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FACILE SYNTHESIS OF β-ALKYL-SUBSTITUTED ESTERS FROM α,β-UNSATURATED ALDEHYDES

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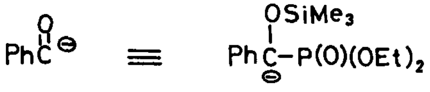
Summary: β-Alkyl-substituted carboxylates were synthesized in good yields from α,β-unsaturated aldehydes by using the 1:1 carbonyl adducts with diethyl bis(trimethylsilyl) phosphite.

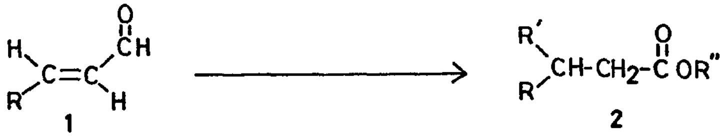
Recently, several studies on acyl anion equivalents utilizing carbonyl insertion reactions have appeared.[2] It has been reported that diethyl trimethylsilyl phosphite (DTSP) reacted with aldehydes to give 1:1 carbonyl adducts in high yields.[3,4,5] In a previous paper[5], we proposed α-trimethylsilyloxybenzylphosphonate anion as a new benzoyl anion equivalent for the unsymmetrical ketone synthesis.

$Me_3SiOP(OEt)_2$
(DTSP)



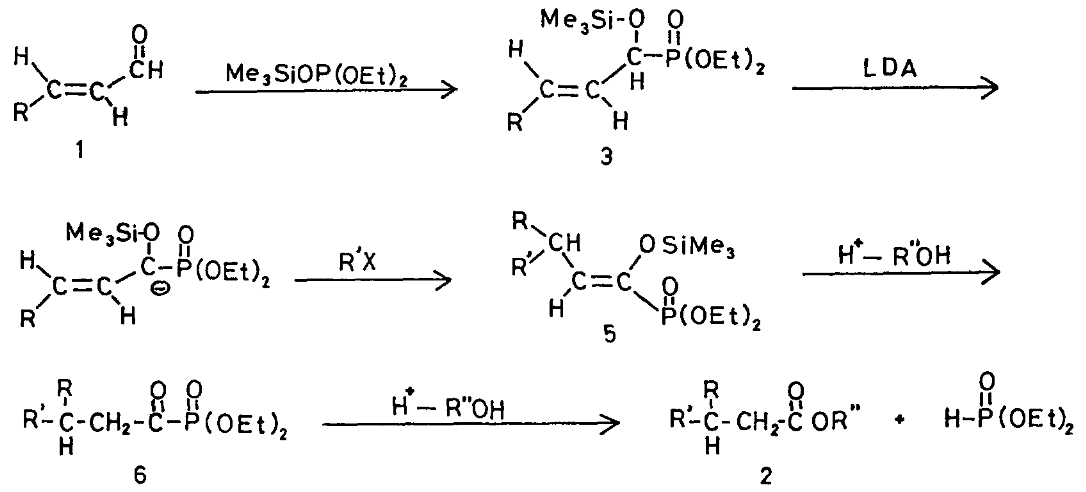
$$PhC(=O)^{\ominus} \equiv PhC^{\ominus}(OSiMe_3)-P(O)(OEt)_2$$

In this paper, we wish to report a new method for the conversion of α,β-unsaturated aldehydes (1) to β-substituted carboxylates (2) utilizing 1:1 carbonyl adducts (3) of 1 with DTSP.



1 2

Diethyl 1-trimethylsilyloxy-2-benzalethylphosphonate (3A) was prepared from DTSP and trans-cinnamaldehyde as described previously.[5] Compound 3A was treated with lithium diisopropylamide (LDA) (1.1 equiv.) in THF at -78°C for 30 min and followed by treatment with methyl iodide (1.1 equiv.) at -78°C for



Scheme I

1 h. The alkylated product (5Aa) was obtained in 43 % yield by rapid separation using column chromatography on silica gel. The NMR spectrum[6] of 5Aa showed that the alkylation proceeded regioselectively at the γ-position to afford stereoselectively E-olefin. Without the isolation of 5Aa the reaction mixture was extracted with methylene chloride and the solvent was evaporated to dryness. Treatment of the residual oil with TsOH(catalytic amount)-EtOH at 60°C for 1 h gave β-methylated ethyl cinnamate (2Aa) in 76 % yield. In the above alkylation, THF was found to be more suitable as the solvent than ether. The conversion of 5Aa to 2Aa might proceed via α-oxophosphonate (6Aa) as depicted in Scheme I. The transformation of 6Aa to 2Aa is explained by the known reactions of β-oxophosphosnates with alcohols to afford esters and dialkyl phosphonates.[7,8] In a similar manner, 1A was alkylated with several alkyl halides and converted to β-alkyl-substituted esters (2Ab-2Ag) in good yields.

The use of trimethylsilyl chloride and bromide as electrophiles gave also β-trimethylsilyl derivative (2Ah) in 49 % and 52 yields, respectively.

The carbonyl adducts (3B-3D) obtained from acrolein, crotonaldehyde, and trans-hexenylaldehyde were also alkylated at the γ-position and converted to the corresponding β-alkyl-substituted esters (2B-2D). The results of these reactions are summarized in Table I. In these reactions, some of initially γ-alkylated products, i.e., 5Ae and 2Ba, could be isolated as the exclusive products in 69 % and 58 % yields, respectively. The structures of 5Ae and 2Ba were also confirmed as E-configuration by their NMR spectra.

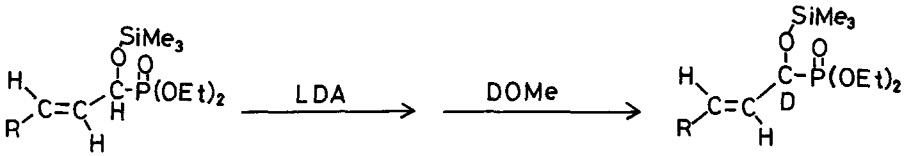
On the other hand, deuteration of the lithio derivatives of 3A-3D at -78°C gave α-deuterated parent 1-trimethylsilyloxyphosphonates (7A-7D) in 73 %, 84 %, 90 %, and 37 % yields, respectively. In all cases, the γ-deuterated products were not isolated. The highly regioselective γ-alkylations might be

Table I Preparation of β-substituted carboxylates (2) from α,β-unsaturated aldehydes (1) via 1:1 carbonyl adducts (3) of 1 with diethyl trimethylsilyl phosphite and deuteration of α-lithio derivatives of 3

3 R	R'X (equiv.)	Condition for alkylation or deuteration Time(h) (Temp.)	R"	Treatment of 5 with TsOH-R"OH Time (h)			Deuteration Yield of 7 (%)
				Time (h)	Product	Yield (%)	
Ph (3A)	MeI(1.08)	1 (-78°)	Et	1	2Aa	63	—
	(1.80)	3 (-78°→r.t.)	Et	2	2Ab	76	—
	n-PrI(1.14)	0.5 (-78°)	Et	2	2Ac	76	—
	i-PrI(1.12)	3 (-78°→r.t.)	Et	2.5	2Ad	84	—
	$PhCH_2Br$(1.18)	0.5 (-78°)	Et	2.5	2Ae	89	—
	$CH_2=CHCH_2Br$(1.11)	0.6 (-78°)	Et	2.5	2Af	81	—
	$PhCH_2CH_2Br$(1.11)	4.5 (-78°→r.t.)	Et	2.5	2Ag	69	—
	Me_3SiCl(1.04)	5 (-78°→r.t.)	Et	2	2Ah	49	—
	Me_3SiBr(1.08)	2 (-78°→r.t.)	Et	4	2Ah	52	—
	CH_3OD(1.5)	3 min (-78°)	—	—	—	—	73 (7A)
n-Pr (3B)	$PhCH_2Br$(1.19)	0.6 (-78°)	Et	2.5	2Ba	51	—
	n-BuI(1.15)	0.5 (-78°)	$PhCH_2CH_2$	3	2Bb	45	—
	(1.10)	0.5 (-78°)	n-Bu	3	2Bc	52	—
	CH_3OD(4.0)	5 min (-78°)	—	—	—	—	84 (7B)
Me (3C)	$PhCH_2Br$(1.08)	0.5 (-78°)	Et	2.5	2Ca	75	—
	$PhCH_2CH_2Br$(1.03)	5 (-78°→r.t.)	Et	2	2Cb	44	—
	CH_3OD(3.5)	5 min (-78°)	—	—	—	—	90 (7C)
H (3D)	$PhCH_2Br$(1.11)	1 (-78°)	Et	6	2Da	11	—
	n-BuI(1.19)	1 (-78°)	Et	6	2Db	5	—
	CH_3OD(4.0)	10 min (-78°)	—	—	—	—	37 (7D)

All of alkylations were carried out in dry tetrahydrofuran.

due to steric hindrance of the neighboring diethoxyphosphinyl group and trimethylsilyloxy group.



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In conclusion, the present reaction sequence provides a convenient method for the synthesis of β-substituted esters from α,β-unsaturated aldehydes. It is also noted that the alkylation took place at the β-position of the starting material 1 and the reaction proceeded highly stereoselectively.$^{9)}$

Further extensions of this work are now in progress.

References and Notes

1) This paper participates as Part 12 in the series of Silyl Phosphites. Part 10 and 11 are now in preparation. Part 9: M. Sekine and T. Hata, Chem. Commun., 285 (1978).

2) For comprehensive reviews, see D. Seyferth and K. -H. Geiss, "New Applications of Organometallic Reactions in Organic Synthesis", Elsivier, Amsterdam, 1976; O. W. Lever, Jr., Tetrahedron, **32**, 1943 (1976).

3) Z. S. Novikova and I. F. Lutsenko, J. Gen. Chem. USSR (Engl. Transl.), **40**, 2110 (1970).

4) Z. S. Novikova, S. N. Mashoshina, T. A. Sapozhnikova, and I. F. Lutsenko, ibid., **41**, 2622 (1971).

5) T. Hata, A. Hashizume, M. Nakajima, and M. Sekine, Tetrahedron Lett., 363 (1978).

6) 5Aa NMR(CCl_4): δ 0.07 (s, 9H, $(C\underline{H}_3)_3Si$), 1.19 (t, 6H, J_{H-H}=7.0 Hz, $C\underline{H}_3CH_2$), 2.90 (d, 1H, J_{H-H}=8.1 Hz, one of $C\underline{H}_2Ph$), 2.91 (d, 1H, J_{H-H}=6.6 Hz, one of $C\underline{H}_2Ph$), 3.87 (m, 4H, $C\underline{H}_2O-P$), 5.97 (t, 1H, $J_{H-H}=J_{H-P}$=10 Hz, $C\underline{H}=C$), 7.00 (s, 5H, ArH), 7.07 (s, 5H, ArH).

7) M. I. Kabachnik and P. A. Rossiiskaya, Bull. acak. sci. U. S. S. S., Classe sci. chim., 597 (1945); Chem. Abstr., **41**, 88 (1945).

8) K. Terauchi and H. Sakurai, Bull. Chem. Soc. Jpn., **43**, 883 (1970).

9) Just after the acceptance of this communication, Evans and his coworkers reported a similar reaction process to afford β-alkylated esters including lactons by the use of the carbonyl addition reaction of phosphorodiamidites with α,β-unsaturated aldehydes: D. A. Evans, J. M. Takacs, and K. M. Hurst, J. Am. Chem. Soc., **101**, 371 (1979).

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