Communications to the Editor

[Chem. Pharm. Bull. 34(8)3488—3491(1986)]

DIELS-ALDER REACTIONS OF (1E),(3E)-2-METHYL-1-TRIMETHYLSILYLOXY-1,3-PENTADIENE AND THE SYNTHESIS OF MULTISTRIATINS FROM THE ADDUCTS

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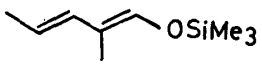
The Diels-Alder reactions of (1E),(3E)-2-methyl-1-trimethylsilyloxy-1,3-pentadiene with methyl acrylate and methyl (2E)-pentenoate were investigated. One of the adducts was used to synthesize some multistriatins.

KEYWORDS——(1E),(3E)-2-methyl-1-trimethylsilyloxy-1,3-pentadiene; Diels-Alder reaction; exo-adduct predominance; multistriatin

The [4+2] cycloaddition is the best way to generate substituted six-membered rings in which silyloxy substituted dienes react with a variety of dienophiles to provide new and effective routes to the oxygenated cyclohexenes so common in natural products.[1] We were interested in silyloxydiene (1), which has two methyl groups located in a 1,3-relationship, because the strong electron donor trimethylsilyloxy substituent on C-1 allows us to expect that the diene will react with electron defficient dienophiles to give ortho adducts, while the dimethyl groups on C-2 and C-4 require the opposite regiochemistry to generate meta-adducts.[1,2]



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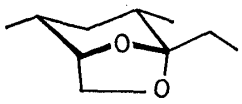

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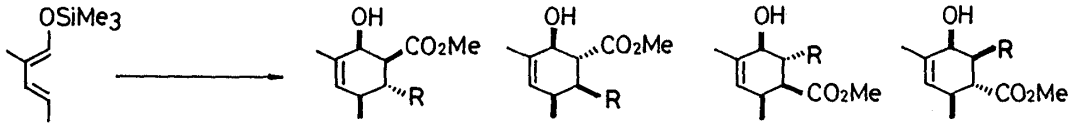
In this paper we report the Diels-Alder reactions of the diene (1) with methyl acrylate and methyl (2E)-pentenoate and the stereochemical outcome of the reaction. Moreover, we used one of the adducts to synthesize some dl-multistriatins. α-Multistriatin (2) is one of three essential components of an aggregation pheromone of the European elm bark beetle, Scolytus multistriatus.[3,4]

Trimethylsilylation of 2-methyl-2-pentenal, obtained from propanal, with Me_3SiCl/Et_3N gave (1E),(3E)-2-methyl-1-trimethylsilyloxy-1,3-pentadiene (1) as a sole product.[5] The Diels-Alder reaction of the diene (1) with methyl acrylate and methyl (2E)-pentenoate gave a chromatographically separable mixture of cycloadducts after hydrolysis. The results are summarized in Tables I and II.

Table I shows that the thermal reaction of 1 and methyl acrylate yielded a 65:35 mixture of ortho and meta adducts. The former adducts were the only product if the reaction was performed in the presence of $AlCl_3$ which affected the



1 3:R=H 4:R=H 5:R=H 6:R=H
7:R=Et 8:R=Et 9:R=Et 10:R=Et

Table I. The Reaction of the Diene (1) and Methyl Acrylate

Solvent (cat.)	Temp (°C)	Time (hr)	Yield (%)	3+4 : 5+6 (ortho:meta)	3 : 4 (endo:exo)	5 : 6 (endo:exo)
Xylene	137	42	89	65 : 35	75 : 25	88 : 12
$CH_2Cl_2(AlCl_3)$	0	1	9	100 : 0	92 : 8	——
Toluene$(AlCl_3)$	-20	2	57	100 : 0	98 : 2	——

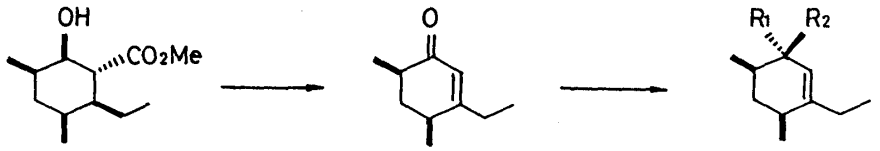
Table II. The Reaction of the Diene (1) and Methyl (2E)-Pentenoate

Solvent	Temp (°C)	Time (day)	Yield (%)	7+8 : 9+10 (ortho:meta)	7 : 8 (endo:exo)	9 : 10 (endo:exo)
Xylene	140	2.7	32	25 : 75	2 : 98	25 : 75
Xylene	162	6.5	84	29 : 71	2 : 98	24 : 76
$o\text{-}C_6H_4Cl_2$	162	6.0	79	35 : 65	2 : 98	27 : 73

rate of the reaction and induced high regio- and stereoselectivities. Other Lewis acids ($ZnCl_2$, $SnCl_4$, $Et_2O{\cdot}BF_3$) catalyzed the reaction but gave the adducts only in low yield.

On the other hand, methyl (2E)-pentenoate was less reactive than methyl acrylate and the reaction with the diene (1) afforded a mixture of four isomers (7), (8), (9), and (10).[5] Table II shows the interesting opposite effects on regiochemistry and stereochemistry, suggesting that serious steric interactions exist between the substituents of 1 and the ethyl group of the dienophile. The overall balance of the substituent effects favored the formation of the meta adducts (9) and (10) regiochemically and the exo adducts (8) and (10) stereochemically. The Lewis acid-catalyzed reaction did not yield any cycloadducts.

In order to confirm the structures of the adducts, 8 was transformed to an allylic alcohol (13), a synthetic intermediate of α-multistriatin.[4i] Trimethylsilylation of 8 followed by catalytic hydrogenation and hydrolysis gave

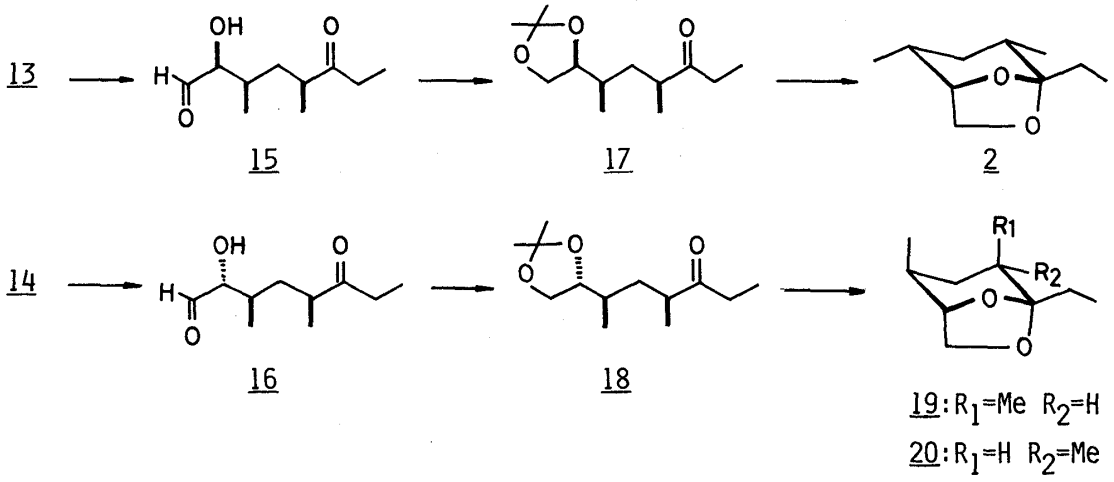


11 12 13:R_1=OH R_2=H
14:R_1=H R_2=OH

exclusively the pentasubstituted cyclohexane (11),[5] whose dimethyl groups existed in 1,3-diaxial configuration. The hydroxy-ester (11) was converted to the enone (12) in 30% overall yield by successive treatments with Jones reagent, DMSO/NaCl, and LDA/PhSeCl followed by H_2O_2 (CH_2Cl_2, 0°C). Reduction of 12 with $LiAlH_4$ (THF, 0°C) gave the trans allylic alcohol (13), whose NMR spectral data were identical with those of the reported compound (13).[4i] The stereochemical assignment for 13 was also supported by the reduction with more bulky L-Selectride (THF, 0°C) which attacked 12 from the less hindered α-side, giving an isomeric alcohol (14)[5] in 92% yield.

The alcohols (13) and (14) were converted to multistriatins according to the procedure of Marino et al.[4i] Oxidative cleavage of the double bonds of 13 and 14 with ozone afforded the keto-aldehydes (15) and (16), respectively. Finally, 15 was transformed to dl-α-multistriatin (2) via 17 in 36% overall yield from 13 by $LiAlH_4$ reduction, acetalization, Jones oxidation, and then acid treatment. The synthetic α-multistriatin (2) showed a single peak by GLC analysis (3% JXR Silicone, 100°C) and the IR and ^{1}H-NMR spectra of 2 were identical with those of an authentic sample.

In the same way, the other acyclic precursor (16) was converted to dl-β- and -δ-multistriatins (19) and (20)[6] in a 5:95 ratio by GLC analysis in 35% overall yield from 14. It is evident that the final acid-catalyzed cyclization of 18 afforded the more stable δ-isomer in preference to the β-isomer to avoid the 1,3-diaxial interaction in 19 by epimerization.[7]



ACKNOWLEDGEMENT We are grateful to Prof. K. Mori of the University of Tokyo for gifts of the spectral data of α, β, γ, and δ-multistriatins.

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5) 1 bp 108°C (81 mmHg). ^{1}H-NMR ($CDCl_3$) δ: 0.12 (9H, s), 1.64 (3H, s), 1.68 (3H, d, J=6Hz), 5.30 (1H, dq, J=15 and 6Hz), 5.84 (1H, d, J=15Hz), 6.16 (1H, s). ^{13}C-NMR ($CDCl_3$) δ: 10.0 (q), 18.8 (q), 119.2 (s), 120.1 (d), 131.9 (d), 139.2 (d). No other isomers were detected by ^{13}C-NMR analysis.
7 ^{1}H-NMR ($CDCl_3$) δ: 0.83 (3H, t, J=7Hz), 1.02 (3H, d, J=7Hz), 1.80 (3H, s), 2.50 (1H, m), 2.57 (1H, dd, J=10, 4Hz), 3.74 (3H, s), 4.08 (1H, d, J=4Hz), 5.38 (1H, s).
8 ^{1}H-NMR ($CDCl_3$) δ: 0.84 (3H, t, J=7Hz), 0.86 (3H, d, J=7Hz), 1.10-1.44 (2H, m), 1.73 (3H, s), 1.80 (1H, m), 1.89 (1H, OH), 2.28 (1H, m), 2.42 (1H, dd, J=9.5, 12Hz), 3.72 (3H, s), 4.35 (1H, d, J=9.5Hz), 5.48 (1H, d, J=4Hz).
9 ^{1}H-NMR (C_5D_5N) δ: 0.96 (3H, t, J=7Hz), 1.00 (3H, d, J=7Hz), 1.84 (2H, m), 1.93 (3H, s), 2.20-2.64 (2H, m), 2.86 (1H, dd, J=10, 5Hz), 3.70 (3H, s), 4.05 (1H, d, J=8Hz), 5.48 (1H, d, J=4Hz).
10 ^{1}H-NMR ($CDCl_3$) δ: 0.95 (3H, d, J=7Hz), 0.96 (3H, t, J=7Hz), 1.20-1.74 (3H, m), 1.80 (3H, t, J=1.5Hz), 2.08 (1H, t, J=10.5Hz), 2.40 (1H, m), 3.68 (3H, s), 3.88 (1H, d, J=2Hz), 5.33 (1H, s).
11 ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J=7Hz), 0.92 (3H, d, J=8Hz), 0.99 (3H, d, J=8Hz), 1.20-1.60 (4H), 1.61-2.20 (4H), 2.65 (1H, t, J=7Hz), 3.66 (3H, s), 3.98 (1H, dd, J=7, 4Hz).
13 ^{1}H-NMR ($CDCl_3$) δ: 0.97 (3H, d, J=7Hz), 1.01 (3H, t, J=8Hz), 1.03 (3H, d, J=7Hz), 1.16-2.40 (7H), 3.76 (1H, d, J=9Hz), 5.37 (1H, s).
14 ^{1}H-NMR ($CDCl_3$) δ: 0.99 (3H, t, J=7Hz), 1.00 (3H, d, J=7Hz), 1.01 (3H, d, J=7Hz), 1.15-1.80 (4H), 1.84-2.36 (3H), 3.86 (1H, t, J=5Hz), 5.62 (1H, d, J=5Hz).

6) The structures of 19 and 20 are depicted in natural configuration.

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(Received April 2, 1986)