Methyl 4-Trimethylsiloxy-2,4-pentadienoate. A Novel Diels-Alder-Reactive Diene

Jakob Oren,[a,b] Martin Demuth,*[a] Benzion Fuchs*[b]

[a] Max-Planck-Institut für Strahlenchemie, D-4330 Mülheim a.d. Ruhr, West Germany
[b] School of Chemistry, Tel-Aviv University, Ramat-Aviv, 69978 Tel-Aviv, Israel

Methyl 4-trimethylsiloxy-2,4-pentadienoate, a novel 1,3-diene of anticipated importance as a precursor of useful intermediates, was prepared and its chemical behavior in Diels-Alder reactions and dimerization was explored.

The Diels-Alder reaction is undoubtedly one of the cornerstones of organic synthesis.[1] In this context, a remarkable number of 1,3-dienes have been prepared with suitably positioned electron-donor or -acceptor substituents rendering the diene thermally reactive and allowing efficient regiocontrol in [4 + 2]cycloadditions.[1b] For current work we required a Diels-Alder component in which the structural features of the two known enophiles, $H_2C{=}C[OSi(CH_3)_3]{-}CH{=}CH_2$ **(1)**[2] and $H_2C{=}CH{-}CH{=}CH{-}COOCH_3$ **(2**, Fluka) are combined. Thus, methyl *trans*-4-oxo-2-pentenoate **(3)**, which is readily accessible from methyl levulinate,[3] was successfully trimethylsilylated to give the desired and hitherto unknown title diene[4] **4** in 75% yield. This material can be stored without noticeable decomposition in cyclohexane solution at 0–10 °C for several weeks.

The anticipated Diels-Alder reactivity of the diene **4** was exemplified by its smooth cycloadditions to *N*-phenylmaleimide, maleic anhydride, and dimethyl acetylenedicarboxylate. The crude reaction products characterized satisfactorily by spectroscopy were transformed in methanol to the more stable corresponding ketones **(8, 9, 10)**. The complete data of these compounds were collected after column chromatography (Tables 1 and 2).

A noteworthy aspect of the chemical behavior of the diene **4** is its dimerization and its cycloaddition with its precursor **3**, both reactions being highly efficient processes. Also in this series, the enol silyl ether moiety of the cycloadducts was cleaved with methanol to obtain the stable cyclohexanones (**13, 14, 16, 18,** and **15** + **17** as a mixture of diastereoisomers) which allowed extensive characterization (Tables). In a cursory examination we found that **16** isomerizes quantitatively as a result of base catalysis (0.1 molar sodium methoxide in methanol at room temperature) to the symmetric diastereosiomer **18**, whereas the mixture **15** + **17** remains unchanged (1 : 1) under the same conditions. Clearly, the moderate regioselectivity (~ 3 : 1) and lack of stereoselectivity indicate that within the FMO interaction concept[5] primary orbital overlap is the main factor controlling the cycloadditions with **3**. Low temperature conditions along with the use of catalysts are being investigated as a possibility to improve the regio- and stereoselectivity of these transformations.

Table 1. Cyclic Products from Methyl 4-Trimethylsiloxy-2,4-pentadienoate **(4)**

Product	Yield (%)[a]	m.p. (°C)	Molecular Formula[b]	MS[c] *m/e* (M^+)
5	84	oil	$C_{19}H_{23}NO_5Si$ (373.2)	373
8[d]	75	150	$C_{16}H_{15}NO_5$ (301.1)	301
9[e]	40	89–90	$C_{12}H_{16}O_7$ (272.1)	272
10[f]	50	oil	$C_{12}H_{14}O_7$ (270.1)	270
13a	[g]	oil	$C_{15}H_{24}O_6Si$ (328.2)	328
13b	[h]	oil	$C_{12}H_{16}O_6$ (256.1)	256
14a	[g]	oil	$C_{15}H_{24}O_6Si$ (328.2)	328
14b	[h]	oil	$C_{12}H_{16}O_6$ (256.1)	256
16	[i]	oil	$C_{12}H_{16}O_6$ (256.1)	256
15 + **17**	[i]	oil	$C_{12}H_{16}O_6$ (256.1)	256
18	[i]	oil	$C_{12}H_{16}O_6$ (256.1)	256

[a] Yield of purified product, based on **4**.
[b] Satisfactory microanalyses obtained: C ± 0.25, H ± 0.12, N ± 0.20, Si ± 0.18.
[c] Recorded on a Varian CH-5 instrument at 70 eV.
[d] Purified by column chromatography on silica gel (petroleum ether/EtOAc 3 : 1).
[e] The two-step sequence affords a keto acid and the dimethyl acetal thereof. Treatment of this mixture with diazomethane in Et_2O followed by acetal cleavage with 15% H_2SO_4 in CH_2Cl_2 (12 h) gives exclusively the *all-cis* triester **9**[6a] which is purified by column chromatography on silica gel (pentane/Et_2O 4 : 1).
[f] *cis*-**10**[6b]/*trans*-**10** = 2 : 1 (^{1}H-NMR); purification by column chromatography on silica gel (pentane/Et_2O 4 : 1).
[g] The 5 : 2 mixture **11** + **12** is hydrolyzed to **13a** + **14a** (5 : 2); overall yield of the product mixture: 73%.
[h] The mixture **13a** + **14a** is treated with tetrabutylammonium fluoride and the resultant product is subjected to column chromatography on silica gel (pentane/Et_2O 4 : 1) to afford **13b** and **14b** in 44% and 25% overall yield, respectively.
[i] Column chromatography on sila gel (pentane/Et_2O 5 : 1) of the product mixture affords pure **16** and **18** whereas **15** and **17** cannot be separated. The total yield amounts to 75%.

In summary, the results show that ester **4** answers our expectations of a synthetically valuable 1,3-diene reagent.

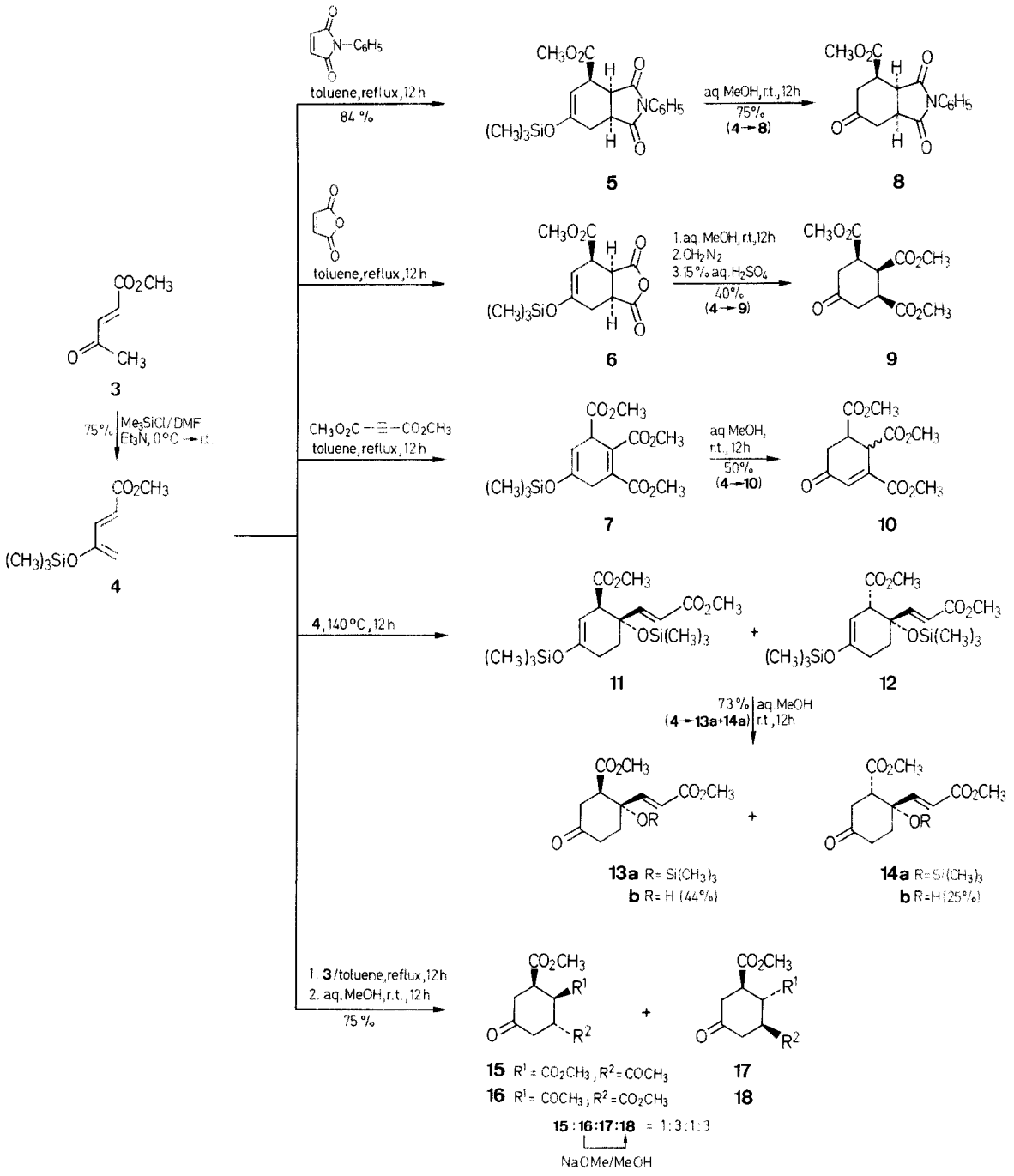

Table 2. Spectral Data of Compounds **5**, **8**, **9**, **10**, **13–18**

Compound	IR ($CHCl_3$)[a] ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[b] δ, J (Hz)	^{13}C-NMR ($CDCl_3$/TMS)[b] δ, J (Hz)
5	1715, 1650	0.2 (s, 9H); 2.49 (dd, 1H, J = 8, 16); 2.64 (dd, 1H, J = 5, 16); 3.2–3.5 (m, 2H); 3.59 (t, 1H, J = 6); 3.66 (s, 3H); 5.19 (d, 1H, J = 6); 7.2–7.5 (m, 5H)	−0.45 (3C), 28.7, 38.6, 39.9, 41.0, 51.5, 98.9, 126.1 (2C), 127.9, 128.5 (2C), 131.9, 152.7, 171.4, 176.2, 177.6
8	1720	2.61 (dd, 1H, J = 5.5, 19); 2.7–2.9 (m, 3H); 3.4–3.6 (m, 3H), 3.74 (s, 3H), 7.2–7.6 (m, 5H)	36.8, 37.4, 39.2, 39.7, 40.3, 52.9, 126.5 (2C), 128.9, 129.3 (2C), 131.9, 172.4, 175.6, 176.6, 205.1
9	1740, 1720	2.65 (dd, 2H, J = 4.4, 15.3); 2.84 (dd, 2H, J = 13.4, 15.3); 2.99 (dt, 2H, J = 4.4, 13.4); 3.71 (s, 3H); 3.76 (s, 6H); 3.88 (t, 1H, J = 4.4)	39.0 (2C), 42.7 (2C), 42.8, 52.1, 52.2 (2C), 170.8, 171.3 (2C), 206.3

Table 2. (Continued)

Compound	IR ($CHCl_3$)[a] ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[b] δ, J(Hz)	^{13}C-NMR ($CDCl_3$/TMS)[b] δ, J(Hz)
10	1735, 1695	*cis:* 2.62 (dd, 1H, J = 5.3, 17.3); 2.88 (dd, 1H, J = 3.1, 17.3); 3.64 (m, 1H); 3.71 (s, 3H); 3.78 (s, 3H); 3.86 (s, 3H); 4.35 (d, 1H, J = 3); 6.77 (bs, 1H) *trans:* 2.75 (dd, 1H, J = 5, 17.6); 2.8–2.9 (m, 1H); 3.3–3.4 (m, 1H), 3.6 (s, 3H); 3.71 (s, 3H); 3.88 (s, 3H); 4.38 (d, 1H, J = 5.5); 6.79 (bs, 1H)	35.9, 41.7, 42.2, 52.2, 52.4, 52.5, 133.1, 142.1, 165.3, 169.8, 171.5, 195.1 35.6, 41.3, 41.8, 51.5, 51.9, 52.3, 133.3, 143.2, 165.7, 170.7, 171.9, 196.6
13a	1730	0.13 (s, 9H); 1.9–2.1 (m, 1H); 2.3–2.45 (m, 3H); 2.45–2.65 (m, 1H); 2.8 (dd, 1H, J = 6, 15); 3.08 (ddd, 1H, J = 2, 4, 6); 3.55 (s, 3H); 3.73 (s, 3H); 5.87 (d, 1H, J = 16); 7.07 (d, 1H, J = 16)	2.1 (3C), 31.9, 36.2, 38.8, 51.8, 51.9, 53.6, 73.0, 120.9, 149.6, 166.1, 172.3, 207.7
13b	3460, 1720	1.9–2.0 (m, 1H); 2.2–2.3 (m, 1H); 2.3–2.6 (m, 3H); 2.82 (dd, 1H, J = 6, 15); 3.03 (dd, 1H, J = 6, 9); 3.66 (s, 3H); 3.71 (s, 3H); 3.72 (s, OH); 6.18 (d, 1H, J = 16); 7.12 (d, 1H, J = 16)	34.8, 36.5, 38.9, 51.5, 51.8, 52.4, 71.2, 121.3, 148.8, 166.5, 172.3, 207.8
14a	1725	0.1 (s, 9H); 1.95–2.1 (m, 1H); 2.2–2.4 (m, 3H); 2.5–2.7 (m, 1H); 2.8–2.9 (m, 2H); 3.64 (s, 3H); 3.74 (s, 3H); 5.97 (d, 1H, J = 16); 7.18 (d, 1H, J = 16)	2.1 (3C), 35.0, 36.4, 39.3, 51.8, 51.9, 52.5, 73.6, 120.4, 150.6, 166.2, 171.0, 207.9
14b	3480, 1720	1.75–1.85 (m, 1H); 1.95–2.05 (m, 1H); 2.2–2.3 (m, 1H); 2.4–2.45 (m, 1H); 2.75–2.9 (m, 2H); 2.95 (dd, 1H, J = 4, 14); 3.63 (s, 3H); 3.69 (s, 3H); 4.17 (s, OH); 6.16 (d, 1H, J = 16); 6.86 (d, 1H, J = 17)	35.8, 36.0, 39.1, 49.0, 51.7, 52.4, 71.0, 120.9, 150.8, 166.4, 173.7, 207.2
16	1735, 1720	2.3 (s, 3H); 2.35 (ddd, 1H, J = 1.2, 9.7, 16); 2.54 (ddd, 1H, J = 1.2, 5.5, 16); 2.6 (ddd, 1H, J = 1.6, 5.5, 16); 2.74 (ddd, 1H, J = 1.6, 5.5, 16); 3.27 (ddd, 1H, J = 5.5, 8.8, 9.7); 3.33 (ddd, 1H, J = 4.2, 5.5, 5.5); 3.46 (dd, 1H, J = 4.2, 8.8); 3.59 (s, 3H); 3.65 (s, 3H)	28.7, 40.4, 40.5, 40.9, 41.5, 50.4, 52.3, 52.4, 172.1, 173.5, 204.3, 206.6
15 + 17	1730	2.16 (s, 3H); 2.22 (s, 3H); 3.63 (s, 3H); 3.65 (s, 3H); 3.66 (s, 3H); 3.67 (s, 3H) **15:** 2.21 (dd, 1H, J = 10, 15); 2.5–2.6 (m, 2H); 2.68 (ddd, 1H, J = 2, 6, 15); 3.38 (dd, 1H, J = 4, 10); 3.4–3.5 (m, 2H) **17:** 2.35 (dd, 1H, J = 13, 15); 2.5–2.6 (m, 3H); 2.95 (ddd, 1H, J = 5.5, 11, 11.5); 3.2 (ddd, 1H, J = 4, 11, 13); 3.3 (t, 1H, J = 11)	28.8, 29.1, 40.6, 40.9, 41.0, 41.4, 42.2, 43.5, 43.9, 44.6, 47.3, 50.3, 52.3, 52.4 (2C), 52.5, 171.7, 172.2, 172.4, 172.6, 204.7, 204.8, 206.7, 208.2
18	1730	2.31 (s, 3H); 2.48 (dd, 2H, J = 13, 15); 2.67 (dd, 2H, J = 3.8, 15); 3.03 (ddd, 2H, J = 3.8, 10.4, 13); 3.44 (t, 1H, J = 10.4); 3.67 (s, 6H)	31.5, 41.5, 44.0, 50.6, 52.6, 172.6, 204.4, 209.4

[a] Recorded on a Perkin-Elmer 297 spectrometer.

[b] Recorded on Bruker WH-90, AM-360, or AM-400 instruments.

Methyl 4-Trimethylsiloxy-2,4-pentadienoate (4); Typical Procedure:
A DMF (50 mL) solution of chlorotrimethylsilane (31.7 mL, 0,25 mol) is added dropwise to a stirred DMF (200 mL) solution of methyl 4-oxo-2-pentenoate (**3**; 25.6 g, 0.2 mol) and triethylamine (35 mL, ~ 0.25 mol) at 0 °C. The mixture is stirred under nitrogen at room temperature for 12 h and then poured into saturated $NaHCO_3$ solution (150 mL) and extracted with pentane (3 × 200 mL). The organic extracts are washed with water (200 mL) and dried (Na_2SO_4). Evaporation of the solvent affords **4** as an oil in > 96% purity; yield: 30.02 g (75%).

$C_9H_{16}O_3Si$ (200.15) calc. C 53.97 H 8.05 Si 14.02
found 53.90 8.00 13.84

MS (70 eV): m/e = 200 (M^+).

IR ($CHCl_3$): ν = 1710, 1645, 1600, 1440, 1330, 1310, 1265, 1220, 1200, 1175 cm^{-1}.

UV (cyclohexane): λ_{max} = 262 nm (ε = 17000).

^{1}H-NMR ($CDCl_3$/TMS): δ = 0.23 (s, 9H); 3.73 (s, 3H); 4.6–4.7 (m, 2H); 6.10 (d, 1H, J = 16 Hz); 7.06 (d, 1H, J = 16 Hz).

^{13}C-NMR ($CDCl_3$/TMS): δ = 0.13, 51.5, 102.9, 118.8, 142.4, 153.4, 167.3.

Cycloadditions of Dienoic Ester 4; General Procedure:

Siloxycyclohexene Derivatives **5,6,7, 11,12**: A toluene (40 mL) solution of methyl 4-trimethylsiloxy-2,4-pentadienoate (**4**; 2.002 g, 10 mmol) and the dienophile (10 mmol) is refluxed for 12 h, followed by removal of the solvent *in vacuo*; only the dimerization (**4** → **11** + **12**) is performed without solvent at 140 °C (12 h). The residues are used in the next step without purification.

Substituted Cyclohexanones **8,9,13–18** *and Cyclohexenones* **10**: The crude product from the foregoing step is dissolved in MeOH/H_2O (4:1; ~ 100 mL) and this solution is stirred at room temperature for 12 h. Most of the MeOH is then removed *in vacuo* and the aqueous residue is extracted with CH_2Cl_2 (3 × 100 mL). The organic phase is separated and dried (Na_2SO_4). The solvent is evaporated and the crude product is chromatographed on a silica gel column (20 cm × 1.5 cm; 230–400 mesh) using the eluents given in Table 1.

A Minerva postdoctoral grant to J.O. is gratefully acknowledged.

Received: 25 July 1986; revised: 25 March 1987

(1) For more recent reviews, see:
(a) Sauer, J., Sustmann, R. *Angew. Chem.* **1980**, *92*, 773; *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 779.
(b) Petrzilka, M., Grayson, J.I. *Synthesis* **1981**, 753.
(c) Weinreb, S.M., Staib, R.R. *Tetrahedron* **1982**, *38*, 3087.

(2) Danishefsky, S., Prisbylla, M.P., Hiner, S. *J. Am. Chem. Soc.* **1978**, *100*, 2918.
Jung, M.E., McCombs, C.A. *Org. Synth.* **1978**, *58*, 163.

(3) El-Ghandour, N. *Bull. Soc. Chim. Fr.* **1972**, 2817.

(4) For two related dienes, see:
(a) Agosta, W.C., Lowrance, W.W. *J. Org. Chem.* **1970**, *35*, 3851.
(b) Davies, C.R., Davies, J.S. *J. Chem. Soc. Perkin Trans. 1* **1976**, 2390.

(5) Fukui, K. *Theory of Orientation and Stereoselection*, Springer Verlag, Berlin, 1975; *Acc. Chem. Res.* **1971**, *4*, 57; *Fortschr. Chem. Forsch.* **1970**, *15*, 1.
Sustmann, R. *Pure Appl. Chem.* **1974**, *40*, 569.
Houk, K.N. *Acc. Chem. Res.* **1975**, *8*, 361.
Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*, John Wiley & Sons, New York, 1976.
Gleiter, R., Bohm, M.C., in: *Stereochemistry and Reactivity of Systems Containing π-Electrons*, Watson, W.H. (ed.), Verlag Chemie, Weinheim, 1983.

(6) (a) The corresponding triethyl ester has been reported previously.[4a]
(b) The corresponding unsaturated triethyl triester, i.e., the *cis*-isomer, has been reported earlier[4]; it exhibits ^{1}H-NMR data similar to those of our *cis*-**10**.