(25), 67 (22), 55 (26). A 2,4-DNP derivative was obtained; mp 166–168 °C (lit.[8b] mp 168.5–170 °C).

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Registry No. 1, 83587-88-6; 2, 83587-89-7; 3, 82976-52-1; 4, 83587-90-0; 5, 83587-91-1; 6, 13621-25-5; 7, 6939-35-1; 8, 83587-92-2; 9, 16776-05-9; 2-allylcyclohexane-1,3-dione, 42738-68-1; ethanol, 64-17-5; 2-bromopropene, 557-93-7.

Acylation of Ketone Silyl Enol Ethers with Acid Chlorides. Synthesis of 1,3-Diketones

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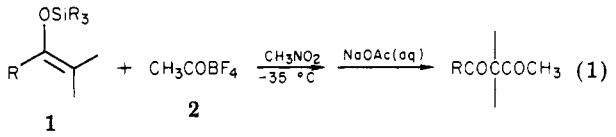
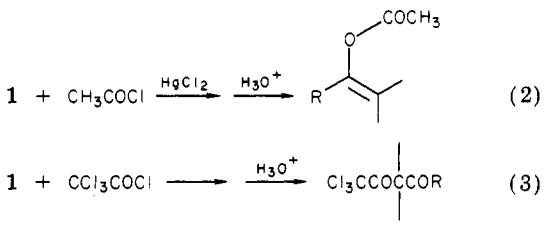
Trimethylsilyl enol ethers of ketones are acylated by a variety of acid chlorides in the presence of zinc chloride or antimony trichloride. The major product of this reaction is the 1,3-diketone resulting from C-acylation. Some O-acylation is observed in most cases. Yields of 1,3-diketones varied but were usually good to excellent.

Recent work in our laboratory has shown that a variety of trialkylsilyl enol ethers **1** are readily acylated with acetyl tetrafluoroborate **2**.[1] This method gives 1,3-diketones in reasonable yields (eq 1). Other methods for the acylation



(1)

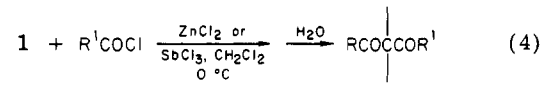
of trialkylsilyl enol ethers give exclusive O-acylation (eq 2)[2] or are restricted to polyhalogenated acid chlorides (eq 3).[3]



(2)

(3)

Further investigation of the acylation of ketone silyl enol ethers has led us to what we believe are more general and convenient methods to accomplish this transformation. Reaction of trialkylsilyl enol ethers with acid chlorides in the presence of zinc chloride or antimony trichloride (Table I) results in good to excellent yields of 1,3-diketones (eq 4). We report here some of the results obtained in our



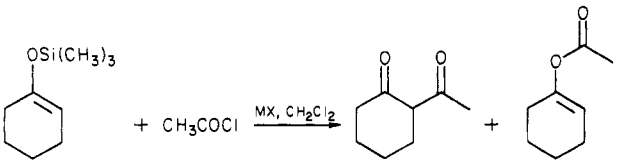
(4)

study of this acylation reaction.

Results and Discussion

Initial experiments involved the survey of a variety of Lewis acids as promoters for the reaction of acetyl chloride,

Table I. Reaction of MX with Cyclohexanone Trimethylsilyl Enol Ether and Acetyl Chloride

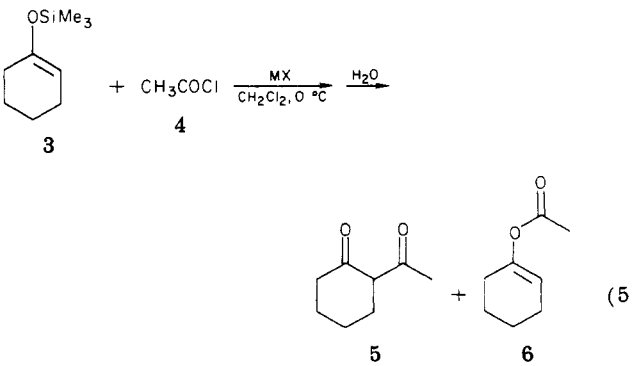


C-acylated O-acylated

entry	MX	% yield[a] C-acylated	% yield[a] O-acylated
I	$ZnCl_2$	63	3
II	$SbCl_3$	65	15
III	$TiCl_4$	48	trace
IV	$SbCl_5$	35	7
V	$SnCl_4$	34	0
VI	BCl_3	27	0
VII	$FeCl_3$	23	0
VIII	$AlCl_3$	22	1
IX	$NiBr_2$	8	0
X	$CoBr_2$	3	trace
XI	$SiCl_4$	trace	0
XII	$CuCl_2$	trace	6
XIII	n-Bu_3SnCl	0	0
XIV	CuCl	0	0

[a] Yields determined by GC analysis.

4, with cyclohexanone trimethylsilyl enol ether, **3**, in methylene chloride at 0 °C (eq 5). Zinc chloride gave a



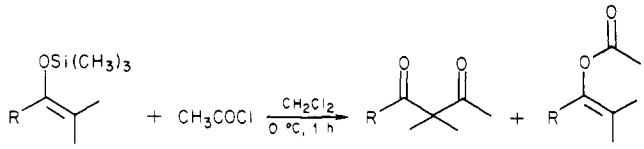
(5)

63% yield of C-acylated product **5** with 3% O-acylated product **6** and approximately 20% recovered cyclohexanone. Antimony trichloride also gave satisfactory

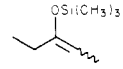
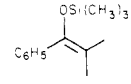
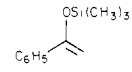
(1) Kopka, I; Rathke, M. W. *J. Org. Chem.* **1981**, *46*, 3771.
(2) Rasmussen, J. K. *Synthesis* **1977**, 91.
(3) (a) Murai, S.; Kuraki, Y.; Hasegawa, K.; Tsutsumi, S. *J. Chem. Soc., Chem. Commun.* **1972**, 946. (b) Kramarova, E. P.; Baukov, Y. I.; Lutsenko, I. F. *Zh. Obshch. Khim.* **1975**, 45, 478. (c) For reaction with oxaloyl chloride see: Murai, S.; Hasegawa, K.; Sonodu, N. *Angew. Chem., Int. Engl. Ed.* **1975**, *14*, 636.

0022-3263/82/1947-5099$01.25/0

Table II. Reaction of Trimethylsilyl Enol Ethers with Acetyl Chloride



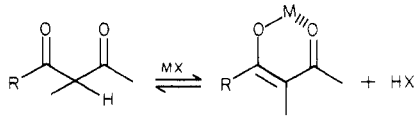
C-acylated O-acylated

entry	silyl enol ether	procedure[a]	% yield[b] C-acylated	% yield[b] O-acylated
I		A	71	5
		B	65	15
II		A	10	0
		B	43	12
III		A	77	5
		B	61	25
IV		A	94	4
		B	61	12
V		A	92	0
		B	70	17
VI		A	0	0
		B	4	10

[a] Procedure A uses zinc chloride and diethyl ether, and B uses antimony trichloride. [b] Yields determined by GC analysis.

results with 65% of 2-acetylcyclohexanone, 15% cyclohexanone enol acetate, and approximately 10% cyclohexanone. The other Lewis acids investigated gave less satisfactory results (Table I). The addition of a small amount of diethyl ether as well as allowing the flask to warm to room temperature before quenching with water significantly increased the yields of 1,3-diketones from the reaction with zinc chloride. The amount of O-acylated product obtained was not altered. The addition of diethyl ether did not increase the yields for the reactions using antimony trichloride.

An important point to consider is the probable formation of a diketonate metal complex (eq 6). Hydrogen halide

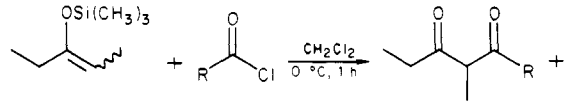


(6)

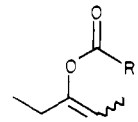
is a product of this reaction, and this material can react with the trimethylsilyl enol ether to give the corresponding ketone. This destruction of starting material is probably an important factor limiting the yields of 1,3-diketone. It appears that in most cases this process is slow enough under our reaction conditions to permit isolation of satisfactory amounts of the desired products. Yields are nearly quantitative when the diketonate–zinc complex cannot be formed as shown by the results for the acylation of the isobutyrophenone and diisopropyl ketone trimethylsilyl enol ethers (Table II entries IV and V). The results of the acylation of a variety of trimethylsilyl enol ethers with acetyl chloride are shown in Table II.

A variety of acid chlorides can also be used as acylating agents in place of acetyl chloride. The results of the reaction of diethyl ketone trimethylsilyl enol ether with different acid chlorides are summarized in Table III.

Table III. Reaction of Various Acid Chlorides with Diethyl Ketone Trimethylsilyl Enol Ether



C-acylated



O-acylated

entry	R	procedure[a]	% yield[b] C-acylated	% yield[b] O-acylated
I	CH_3	A	77	5
		B	61	25
II	C_6H_5	A	63	4
		B	36	
III	CH_3CH_2	A	83	6
		B	61	26
IV	$(CH_3)_2CH$	A	81	5
		B	63	24
V	$(CH_3)_3C$	A	90	0
		B	63	17

[a] Procedure A uses zinc chloride and diethyl ether, and B uses antimony trichloride. [b] Yields determined by GC analysis.

Conclusion

The procedure described here appears to offer serveral advantages over previous methods for the acylation of ketone silyl enol ethers. It combines convenience and generality in substrate and acylating agent as well as a predominant selectivity for C-acylation over O-acylation. We believe it will complement other methods described in the literature[4-7] for the C-acylation of ketones.

Experimental Section

Reagent grade methylene chloride was dried over 4A sieves. ^1H NMR spectra were obtained on a Varian T-60 spectrometer at 60 MHz. Chemical shifts are reported in parts per million in the δ scale relative to an internal Me_4Si standard. Infrared spectra were recorded on a Perkin-Elmer 237B spectrophotometer. Mass spectral data were obtained with a Finnigan Model 4000 gas chromatograph–mass spectrometer equipped with a 6 ft × 0.25 in. column packed with 10% SE-30 on Chromosorb W. Gas chromtographic analyses were obtained with Varian 920 and 90-P chromotographs equipped with 6 ft × 0.25 in. stainless steel columns packed with 15% SE-30 on Chromosorb W. All product yields were determined by GC analysis with *n*-alkanes as internal standards. Acid chlorides were purified by distillation when necessary.

Silyl Enol Ethers. Trimethylsilyl enol ethers were prepared from the corresponding ketone by reaction with trimethylchlorosilane, triethylamine, and sodium iodide in acetonitrile according to the procedure of Duboudin.[8] Isolation and puri-

(4) Beck, A. K.; Hoekstra, M. S.; Seebach, D. *Tetrahedron Lett.* **1977**, 1187.
(5) Howard, H. J.; Meerholz, C. A.; Michael, J. P. *Tetrahedron Lett.* **1979**, 1339.
(6) See: House, H. O. "Modern Synthetic Reactions", 2nd ed.; W. A. Benjamin: New York, 1972; Chapter 11.
(7) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2341.
(8) Cazlau, P.; Moulines, F.; Laporte, O.; Duboudin, F. *J. Organomet. Chem.* **1980**, *201*, C9.

fication were accomplished by distillation through a short Vigreux column.

Cyclohexanone trimethylsilyl enol ether was prepared by the above method: ^{1}H NMR ($CDCl_3$) 0.2 (9 H, s), 1.57 (4 H, m), 1.93 (4 H, m), 4.75 (1 H, m).

Cyclohexanone trimethylsilyl enol ether was prepared as above: ^{1}H NMR ($CDCl_3$) 0.2 (9 H, m), 1.6–2.4 (6 H, m), 4.5 (1 H, br s).

3-Pentanone trimethylsilyl enol ether was prepared as above: ^{1}H NMR ($CDCl_3$) 0.2 (9 H, s), 1.0 (3 H, t, J = 7 Hz), 1.45 (3 H, d, J = 6 Hz), 1.95 (2 H, m), 4.45 (1 H, 9, J = 5 Hz).

2,4-Dimethyl-3-pentanone trimethylsilyl enol ether was prepared as above: ^{1}H NMR ($CDCl_3$) 0.2 (9 H, s) 0.95 (6 H, d, J = 7 Hz), 1.55 (3 H, s), 1.6 (3 H, s), 2.73 (1 H, septet, J = 7 Hz).

Acetophenone trimethylsilyl enol ether was prepared as above: ^{1}H NMR ($CDCl_3$) 0.2 (9 H, s), 4.35 (1 H, d, J = 2 Hz), 4.75 (1 H, d, J = 2 Hz), 7.0–7.5 (5 H, m).

Isobutyrophenone trimethylsilyl enol ether was prepared as above: ^{1}H NMR ($CDCl_3$) 0.2 (9 H, s), 4.25 (1 H, d, J = 2 Hz), 4.8 (1 H, d, J = 2 Hz), 7.0–7.5 (5 H, m).

Zinc Chloride. Zinc chloride was dried by refluxing in thionyl chloride until gas evolution ceased. After the removal of the excess thionyl chloride the zinc chloride was stored in a desicator over KOH for 12 h.[9] It was then transferred to a dry bottle and stored in a desiccator over P_2O_5. All transfers of zinc chloride were done in a glovebag under argon.

Antimony Trichloride. Antimony trichloride was sublimed [60 °C (~0.1 mmHg)] to give white crystals which were transferred to a dry bottle and stored in a desiccator over P_2O_5. All transfers of antimony trichloride were done in a glovebag under argon.

Acylation of Ketone Silyl Enol Ethers. Procedure A. A 50-mL flask with a septum inlet and magnetic stir bar was flame dried and flushed with argon. Zinc chloride (0.79g, 5.8 mmol) was transferred in a glovebag to the reaction flask. The flask was removed from the glovebag and connected to a mercury bubbler. This was followed by the introduction of 5.8 mL of methylene chloride and 0.93 mL of diethyl ether. After the flask was cooled to 0 °C, the acid chloride (5.8 mmol) was added, followed shortly by the dropwise addition of trimethylsilyl enol ether (5.8 mmol). After being stirred 1 h at 0 °C, the reaction mixture was allowed to warm to room temperature and was quenched with approximately 10 mL of water. The layers were separated, and the aqueous layer was washed with methylene chloride. The methylene chloride layers were combined and washed with a saturated sodium hydrogen carbonate solution. The organic extract was dried over sodium sulfate and analyzed by GC for C- and O-acylated ketone. Pure samples of product were obtained for spectral analysis by preparative GC.

Acylation of Ketone Silyl Enol Ethers. Procedure B. A 50-mL flask with a septum inlet and magnetic stir bar was flame dried and flushed with argon. Antimony trichloride (1.28 g, 5.6 mmol) was added to the flask in a glovebag. The flask was removed from the glovebag and connected to a mercury bubbler. Methylene chloride (5.6 mL) was added to the flask, and it was cooled to 0 °C. The acid chloride (5.6 mmol) was added followed by the dropwise addition of the trimethylsilyl enol ether (5.6 mmol). After the mixture was stirred 1 h at 0 °C, the flask was warmed to room temperature, and the reaction was quenched with approximately 10 mL of H_2O. The method for the work up was as described for procedure A above.

Spectral analyses of all products were performed on pure samples obtained by preparative GC. Those products resulting from C-acylation gave mass spectral, ^{1}H NMR, and IR data consistent with their structural assignments. Enol esters obtained by O-acylation were identified by their mass and ^{1}H NMR spectra.

2-Acetylcyclohexanone[10] was prepared from cyclohexanone trimethylsilyl enol ether and acetyl chloride by procedures A and B. GC analysis of the crude product after workup showed four components with the following identities and retention times: cyclohexanone (1.6 min), cyclohexanone enol acetate (3.5 min), undecane (4.2 min), 2-acetylcyclohexanone (6.6 min). Spectral analysis of 2-acetylcyclohexanone gave the following: ^{1}H NMR ($CDCl_3$) 1.70 (4 H, m), 2.05 (3 H, s), 2.31 (4 H, m), 15.2 (1 H, s); IR (neat) 1730, 1705 cm^{-1} (C=O, keto form), 1610 (C=C, enol form).

2-Acetylcylopentanone[10] was prepared by both procedures A and B from cyclopentanone trimethylsilyl enol ether and acetyl chloride. GC analysis of the crude product shows four components [component identity (retention time)]: cyclopentanone (1 min), cyclopentanone enol acetate (1.9 min), 2-acetylcylopentanone (3.4 min), dodecane (6.6 min). Spectral analysis of 2-acetylcyclopentanone gave the following: ^{1}H NMR ($CDCl_3$) 1.96 (s), 1.65–2.7 (m), 2.20 (s), 3.3 (m), 13.3 (s), spectrum shows keto and two enol forms; IR (neat) 1710, 1745 (C=O, keto form), 1650 cm^{-1} (C=C, enol form).

Cyclopentanone enol acetate was isolated from the reaction of cyclopentanone trimethylsilyl enol ether and acetyl chloride: ^{1}H NMR ($CDCl_3$) 5.3 (1 H, m), 2.1–2.6 (6 H, m), 2.05 (3 H, s).

3-Methyl-2,4-hexanedione[10] was prepared by methods A and B from diethyl ketone trimethylsilyl enol ether and acetyl chloride. The crude product was subjected to GC analysis which showed a four-component mixture [identity (retention time)]: diethyl ketone (0.6 min), diethyl ketone enol acetate (1.5 min), 3-methyl-2,4-hexanedione (2.5 min), undecane (5.4 min). Spectral analysis of 3-methyl-2,4-hexanedione gave the following: ^{1}H NMR ($CDCl_3$) 1.0 (3 H, t), 2.15 and 2.05 (3 H, both s), 1.9 and 1.3 (3 H, s and d), 2.3 (2 H, q), 3.65 and 16.2 (1 H, q and s), spectrum shows keto and two enol forms; IR (neat) 1690, 1725 (C=O, keto form) 1600 cm^{-1} (br, C=C, enol form).

Diethyl ketone enol acetate was prepared by methods A and B: ^{1}H NMR ($CDCl_3$) 5.0 (1 H, q), 1.4 (3 H, d), 1.0 (3 H, t), 2.0–2.3 (5 H, overlapping m and s).

3,3,5-Trimethyl-2,4-hexanedione[11] was prepared by methods A and B from diisopropyl ketone trimethylsilyl enol ether and acetyl chloride. GC analysis of the crude product showed a four-component mixture [identity (retention time)]: diisopropyl ketone (0.9 min), diisopropyl ketone enol acetate (1.9 min), dodecane (2.8 min), 3,3,5-trimethyl-2,4-hexanedione (6.1 min). Spectral analysis of 3,3,5-trimethyl-2,4-hexanedione gave the following: ^{1}H NMR ($CDCl_3$) 1.05 (6 H, d), 1.3 (6 H, s), 2.1 (3 H, s), 2.85 (1 H, septet); IR(neat) 1710, 1730 cm^{-1} (C=O).

Diisopropyl ketone enol acetate was prepared from diisopropyl ketone trimethylsilyl enol ether and acetyl chloride by using both procedures A and B: ^{1}H NMR ($CDCl_3$) 2.05 (3 H, s), 0.95 (6 H, d), 1.45 (3 H, s), 1.7 (3 H, s).

1-Phenyl-1,3-butanedione[10] was prepared from acetophenone trimethylsilyl enol ether and acetyl chloride by using procedure B. GC analysis of the crude product mixture showed five components [identity (retention time)]: acetophenone (1.5 min), acetophenone enol acetate (2.5 min), benzoylacetone (4.9 min), hexadecane (8.8 min), unidentified high-boiling fraction. Spectral analysis of benzoylacetone gave the following: ^{1}H NMR ($CDCl_3$) 2.13 and 2.24 (3 H, both s), 4.03 (s), 6.12 (s), 7.2–7.5 (3 H, m), 7.65 (2 H, m); IR 1600 cm^{-1} (br).

Acetophenone enol acetate was prepared by method B: ^{1}H NMR ($CDCl_3$) 2.2 (3 H, s), 4.9 (1 H, d), 5.35 (1 H, d), 7.1–7.5 (5 H, m).

1-Phenyl-2,2-dimethyl-1,3-butanedione[12] was prepared from isobutyrophenone trimethylsilyl enol ether and acetyl chloride by using both procedures A and B. GC analysis of the crude product identified four major components [identity (retention time)]: isobutyrophenone (2.8 min), isobutyrophenone enol acetate (4.0 min), 1-phenyl-2,2-dimethyl-1,3-butanedione (5.8 min), pentadecane (7.9 min). Spectral analysis of 1-phenyl-2,2-dimethyl-1,3-butanedione gave the following: ^{1}H NMR 1.45 (6 H, s), 2.05 (3 H, s), 7.1–7.4 (3 H, m), 7.65 (2 H, m); IR (neat) 1675, 1715 (C=O), 1600, 1580 cm^{-1} (monosubstituted benzene).

1-Phenyl-2-methyl-1,3-pentanedione[13] was prepared from diethyl ketone trimethylsilyl enol ether and benzoyl chloride by methods A and B. GC analysis of the crude product showed three major components [identity (retention time)]: diethyl ketone enol

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(10) Mao, C. L.; Frostick, F. C.; Man, E. H.; Manik, R. M.; Wells, R. L.; Hauser, C. R. *J. Org. Chem.* **1969**, *34* 1425.
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(13) Muir, W. M.; Ritchie, P. D.; Lyman, D. J. *J. Org. Chem.* **1966**, *31*, 3790.

benzoate (5.3 min), 1-phenyl-2-methyl-1,3-pentanedione gave the following: ^{1}H NMR ($CDCl_3$) 1.0 (3 H, t), 1.4 (3 H, d), 2.4 (2 H, q), 4.4 (1 H, q), 7.2–7.5 (3 H, m), 7.85 (2 H, m), no enol seen; IR (neat) 1690, 1720 cm^{-1} (C=O).

2,4-Dimethyl-3,5-heptanedione[5] was prepared from isobutyryl chloride and diethyl ketone trimethylsilyl enol ether by procedures A and B. GC analysis of the crude product identified three components [identity (retention time)]: diethyl ketone enol isobutyrate (2.2 min), 2,4-dimethyl-3,5-heptanedione (3.7 min), dodecane (6.4 min). Spectral analysis of 2,4-dimethyl-3,5-heptanedione gave the following: ^{1}H NMR ($CDCl_3$) 3.8 and 16.5 (1 H, q and s), 2.2–3.0 (3 H, overlapping septet and quartet), 1.8 and 1.15 (3 H, s and d), 0.9–1.1 (9 H, overlapping t and d), spectrum shows keto and enol forms; IR (neat) 1700, 1725 (C=O, keto form), 1580 cm^{-1} (C=C, enol form).

4-Methyl-3,5-heptanedione[14] was prepared by methods A and B from diethyl ketone trimethylsilyl enol ether and propionyl chloride. GC analysis of the crude products showed four components [identity (retention time)]: diethyl ketone (0.8 min), diethyl ketone enol proprionate) (3.9 min), 4-methyl-3,5-heptanedione (6.7 min), undecane (10 min). Spectral analysis of 4-methyl-3,5-heptanedione gave the following: ^{1}H NMR ($CDCl_3$) 3.65 and 16.3 (1 H, q and s), 2.5 (4 H, q), 1.8 and 1.25 (3 H, s and d), 1.05 (6 H, t), spectrum shows keto and enol forms; IR (neat) 1725, 1700 (C=O, keto form), 1600 cm^{-1} (C=C, enol form).

Diethyl ketone enol propionate was prepared by both methods A and B: ^{1}H NMR ($CDCl_3$) 5.0 (1 H, q), 1.9–2.6 (4 H, m), 1.45 (3 H, d), 0.9–1.3 (6 H, m).

2,2,4-Trimethyl-3,5-heptanedione was prepared by both procedures A and B from pivaloyl chloride and diethyl ketone trimethylsilyl enol ether. GC analysis of the crude product showed four major components [identity (retention time)]: diethyl ketone (1.0 min), diethyl ketone enol trimethyl acetate (3.0 min), 2,2,4-trimethyl-3,5-heptanedione (5.2 min), dodecane (6.9 min). Spectral analysis of 2,2,4-trimethyl3,5-heptanedione gave the following: ^{1}H NMR ($CDCl_3$) 4.1 (1 H, q), 2.5 (2 H, q), 1.35 (3 H, d), 0.9–1.1 (12 H, overlapping t and s), no enol seen; IR (neat) 1700, 1725 cm^{-1}; mass spectrum, *m/e* (relative intensity), 41 (13), 57 (100), 85 (15), 86 (34), 99 (6), 114 (4), 142 (0.3), 170 (M^+, 1). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found C, 70.64; H, 10.80.

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Registry No. Cyclohexanone trimethylsilyl enol ether, 6651-36-1; cyclopentanone trimethylsilyl enol ether, 19980-43-9; 3-pentanone trimethylsilyl enol ether, 17510-47-3; 2,4-dimethyl-3-pentanone trimethylsilyl enol ether, 55339-64-5; isobutyrophenone trimethylsilyl enol ether, 39158-85-5; acetophenone trimethylsilyl enol ether, 13735-81-4; cyclohexanone, 108-94-1; cyclopentanone, 120-92-3; 3-pentanone, 96-22-0; 2,4-dimethyl-3-pentanone, 565-80-0; acetophenone, 98-86-2; isobutyrophenone, 611-70-1; 2-acetylcyclohexanone, 874-23-7; cyclohexanone enol acetate, 1424-22-2; 2-acetylcyclopentanone, 1670-46-8; cyclopentanone enol acetate, 933-06-2; 3-methyl-2,4-hexanedione, 4220-52-4; diethyl ketone enol acetate, 13893-75-9; 3,3,5-trimethyl-2,4-hexanedione, 42412-60-2; diisopropyl ketone enol acetate, 4007-46-9; 1-phenyl-1,3-butanedione, 93-91-4; acetophenone enol acetate, 2206-94-2; 1-phenyl-2,2-dimethyl-1,3-butanedione, 3815-34-7; isobutyrophenone enol acetate, 5170-76-3; 1-phenyl-2-methyl-1,3-pentanedione, 13618-19-4; diethyl ketone enol benzoate, 13893-94-2; 2,4-dimethyl-3,5-heptanedione, 37484-68-7; diethyl ketone enol isobutyrate, 83710-44-5; 4-methyl-3,5-heptanedione, 1187-04-8; diethyl ketone enol propionate, 83710-42-3; 2,2,4-trimethyl-3,5-heptanedione, 83710-43-4; diethyl ketone enol trimethyl acetate, 83710-45-6; CH_3COCl, 75-36-5; PhCOCl, 98-88-4; CH_3CH_2COCl, 79-03-8; $(CH_3)_2CHCOCl$, 79-30-1; $(CH_3)_3CCOCl$, 3282-30-2; $ZnCl_2$, 7646-85-7; $SbCl_3$, 10025-91-9; $TiCl_4$, 7550-45-0; $SbCl_5$, 7647-18-9; $SnCl_4$, 7646-78-8; BCl_3, 10294-34-5; $FeCl_3$, 7705-08-0; $AlCl_3$, 7446-70-0.

Synthesis and Proton Nuclear Magnetic Resonance Spectra of Diastereomeric β-Hydroxy Esters. An Unusual Hydroxy to Methyl Coupling through Four σ Bonds

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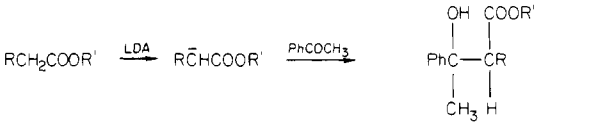
A series of 3-hydroxy-3-phenyl-2-alkylbutyrate esters has been prepared by the reaction of various ester enolates with acetophenone. A 1:1 mixture of diastereoisomers was obtained in each case which was conveniently separated by HPLC. The two isomers, erythro (e) or threo (t), were identified on the basis of their IR and proton NMR spectra. In $CDCl_3$ solution only the erythro isomers exhibited a 1-Hz coupling constant between the hydroxyl and geminal methyl protons. This coupling is transmitted through four σ bonds which are arranged in a "W" configuration. In Me_2SO solution, the intramolecular hydrogen bond which allows the "W" configuration is disrupted, causing coupling to disappear and the spectra of the erythro and threo isomers to become nearly equivalent.

Compounds with two adjacent asymmetric centers which exist in two diastereomeric forms have frequently been studied by NMR spectroscopy.[1] The stereochemistry of a series of diastereomeric ethyl 3-hydroxy-3-(para-substituted phenyl)butyrates has been previously determined by Balsamo et al. using careful analysis of the proton chemical shifts.[2] We have extended and generalized this early study by applying similar methods to various 3-hydroxy-3-phenyl-2-alkylbutyrate esters. In particular, we report the observation of a long-range spin–spin coupling between the protons of the methyl group and the geminal

Scheme I



1, R = CH_3; R' = CH_3
2, R = $CH_2CH_2CH_3$; R' = CH_2CH_3
3, R = $CH(CH_3)_2$; R' = CH_2CH_3

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