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HIGHLY SELECTIVE FORMATION OF LINEAR-CONJUGATED DIENOLATE ANIONS FROM CONJUGATED ENONES

Mituyosi KAWANISI, Yasuko ITOH, Takanori HIEDA, Sinpei KOZIMA,*† Torazo HITOMI,† and Kazuko KOBAYASHI††

Department of Industrial Chemistry, Faculty of Engineering,
Kyoto University, Kyoto, 606
†Department of Chemistry, School of Liberal Arts & Sciences,
Kyoto University, Kyoto, 606
††Meiji College of Oriental Medicine, Hiyoshi, Funai-gun, Kyoto,
629-03

Treatment of conjugated enones having both α'- and γ-hydrogens with $KN(SiMe_3)_2$ (KHMSA) in a mixed solvent of DMF with THF at -78 °C afforded preferentially linear-conjugated dienolate anions, which were trapped by methyl chloroformate to give the corresponding dienyl methyl carbonates.

Selective formation of cross-conjugated dienolate anions by α'-deprotonation of conjugated enones with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) has been generally recognized.[1,2] In contrast, not a few combinations of base and solvent were reported in order to generate linear-conjugated dienolates, i.e., Et_3N/DMF,[3] t-BuOK/t-BuOH,[4] t-BuOK/DMF,[5] and Ph_3CLi/THF[6] for 4a-methyl-4,4a,5,6,7,8-hexahydro-2(3*H*)-naphthalenone (4), $NaNH_2$/liq.NH_3[7] for 3-methyl-2-cyclohexen-1-one (2), and Fe(0)/Et_2O[8] for 3,5,5-trimethyl-2-cyclohexen-1-one (3). More recently there was reported a general procedure to obtain end- or exocyclic

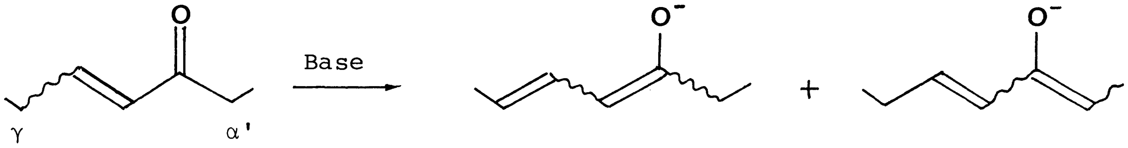
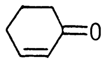
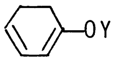
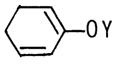
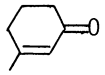
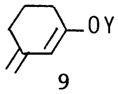
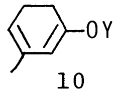
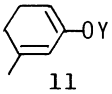
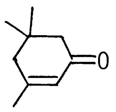
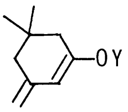
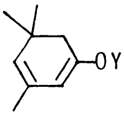
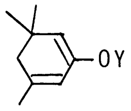
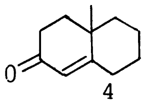
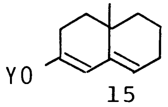
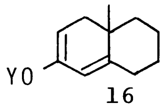
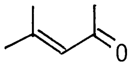
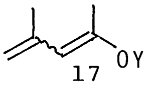
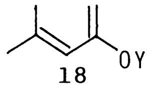
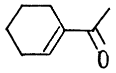
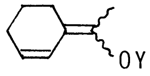
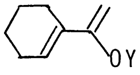


Table 1. Preparation of dienyl methyl carbonates from conjugated enones

Entry	Enone	Base	Solvent	Product (Y = CO_2Me)			Yield / %
	 1			 7	 8		
1		KHMSA	DMF·THF	>99	--		34
2		LiHMSA	DMF·THF	75	25		68
3		LDA	THF	--	>99		44
	 2			 9	 10	 11	
4		KHMSA	DMF·THF	87	13	--	56
5		KHMSA	DMF·THF$^{a)}$	96	4	--	44
6		KHMSA	THF	64	18	17	25
7		LiHMSA	DMF·THF	74	20	6	67
8		LDA	THF	--	--	>99	62
	 3			 12	 13	 14	
9		KHSMA	DMF·THF	96	4	--	60
10		KHMSA	THF	76	13	11	36
11		LiHMSA	DMF·THF	93	7	--	70
12		LiHMSA	THF	37	7	56	64
13		LDA	THF	--	--	>99	63
	 4			 15	 16		
14		KHMSA	DMF·THF	84	16		34
15		LDA	THF	--	>99		39
	 5			 17	 18		
16		KHMSA	DMF·THF	99	--		52
17		LDA	THF	16	84		50
	 6			 19	 20		
18		KHMSA	DMF·THF	--	>99		25
19		LDA	THF	--	>99		42

a) The dienolate anions were trapped by chlorotrimethylsilane (Y = TMS).

linear-conjugated cyclohexadienolate anions selectively from conjugated cyclohexenones having 3-alkyl substituents by using an activated Fe(0)/MeMgBr/DME or Fe(0)/Et_3N.[9) However, selective conversion of a simpler compound, 2-cyclohexen-1-one (**1**), into the linear-conjugated 1,3-cyclohexadienolate anion has never been presented. Recent communications by Krafft and Holton[8,9) prompted us to disclose an alternative and profitable method for the formation of linear-conjugated dienolate anions from the corresponding conjugated enone by treatment with potassium hexamethyldisilazanide (KHMSA) in a mixed solvent of DMF with THF.

A typical procedure is as follows: To a DMF THF (DMF 10 ml, THF 5 ml) solution of KHMSA (2.05 mmol)[10,11) was slowly added the relevant conjugated enone (2.00 mmol) at -78 °C with stirring, and the mixture was kept at -78 °C for 2 h. Soon after removing the dry ice-acetone bath, hexamethylphosphoric triamide (2 ml) and then methyl chloroformate (0.3 ml) were added to the mixture. The reaction mixture was kept at room temperature for 20 min, and was treated with pentane (10 ml) and a cold saturated aqueous solution of sodium hydrogen carbonate (20 ml, 0 °C). The dienyl methyl carbonates produced were separated from the pentane solution by elution chromatography (silica gel, hexane/AcOEt = 9/1), and the isomer ratios of the carbonates were analyzed by glc and ^{1}H-NMR spectroscopy. The results are summarized in Table 1. The dienyl carbonates were identified by ^{1}H and ^{13}C NMR spectroscopy.[12)

Linear-conjugated 1,3-cyclohexadienolate anion could be formed exclusively from **1** with KHMSA/DMF·THF (entry 1). Predominant γ-deprotonation at the 3-methyl group in **2** and **3** with KHMSA/DMF·THF afforded the exocyclic linear-conjugated dienolate anions (entries 4, 5, and 9). Lower selectivity was observed with KHMSA/THF (entries 6 and 10) or lithium hexamethyldisilazanide (LiHMSA)/DMF·THF (entries 2, 7 and 11). Treatment of **4** and **5** with KHMSA/DMF·THF gave the linear-conjugated derivatives (entries 14 and 16). However, 1-acetyl-1-cyclohexene (**6**) was found to be an exceptional case; the linear-conjugated dienolate (**19**) was not detected in the product, but the cross-conjugated dienolate (**20**) was exclusively produced even with KHMSA/DMF·THF (entry 18). In all entries, the yields of the carbonates were not satisfactory. This is ascribed to the facile oligomerization of the conjugated enones, even though the reaction was carried out at -78 °C.

We have already shown that the dienyl methyl carbonates are promising precursors for organotin dienolates.[13) In view of the recent keen interests in generating the metal dienolates and their application in synthesis,[3,5,9,14) the present methodology provides the efficient means of forming linear-conjugated dienolate anions specifically.

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10) KHMSA was prepared from KH and 1,1,1,3,3,3-hexamethyldisilazane in THF.[11] The mixed solvent of DMF•THF (2:1) does not solidify at -78 $^{\circ}$C.

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12) Dienic and the other characteristic peaks in ^{1}H and ^{13}C NMR spectra (CDCl$_3$, 89.55 and 22.49 MHz) of the dienyl carbonates (7 -20) are given as follows. 7: ^{1}H-NMR δ 5.54-6.00 (m, 3H); ^{13}C-NMR δ 110.7 (d), 122.7 (d), 123.8 (d), 149.2 (s). 8: ^{1}H-NMR δ 5.46 (m, 1H), 5.63-6.07 (m, 2H); ^{13}C-NMR δ110.7 (d), 122.5 (d), 129.4 (d), 146.2 (s). 9: ^{1}H-NMR δ 4.80 (s, 2H), 5.98 (s, 1H); ^{13}C-NMR δ 111.6 (t), 117.5 (d), 141.4 (s), 151.4 (s). 10: ^{1}H-NMR δ 5.21-5.39 (m, 1H), 5.58 (s, 1H); ^{13}C-NMR δ 23.9 (q), 114.3 (d), 117.9 (d), 130.4 (s), 149.3 (s). 11: ^{1}H-NMR δ 1.80 (s, 3H), 5.16-5.33 (m, 1H), 5.41-5.53 (m, 1H); ^{13}C-NMR δ 23.0 (q), 107.5 (d), 117.3 (d), 139.6 (s), 146.7 (s). 12: ^{1}H-NMR δ 4.83 (s, 2H), 5.96 (s, 1H); ^{13}C-NMR δ 112.8 (t), 116.5 (d), 140.6 (s), 150.2 (s). 13: ^{1}H-NMR δ 5.40-5.47 (m, 1H), 5.52-5.60 (m, 1H); ^{13}C-NMR δ 113.0 (d), 116.5 (d), 129.9 (s). 14: ^{1}H-NMR δ 1.79 (s, 3H), 5.09 (s, 1H), 5.52 (m, 1H); ^{13}C-NMR δ 116.3 (d), 118.5 (d), 130.1 (s), 145.5 (s). 15: ^{1}H-NMR δ 5.37 (t, 1H), 5.75 (d, 1H); ^{13}C-NMR δ 116.9 (d), 124.9 (d), 138.3 (s), 147.4 (s). 16: ^{1}H-NMR δ 5.18-5.47 (m, 1H), 5.39 (s, 1H). ^{13}C-NMR δ 107.2 (d), 111.5 (d), 145.6 (s), 148.7 (s). 17: ^{1}H-NMR δ 4.88 (bs, 2H), 5.54 (s, 1H); ^{13}C-NMR δ 116.8 (t), 119.0 (d), 138.9 (s), 144.9 (s). 18: ^{1}H-NMR δ 4.78 (s, 1H), 4.94 (s, 1H), 5.64 (bs, 1H); ^{13}C-NMR δ 104.0 (t), 118.9 (d), 139.9 (s), 152.3 (s). 20: ^{1}H-NMR δ 4.77 (d, 1H), 4.90 (d, 1H), 5.91-6.09 (t, 1H); ^{13}C-NMR δ 99.7 (t), 126.1 (d), 130.1 (s), 130.5 (s).

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