J. Org. Chem. 1981, 46, 196-197

triacetate was obtained in 87% yield, mp 116–117.5 °C (lit.[12] mp 110 °C).

Mass spectral data [m/z (relative intensity)] of 1–4 are as follows.

1: 227 (15), 226 (96), 225 (11), 196 (30), 181 (26), 121 (26), 120 (100), 92 (44), 77 (41), 51 (93), 42 (37).

2: 546 (12), 544 (42), 542 (64), 540 (36), 538 (11), 499 (6), 497 (10), 495 (7), 464 (9), 462 (24), 460 (25), 458 (11), 431 (5), 433 (15), 435 (14), 437 (7), 393 (4), 280 (82), 278 (100), 276 (88), 252 (6), 250 (10), 248 (6), 198 (8), 196 (9), 185 (18), 183 (19), 157 (9), 156 (19), 155 (17), 154 (19), 153 (11), 143 (11), 141 (11), 76 (11), 75 (64), 74 (34), 63 (21), 62 (14), 53 (10), 50 (8), 28 (9).

3: 327 (16), 326 (63), 298 (13), 297 (45), 280 (23), 279 (100), 243 (3), 170 (20), 169 (84), 153 (10), 152 (11), 151 (18), 146 (15), 141 (19), 128 (29), 127 (36), 126 (29), 115 (26), 114 (31), 78 (23), 76 (13).

4: 318 (5), 317 (11), 316 (57), 300 (8), 299 (27), 283 (5), 273 (19), 272 (5), 274 (24), 244 (11), 243 (24), 228 (8), 199 (14), 198 (8), 171 (19), 170 (100), 144 (19), 140 (30), 124 (14), 123 (11), 110 (32), 108 (14), 106 (12), 96 (16), 95 (19), 85 (30), 83 (34), 82 (65), 81 (49), 80 (16), 69 (27), 68 (22), 67 (43), 58 (19), 57 (14), 56 (38), 55 (65).

Acknowledgment. We are grateful to the National Science Foundation for a major instrument grant used to purchase the FX-90 spectrometer.

Registry No. 1, 252-72-2; 2, 75625-88-6; 3, 52243-98-8; 4, 75625-89-7.

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An Improved Synthesis of Ketene Dimethyl Thioacetal Monoxide

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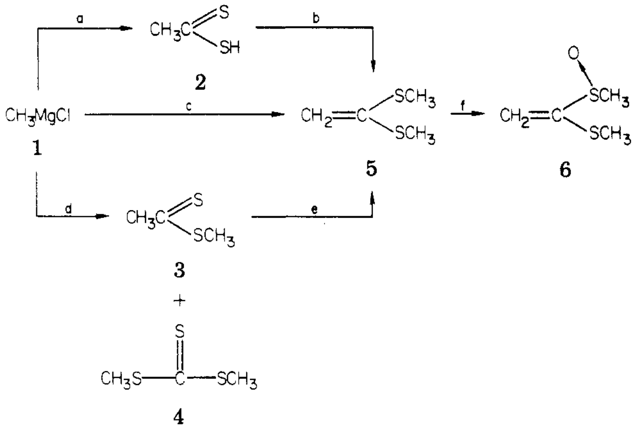
Ketene dimethyl thioacetal monoxide (**6**) has found varied use as a formylmethyl synthon[1] since it reacts as a Michael acceptor with a variety of enolate anions to yield, after hydrolysis of the intermediate adduct, 1,4-dicarbonyl compounds in which the carbonyl group derived from **6** is an aldehyde.

Our research required substantial quantities of **6** and we found the reported six-step route[1a] unsatisfactory because of cost in time and reagents. In view of Ziegler and Chan's recent synthesis of ketene thioacetals from dithioic acid dianions[2] we undertook an investigation of the synthesis of **6** by the related routes outlined in Scheme I.

Scheme I[a]



[a] a, CS_2/THF, 40-45 °C, 2 h, H^+, room temp; b, 2 n-BuLi/THF, -78 °C, 2 $(CH_3O)_2SO_2$, -78 °C; c, CS_2/THF, 1 LDA, 2 $(CH_3O)SO_2$; d, CS_2/THF, 40-45 °C, 2 h, 1 $(CH_3O)_2SO_2$, room temp; e, LDA/THF, -78 °C, 2 h, 1 $(CH_3O)_2SO_2$, -78 °C; f, m-CPBA, CH_2Cl_2, -5 °C.

We have found the most efficient preparation of the intermediate, ketene dimethyl thioacetal (**5**), to be a "one-pot" synthesis from methylmagnesium chloride. Thus, reaction of **1** with carbon disulfide, followed by reaction of the adduct with lithium diisopropylamide (LDA) at -78 °C and then with dimethyl sulfate afforded **5** in 60% yield. In this synthesis, if the temperature of the reaction mixture was allowed to increase above 0 °C then tar formation occurred with a lowering of the yield of **5**. Further, small amounts of dimethyl trithiocarbonate (**4**)[3] were formed in the reaction, requiring purification of the ketene before its conversion to the monoxide. In a similar procedure, with n-butyllithium substituted for LDA, **5** was obtained in lower yield along with other unidentified products.

Oxidation of **5** with m-chloroperbenzoic acid gave virtually pure ketene monoxide **6** uncontaminated with starting **5** or the other possible oxidation products (sulfone, bis sulfoxide or epoxide derived from **5**) as determined by NMR analysis. Similarly, oxidation of **5** with sodium metaperiodate by a slight modification of Johnson's method[4] gave monoxide **6** as the major product along with some unidentified compounds, necessitating purification of the crude material. Attempts to oxidize **5** to **6** with N-chlorosuccinimide and pyridinium chlorochromate failed to give the expected monoxide.

The intermediate ketene thioacetal **5** was also prepared by two other routes related to the "one-pot" procedure. In one route, dithioacetic acid (**2**), prepared in 56% yield[5] from Grignard **1**, was allowed to react with 2 equiv of n-butyllithium in THF/hexane at -78 °C followed by treatment of the intermediate dianion with dimethyl sulfate to give **5** in 70% yield. In the other route, methyl dithioacetate (**3**), prepared in 55% yield from Grignard **1**, was allowed to react with 1 equiv of LDA in THF at -78 °C followed by treatment of the intermediate anion with dimethyl sulfate to give **5** in 94% yield.

We have found both dithioacetic acid and ketene dimethyl thioacetal to be unstable under normal conditions. The acid polymerizes over a period of several months even when stored at 0 °C [6] and the thioacetal reacts slowly with air and will darken noticably within a few hours when exposed to a stream of oxygen. The oxidation products of this last reaction are currently under investigation.

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(3) Dimethyl trithiocarbonate was purified by fractional distillation, bp 106-110 °C (27 mm) [lit.[3a] bp 86-88 °C (5.4 mm)], and identified by comparison of its IR and NMR spectra with those of an authentic sample. (a) H. C. Godt, Jr., and R. E. Wann, *J. Org. Chem.* **26**, 4047 (1961).

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(5) This yield of **2** represents a substantial increase over the lower yields of about 20% which have been reported.[2,5a] (a) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances", Prentice-Hall, Englewood Cliffs, NJ, 1954, p 1287.

(6) A. Ohno and S. Oae in "Organic Chemistry of Sulfur", S. Oae, Ed., Plenum, New York, 1977, p 173, report that "dithioacetic acid kept standing for a prolonged period affords tetramethylhexathioadamantane".

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Ketene dimethyl thioacetal monoxide (**6**) can thus be prepared in moderate yield by a convenient two-step reaction sequence representing a significant improvement over the previously reported method both in terms of preparation time and cost of reagents.

Experimental Section

Proton NMR spectra were recorded on a Hitachi Perkin-Elmer R-24B instrument with tetramethylsilane as internal standard. Infrared spectra were recorded on a Perkin-Elmer Model 621 grating instrument and mass spectra were obtained from a Hitachi Perkin-Elmer RMU-6E double-focusing instrument. Elemental analyses were performed by Midwest Microlab, Ltd., Indianapolis, IN.

Tetrahydrofuran (THF) was dried and purified by distillation from sodium-potassium alloy prior to use. Diisopropylamine was distilled from calcium oxide and stored over 3-Å molecular sieves. Standardization of *n*-butyllithium and methylmagnesium chloride was performed by reaction with excess standard acid and back titration with standard base to a phenolphthalein end point.

Ketene Dimethyl Thioacetal (5). A solution of 90.0 mL (2.8 M, 252 mmol) of methylmagnesium chloride in THF under N_2 was diluted with THF to make a 1 M solution. Then a solution made by diluting 28.55 g (375 mmol) of carbon disulfide with an equal volume of THF was added to the mechanically stirred[7] Grignard reagent at a rate sufficient to increase the temperature of the reaction mixture to 40-45 °C and maintain this temperature range during the remainder of the carbon disulfide addition. After addition was complete the reaction mixture was stirred for 2 h, maintaining the temperature between 40-45 °C, and then cooled to -78 °C with a dry ice-acetone bath. Then a 0 °C solution of lithium diisopropylamide[8] was added dropwise, during 30 min, to the cold reaction mixture. The resulting solution was stirred at -78 °C for 2 h and then 63.6 g (504 mmol) of dimethyl sulfate was added during 1 h while the same low temperature was maintained. The resulting mixture was allowed to warm to room temperature and stirred at this temperature for 2 h. Then 300 mL of ether was added and after being stirred briefly the solution was allowed to stand during which time inorganic salts precipitated. The supernatant solution was decanted from the salts into 500 mL of 1% aqueous $NaHCO_3$ solution and the salts were washed with ether. The combined ether washings were added to the $NaHCO_3$ solution, the resulting mixture was shaken, and the layers were separated. The aqueous layer was extracted with two 150-mL portions of ether which were then added to the organic layer. The resulting organic solution was washed with two 100-mL portions of water, dried ($MgSO_4$), and distilled of solvent on a rotary evaporator to give 28.8 g (95%) of the crude product which was distilled under reduced pressure to give 18.2 g (60%) of a yellow liquid: bp 76-78 °C (26 mm); ^1H NMR ($CDCl_3$) δ 2.28 (6 H, s), 5.08 (2 H, s); IR (neat) 1580, 1560, 1445, 1430, 1327, 1108, 983, 802-865 cm^{-1}; mass spectrum (70 eV), *m/e* (relative intensity) 120 (79.5, M^+), 105 (18.8), 73 (100.0), 61 (40.6), 58 (49.7), 45 (53.0).

Anal. Calcd for $C_4H_8S_2$: C, 39.96; H, 6.71. Found: C, 40.11; H, 6.76.

Ketene Dimethyl Thioacetal Monoxide (6). To a solution of 6.8 g (50 mmol) of **5** in 100 mL of CH_2Cl_2 under an atmosphere of N_2 and maintained at -5 °C with a ice-salt bath was added 10.2 g (50 mmol) of 85% *m*-chloroperbenzoic acid in portions at such a rate that the temperature did not exceed 0 °C. The resulting solution was allowed to stir for 15 min at -5 °C and then for 1 h at room temperature after which time the reaction mixture was poured into 200 mL of 5% aqueous $NaHCO_3$ solution. The aqueous layer was extracted with two 50-mL portions of CH_2CL_2 which were combined with the organic layer. The resulting solution was dried ($MgSO_4$) and distilled of solvent on a rotary evaporator to give 5.8 g (85%) of **6** sufficiently pure (NMR analysis) for most purposes. Further purification by distillation under reduced pressure gave 4.8 g (71%) of a yellow liquid: bp 145-150 °C (27 mm); ^1H NMR ($CDCl_3$) δ 2.38 (3 H, s), 2.64 (3 H, s), 5.51 (1 H, d, $J = 2$ Hz), 6.01 (1 H, d, $J = 2$ Hz); IR (neat) 3490, 1593, 1429, 1330, 1070, 970, 893 cm^{-1}; mass spectrum (70 eV), *m/e* (relative intensity) 136 (5.9, M^+), 126 (0.8), 120 (1.6), 108 (3.2), 90 (8.4), 73 (100.0), 58 (15.1).

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Registry No. 2, 594-03-6; **3**, 2168-84-5; **5**, 51102-74-0; **6**, 51534-42-0; methyl chloride, 74-87-3; carbon disulfide, 75-15-0; dimethyl sulfate, 77-78-1.

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[7] Mechanical stirring is necessary because when the intermediate dianion is formed the reaction mixture is too viscous to permit the use of magnetic stirring.

[8] The LDA was made by adding 158 mL (1.6 M, 252 mmol) of *n*-butyl lithium in hexane to a solution of 25.5 g (252 mmol) of diisopropylamine in THF under N_2 and cooled in a salt-ice bath at such a rate that the temperature of the reaction mixture did not rise above 0 °C. The resulting solution was allowed to react for 0.5 h and then added to the ketene acetal reaction mixture.

Enone Mesylates. Precursors to β-Substituted Cyclohexenones

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β-Substituted cyclohexenones are valuable synthetic intermediates which are frequently employed in various schemes. Piers uses the conjugate addition of a suitable cyclopropylcuprate to 3-iodo-2-cyclohexenone in his approach to β-himachalene.[1] Wender generates spiro compounds by adding an organobiscuprate to β-chlorocyclohexenones.[2] Okamura's approach to the vitamin D system employs 3-iodo-2-methylcyclohexenone,[3] while Stork's widely used entry into 4-alkylcyclohexenones starts from β-alkoxycyclohexenones.[4] β-Aminocyclohexenones are important intermediates in Mariano's amino-Claisen rearrangement,[5] and the thioalkyl-substituted enones are starting materials for Bryson in forming functionalized 3-alkylcyclohexenones.[6] These represent but a few of the many uses to which such compounds have been put.

As a result of their importance, β-substituted cyclohexenones have been prepared by numerous methods.[1-6] Significant improvements have recently been made by Piers[7] and Heathcock[8] in approaches to the haloenones from 1,3-diones, their usual precursors. Both the orthoester approach[9] and "Organic Syntheses" procedure[10] allow formation of 3-alkoxycyclohexenones from the 1,3-diones. Other procedures are used to prepare amino-[5] and mercapto-substituted[6] enones. Despite these advances and others, however, there is no simple, general route which

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