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SYNTHESIS OF PHENOLS BY THE INTRAMOLECULAR CONDENSATION OF β, β',δ, δ'-TETRAOXOALKANEDIOATES A NOVEL BF_3-PROMOTED CLAISEN CONDENSATION OF ACETOACETATE DIANION WITH ESTERS AND AMIDES

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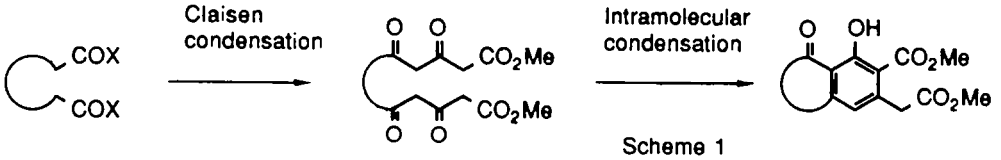
Abstract: The aromatization process of β, β',δ, δ'-tetraoxoalkanedioates, which were synthesized by the BF_3-promoted Claisen condensation, was examined.

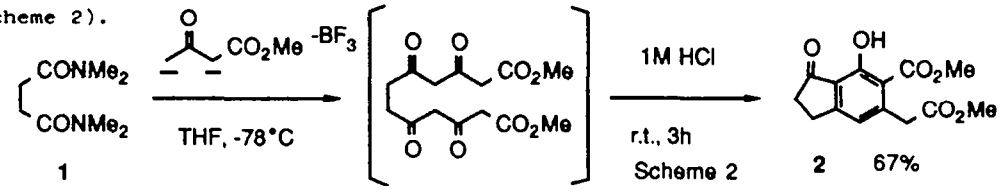
Polyketides are one of the important intermediates in the biosynthesis of naturally occurring aromatic compounds. It is considered that the intramolecular condensation of these linear molecules constructs the aromatic nuclei.[1] We have been studying a new synthetic method of aromatics, which consists of the Claisen-type condensation of dicarboxylic acid derivatives with acetoacetate dianion and the aromatization by the intramolecular condensation of the β, β',δ, δ'-tetraoxoalkanedioates (Scheme 1). The methodology turned out to be useful for the synthesis of linear polycyclic aromatic compounds such as anthracenes, naphthacenes, or pentacenes starting from glutaric acid derivatives.[2, 3] When we started the work only a few examples[4] of this type of the arene synthesis were known, and the aromatization procedures of the polyketo esters had to be established.[5] In this report, we wish to describe our results of the studies on the intramolecular condensation reactions of β, β',δ, δ'-tetraoxoalkanedioates,[6] which are synthesized by a novel BF_3-promoted Claisen condensation of acetoacetate dianion.[7] The scope and the limitation of this Claisen reaction are also included.



Scheme 1

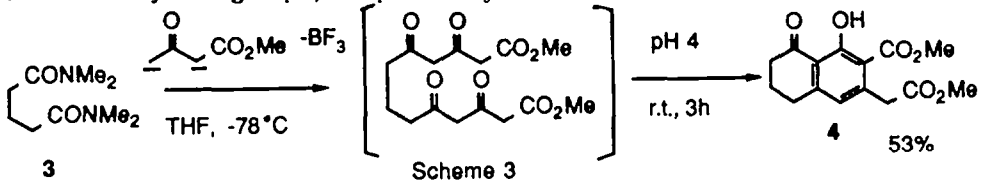
At first, succinic acid derivatives were selected as the precursor of the tetraoxoalkanedioates. Since we were aware that, in the presence of $BF_3 \cdot OEt_2$,[8] tertiary amides reacted with organolithium compounds quite effectively, tertiary amide of succinic acid was chosen as the substrate. The BF_3-promoted Claisen condensation of N,N,N',N'-tetramethylsuccinamide (1) with lithium sodium

dianion proceeded smoothly, and the crude product was treated with 1M hydrochloric acid at r.t. for 3 h for the aromatization. The expected 7-hydroxy-6-methoxycarbonyl-5-methoxycarbonylmethyl-1-indanone (2) was obtained in 67% yield (Scheme 2).



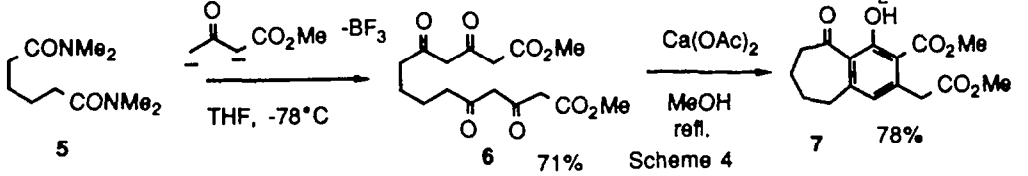
Scheme 2

N,N,N',N'-Tetramethylglutaramide (3) was also treated with the dianion. The six-membered ring formation, however, did not proceed under the acidic (pH 1) or basic (pH 10) condition. The aromatization occurred only in neutral region, and 8-hydroxy-6-methoxycarbonyl-7-methoxycarbonylmethyl-1-oxo-1,2,3,4-tetrahydronaphthalene (4) was isolated in 53% yield at pH 4 for 3h; 61% yield at pH 6 for 3 h, and 25% at pH 8 for 3 h (Scheme 3). It is considered that the cyclohexenone formation requires both acidic and basic species wich activate carbonyl and active methylene groups, respectively.



Scheme 3

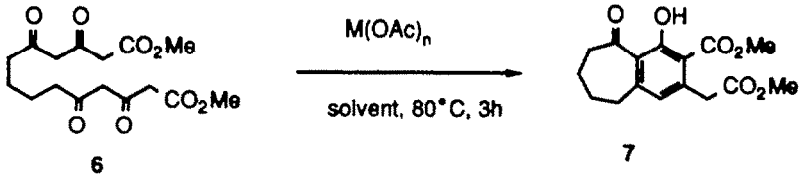
The attention was next turned to the seven-membered ring formation. The BF_3-promoted Claisen condensation of N,N,N',N'-tetramethyladipamide (5) gave dimethyl 3,5,10,12-tetraoxotetradecanedioate (6), which was isolated by silica gel chromatography (71 % yield). Since 6 did not aromatize by simply adjusting the pH of the aqueous solution, the effect of the metal salts was examined. Of various salts tested, $Mn(OAc)_2 \cdot 4H_2O$ was found to catalyze the reaction in refluxing methanol, and 1-hydroxy-2-methoxycarbonyl-3-methoxycarbonylmethyl-9-oxo-6,7,8,9-tetrahydro-5H-benzocycloheptene (7) was obtained in 40% yield. Interestingly, other manganase salts such as $MnCl_2 \cdot 4H_2O$, $Mn(NO_3)_2 \cdot 6H_2O$, $Mn(acac)_2$, or $Mn(H_2PO_4)_2 \cdot 4H_2O$ was not effective at all. The yield was raised to 78% with $Ca(OAc)_2$ (Scheme 4).



Scheme 4

As a model for the aromatization process of polyketides, the reaction was examined further. The effect of the solvent and metal acetate are summarized in Table 1. In general, alkali or alkaliearth metal acetates gave good results. Several transition metal acetates such as Mn(II), Co(II), or Ni(II) were also effective. An interesting solvent effect was observed. Sodium, potassium, or zinc acetate promoted the reaction in methanol or water, and were not effective in acetic acid. While Ni(II) or Co(II) acetate catalyzed the reaction in acetic acid. Presumably, the requirement of both acidic and basic species is playing an important role in these phenomena. It was also noted that the use of the protic solvents was essential and 7 was not detected in methylene chloride, THF, or toluene with $Mn(OAc)_2$. Although we are not fully able to explain these results,

Table 1. The Effect of Metal Acetate and Solvent on the Aromatization of 6.



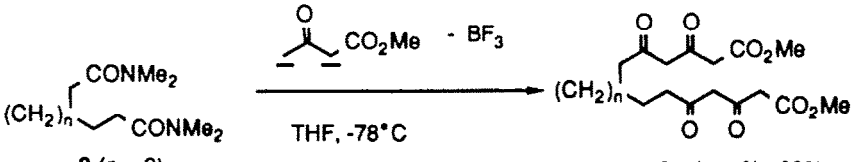
6 7

$M(OAc)_n$ \ solvent	Yield of 7 (%)[a] methanol	water	acetic acid
NaOAc	47	35	—
KOAc	42	35	—
$Mg(OAc)_2$	8	18	30
$Ca(OAc)_2$	78	31	41
$Ba(OAc)_2$	54	38	21
$Mn(OAc)_2$	40	39	38
$Co(OAc)_2$	8	33	15
$Ni(OAc)_2$	—	—	63
$Cu(OAc)_2$	—	—	26
$Zn(OAc)_2$	9	15	—
$Cd(OAc)_2$	19	21	22
none	—	—	—

a) When 7 was not detected, they are shown by —.

the use of $Ca(OAc)_2$ in methanol gave a satisfactory result from the synthetic standpoint of view, and it was used in the synthesis of polycyclic aromatic compounds.[2, 3]

N,N,N',N'-Tetramethylheptanamide (8) and octanamide(10) were also subjected to the Claisen condensation, and the corresponding tetraoxoalkanedioates 9 and 11 were isolated in 69 and 43% yields, respectively (Scheme 5). However, 9 and 11 did not aromatize under various reaction conditions.



8 (n = 2)
10 (n = 3)

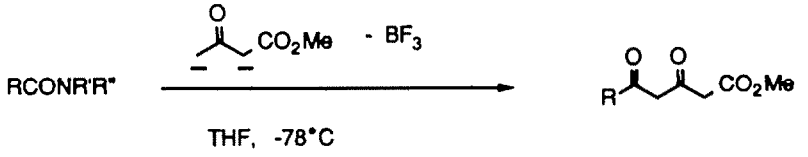
Scheme 5

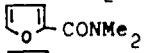
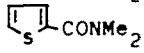
9 (n = 2) 69%
11 (n = 3) 43%

As the BF_3-promoted Claisen condensation worked well for the synthesis of β,β',δ,δ'-tetraoxoalkanedioates, the reaction was examined in detail. As shown in Table 2, various 3,5-dioxoalkanoates were obtained by the treatment of tertiary amides with acetoacetate dianion in the presence of the Lewis acid. The method is also applicable to esters (Table 3), although amides gave a higher yield of the products. In conventional method, ester exchange or hydrolysis of the products were observed for certain substrates.[7] However, these by-products were not detected in the present reaction.

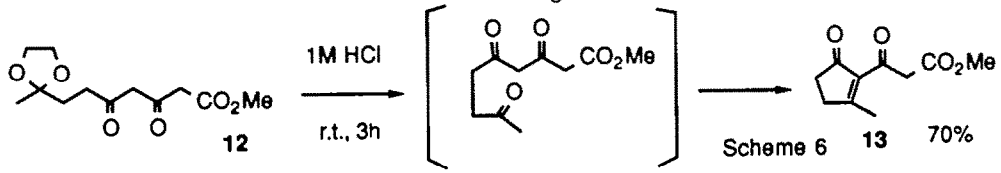
In spite of the use of the Lewis acid, ethylene acetal was not affected.

Table 2. Synthesis of 3,5-Dioxoalkanoates from Tertiary Amides.



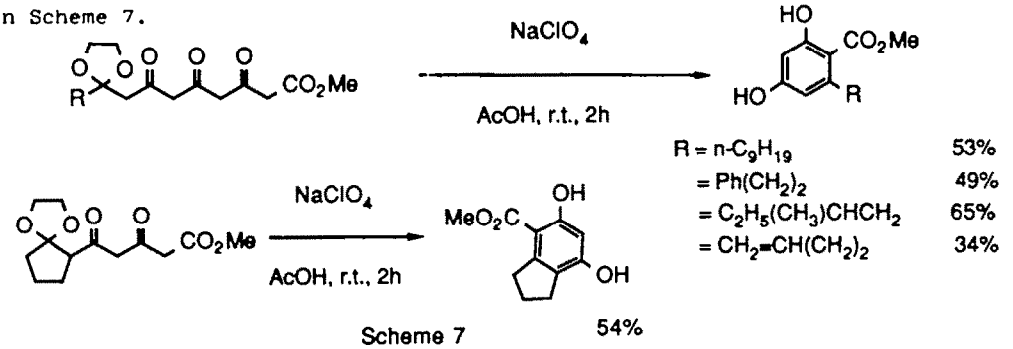
Amides	Yields (%)
CH_3CONMe_2	77
$n\text{-}C_5H_{11}CONMe_2$	73
$n\text{-}C_9H_{19}CONMe_2$	74
$Ph(CH_2)_3CONMe_2$	85
$Ph(CH_2)_3CON$	57
$CH_3\text{-}C(O_2C_2H_4)\text{-}(CH_2)_2CONMe_2$	62
$PhCONMe_2$	84
	77
	86

Keto acetal 12, synthesized from N,N-dimethyl-4-oxopentanamide, was treated with acid for the deprotection. The intramolecular condensation proceeded under the acidic condition, and 2-(2-methoxycarbonyl-1-oxoethyl)-3-methyl-2-cyclopentenone(13) was obtained (70% yield) as shown in Scheme 6. Cyclopentenone 13 existed as a mixture of keto- and enol-tautomers in $CDCl_3$. The treatment of 2-(5-methoxy-



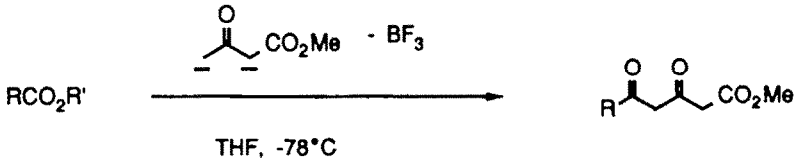
Scheme 6

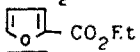
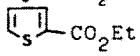
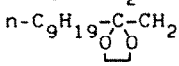
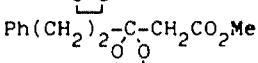
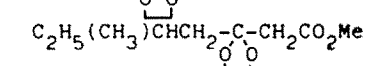
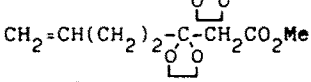
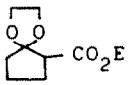
carbonyl-2,4-dioxopentyl)-2-nonyl-1,3-dioxolane with 2M HCl at r.t. gave 2-methoxycarbonylmethyl-6-nonyl-4-pyrone. It was reported in a literature that the acid treatment of 3,6,9-trioxodecanoate resulted in the pyrone and not the benzoate.[9] After the examination of the reaction conditions, the presence of sodium perchlorate was found to give the carbon-carbon bond formation product in acetic acid. The examples of the synthesis of benzoates from dioxoacetals are shown in Scheme 7.



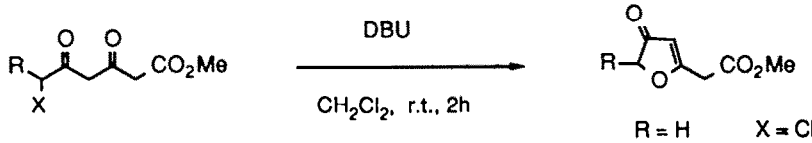
Scheme 7

Table 3. Synthesis of 3,5-Dioxoalaknoates from Esters.



Esters	Yields (%)
$n\text{-}C_5H_{11}CO_2Et$	44
$n\text{-}C_9H_{19}CO_2Et$	60
$PhCO_2Et$	72
	55
	52
	71
	55
	43
	45
$ClCH_2CO_2Me$	43
$CH_3CHClCO_2Me$	74
$n\text{-}C_3H_7CHBrCO_2Me$	56
	81

As the present BF_3-promoted Claisen condensation proceeds under mild reaction conditions, halogen was also not affected. 6-Halo-3,5-dioxoalkanoates were obtained from α-haloesters in good yields (Table 3). In contrast, the reaction of α-haloesters with acetoacetate dianion at 0 °C in the absence of the Lewis acid gave a complex mixture. With DBU in methylene chloride, 6-halo-3,5-dioxoalkanoate was converted to 2-alkyl-3(2H)-furanone by the intramolecular alkylation (Scheme 8).

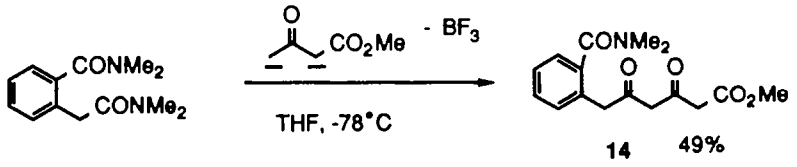


R = H X = Cl 61%
Me Cl 74%
n-Pr Br 80%

Scheme 8

A variety of 3,5-dioxoalkanoates are synthesized by employing the present method starting from amides or esters. The reaction, however, is not quite effective for rather hindered substrates. For example, the treatment of N,N-dimethyl-o-(N,N-dimethylcarbamoyl)phenylacetamide with dianion in the presence of $BF_3 \cdot OEt_2$ gave N,N-dimethyl-(o-N,N-dimethylcarbamoylphenyl)-3,5-dioxohexanamide (14) in 49% yield (Scheme 9). While, the reaction of the

corresponding diester with acetoacetate dianion in THF-HMPA at r.t. in the absence of BF_3 gave the dual condensation product, which was converted to the anthracene derivatives by the intramolecular condensation.[2, 3] In spite of the drawback, the Lewis acid promoted Claisen condensation is useful; it proceeds under mild reaction conditions, which minimize the formation of the by-products — hydrolysis or ester exchange — and it tolerates the sensitive functional group such as halogen.



14 49%

Scheme 9

In summary, several β,β',γ,γ'-tetraoxoalkanedioates were synthesized by the BF_3-promoted Claisen condensation of N,N,N',N'-tetramethylalkanediamides with acetoacetate dianion. The aromatization of the polyketoesters was examined and metal acetates were found to catalyze the intramolecular condensation effectively. The scope and the limitation of the Lewis acid promoted condensation reaction was also studied.

EXPERIMENTAL

NMR spectra were obtained on a JEOL JNM-FX-60. Chemical shift values are given in ppm relative to internal Me_4Si. IR spectra were recorded on a Shimadzu IR-408. High resolution mass spectra were taken with JEOL JMS-DX-300. Distillations were performed by Kugel-rohr using Shibata Glass Tube Oven GTO-250, and bath temperatures were recorded. Melting points were not corrected. Chromatographies (silica gel) were conducted on Wako gel B5F or C-200 (Wako Pure Chemical Industries LTD.).

7-Hydroxy-6-methoxycarbonyl-5-methoxycarbonylmethyl-1-indanone (2). Under a nitrogen atmosphere, methyl acetoactate (290 mg, 2.5 mmol) in THF (2 ml) was added to a suspension of sodium hydride (66 mg, 2.75 mmol) in THF (1 ml) at 0 °C. After 10 min, a hexane solution (1.6 ml) of n-butyllithium (2.5 mmol) was added, and the mixture was stirred for 10 min at 0 °C. On cooling to -78 °C, a THF (2 ml) solution of N,N,N',N'-tetramethylsuccinamide (1) (50 mg, 0.3 mmol) and $BF_3 \cdot OEt_2$ (0.4 ml, 2.9 mmol) were added successively. The mixture was slowly warmed to 0 °C for 1 h, and 1M hydrochloric acid was added. After stirring for 3 h at room temperature, organic materails were extracted with ethyl acetate, washed with aqueous sodium bicarbonate and brine, dried over sodium sulfate, and concentrated. The residue was chromatographed over silica gel with ethyl acetate-benzene to give 2 (37 mg, 67%). NMR ($CDCl_3$) δ 2.5-2.8 (2H,m), 3.0-3.2 (2H,m), 3.69 (3H,s), 3.85 (2H,s), 3.92 (3H,s), 6.81 (1H,s), 10.91 (1H,s). IR (KBr) 1740, 1700, 1610 cm^{-1}. Exact mass calcd for $C_{14}H_{14}O_6$: 278.0789. Found: 278.0763. Mp 129-131 °C (ether-hexane).

8-Hydroxy-6-methoxycarbonyl-7-methoxycarbonylmethyl-1-oxo-1,2,3,4-tetrahydronaphthalene (4). Synthesized as above except that the reaction mixture was treated with 1M hydrochloric acid and 1M aqueous sodium hydroxide to pH 4. H-NMR ($CDCl_3$) δ 1.9-2.3 (2H,m), 2.60 (2H,t,J=6Hz), 2.83 (2H,t,J=6Hz), 3.70 (5H,s), 6.66 (1H,s), 13.04 (1H,s). IR (KBr) 1730, 1715, 1620 cm^{-1}. Exact mass calcd for $C_{15}H_{16}O_6$: 292.0945. Found: 292.0920. Mp 92.5-93.0 °C (ether).

Dimethyl 3,5,10,12-Tetraoxotetradecanedioate (6). To a THF-hexane (20+10 ml) solution of acetoacetate dianion (16 mmol), generated from methyl acetoacetate as above, was added a THF (2.5 ml) solution of N,N,N',N'-tetrametnyladipamide (5) (1.0 g, 5 mmol) and $BF_3 \cdot OEt_2$ (2.0 ml, 15 mmol) at -78 °C. The mixture was warmed to 0 °C for 1 h, and added to 2M hydrochloric acid. Organic materials were extracted with ethyl acetate, washed with aqueous sodium bicarbonate and brine, dried over sodium sulfate, and concentrated. The product 4 (1.22 g, 71%) was isolated by silica gel chromatography (ethyl acetate-hexane). H-NMR ($CDCl_3$-CCl_4) δ 1.0-1.6 (4H,m), 1.6-2.3 (4H,m), 3.31 (4H,s), 3.73 (6H,s), 5.52 (2H,s), 14.78 (2H, br). IR (neat) 3500-2300, 1730, 1600 cm^{-1}. Exact mass calcd for $C_{16}H_{22}O_8$: 342.1304. Found: 342.1269.

Dimethyl 3,5,12,14-tetraoxohexadecanedioate (9). H-NMR ($CDCl_3$-CCl_4) δ 1.1-1.9 (6H,m), 2.0-3.0 (4H,m), 3.32 (4H,s), 3.74 (6H,s), 5.56 (2H,s), 14.91 (2H,br). IR (neat) 3500-2300, 1735, 1600 cm^{-1}. Exact mass calcd for $C_{17}H_{24}O_8$: 356.1471.

Found: 356.1519.

Dimethyl 3,5,14,16-Tetraoxooctadecanedioate (11). H-NMR ($CDCl_3$-CCl_4) δ 1.1-1.9 (8H,m), 2.0-2.7 (4H,m), 3.36 (4H,s), 3.74 (6H,s), 5.60 (2H,s), 15.0 (2H,br). IR (Neat) 3500-2300, 1740, 1630 cm^{-1}.

1-Hydroxy-2-methoxycarbonyl-3-methoxycarbonylmethyl-9-oxo-6,7,8,9-tetrahydro-5H-benzocycloheptene (7). A mixture of $Ca(OAc)_2 \cdot H_2O$ (113 mg, 0.64 mmol), 6 (88 mg, 0.26 mmol), and methanol (3 ml) was stirred under reflux for 3 h. On cooling, 1M hydrochloric acid was added and organic materials were extracted with ethyl acetate, washed with brine, dried over sodium sulfate, and concentrated. The product 7 (61 mg, 78%) was isolated by silica gel chromatography (ethyl acetate-hexane). H-NMR ($CDCl_3$) δ 1.6-2.0 (4H,m), 2.6-3.0 (4H,m), 3.79 (5H,s), 3.92 (3H,s), 6.06 (1H,s), 12.90 (1H,s). IR (KBr) 3500, 2900, 1720, 1630, 1610 cm^{-1}. Exact mass calcd for $C_{16}H_{18}O_6$: 306.1103. Found: 306.1112. Mp 114-6 °C (benzene-hexane).

N,N-Dimethyl-(o-N',N'-dimethylcarbamoylphenyl)-3,5-dioxohexanamide (14). H-NMR ($CDCl_3$) δ 2.82 (3H,s), 3.09 (3H,s), 3.32 (2H,s), 3.72 (5H,s), 5.63 (1H,s), 7.0-7.5 (4H,m). IR (neat) 3600, 1740, 1620 cm^{-1}. Exact mass calcd for $C_{16}H_{19}NO_5$: 305.1262. Found: 305.1252.

Synthesis of Methyl 3,5-Dioxoalkanoates from Amides. A Typical Procedure. Under a nitrogen atmosphere, a THF-hexane (2 and 1.3 ml) solution of methyl acetoacetate dianion (2.0 mmol) was prepared as above. The mixture was cooled to -78 °C, and a THF (2 ml) solution of N,N-dimethylhexanamide (72 mg, 0.5 mmol) and $BF_3 \cdot OEt_2$ (0.4 ml, 2.9 mmol) were added successively. The mixture was warmed to 0 °C for 2 h, and poured on silica gel (10 g), which was allowed to stand overnight. Organic materials were eluted with ethyl acetate, concentrated, and chromatographed on silica gel (ethyl acetate-hexane) to give methyl 3,5-dioxodecanoate (78 mg, 73%). H-NMR ($CDCl_3$) δ 0.91 (3H,t,J=5Hz), 1.0-2.0 (6H,m), 2.1-2.5 (2H,m), 3.31 (2H,s), 3.74 (3H,s), 5.56 (1H,s), 15.0 (1H,br). IR (neat) 1740, 1600 cm^{-1}. Exact mass calcd for $C_{11}H_{18}O_4$: 214.1204. Found: 214.1204. Bp 100 °C/ 1mm. In cases of larger scale synthesis, the same workup with the preparation of 6 was conducted, which gave a similar yield of the product.

Methyl 3,5-Dioxohexanoate. H-NMR ($CDCl_3$-CCl_4) δ 2.06 (3H,s), 3.30 (2H,s), 3.73 (3H,s), 5.58 (1H,s). IR (neat 3600-2200, 1730, 1600 cm^{-1}.

Methyl 3,5-Dioxotetradecanoate. H-NMR ($CDCl_3$-CCl_4) δ 0.7-1.1 (3H,m), 1.1-2.0 (14H,m), 2.0-3.0 (2H,m), 3.35 (2H,s), 3.74 (3H,s), 5.59 (1H,s), 14.85 (1H,br). IR (neat) 3600-2300, 1740, 1600 cm^{-1}. Exact mass calcd for $C_{15}H_{26}O_4$: 270.1831. Found: 270.1854. Bp 150 °C/ 1mm.

Methyl 8-Phenyl-3,5-dioxooctanoate. H-NMR ($CDCl_3$-CCl_4) δ 1.8-2.0 (6H,m), 3.33 (2H,s), 3.72 (3H,s), 5.57 (1H,s), 7.21 (5H,s). IR (neat) 3600-2400, 1740, 1600 cm^{-1}. Exact mass calcd for $C_{15}H_{18}O_4$: 262.1204. Found: 262.1159. Bp 200 °C/ 1mm.

2-(2-Methoxycarbonyl-1-oxoethyl)-3-methyl-2-cyclopenten-1-one (12). H-NMR ($CDCl_3$-CCl_4) δ 1.35 (3H,s), 1.8-2.2 (2H,m), 2.2-2.8 (2H,m), 3.36 (2H,m), 3.77 (3H,s), 3.97 (2H,s), 5.64 (1H,s). IR (neat) 3600-2300, 1740, 1600 cm^{-1}. Exact mass calcd for $C_{12}H_{18}O_6$: 258.1103. Found: 258.1046.

Methyl 3,5-Dioxo-5-phenylpentanoate. H-NMR ($CDCl_3$-CCl_4) δ 3.43 (2H,s), 3.73 (3H,s), 6.24 (1H,s), 7.2-7.6 (3H,m), 7.6-8.0 (2H,m), 15.53 (1H,br). IR (neat) 3500-2200, 1740, 1600 cm^{-1}. Bp 170 °C/ 1mm.

Methyl 3,5-Dioxo-5-(2-furyl)pentanoate. H-NMR ($CDCl_3$-CCl_4) δ 3.40 (2H,s), 3.75 (3H,s), 6.16 (1H,s), 6.5-6.6 (1H,m), 7.1-7.2 (1H,m), 7.5-7.6 (1H,m), 13.0 (1H,br). IR (neat) 3600-2300, 1730, 1600 cm^{-1}. Exact mass calcd for $C_{10}H_{10}O_5$: 210.0528. Found: 210.0552. Bp 150 °C/ 0.8 mm.

Methyl 3,5-Dioxo-5-(2-thienyl)pentanoate. H-NMR ($CDCl_3$-CCl_4) δ 3.42 (2H,s), 3.76 (3H,s), 6.14 (2H,s), 7.0-7.3 (1H,m), 7.5-7.8 (2H,m), 13.85 (1H,br). IR (neat) 3600-2300, 1740, 1600 cm^{-1}. Exact mass calcd for $C_{10}H_{10}O_4S$: 226.0300. Found: 226.0308. Bp 200 °C/ 2 mm.

Synthesis of Methyl 3,5-Dioxoalkanoates from Esters. A Typical Procedure. Under a nitrogen atmosphere, a THF-hexane (20 and 12.8 ml) solution of acetoacetate dianion (20 mmol) was prepares as above. On cooling to -78 °C, methyl 3-oxododecanoate ethylene acetal (1.3 g, 4.8 mmol) in THF (5 ml) and $BF_3 \cdot OEt_2$ (1 ml, 7.7 mmol) were added successively. The mixture was warmed to 0 °C for 30 min, and poured on 2M hydrochloric acid. Organic materials were extracted with ethyl acetate, washed with aqueous sodium bicarbonate and brine, dried over sodium sulfate, and concentrated. 2-(5-Methoxycarbonyl-2,4-dioxopentyl)-2-nonyl-1,3-dioxolane (1.2 g, 71%) was obtained by silica gel chromatography (ethyl acetate-hexane). H-NMR ($CDCl_3$) δ 0.7-1.0 (3H,m), 1.0-1.8 (14H,m), 2.61 (2H,s), 3.37 (3H,s), 3.77 (3H,s), 3.96 (4H,s), 5.72 (1H,s), 14.3 (1H,br). IR (neat) 3400-2300, 1740, 1600 cm^{-1}.

2-(5-Methoxycarbonyl-2,4- dioxopentyl)-2-(2-phenylethyl)-1,3-dioxolane. H-NMR ($CDCl_3$) δ 1.9-2.2 (2H,m), 2.5-3.0 (2H,m), 2.61 (2H,s), 3.32 (2H,s), 3.71 (3H,s), 3.99 (4H,s), 5.68 (1H,s), 7.18 (5H,s), 14.5 (1H,br). IR (neat) 3600-2200, 1740, 1600 cm^{-1}. Exact mass Calcd for $C_{18}H_{22}O_6$: 334.1416. Found: 334.1403.

2-(2-Methylbutyl)-2-(5-methoxycarbonyl-2,4-dioxopentyl)-1,3-dioxolane. H-NMR ($CDCl_3$) δ 0.7-1.0 (6H,m), 1.0-1.8 (5H,m), 2.58 (2H,s), 3.33 (2H,s), 3.73 (3H,s), 3.94 (4H,s), 5.69 (1H,s), 13.6 (1H,br). IR (neat) 3600-2400, 1740, 1600 cm^{-1}.

2-(3-Butenyl)-2-(5-methoxycarbonyl-2,4-dioxopentyl)-1,3-dioxolane. H-NMR ($CDCl_3$) δ 1.0-2.3 (6H,m), 2.58 (2H,s), 3.33 (2H,s), 3.74 (3H,s), 3.95 (4H,s), 4.8-5.1 (2H,m), 5.7-6.4 (1H,m), 5.68 (2H,s), 15.0 (1H,br). IR (neat) 3600-2400, 1740, 1600 cm^{-1}. Exact mass calcd for $C_{15}H_{22}O_6$: 298.1120. Found: 298.1170.

Methyl 6-Chloro-3,5-dioxohexanoate. H-NMR ($CDCl_3$-CCl_4) δ 3.38 (2H,s), 3.75 (3H,s), 4.04 (2H,s), 5.96 (1H,s). IR (neat) 3400-2300, 1720, 1600 cm^{-1}.

Methyl 6-Chloro-3,5-dioxoheptanoate. H-NMR ($CDCl_3$-CCl_4) δ 1.69 (3H,d,J=7HZ), 3.40 (2H,s), 3.76 (3H,s), 4.40 (1H,q,J=7Hz), 5.95 (1H,s). IR (neat) 3400-2200, 1740, 1600 cm^{-1}.

Methyl 6-Bromo-3,5-dioxodecanoate. H-NMR ($CDCl_3$-CCl_4) δ 0.7-1.1 (3H,m), 1.1-1.7 (2H,m), 1.7-3.0 (2H,m), 3.36 (2H,s), 3.74 (3H,s), 3.9-4.3 (1H,m), 5.58 (1H,s), 13.5 (1H,br). IR (neat) 3400-2600, 1720, 1615 cm^{-1}.

6-(4-Methoxycarbonyl-1,3-dioxobutyl)-1,4-dioxaspiro[4,4]nonane. H-NMR ($CDCl_3$) δ 1.6-2.1 (6H,m), 2.87 (1H,t,J=8Hz), 3.35 (2H,s), 3.74 (3H,s), 3.7-4.0 (4H,m), 5.69 (1H,s), 15.08 (1H,br). IR (neat) 3600-2400, 1730, 1600 cm^{-1}. Exact mass calcd for $C_{13}H_{18}O_6$: 270.1103. Found: 270.1125.

2-(2-Methoxycarbonyl-1-oxoethyl)-3-methyl-2-cyclopenten-1-one (13). A mixture of 2-(2-methoxycarbonyl-1-oxoethyl)-2-methyl-1,3-dioxolane (12) (99 mg, 0.38 mmol), THF (3 ml), and 1M hydrochloric acid (3 ml) was stirred for 3 h at room temperature. Then, it was diluted with water, extracted with ethyl acetate, washed with brine, and dried over sodium sulfate. After the removal of the solvents, 13 (52 mg, 70%) was isolated by silica gel chromatography (ethyl acetate-hexane). H-NMR ($CDCl_3$) δ 2.4-2.8 (4H,m), 2.48 (3H,s), 3.27 and 3.76 (3H,s and s), 3.92 (1.6H,s), 5.97 (0.2H,s). 12.21 (0.2H,s). C-NMR ($CDCl_3$) δ 20.2, 32.9, 33.4, 34.9, 35.3, 48.6, 51.3, 52.1, 91.9, 132.3, 136.8, 165.4, 168.4, 181.1, 189.2, 190.9, 204.7, 205.2. IR (neat) 1700, 1630 cm^{-1}. Exact mass calcd for $C_{10}H_{12}O_4$: 196.0735. Found: 196.0747.

Synthesis of Methyl 2,4-Dihydroxybenzoates. A Typical Procedure. A mixture of 2-(5-methoxycarbonyl-2,4-dioxopental)-2-nonyl-1,3-dioxolane (50 mg, 0.14 mmol), sodium perchlorate (50 mg, 0.42 mmol), and acetic acid (2 ml) was stirred for 2 h at room temperature. The mixture was diluted with water, and organic materials were extracted with ethyl acetate. The organic layer was washed with aqueous sodium bicarbonate and brine, dried over sodium sulfate, and concentrated. Methyl 2,4-dihydroxy-6-nonylbenzoate (22 mg, 53%) was isolated by silica gel chromatography (ethyl acetate-hexane). H-NMR ($CDCl_3$) δ 0.7-1.0 (3H,m), 1.0-1.7 (14H,m), 2.5-3.0 (2H,m), 3.91 (3H,s), 5.53 (1H,br), 6.24 (2H,s), 11.68 (1H,s). IR (KBr) 3400-2200, 1750, 1680 cm^{-1}. Exact mass calcd for $C_{17}H_{26}O_4$: 294.1830. Found: 294.1817. Mp 80-81 °C (hexane).

Methyl 2,4-Dihydroxy-6-(2-phenylethyl)benzoate. H-NMR ($CDCl_3$) δ 2.5-3.3 (4H,m), 3.94 (3H,s), 4.6 (1H,br), 4.7-5.0 (2H,m), 7.18 (5H,s), 11.66 (1H,s). IR (neat) 3300-2500, 1740, 1650 cm^{-1}. Exact mass calcd for $C_{16}H_{16}O_4$: 272.1049. Found: 272.1059.

Methyl 2,4-Dihydroxy-6-(2-methylbutyl)benzoate. H-NMR ($CDCl_3$) δ 0.7-1.1 (6H,m), 1.1-2.0 (3H,m), 2.0-3.2 (2H,m), 3.92 (3H,s), 5.67 (1H,br), 6.14 (1H,d,J=2.5 Hz), 6.25 (1H,d,J=2.5Hz), 11.62 (1H,s). IR (neat) 3600-2200, 1710, 1600 cm^{-1}. Exact massclacd for $C_{13}H_{18}O_4$: 238.1205. Found: 238.1191.

Methyl 6-(3-Butenyl)-2,4-dihydroxybenzoate. H-NMR ($CDCl_3$) δ 1.1-3.0 (6H,m), 3.91 (3H,s), 4.7-5.3 (2H,m), 5.5-6.0 (1H,m), 6.0-6.3 (2H,m), 11.65 (1H,s). IR (neat) 3600-2400, 1710, 1600 cm^{-1}. Exact mass calcd for $C_{13}H_{16}O_4$: 236.1047. Found: 236.1041.

4,6-Dihydroxy-7-methoxycarbonylindan. H-NMR ($CDCl_3$) δ 1.9-2.3 (2H,m), 2.77 (2H,t,J=8HZ), 3.18 (2H,t,J=7Hz), 3.90 (3H,s), 5.31 (1H,s), 6.25 (2H,s), 11.33 (1H,s). IR (KBr) 3500-2700, 1740, 1710 cm^{-1}. Exact mass Calcd for $C_{11}H_{13}O_4$: 209.0813. Found: 209.0807. Mp 147-51 °C ($CHCl_3$-hexane).

Synthesis of 2-Alkyl-3(2H)-furanones. A Typical Procedure. Under a nitrogen atmosphere, 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU, 0.3 ml, 2 mmol) was added to a THF (5 ml) solution of methyl 6-chloro-3,5-dioxohexanoate (195 mg, 1 mmol), and the mixture was stirred for 2 h at room temperature. Acetic acid (0.6 ml) was added, and the solvents were removed under reduced pressure. 3(2H)-Furanone (128 mg, 74%) was isolated by silica gel chromatography (ethyl acetate-hexane). H-NMR ($CDCl_3$-CCl_4) δ 3.56 (2H,s), 3.77 (3H,s), 4.51 (2H,s), 5.68 (1H,s). IR (neat) 1740, 1700, 1600 cm^{-1}. Exact mass calcd for $C_7H_8O_4$: 156.0423. Found: 156.0416.

2-Methyl-3(2H)-furanone. H-NMR ($CDCl_3$-CCl_4) δ 1.44 (3H,d,J=7Hz), 3.55 (2H,s), 3.16 (3H,s), 4.50 (1H,q,J=7Hz), 5.61 (1H,s). IR (neat) 1750, 1700, 1600 cm^{-1}.

2-Propyl-3(2H)-furanone. H-NMR ($CDCl_3$-CCl_4) δ 0.7-1.1 (3H,m), 1.1-2.1 (4H,m), 3.54 (2H,s), 3.76 (3H,s), 4.3-4.6 (1H,m), 5.62 (1H,s). IR (neat) 1750, 1700, 1600 cm^{-1}.

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