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STEREOSELECTIVE TRANSFORMATION OF 2,4-ALKADIENOIC ESTERS TO THE 3,5-DIENOIC ISOMERS WITH LITHIUM DIISOPROPYLAMIDE (LDA)

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Treatment of 2(E),4(Z)-alkadienoic esters with lithium diisopropylamide (LDA) at -80 °C gave 3(E),5(E)-isomers with 81-98% stereoselectivity. In contrast, treatment of 2(E),4(E)-isomers with LDA gave 3(E),5(Z)-isomers with 72-80% stereoselectivity.

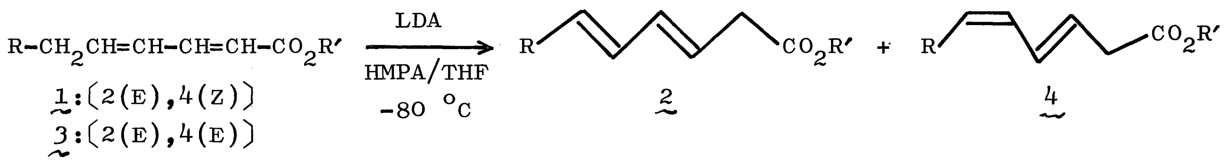
Recently we reported the highly stereoselective synthesis of 2(E),4(Z)-alkadienoic esters (**1**) with alumina as a promoter.$^{1)}$ As a part of its application to organic syntheses, we carried out the base-catalyzed rearrangement of 2,4-alkadienoic esters to the 3,5-dienoic isomers. This communication deals with a stereoselective synthesis of 3(E),5(E)- and 3(E),5(Z)-alkadienoic esters from 2,4-dienoic isomers.

Treatment of 2(E),4(Z)-alkadienoates (**1**) with lithium diisopropylamide (LDA)/hexamethylphosphoramide in THF at -80 °C gave 3(E),5(E)-isomers (**2**)$^{2)}$ in 56-87% yield with 81-98% stereoselectivity. On the other hand, 2(E),4(E)-alkadienoates (**3**)$^{3)}$ were similarly treated with LDA to give 3(E),5(Z)-isomers (**4**)$^{2)}$ in 51-75% yield with 72-80% stereoselectivity. The results are summarized in Table 1. A typical experiment is described below.

To a solution of diisopropylamine (0.19 ml, 1.33 mmol) in dry THF (2.5 ml) was added dropwise 1.65 M butyllithium in hexane (0.73 ml, 1.3 mmol) at -15 °C. After 30 min HMPA (0.3 ml) was added and a solution of ethyl 2(E),4(Z)-tridecadienoate (236 mg, 0.992 mmol) in dry THF (1.5 ml) was added dropwise at -80 °C. The mixture was stirred for 60 min and then water (10 ml) was added. After extraction with ether, drying (anhydrous $MgSO_4$), and evaporation of the solvent, the residue (181 mg) was analyzed with GLC (SE-30 silicone gum rubber, 0.5 mm x 45 m, 200 °C) to be a mixture of **2d** and **4d** (85:15). Preparative GLC gave the analytical sample of **2d**: IR (neat) 1740, 1630, 1590 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.88 (t, 3H), 1.28 (m, 13H), 2.07 (m, 2H), 3.08 (d, J = 7 Hz, 2H), 4.16 (q, J = 7 Hz, 2H), 5.4-6.4 (m, 4H). Found: C, 75.77; H, 10.80%. Calcd for $C_{15}H_{26}O_2$: C, 75.78; H, 10.99%.

Double bond migrations of 2-alkenoates to the 3-alkenoate with LDA are well known.$^{4,5)}$ However, that of 6-alkyl-2,4-alkadienoates to the 3,5-dienoic isomers

Table 1. Transformation of 2,4-Alkadienoates to the 3,5-Dienoic Isomers[a)]



2,4-Alkadienoates			Yields of products/%[b)]			Stereoselectivity[c)]
Compd	R	R'	**1**	**2**	**4**	%
1a	C_2H_5	CH_3	2	77	3	96
1b	C_3H_7	CH_3		56	1	98
1c	C_4H_9	C_2H_5		87	10	90
1d	C_7H_{15}	C_2H_5		68	12	85
1e	C_8H_{17}	CH_3	23	62	15	81
3a	C_2H_5	CH_3		13	51	80
3b	C_3H_7	CH_3		22	66	75
3c	C_4H_9	C_2H_5		28	72	72
3e	C_8H_{17}	CH_3		19	75	80

a) All experiments are not optimized. b) Analyzed by GLC fitted with Golay column (SE-30 silicone gum rubbers, 0.5 mm x 45 m) or 10% SE-30 on Chromosorb W column (3 mm x 1 m), and/or by ^{13}C NMR spectra. c) Percentages of the main product except the starting material.

with LDA is, to our knowledge, the first example. The present method is useful for the preparation of polyene compounds such as leukotrienes, insect pheromones, and latex components of plants. For example, the methyl ester of megatomoic acid (**4e**), sex attractant of black carpet beetle, was prepared by the present synthesis in the total yield which was best among the known methods.[6)]

References

1) S. Tsuboi, T. Masuda, and A. Takeda, J. Org. Chem., **47**, 4478 (1982).
2) The geometry was determined by ^1H NMR spectral data with the aids of a shift reagent [Eu(dpm)$_3$] and the proton decoupling technique: for example, **2c** (E,E), $J_{3,4} = J_{5,6} = 15$ Hz; **4c** (E,Z), $J_{3,4} = 15.4$ Hz and $J_{5,6} = 10.8$ Hz.
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