (consisting of exergonic C,O-bond formation and of exergonic O,O$_2$-bond cleavage energy). 3) These intermediates would belong to the known class of C,O-cleaved oxirane radical cations[21]. Ring-closed oxirane cations prefer to isomerise to C,C-cleaved isomers[22] which are autoxidisable carbon radicals. Principally, oxiranyl ethers are sometimes formed during ozonation of enol ethers[23]. On the other hand, vinylogous esters (β-acyl vinylethers) are easily epoxidised by means of dimethyldioxirane[24]. In any case these compounds are rather unstable and must be characterised spectroscopically and by their reactions. It has been found that even more stable oxiranes **29a** from 2-benzylidene indane-1,3-diones suffer easy C,C-cleavages under gentle thermolysis conditions to give carbonyl ylides **29b** which undergo various [3+2] cycloadditions (Scheme 9)[25].

Scheme 9: Carbonyl ylides from donor-acceptor substituted oxiranes according to Anokhina, Krysin, Zalukaev et al.[25]
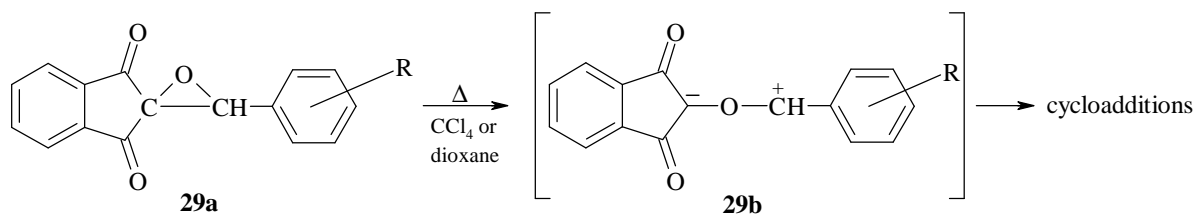

These C,C-cleavages remind of „*equilibria among anions of **a**-hydroxy ß-diketones and **a**-ketol esters*" for which Rubin and Inbar[26] claimed vicinal donor-acceptor substituted oxiranes as intermediates (Scheme 10).

Scheme 10: C,C-cleavages in 2-hydroxy-1,3-diketones in the presence of base via presumable oxirane intermediates according to Rubin and Inbar[26]
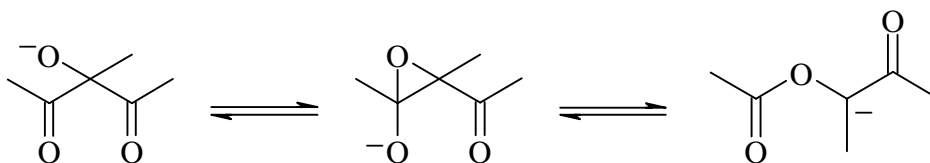
As we have already shown[2f] a ß,ß-diarenesulfonyl vinyl ether (a vinylogous sulfonate) which did not form an oxirane intermediate during ozonation because of competing elimination of sulfinate did not lead to ester formation from enol ether α-carbon (Scheme 11).

Scheme 11: Ozonolytic degradation of (ß,ß-bisbenzenesulfonyl)vinyl methyl ether[2f]
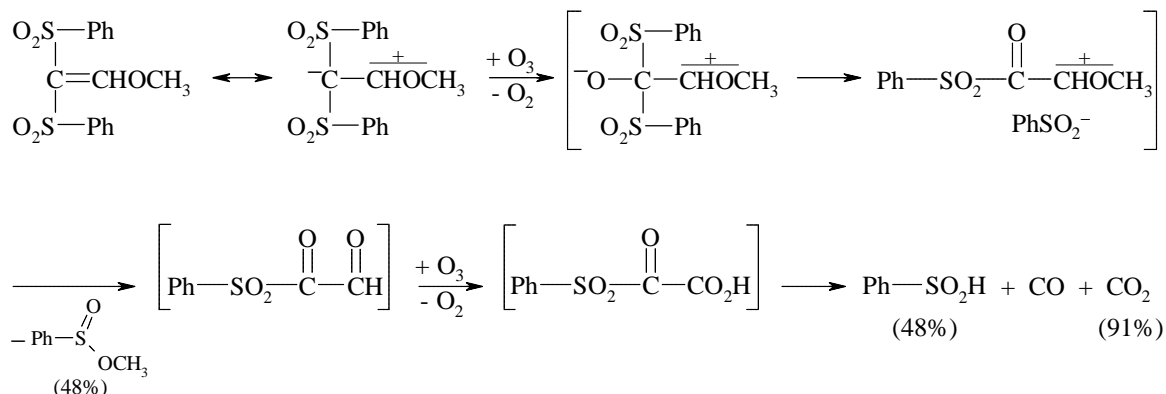
Instead, olefinic carbons were oxidised yielding carbon monoxide (not quantitatively determined) and carbon dioxide. The latter must result from oxidation of a suitable precursor because Griesbaum[27] has found that carbon monoxide is not oxidised to carbon dioxide under usual ozonolysis conditions. 4) [3+2] cycloadditions of C,C-cleaved oxirane radical cations are known to yield ozonides[26] (for careful mechanistic investigations during „stereoselective oxygenation of 2,3-diaryl oxiranes by irradiation of EDA-complexes of TCNE" cf. ref.[26b]), their autoxidation and final SET should lead to open-chain carboxonium peroxides which possess three possibilities for final *intra*molecular reactions:

I   Grob fragmentation yielding oxygen and two carbonyl compounds

II   Ring closure yielding ozonides

III Intramolecular nucleophilic substitution yielding dioxirane species or their rearranged Baeyer-Villiger like products (Scheme 12).

Scheme 12: Proposal of a summarising reaction scheme as a result of observed reactions and suitable reference
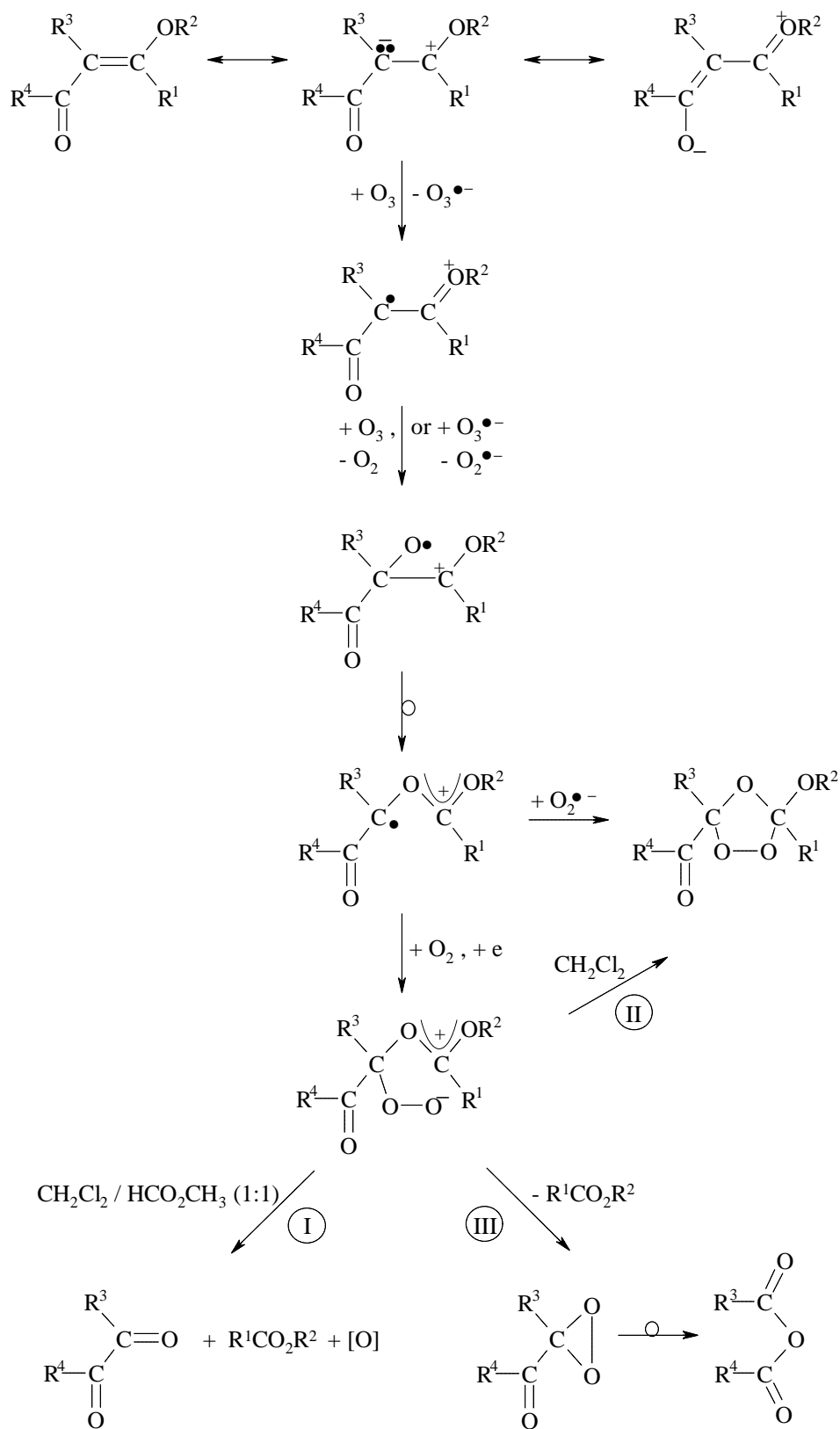
A proof of atomic oxygen according to I in the presence of molecular oxygen and of ozone seems to be impossible because the former generates ozone whereas the latter decompose it generating molecular oxygen : $[O] + O_2 \rightarrow O_3$; $O_3 + [O] \rightarrow 2\,O_2$

Thus the role of methyl formate could be a prevention of suitable ring closures, favouring I and hindering II and III.

Experimental Section

Starting materials Meldrum's Acid, 4-butyrolactone, 1-tetralone, 1-indanone and 1,3-indane-dione are commercially available. Alkoxyalkenylations of their active methylene groups are carried out either according to known procedures or are described here. Ozonolyses are carried out using a Fischer 503 or a Sander 301.7 ozoniser both affording an ozone-oxygen stream of ca. 1.9-2 mmol ozone/min at a gas flow rate of 60 l/h. TLC foils Alugram SILG/ UV_{254} or Polygram Alox N/UV_{254} (Macherey and Nagel) are used for continuous controls of reaction mixtures. Qualitative and quantitative determinations of peroxide contents used aqueous potassium iodide in the presence of acetic acid. Melting and decomposition temperatures are determined by use of a Kofler heating table. IR spectra are recorded by use of a Beckman IR-33, NMR spectra (CDCl$_3$/TMS as internal standard, if not mentioned otherwise) are recorded either by a Bruker WH90 (^{1}H) or by a Bruker AM400 (^{1}H at 400 MHz, ^{13}C at 100 MHz). Subsequent compounds are prepared as described: 2-Formyl-4-butyrolactone sodium salt (**9**)[29], 2-methoxymethylene-1-tetralone (**16a**)[30a,b], 2-methoxymethy-lene-1-indanone (**16b**)[30a], 2-anilinomethylene-1,3-indanedione (three-component-method)[31], 2-hydroxymethylene-1,3-indandione[14], 2-(1-ethoxy-1-ethylidene)-1,3-indanedione (**19d**)[15], 2,2-dicyanovinyl methyl ether (**22**)[32], triethyloxonium tetrafluoroborate[33], 3-(2-carboxyphenyl) propionic acid[34] and its dimethyl ester[35].

a) *2-(1-Methoxy-1-ethylidene) Meldrum's Acid (1b)* (in analogy to ref.[12]): A mixture of Meldrum's Acid (5.00 g, 35 mmol) and trimethyl orthoacetate (21.0 g, 174 mmol) are heated to 85-90°C for 2 h. Volatile ester is removed i.vac., a few ml absol. methanol are added to the residue and the mixture is stored in a refrigerator overnight. Colourless crystals are formed (2.24 g, 32%), mp 81°C (from methanol). IR (KBr), ν_{max}/cm^{-1} 1750, 1710; δ_H/ppm 1.71 (s, 6H, CH$_3$), 2.75 (s, 3H, CH$_3$), 4.13 (s, 3H, OCH$_3$); δ_C/ppm 17.7, 30.0 (CH$_3$), 57.6 (OCH$_3$), 102.8 (C$_{quart}$), 159.4 ($\underline{C}$=C$-$O), 163.3 (C=$\underline{C}$$-$O), 186.7 (C=O).

b) *2-(methoxycarbonyloxymethylene)-4-butyrolactone (11)*: 2-Formyl-4-butyrolactone sodium salt (**9**) (2.72 g, 20 mmol) in absol. THF (100 ml) are treated with methyl chloroformate (3.78 g, 40 mmol) as described[13]. Obtained product (2.79 g, 81%) melted at 114-115°C (from dichloromethane - petrol ether 1:1) (ref.[13] 117-118°C); IR (KBr): ν_{max}/cm^{-1} 1785, 1670. δ_H/ppm 2.99-3.02 (t, d, 2H, J^1 3.0 Hz, J^2 7.5 Hz, CH$_2$), 3.95 (s, 3H, OCH$_3$), 4.42 (t, 2H, J 7.5 Hz, OCH$_2$), 8.07 (t, 1H, J 3 Hz, H$_{vinyl}$); δ_C/ppm 24.0 (CH$_2$), 56.1 (OCH$_3$), 65.8 (OCH$_2$), 110.6 (CH=C), 143.9 (CH=C), 152.1, 170.8 (CO).

c) *(E) 2-Methoxymethylene-4-butyrolactone (13)*: A suspension of **9** (20.0 g, 147 mmol) and anhydrous potassium carbonate (40.6 g, 0.3 mol) in absol. acetone (100 ml) is refluxed for 6h with dimethyl sulfate (18.6 g, 147 mmol). Solid material is filtered by suction and washed several times with fresh absol. acetone. The mother liquor is worked up by distillation, at last i. vacuo. (E) **13** (12.3 g, 64%) is obtained as colourless liquid of bp$_{13\ Torr}$ 143°C, crystallising < -10°C and melting before reaching RT. IR (liquid): ν_{max}/cm^{-1} 1750, 1685; δ_H/ppm 2.86 (t, d, 2H, J^1 2.6 Hz, J^2 7.5 Hz, CH$_2$), 3.89 (s, 3H, OCH$_3$), 4.35 (t, 2H, J 7.5 Hz, OCH$_2$), 7.27 (t, 1H, J 2.6 Hz, H$_{vinyl}$); δ_C/ppm 23.5 (CH$_2$), 61.6 (OCH$_3$), 65.5 (OCH$_2$), 101.5 (CH=C), 156.1 (CH=C), 172.6 (CO).

d) *2-Methoxymethylene-1-indanone (16b)*: Although **16b** is prepared according to ref.[30a], ^{1}H-NMR data found do not correspond to those mentioned. Therefore, measured data together with ^{13}C-NMR data are supplemented here: **16b**, δ_H/ppm 3.63 (s, 2H, CH$_2$), 3.94 (s, 3H, OCH$_3$), 7.39 (t, 1H, J 7.7 Hz, H$_{ar}$), 7.45 (t, 1H, J 7.7 Hz, H$_{ar}$), 7.46 (s, 1H, H$_{vinyl}$), 7.55 (t, 1H, J 7.6 Hz, H$_{ar}$), 7.81 (d, 1H, J 7.8 Hz, H$_{ar}$); δ_C/ppm 28.6 (CH$_2$), 61.9 (OCH$_3$), 115.5 (CH$_{vinyl}$), 123.6, 126.2, 127.2, 133.7, 139.5, 148.6 (C$_{ar}$), 155.6 (C-2), 189.3 (C=O).

e) *2-Methoxymethylene-1,3-indanedione (19c)*: *1)* A solution of diazomethane in ether (0.39 M, 100 ml) is dropped to a stirred suspension of 2-hydroxymethylene-1,3-indandione[14] **19a** (3.4 g, 18 mmol) in ether (300 ml). Stirring is continued for 24 h, non-consumed starting material is removed by filtration (absence of diazomethane !) and solvent is evaporated. The remaining residue is recrystallised twice from methanol affording pink crystals (1.47 g, 40%), mp 162-163 °C. IR (KBr): ν_{max}/cm^{-1} 1640, 1700, 1740; δ_H/ppm 4.23 (s, 3H, OCH$_3$), 7.60 (s, 1H, H$_{vinyl}$), 7.72-7.79 (m, 2H$_{ar}$), 7.88-7.92 (m, 2H$_{ar}$); δ_C/ppm 65.2 (OCH$_3$), 112.6 (CH$_{vinyl}$), 122.6, 122.8, 134.4, 134.7, 140.4, 141.3 (C$_{ar}$), 164.1 (C-2), 187.8, 190.4 (C=O). *2)* Triethyloxonium tetrafluoroborate[33] (6 g, 20 mmol) in dry dichloromethane (50 ml) is added dropwise to a solution of 2-hydroxymethylene-1,3-indanedione (3.4 g, 18 mmol) in dichloro-

methane (250 ml). After stirring for 24 h at ambient temperature solvent is evaporated and the crude residue of **19b** is refluxed with methanol (100 ml) for 3 h. The hot solution is filtered and cooled, yielding **19c** (2.8 g, 74%).

General procedure for ozonolyses: A *dry* gas stream of ozonised oxygen is bubbled through *anhydrous* solutions of vinylogous esters according to table 1 until the double bonds are completely cleaved (TLC-controls). Unreactive enol ethers need application of an excess ozone, although all ozonolytic cleavages described here need ozone in equimolar amounts as can be recognised iodometrically (quantitative ozone absorption by potassium iodide solutions as traps behind the apparatus). Excess of ozone in reaction mixtures is blown out first by oxygen at reaction temperature, finally ozonised solutions are warmed up to RT during introduction of a stream of *dry* nitrogen. Peroxide formation (or not) is determined quantitatively by iodometric titration and solvents are removed i.vac. without external heating (Table 1).

Ozonolysis of 1b, isolation of spiro[6.5]-2,4,6,7,9-pentaoxa-8-methoxy-3,3,8-trimethyl-1,5-decanedione (**6b**): The solution of entry 1 (titrated peroxide content 100%) is cooled to -20°C. At this temperature **6b** separated out crystaline. Filtration is carried out under low temperature conditions by fast suction because **6b** liquifies already below RT yielding a colourless viscous liquid (2.23, 100%). IR (CCl_4 solution): ν_{max}/cm^{-1} 1795, 1765; δ_H/ppm 1.84 (s, 3H, CH_3), 1.88 (s, 3H, CH_3), 1.92 (s, 3H, CH_3), 3.60 (s, 3H, OCH_3); δ_C/ppm 21.2, 28.8, 29.0 (CH_3), 51.6 (OCH_3), 106.7, 124.9, 147.1 (C_{quart}), 158.2, 159.6 (C=O).

Ozonolysis of 13, a) isolation of one from four possible configuration isomers of spiro[5.5]-3-methoxy-1,2,4,6-tetraoxanonan-5-one (**14**): The solution of entry 2 displays a titrated peroxide content of 88% due to different ozonide diastereomers. One of these decomposes already during removal of solvent below RT, it can be identified only by difference ^{1}H-NMR spectroscopy within the crude reaction mixture. A residue obtained from crude $CDCl_3$ solution (40 ml) is separated by LC (silica gel, ethyl acetate). Ozonide **6b** is obtained as colourless oil from first fraction (1.96 g, 65.4%) which explodes on warming. IR (liquid): ν_{max}/cm^{-1} 2970, 1840, 1780; δ_H/ppm 2.56 - 2.62 (m, 1H, CH_2), 2.83 - 2.91 (m, 1H, CH_2), 3.47 (s, 3H, OCH_3), 4.34 - 4.38 (m, 2H, OCH_2), 6.35 (s, 1H, CH); δ_C/ppm 27.3 (CH_2), 51.5 (OCH_3), 63.9 (OCH_2), 103.6 (CH), 113.9 (C_{quart}), 168.4 (C=O). The portion of second isomer can be found by ^{1}H-NMR evaluation of the crude reaction mixture in $CDCl_3$ before and after LC separation (22.6% on the base of 88% peroxide): δ_H/ppm 2.51 - 2.61 (m, 2H, CH_2) 3.61 (s, 3H, OCH_3),

4.34 - 4.49 (m, 2H, OCH$_2$), 6.22 (s, 1H, CH); δ_C/ppm 31.8 (CH$_2$), 51.8 (OCH$_3$), 64.4 (OCH$_2$), 103.5 (CH), 113.8 (C$_{quart}$), 168.4 (C=O). 2.5-Dihydro-3-hydroxy-furan-2-one (**15**, enol form) is collected as second fraction, yielding colourless crystals (200 mg, 11.6%), mp 110°C (from ether) (mp[36] 111°C). b) Reduction of a second part of the crude reaction mixture (40 ml) by means of triphenyl phosphine (1.75 g, 6.7 mmol) in absol. dichloromethane (20ml) (dropwise addition and final stirring for 6 h at RT) yields **15** after chromatographic purification (silica gel, ethyl acetate) colourless crystals (0.76, 100%) as before and is additionally characterised by spectroscopy. IR (KBr): ν_{max}/cm^{-1} 3600 (broad OH), 2900, 1760; δ_H/ppm 4.69 (d, 2H, J 2.1 Hz, OCH$_2$), 6.18 (t, 1H, J 2.2 Hz), 9.30 (broad, 1H, OH); δ_C/ppm 67.5 (OCH$_2$), 114.3 (CH=C), 142.9 (CH=C), 168.8 (C=O).

Ozonolysis of 16a: Peroxide-free solution of entry 3 is evaporated to dryness yielding anhydride **17a** (1.58 g, 100%) which polymerises showly (cf. ref.[37]) and cannot be characterised by a mp. IR (CCl$_4$ solution): ν_{max}/cm^{-1} 1800, 1725, 1600; δ_H/ppm 2.60 - 3.65 (m, 4H, CH$_2$), 7.05 - 7.70 (m, 3H$_{ar}$), 7.70 - 8.10 (m, 1H$_{ar}$); δ_C/ppm 28.1, 37.4 (CH$_2$), 128.1, 129.3, 131.4, 133.8, 139.2 (C$_{ar}$), 162.7, 166.6 (C=O). For additional characterisation it is advantageous to add absol. methanol (10 ml) to the cold solution of a further batch and to stir for 24 h at RT. After removal of the solvent an oily mixture results consisting of aliphatic hemimethyl ester **18** and of aromatic hemimethyl ester **18'** (ratio ~ 6:1 (1.87 g, 100%). A corresponding mixture can be obtained by methanolysis of independently prepared anhydride **17a**.

Ozonolysis of 16b: Peroxide-free solution of entry 4 is evaporated to dryness yielding colourless crystals of homopthalic acid anhydride (**17b**) (0.54 g, 98%), mp 140°C (from acetic acid anhydride) (mp[38] 140-141°C). IR and NMR data correspond to those already mentioned[37]. Stirring of **17b** (0.54 g, 3.4 mmol) in absol. methnaol (50 ml) for 24 h afforded exclusively aliphatic hemimethyl ester **18b**, colourless crystals (0.64 g, 100%) of mp 96°C (from petrol ether) (mp[39] 96-98°C).

Ozonolysis of 19c: Peroxide-free greenish solution of entry 5 is evaporated to dryness yielding greenish crystals of phthalonic acid anhydride **20** (0.47 g, 99%), mp 187.5°C (from ethyl acetate) (mp[40] 185-186°C). Stirring of **20** (0.5 g, 2.3 mmol) in absol. methanol (20 ml) for 24 h affords exclusively aliphatic hemimethyl ester **21** (0.48 g, 100%), mp 74°C from ether) (mp[41] 74-85°C by conventional copper block measure method). Peroxide-free coloured (green to red depending on temperature and on concentration of **22** formed, provided the solution is protected from moisture) solution of entry 6 is evaporated to dryness and the residue (0.37 g)

is stirred with absol. methanol (20 ml) for 24 h at RT. Methanol is evaporated i.vac. and the remaining residue (0.41 g) is dissolved in CDCl$_3$, hemiester **21**: hemiacetal **23** ratio is ^{1}H-NMR analysed to be 82 : 18. For comparison, **23** is prepared by stirring ninhydrin (2 g, 11.2 mmol) with absol. methanol (10 ml) for 24 h at RT. Obtained colourless powder (2.17 g, quantitative) has mp 88-89°C (from ether) and decomposes like **21** on melting.

Ozonolyses of 19d are carried out as fore-mentioned (cf. table 1, entries 7 and 8). Entry 8 affords only a 4% yield of **23**.

Ozonolysis of 24. Peroxidic (54%) solution of entry 9 is treated according to footnote f) in table 1 yielding a mixture of mixed anhydride **26** and triketone **27** which cannot be separated undecomposed. Whereas unsolvated **27** can be identified via known spectroscopic data[42] (δ_H/ppm 2.44 (s)), sensitive mixed anhydride **26** is generated as follows: Oxalyl chloride (12.7 g, 0.1 mol) in absol. ether (20 ml) is dropped to a well stirred mixture of pyruvic acid (8.8 g, 0.1 mol), anhydrous sodium carbonate (5.3 g, 50 mmol) and three drops of absol. DMF in absol. ether (60 ml) at 0°C. Stirring is continued for 24 h at RT. The suspension is filtered and resulting yellowish solution is stirred for further 12 h with anhydrous sodium acetate (8.2 g, 0.1 mol). After filtration and cautious evaporation resulting crude oil of **26** is investigated by ^{1}H-NMR: δ_H/ppm 2.12 (s, 3H, CH$_3$CO), 2.51 (s, 3H, CH$_3$COCO). With data known for **24**, **26**, **27** and ethyl formate (δ_H/ppm 1.30 (t, 3H, CH$_2$–$\underline{CH_3}$), 4.24 (q, 2H, $\underline{CH_2}$–CH$_3$), 8.05 (s, 1H, CHO) peroxidic solution of entry 10 can be analysed via ^{1}H-NMR for structural determination of ozonide **25**: δ_H/ppm 1.26 (t, 3H, CH$_2$–$\underline{CH_3}$), 2.32 (s, 3H, Ac), 2.38 (s, 3H, Ac), 3.77 (q, 2H, $\underline{CH_2}$-CH$_3$), 6.06 (s, 1H, CH). **25** : **26** : ethyl formate ratio is found to be 52 : 30 : 28.

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