A New Synthesis of 3,4-Bis[methylene]-hexanedioic Esters from 2-Butynediol via Claisen Orthoester Rearrangement

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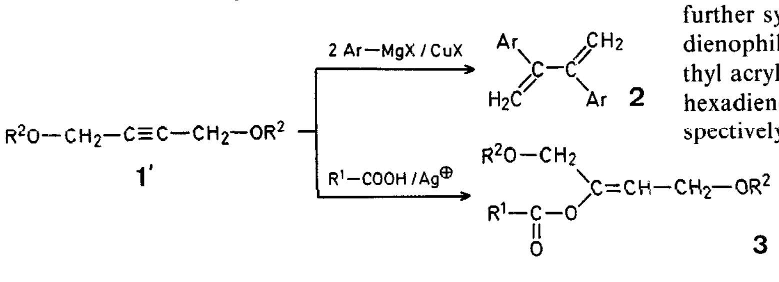
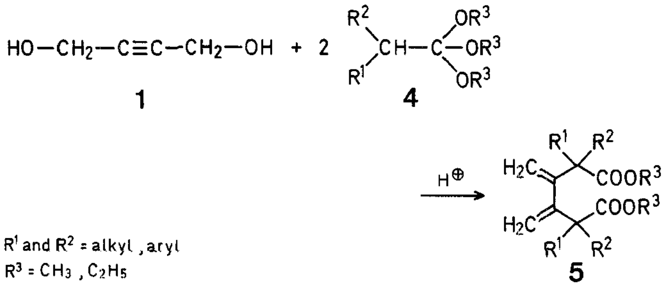
We have recently reported the facile synthesis of 2,3-diaryl-1,3-butadienes[1] (2) and 2-acyloxy-2-butenes[2] (3) starting from derivatives 1′ of 2-butynediol.

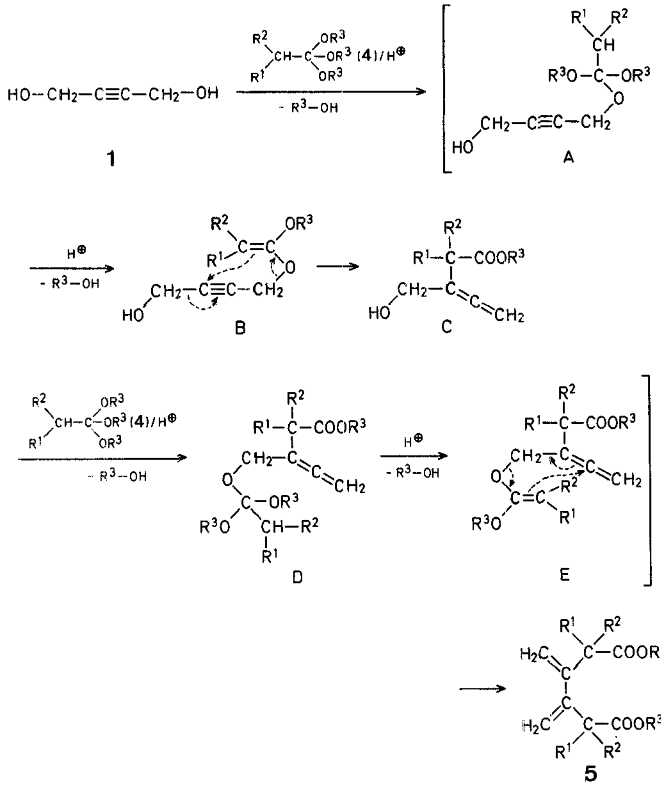


In the present communication, we describe a convenient new synthesis of 2,3-bis[1-alkoxycarbonylalkyl]-1,3-butadienes (5, dialkyl 3,4-bis[methylene]hexanedioates) from 2-butynediol (1) via a "Double Claisen Orthoester Rearrangement". This method provides a useful access to compounds 5.



The reaction is performed by heating diol 1 with an excess of the orthoester 4 at 110 °C in the presence of a catalytic amount of propanoic acid and allowing the low-boiling alcohol R^3—OH formed in the reaction to distil off continuously.

In analogy to the mechanism proposed for the conventional Claisen orthoester rearrangement[3], we assume that the reaction proceeds through the initial formation of the ketene acetals B followed first by a [3,3]sigmatropic rearrangement to give the 3-hydroxymethyl-3,4-alkadienoic esters C which are then converted into products 5 via D and E by a second orthoester rearrangement[4,5].



As an example of the potential application of compounds 5 in further syntheses we describe their Diels-Alder reaction with dienophiles such as dimethyl acetylenedicarboxylate (6), methyl acrylate (7a), or maleic anhydride (7b) to give 1,4-cyclohexadiene derivatives (8) or cyclohexene derivatives (9), respectively (Table 2).

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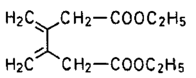
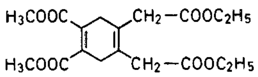
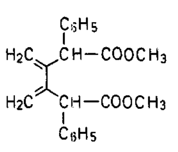
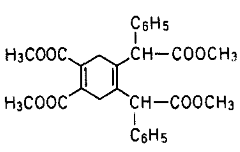
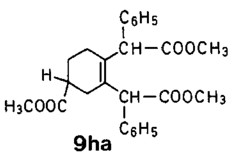
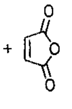
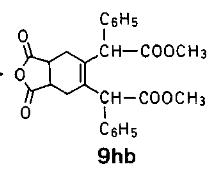
Table 1. 3,4-Bis[methylene]-hexanedioic Esters (**5**) prepared

5	R[1]	R[2]	R[3]	Yield[a] [%]	m.p.[b] [°C]	Molecular formula[c]	I.R., $\nu_{C=O}$ [cm^{-1}]	^{1}H-N.M.R. (CCl_4 or $CDCl_3$/TMS_{int}) δ [ppm]
a	H	H	C_2H_5	51	oil	$C_{12}H_{18}O_4$ (226.3)	1770	1.27 (m, 6H); 3.30 (s, 4H); 4.17 (m, 4H); 5.03 (s, 2H); 5.39 (s, 2H)
b	CH_3	H	CH_3	88	oil	$C_{12}H_{18}O_4$ (226.3)	1738	1.28 (d, 6H); 3.40 (q, 2H); 3.52 (s, 6H); 5.12 (q, 4H)
c	CH_3	H	C_2H_5	84	oil	$C_{14}H_{22}O_4$ (254.3)	1739	1.26 (m, 12H); 3.42 (q, 2H); 4.12 (q, 4H); 5.18 (q, 4H)
d	C_2H_5	H	C_2H_5	92	oil	$C_{16}H_{26}O_4$ (282.4)	1730	0.94 (t, 6H); 1.28 (t, 6H); 1.72 (m, 4H); 3.20 (t, 2H); 4.16 (q, 4H); 5.24 (q, 4H)
e	CH_3	CH_3	C_2H_5	47	oil	$C_{16}H_{26}O_4$ (282.4)	1727	1.32 (m, 18H); 4.07 (q, 4H); 4.95 (s, 2H); 5.21 (s, 2H)
f	Cl	H	C_2H_5	87	oil	$C_{12}H_{16}Cl_2O_4$ (295.2)	1754	1.32 (m, 6H); 4.31 (q, 4H); 5.14 (s, 2H); 5.64 (s, 2H); 5.78 (s, 2H)
g	NC—CH_2—	H	C_2H_5	84	oil	$C_{16}H_{20}N_2O_4$ (304.3)	1739	1.32 (t, 6H); 2.84 (q, 4H); 3.80 (t, 2H); 4.31 (m, 4H); 5.43 (s, 2H); 5.62 (s, 2H)
h	C_6H_5	H	CH_3	89	136–140°	$C_{22}H_{22}O_4$ (350.4)	1727	3.66 (s, 6H); 4.72 (s, 2H); 4.96 (s, 2H); 5.40 (s, 2H); 7.27 (m, 10H)
i	4-H_3C—C_6H_4—	H	CH_3	94	162–164°	$C_{24}H_{26}O_4$ (380.5)	1730	2.37 (s, 6H); 3.75 (s, 6H); 4.83 (s, 2H); 5.07 (s, 2H); 5.51 (s, 2H); 7.27 (m, 8H)
j	4-Cl—C_6H_4—	H	CH_3	76	183–186°	$C_{22}H_{20}Cl_2O_4$ (419.3)	1730	3.80 (s, 6H); 4.83 (s, 2H); 5.12 (s, 2H); 5.54 (s, 2H); 7.44 (m, 8H)
k	4-H_3CO—C_6H_4—	H	CH_3	88	150–152°	$C_{24}H_{26}O_6$ (412.5)	1748	3.72 (s, 6H); 3.84 (s, 6H); 4.75 (s, 2H); 5.04 (s, 2H); 5.46 (s, 2H); 7.06 (m, 8H)

[a] Yield of isolated product.
[b] Uncorrected. G.L.C. analysis of the oils showed that these products possessed a purity of >97% (conditions: column temperature 130 °C, carrier gas N_2, column, OV 1, 1.5 m).
[c] The microanalyses showed the following maximum deviations from the calculated values: C, ±0.30; H, ±0.20.

Table 2. Diels-Alder Reactions of Compounds **5**

Diene 5	Dienophile	Product	Yield[a] [%]	m.p.[b] [°C]	Molecular formula[c]	^{1}H-N.M.R. (CCl_4 or $CDCl_3$/TMS_{int}) δ [ppm]
 **5a**	+ H_3COOC—C≡C—$COOCH_3$ → **6**	 **8a**	88	61–63°	$C_{18}H_{24}O_8$ (368.4)	1.22 (t, 6H); 3.12 (s, 8H); 3.76 (s, 6H); 4.12 (q, 4H)
 **5h**	+ H_3COOC—C≡C—$COOCH_3$ → **6**	 **8h**	77	140–146°	$C_{28}H_{28}O_8$ (492.5)	3.0 (m, 4H); 3.66 (d, 12H); 5.08 (s, 2H); 7.2 (m, 10H)
	+ H_2C=CH—$COOCH_3$ → **7a**	 **9ha**	96	oil	$C_{26}H_{28}O_6$ (436.5)	2.0 (m, 7H); 3.61 (m, 9H); 4.96 (d, 2H); 7.2 (m, 10)
	+  → **7b**	 **9hb**	52	oil	$C_{26}H_{24}O_7$ (448.5)	2.01 (s, 4H); 3.10 (s, 2H); 3.61 (s, 6H); 5.07 (s, 2H); 7.27 (m, 10)

[a] Yield of isolated product.
[b] Uncorrected. Purity of the liquid products: 97% (G.L.C. conditions; column temperature 260 °C, carrier gas N_2, column, OV 1, 1.5 m).
[c] The microanalyses showed the following maximum deviations from the calculated values: C, ±0.30; H, ±0.20.

3,4-Bis[methylene]-hexanedioic Esters (2,3-Bis[alkoxycarbonylmethyl]-butadienes, 5); General Procedure:

To a mixture of 2-butynediol (**1**; 861 mg, 10 mmol) and a trialkyl orthoalkanoate (**4**; 40 mmol), propanoic acid (500 mg, 6.8 mmol) is added at 50 °C and the mixture is stirred at 110 °C for 3 h, the low-boiling alcohol R^3—OH being allowed to distil from the mixture as it is formed. The residue is poured into water (50 ml) and this mixture extracted with ether (3 × 50 ml). The combined ether phase is washed with saturated sodium hydrogen carbonate solution (100 ml) and dried with magnesium sulfate. The ether is evaporated and the product **5** is isolated by column chromatography of the residue on silica gel (particle size 74-149 μ) using chloroform as eluent.

Diels-Alder Reaction of Compounds 5 with Dimethyl Acetylenedicarboxylate (6):

A mixture of the respective compound **5** (10 mmol) and dimethyl acetylenedicarboxylate (**6**; 2.843 g, 20 mmol) is heated at 140 °C under nitrogen for 5 h. The cooled mixture is extracted with chloroform (3 × 50 ml), the chloroform extract is washed with saturated aqueous sodium carbonate (100 ml), and dried with magnesium sulfate. The solvent is evaporated and the product **8** isolated by column chromatography of the residue on silica gel (particle size 74-149 μ) using benzene/ethyl acetate (10/1) as eluent.

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[1] Y. Ishino, I. Nishiguchi, F. Takihira, T. Hirashima, *Tetrahedron Lett.* **21**, 1527 (1980).

[2] Y. Ishino, I. Nishiguchi, S. Nakao, T. Hirashima, *Chem. Lett.* **1981**, 641.

[3] W. S. Johnson et al., *J. Am. Chem. Soc.* **92**, 741 (1970).
J. K. Crandall, G. L. Tindell, *J. Chem. Soc. Chem. Commun.* **1970**, 1411.
D. K. Black, Z. T. Fomum, P. D. Landor, S. R. Landor, *J. Chem. Soc. Perkin Trans. 1* **1973**, 1349; and references cited therein.

[4] It is noteworthy that under similar conditions but using pivalic acid as catalyst alkylation of the methylene groups of 2-butynediol (**1**) occurred and led to the predominant formation of unsaturated γ-lactones[5].

[5] G. Bennett, *Chem. Lett.* **1975**, 939.

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