Reaction of Ketene Alkyl Trimethylsilyl Acetals with Dimethyl Acetylenedicarboxylate Catalyzed with Zirconium Tetrachloride

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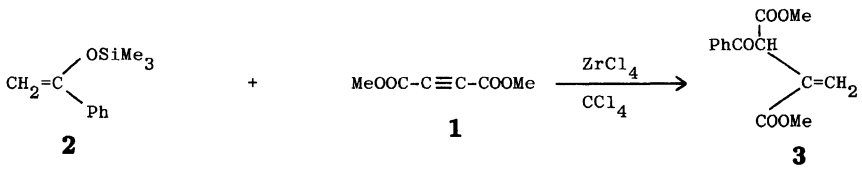
When dimethyl acetylenedicarboxylate is reacted with ketene alkyl trimethylsilyl acetals in the presence of a catalytic amount of zirconium tetrachloride, dimethyl 2-alkoxycarbonyl-3-alkylidenebutanedioates are afforded. Although the silyl enol ether from acetophenone undergoes the same type of reaction, other trisubstituted silyl enol ethers such as those from butyrophenone and 3-pentanone fail to react with dimethyl acetylenedicarboxylate under these conditions.

The Lewis acid catalyzed reaction of silyl enol ethers or ketene alkyl silyl acetals with conjugated ynones has been reported to have a variety of reaction patterns such as a [2+2] cycloaddition,[1] a Michael addition,[2] or a 1,2-addition,[3] but conjugated enones do almost exclusively a Michael addition in the related reaction.[4] The [2+2] cycloaddition reaction with ynones might be anticipated to supply a useful method to introduce different groups to each position of the yne moiety by cleavage of the silyl substrate-originated bond of the resulting cyclobutene ring. As for silyl enol ethers, those from cycloalkanones have been transformed to the ring-expanded products though the [2+2] addition reaction with acetylenic esters followed by acid treatment[5] although, in this case, the *t*-butyldimethylsilyl group is appropriate and the trimethylsilyl group is inclined to be cleaved before the cycloaddition.[1] This type of reaction using the silyl enol ethers, however, has been almost entirely limited to those from cyclic ketones and few investigations concern those of acyclic ketones. In this investigation, we have found that zirconium tetrachloride catalyzes the reaction of ketene alkyl trimethylsilyl acetals or a trimethylsilyl enol ether with dimethylacetylenedicarboxylate (**1**) to furnish the products constituted by introduction of the different groups to both positions of the carbon-carbon triple bond of **1**, which seem to be formally derived through the desilylative ring opening of the cycloadducts. The results of the ring opening following cycloaddition of enamines,[6] ketene acetals,[7] and enol ethers[8] with acetylenic esters have been shown. This type of reaction using ketene alkyl silyl acetals, however, has not been so far investigated to our knowledge although the reaction of ketene alkyl silyl acetals with ethyl propiolate in the presence of titanium tetrachloride has been reported to form the titanium intermediates induced form the Michael addition, which, in turn, afford products differently functionalized at each position of the acetylenic bond through the trap with electrophiles.[2]

Results and Discussion

Reaction with Silyl Enol Ethers. We have shown that trimethylsilyl enol ethers react with conjugated enones under photoirradiation to form the [2+2] cycloadducts, which are subsequently electrolyzed to introduce the different groups to both positions of the ene moieties of the starting enones by the collapse of the cyclobutane ring.[9] Thus, at first, the photoreaction of 1-phenyl-1-trimethylsiloxy-ethylene (**2**) with **1** was done with expectation of the formation of the [2+2] cycloadduct. The adduct, however, was not formed at all. Next, the $TiCl_4$-catalyzed reaction of **2** with **1** was examined since titanium tetrachloride has been known to promote the cycloaddition of silyl enol ethers with acetylenic esters.[1] The result was only the formation of benzophenone, which is a precursor of **2**, and its aldol-type product. As titanium tetrachloride preferentially cleaved the trimethylsilyl group without the production of the cycloadduct, the weaker Lewis acids, such as titanium tetraisopropoxide, titanium diisopropoxide dichloride,[10] ethylaluminium dichloride, or diethylaluminium chloride, were investigated. These, however, also failed to perform the cycloaddition. Finally, the $ZrCl_4$-catalyzed reaction of **2** with **1** in an equimolar ratio was done in a CCl_4 solution at room temperature to afford dimethyl 2-benzoyl-3-methylenebutanedioate (**3**) in 18% yield (Scheme 1). Lowering the reaction temperature to 0 °C did not give **3**. Use of two equivalents of **2** at room temperature rather decreased the yield of **3**, resulting in the formation of a complex mixture.



Scheme 1.

The trisubstituted silyl enol ethers, i.e., those from butyrophenone and 3-pentanone, did not yield the 2-acyl-3-methylenebutanedioates by the $ZrCl_4$-catalyzed reaction with **1** at room temperature and even at reflux, remaining intact.

Reaction with Ketene Alkyl Silyl Acetals. Next, ketene alkyl trimethylsilyl acetals **4** were tried in the $ZrCl_4$-catalyzed reaction with **1**. When the ketene alkyl silyl acetal from ethyl hexanoate, **4a**, was reacted with an equimolar amount of **1** at room temperature, dimethyl 2-ethoxycarbonyl-3-pentylidenebutanedioate (**5a**) was afforded in 22% yield (Scheme 2). Use of two equivalents of **4a** raised the yield of **5a** to 55%. GC analysis found that **5a** was composed of a single stereoisomer which seems to be a *Z*-form from comparison of the observed chemical shift of olefinic H-4 (δ=6.08) with that calculated according to the literature[11] (δ=5.99 and 6.55 for *Z*- and *E*-form, respectively). While the reaction of two equivalents of the ketene alkyl silyl acetal from propyl hexanoate, **4b**, with **1** at room temperature for 20 h afforded **5b** in 47% yield, lowering of the reaction temperature (0 °C for 5 h followed by room temperature for 15 h) raised the yield of **5b** to 80%. On the other hand, the yield of **5b** was not affected by increasing the amount of **4b** to three equivalents (77%). Thus, a variety of **4** were tried in the $ZrCl_4$-catalyzed reaction with **1** under the standard conditions, in which a CCl_4 solution containing **1**, **4**, and $ZrCl_4$ in 1:2:0.1 molar ratio was stirred at 0 °C (5 h) and then room temperature (15 h), although the reaction was done with refluxing in the case of sluggish consumption of the starting substrates. The results are collected in Table 1. The ketene alkyl silyl acetal from ethyl oleate, **4c**, afforded **5c** in 27% yield under the standard conditions while use of an increased amount of **4c** (5 equiv) raised the yield of **5c** to 81%. In turn, and increase of the amount of zirconium tetrachloride (0.5 equiv) rather diminished the yield of **5c** to 18%. Although the products from the ketene alkyl silyl acetals **4b**—**f** may have the stereochemistry of *Z*- and *E*-forms, GC analysis demonstrated that those are composed of the sole stereoisomers which are likely to be all the *Z*-forms, judged from similarity of the observed chemical shifts of olefinic H-4 of **5b**—**e**, i.e., δ=6.08, 6.09, 6.18, and 6.11, with that of **5a** (above), and comparison of the H-4 observed chemical shift of **5f** (δ=7.02) with the calculated chemical shift[11] (δ=6.90 and 7.46 for *Z*- and *E*-forms, respectively). The product **5g** was also composed of the single steroisomer although its accurate configuration cannot be ascertained at this stage.

Table 1. Reaction of Ketene Alkyl Silyl Acetals **4** with **1** in the Presence of $ZrCl_4$ (0.1 equiv)

4	**4**/**1** mole ratio	T/°C	Yield **5**/%[a]
a	1	0 → r.t.	22
a	2	0 → r.t.	55
b	2	r.t.	47
b	2	0 → r.t.	80
b	3	0 → r.t.	77 (56)[b]
c	2	0 → r.t.	(27)[c]
c	5	0 → r.t.	(81)[c]
c	5	0 → r.t.	(18)[c,d]
d	2	0 → r.t.	48
e	2	0 → r.t.	(20)[c]
f	2	76	(41)[c]
g	2	76	(62)[c]
h	2	76	50 (33)[b]

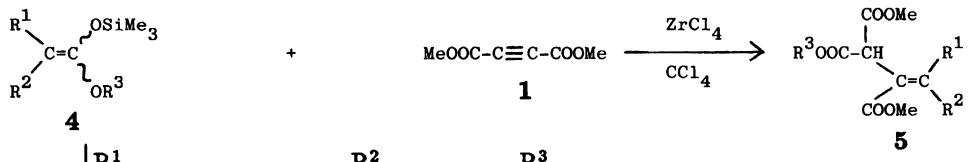
a) Determined by GC. b) After purification by column chromatography. c) After purification by preparative TLC. d) Reaction in the presence of 0.5 equiv of $ZrCl_4$.

Ketene alkyl silyl acetals proved to be more susceptive for this reaction than silyl enol ethers, as exemplified by the results that tri- and even tetrasubstituted ketene alkyl silyl acetals were able to yield **5** but trisubstituted silyl enol ethers failed to react with **1** (above). Thus, electron abundance of an ene moiety seems to be critical for the $ZrCl_4$-catalyzed reaction with **1**. Actually, the ketene alkyl silyl acetals bearing the electron-withdrawing substituents such as phenylthio, chloro, or bromo, **4i**—**k**, were not successful in formation of **5**. On the other hand, 2-dimethylamino-1-methoxy-1-trimethylsiloxyethylene (**4l**), which is a highly electron-rich ketene alkyl silyl acetal, underwent a reaction with carbon tetrachloride as a solvent before that with **1**, forming *N*,*N*-dimethyl-2-(trichloromethyl)glycine methyl ester (**6**) (Scheme 3).

Other conjugated alkynes than **1** such as ethyl propiolate and 4-phenyl-3-butyn-2-one, or the alkene analogue of **1**, i.e., diethyl maleate, afforded no product by the $ZrCl_4$-catalyzed reaction with **4b**.

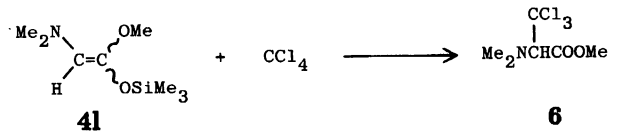
Effects of Solvents. The effects of solvents on this reaction were explored, and carbon tetrachloride was proved to be best of the solvents examined, i.e., THF, CH_2Cl_2, CH_3CN, and CCl_4, as exemplified by the results of the reaction of **4d** with **1** in those solvents which are shown in Table 2.

Mechanism. As the mechanism for the formation of **5**, a pathway via the [2+2] cycloadduct **7** as shown in



	R^1	R^2	R^3
a	H	Bu	Et
b	H	Bu	Pr
c	H	$C_{16}H_{31}$	Et
d	H	Me	Me
e	H	$CH_2CH=CH_2$	Et
f	H	Ph	Me
g	$-CH_2CH=CH(CH_2)_2$	–	Et
h	Me	Me	Et
i	H	SPh	Et
j	H	Cl	Et
k	H	Br	Et

Scheme 2.



Scheme 3.

Table 2. Effect of Solvent of the $ZrCl_4$-Catalyzed Reaction of **4d** with **1**

Solvent	Yield **5d**/%
CCl_4	48
CH_2Cl_2	40
THF	8
CH_3CN	19

Scheme 4 may be tentatively supposed although other possibilities, e.g., the route by way of the Michael-type reaction, cannot be excluded at this stage. Actually, in the reaction of **4h** with **1**, the formation of the cycloadduct **7h** besides **5h** was ascertained. Furthermore, the reaction of the ketene alkyl silyl acetal from γ-butyrolactone, **4m**, with **1** also afforded the cycloadduct **7m** (Scheme 5). Although the desilylative ring-expanded product was not formed in this case, that may be possibly rationalized by the lesser stability of the seven-membered ring compared with the five-membered ring of **7m**.

Conclusion

When a highly electron-deficient alkyne, i.e., **1**, is reacted with ketene alkyl trimethylsilyl acetals in the presence of a catalytic amount of zirconium tetrachloride, **5** which is a product resulting from the overall introduction of a different group to each acetylenic carbon of **1** is afforded. In the case of the silyl enol ether, which is a slightly less electron-rich substrate compared with the ketene alkyl silyl acetal, only the 1,1-disubstituted one (i.e., **2**) reacts similarly.

Experimental

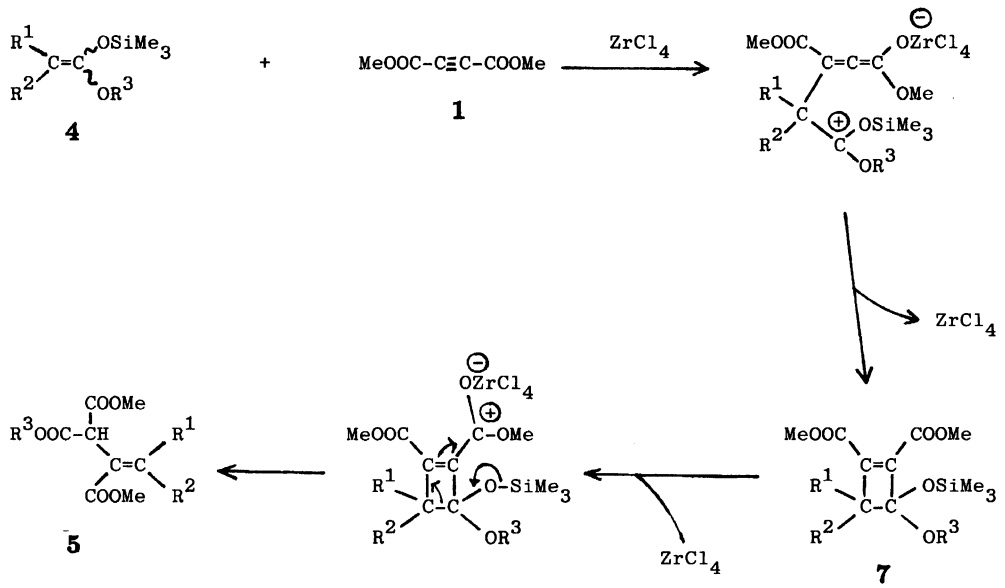
IR spectra were recorded on a Hitachi EPI-G3 spectrometer as neat oils. ^1H (60 MHz) and ^{13}C (15 MHz) NMR spectra were recorded with a JEOL FX60 spectrometer for $CDCl_3/CCl_4$ solutions, using Me_4Si as internal standard. Mass spectra were obtained at 70 eV using a Hitachi M-80B instrument. Preparative TLC was done on Merck $60F_{254}$ silica gel and column chromatography was done on silica gel with a Yamazen MPLC instrument. GC was done using a Shimadzu GC-12A.

Materials. Trimethylsilyl enol ether **2** and ketene alkyl trimethylsilyl acetals **4a**—**m** were prepared by the methods of House[12] and Ainsworth,[13] respectively.

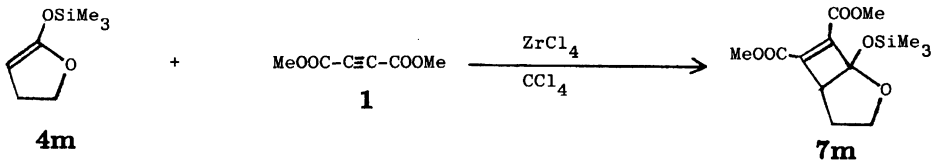
Standard Procedure. To a stirred solution of dimethyl acetylenedicarboxylate **1** (0.284 g, 2 mmol), the ketene alkyl silyl acetal **4** (4 mmol), and carbon tetrachloride (5 cm^3) at 0 °C, zirconium tetrachloride (46.6 mg, 0.2 mmol) was added at one portion. The resulting solution was stirred at 0 °C for 5 h and then at room temperature for 15 h. The reaction mixture was poured into water (50 cm^3) and extracted with diethyl ether (2×25 cm^3). After this was dried over $MgSO_4$, diethyl ether was removed under reduced pressure and the residue was purified by preparative GC, column chromatography, or preparative TLC.

Dimethyl 2- Benzoyl- 3- methylenebutanedioate (3). IR 3026, 1755, 1710, 1644, 1572 cm^{-1}; ^1H NMR δ=8.28—7.17 (5H, m, Ph), 5.95 (1H, s, H-4), 5.58 (1H, s, H-4), 4.58 (1H, s, H-2), 3.64 (6H, s, COOMe); ^{13}C NMR δ=132.10, 129.04, 127.62, 127.48, 53.16, 51.31, 51.12; MS-(EI) m/z 262 (M^+, 1), 105 (100), 77 (48). HRMS: Found: M^+, m/z 262.0859. Calcd for $C_{14}H_{14}O_5$: M, 262.0841.

Dimethyl (*Z*)-2-Ethoxycarbonyl-3-pentylidenebutanedioate (5a). IR 3027, 1736, 1647 cm^{-1}; ^1H NMR δ=6.08 (1H, t, J=7.7 Hz, H-4), 4.24 (1H, s, H-2), 4.09 (2H, q, J=7.7 Hz, $COOCH_2$), 3.67 (6H, s, COOMe), 2.73—2.39 (2H, m, H-5), 1.80—1.30 (4H, m, H-6, H-7), 1.36 (3H, t,



Scheme 4.



Scheme 5.

J=7.7 Hz, $COOCH_2C\underline{H}_3$), 0.96 (3H, t, J=6.0 Hz, H-8); ^{13}C NMR δ=148.09, 61.06, 54.87, 52.19, 51.22, 30.99, 29.24, 22.12, 13.82, 13.79; MS(EI) m/z 286 (M^+, 10), 254 (85), 227 (81), 213 (56), 93 (100), 59 (98). HRMS: Found: M^+, m/z 286.1409. Calcd for $C_{14}H_{22}O_6$: M, 286.1414.

Dimethyl (*Z*)-2-Pentylidene-3-(propoxycarbonyl)-butanedioate (5b). IR 3035, 1736, 1642 cm^{-1}; ^{1}H NMR δ=6.08 (1H, t, J=7.7 Hz, H-4), 4.31 (1H, s, H-2), 4.01 (2H, t, J=7.2 Hz, $COOCH_2$), 3.65 (6H, s, COOMe), 2.70—2.43 (2H, m, H-5), 1.83—1.20 (4H, m, H-6, H-7), 0.98 (3H, t, J=6.8 Hz, $COO(CH_2)_2C\underline{H}_3$), 0.96 (3H, t, J=6.8 Hz, H-8); ^{13}C NMR δ=148.04, 66.66, 54.87, 52.04, 50.97, 30.99, 29.24, 22.12, 21.73, 13.79, 10.18; MS(EI) m/z 300 (M^+, 8), 268 (86), 241 (95), 226 (100), 93 (93). HRMS: Found: M^+, m/z 300.1573. Calcd for $C_{15}H_{24}O_6$: M, 300.1571.

Dimethyl (*Z*)-2-Ethoxycarbonyl-3-[(*Z*)-9-heptadecenylidene]butanedioate (5c). IR 3008, 1732, 1644 cm^{-1}; ^{1}H NMR δ=6.09 (1H, t, J=7.7 Hz, H-4), 5.21 (2H, t, J=5.1 Hz, H-11, H-12), 4.32 (1H, s, H-2), 4.12 (2H, q, J=7.7 Hz, $COOCH_2$), 3.69 (3H, s, COOMe-3), 3.66 (3H, s, OMe-1), 2.76—2.41 (2H, m, H-5), 2.13—1.84 (4H, m, H-10, H-13), 1.62—1.18 (23H, m, $COOCH_2C\underline{H}_3$, H-6—H-9, H-14—H-19), 0.93 (3H, t, J=6.0 Hz, H-20); ^{13}C NMR δ=146.78, 128.31, 128.11, 59.74, 53.56, 50.78, 49.90, 30.46, 28.26, 27.87, 27.61, 27.49, 26.87, 26.22, 25.78, 21.25, 13.80, 12.72; MS(EI) m/z 452 (M^+, 5), 421 (25), 55 (100). HRMS: Found: M^+, m/z 452.3141. Calcd for $C_{26}H_{44}O_6$: M, 452.3136.

Dimethyl (*Z*)-2-Ethylidene-3-(methoxycarbonyl)-butanedioate (5d). IR 3005, 1736, 1652 cm^{-1}; ^{1}H NMR δ=6.18 (1H, q, J=7.7 Hz, H-4), 4.29 (1H, s, H-2), 3.64 (9H, s, COOMe), 2.09 (3H, d, J=7.7 Hz, H-5); ^{13}C NMR δ=142.24, 54.80, 52.39, 51.58, 15.54; MS(EI) m/z 230 (M^+, 3), 171 (100), 139 (95), 111 (90), 59 (90). HRMS: Found: M^+, m/z 230.0809. Calcd for $C_{10}H_{14}O_6$: M, 230.0789.

Dimethyl (*Z*)-2-(3-Butenylidene)-3-(ethoxycarbonyl)butanedioate (5e). IR 3080, 1732, 1634 cm^{-1}; ^{1}H NMR δ=6.11 (1H, t, J=7.7 Hz, H-4), 5.88—5.43 (1H, m, H-6), 5.26—4.76 (2H, m, H-7), 4.32 (1H, s, H-2), 4.12 (2H, q, J=7.7 Hz, $COOCH_2$), 3.66 (6H, s, COOMe), 3.31 (2H, t, J=7.7 Hz, H-5), 1.32 (3H, t, J=7.7 Hz, $COOCH_2C\underline{H}_3$); ^{13}C NMR δ=144.38, 144.07, 116.12, 61.06, 54.82, 52.09, 51.29, 33.53, 13.89, MS(EI) m/z 270 (M^+, 1), 238 (100), 211 (25), 160 (75), 137 (80). HRMS: Found: $(M-COOMe)^+$, m/z 211.0988. Calcd for $C_{11}H_{15}O_4$: (M−COOMe), 211.0969.

Dimethyl (*Z*)-Benzylidene-3-(methoxycarbonyl)-butanedioate (5f). IR 3063, 3036, 3003, 1740, 1634, 1598, 1500 cm^{-1}; ^{1}H NMR δ=7.31 (5H, br s, Ph), 7.02 (1H, s, H-4), 4.37 (1H, s, H-2), 3.69 (3H, s, COOMe-3), 3.66 (6H, s, OMe-1, COOMe-2); ^{13}C NMR δ=142.43, 128.70, 128.06, 127.33, 55.70, 52.34, 51.26; MS(EI) m/z 292 (M^+, 31), 233 (45), 173 (64), 107 (100), 77 (53). HRMS: Found: M^+, m/z 292.0952. Calcd fro $C_{15}H_{16}O_6$: M, 292.0946.

Dimethyl 2-(3-Cyclohexenylidene)-3-(ethoxycarbonyl)butanedionate (5g). IR 3036, 1732, 1660 cm^{-1}; ^{1}H NMR δ=5.51 (2H, br s, $C\underline{H}$=$C\underline{H}$), 4.39 (1H, s, H-2), 4.04 (2H, q, J=7.7 Hz, $COOCH_2$), 3.62 (6H, s, COOMe), 3.47 (2H, d, J=5.0 Hz, C=C$C\underline{H}_2$CH=C), 3.08—2.64 (4H, m, C=C$C\underline{H}_2C\underline{H}_2$CH=C), 1.24 (3H, t, J=7.7 Hz, $COOCH_2C\underline{H}_3$); ^{13}C NMR δ=124.60, 123.58, 59.07, 51.46, 50.39, 48.51, 32.99, 29.63, 21.54, 13.06; MS(EI) m/z 296 (M^+, 1), 264 (45), 190 (85), 162 (100). HRMS: Found: $(M-CH_3OH)^+$, m/z 264.1015. Calcd for $C_{14}H_{16}O_5$: (M−CH_3OH), 264.0997.

Dimethyl 2-Ethoxycarbonyl-3-isopropylidenebutanedioate (5h). IR 1732, 1640 cm^{-1}; ^1H NMR δ=4.42 (1H, s, H-2), 4.15 (2H, q, J=7.7 Hz, $COOCH_2$), 3.64 (3H, s, COOMe-3), 3.61 (3H, s, OMe-1), 2.12 (3H, s, Me-4), 1.90 (3H, s, H-5), 1.36 (3H, t, J=7.7 Hz, $COOCH_2C\underline{H}_3$); ^{13}C NMR δ=61.11, 52.19, 51.88, 51.07, 23.39, 22.81, 13.94; MS(EI) m/z 258 (M^+, 33), 199 (9), 185 (15), 154 (100), 126 (73). HRMS: Found: M^+, m/z 258.1098. Calcd for $C_{12}H_{18}O_6$: M, 258.1101.

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