# Polarized Ketene Dithioacetals. 28. A New General Highly Stereoselective and Regiospecific Method for Homologation of Ketones to α,β-Unsaturated Esters via α-Oxoketene Dithioacetals[1]

Bekington Myrboh, Hiriyakkanavar Ila,* and Hiriyakkanavar Junjappa*

*Department of Chemistry, North-Eastern Hill University, Shillong 793003 (Meghalaya), India*

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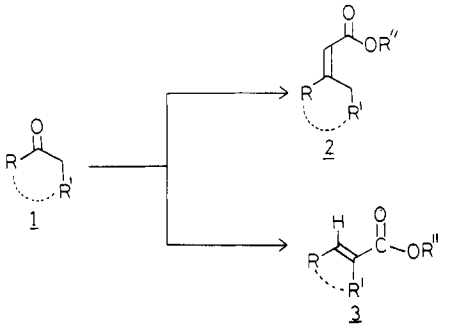
A new highly stereoselective and regiospecific general method for the conversion of active methylene ketones to α,β-unsaturated *O*-methyl esters, *S*-methyl esters, and aldehydes via the corresponding oxoketene dithioacetals has been developed. Thus the [bis(methylthio)methylene]carbinols **7a–g** obtained by sodium borohydride reduction of the corresponding oxoketene dithioacetals **6a–g**, derived from acetophenones and their higher homologues, have been shown to undergo boron trifluoride etherate assisted methanolysis to give the corresponding (*E*)-methylcinnamates **3a–d** and their α-alkyl derivatives **3e–g** in high yields. Also the acetals **6h–k** derived from alkylmethyl ketones gave the corresponding (*E*)-methylcrotonates **3h–k**. Similarly, the acetals **6l–p** derived from alicyclic ketones gave the corresponding cyclic ene esters **3l–p** under identical conditions. A few [bis(methylthio)methylene]carbinols, **7a–d**, were shown to undergo partial hydrolysis in the presence of boron trifluoride etherate/water to give the corresponding *S*-methyl thiocinnamates **8a–d**. The cyclic acetals **6l–n** were also similarly converted to the corresponding cyclic *S*-methylene thio esters **8e–g**. The (methylthio)alkenyl ketones **20a–d** and **18** after borohydride reduction and acidic hydrolysis gave the corresponding (*E*)-α,β-unsaturated aldehydes **22a–d** and **19**. The mechanism governing these transformations has been proposed.

The α,β-unsaturated esters of the general formulas **2** and **3** (Scheme I) are widely used intermediates in organic synthesis. The syntheses of **2** have been generally achieved by treating **1** under one of the variants of aldol condensation,[2-4] which is considered to involve a two-carbon homologation using a carbonyl group as the backbone of the ketone skeleton.

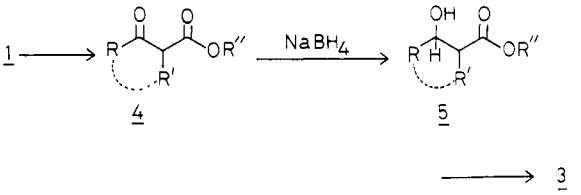
Surprisingly, there is only one method reported in the literature for the conversion of **1** to **3** (Scheme II). It involves the 1,2-reduction of β-keto esters followed by dehydration of the resultant alcohols to the corresponding α,β-unsaturated esters. The method, however, suffers from the formation of complex product mixtures and poor yields.[5] It is therefore desirable to develop a method for the conversion of **1** to **3**.

Consequently, we decided to examine the oxoketene dithioacetals **6** (Scheme III) as potential intermediates for the conversion of **1** to **3** via **7**. The methods of preparation of **6** from **1** have been well established in one-pot reactions in good to excellent yields,[6] and they have additional advantages as starting materials over the β-keto esters in more than one way. They can be considered as masked carboalkoxy groups, which are known to be resistant to 1,4-reduction by metal hydrides.[7] Second, they provide greater structural flexibility through provision for modification of the bis(methylthio)methylene group,[8] thereby ensuring wider choice of substrates. Our results in this

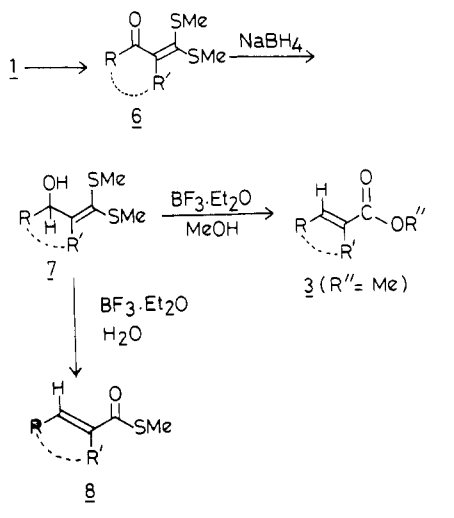
Scheme I



Scheme II



Scheme III



(1) The previous paper in this series: S. Apparao, H. Ila, and H. Junjappa, *J. Chem. Soc., Perkin Trans. 1*, in press.

(2) For a discussion on recent methods for the preparation of α,β-unsaturated acids/esters, see: G. Jones, *Org. React.* **15**, 262–263 (1967).

(3) A. Maercker, *Org. React.* **14**, 270 (1965).

(4) For a recent review on directed Aldol reactions, see: T. Mukaiyama, *Org. React.*, **28**, 203–331 (1982).

(5) (a) J. A. Katzenellenbogen and T. Utawanit, *J. Am. Chem. Soc.*, **96**, 6153 (1974), and references therein; (b) T. Sakai, K. Morita, C. Matsummura, A. Sudo, S. Tsuboi, and A. Takeda, *J. Org. Chem.*, **46**, 4774 (1981); (c) J. Jacques and A. Horeau, *Bull. Soc. Chim. Fr.*, 512 (1950); *Chem. Abstr.*, **45**, 2457 (1951); (d) M. Giani, L. Molteni, and A. Trebbi, *Farmaco, Ed. Sci.*, **14**, 784 (1959). (e) B. S. Nargund, *Proc.—Indian Acad. Sci., Sect. A*, **11A**, 409 (1940).

(6) S. M. S. Chauhan and H. Junjappa, *Tetrahedron*, **32**, 1779 (1976).

(7) These observations are similar to those reported by Ireland, who has noted that metal hydride reduction on (*n*-butylthio)methylene ketones affords only 1,2-reduction, while use of groups other than (*n*-butylthio)methylene (e.g., enol ether, enamine etc.) results in 20% 1,4-reduction: R. F. Church, R. E. Ireland, and J. A. Marshall, *J. Org. Chem.*, **27**, 1118 (1962). See also P. R. Bernstein, *Tetrahedron Lett.*, 1015 (1979).

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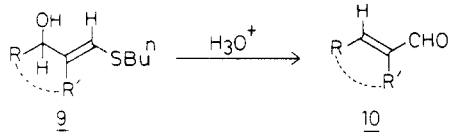
Scheme IV



paper are concerned with these transformations (7 → 3 and 7 → 8).

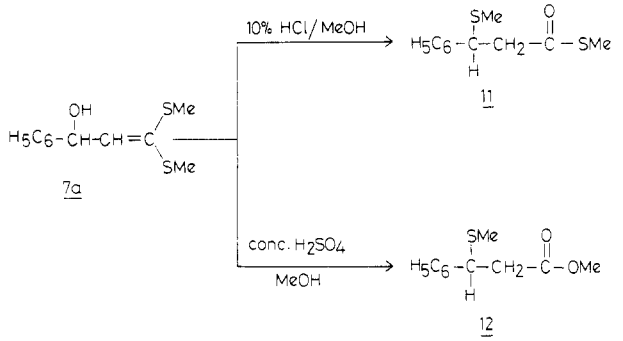
Our literature survey at this stage on related studies revealed that Thuillier and co-workers[9] have reported the sodium borohydride reduction of several oxoketene dithioacetals to the corresponding carbinols in excellent yields. They have also shown that these carbinols, on subsequent treatment with *p*-toluenesulfonic acid in refluxing benzene, yielded a mixture of several products from which the *S*-methyl α,β-unsaturated thio esters were obtained in low yields. Apparently their studies were not intended for use in the preparation of either **3** or **8**. Interestingly, the idea of using this approach for the synthesis of α,β-unsaturated aldehydes (Scheme IV) from cyclic ketones has been elegantly accomplished by Ireland and Marshall.[10] Their method includes the hydrolytic rearrangement of the carbinol **9** to the aldehyde **10**. However, they obtained **9** by treating the α-formyl ketones with *n*-butyl mercaptan followed by sodium borohydride reduction. The method is efficient and related to the present ester synthesis.

## Results and Discussion

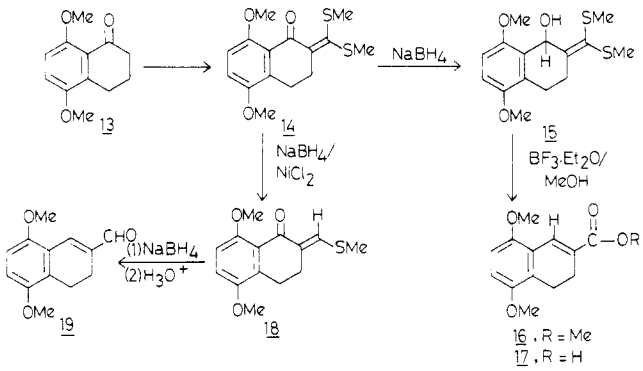
**Reduction of Oxoketene Dithioacetals.** A few representative examples of linear, cyclic aliphatic, and aromatic ketones were selected for the present studies. These ketones were converted to the corresponding α-oxoketene dithioacetals **6** by reported procedures.[6] They were then reduced with sodium borohydride in refluxing absolute ethanol to give, after the workup, the corresponding carbinols **7** in almost quantitative yields. The crude carbinols **7** were used directly without further purification for solvolytic and hydrolytic reactions to yield the corresponding α,β-unsaturated O-methyl esters, *S*-methyl esters, and aldehydes, respectively.

**Preparation of α,β-Unsaturated *O*-Methyl Esters, Aldehydes, and *S*-Methyl Esters.** The above carbinols **7** were initially treated under acid-catalyzed hydrolytic conditions, and a mixture of several products, identical with those obtained by Thuillier and co-workers,[9] was formed. No sulfur-free compound was obtained in any of these experiments. The resistance of these dithioacetals to acid-catalyzed hydrolysis to yield the sulfur-free products is well documented.[11] In one of the pilot experiments, when **7a** was stirred with 10% hydrochloric acid in methanol at room temperature, a mixture of several products (TLC) was formed from which only the rearranged *S*-methyl 3-(methylthio)-3-phenylpropanethiolate (**11**) was isolated in 45% yield (Scheme V). However, when **7a** was refluxed in 80% aqueous trifluoroacetic acid,[12] **11** was obtained in improved yields (65%). Similarly, **7a** in refluxing methanol and concentrated sulfuric acid yielded only methyl 3-(methylthio)-3-phenylpropionate (**12**, Scheme V) in 43% yield along with an undesirable product mixture. The mechanism governing these rearrangements has been studied by Thuillier and co-workers.[13]

Scheme V



Scheme VI



In one of these experiments, when **7a** was refluxed with boron trifluoride etherate in methanol, the corresponding methyl cinnamate **3a** (R = $C_6H_5$; R′ = H) was formed in 70% yield (Scheme III). The reaction was clean, with only one major spot (TLC) corresponding to **3a**, and was found to be general when extended to other carbinols (Table I). No efforts were made to optimize the yields.

Entries 1–4 and 5–7 (Table I) represent the direct conversion of the acetophenones and their higher homologues to the corrsponding methyl cinnamates **3a–d** and the α-alkylcinnamates **3e–g**, respectively, in excellent yields.[14] The geometry of these cinnamates was assigned on the basis of their $^1H$ NMR signals, and they were found to be formed exclusively as *E* isomers. No trace of the isomeric mixture was observed in any of these experiments. Entries 8–11 similarly represent the conversion of alicyclic ketones to the corresponding 2-alkylcrotonates[15] **3h–k**. Here again

(8) The oxoketene dithioacetals can be parent compounds to the following. (a) (Alkylthio)methylene ketones: B. Myrboh, H. Ila, and H. Junjappa, *Synthesis*, 317 (1982). (b) (Alkylthio)alkylidene ketones by conjugate addition with lithium dialkylcopper compounds: E. J. Corey and R. H. K. Chen, *Tetrahedron Lett.*, 3817 (1973).

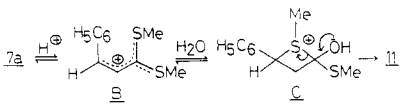
(9) M. Saquet and A. Thuillier, *Bull. Soc. Chim. Fr.*, 3969 (1966).

(10) (a) R. E. Ireland and J. A. Marshall, *J. Org. Chem.*, **27**, 1622 (1962); (b) R. F. Church and R. E. Ireland, *Tetrahedron Lett.*, 495 (1961); (c) S. Akiyama, S. Nakatsuji, and T. Hamamura, *Ibid.*, 2809 (1979); (d) J. A. Marshall and P. C. Johnson, *J. Org. Chem.*, **35**, 193 (1970); (e) T. Nishio and Y. Omote, *Chem. Lett.*, 365 (1979).

(11) B.-T. Grobel and D. Seebach, *Synthesis*, 360 (1977), and references therein under "hydrolysis of *S,S*-acetals".

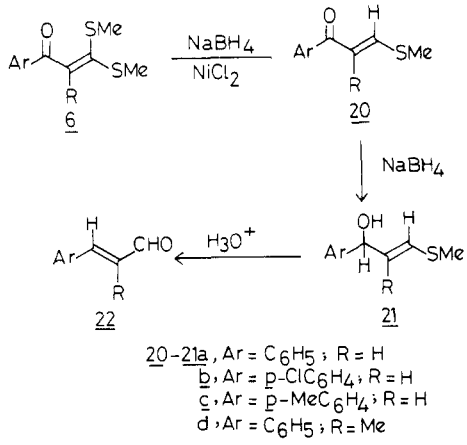
(12) D. Seebach and R. Burstinghaus, *Synthesis*, 461 (1975).

(13) Although Thuillier has suggested formation of **11** by Michael addition of methyl mercaptan to α,β-unsaturated thio esters, an alternate mechanism involving thiatenium ion intermediate C formed by $R_2S$-4 interaction of bivalent sulfur with a developing cationic center can not be ruled out. See: L. A. Paquette, G. V. Meehan, and L. D. Wise, *J. Am. Chem. Soc.*, **91**, 3231 (1969), and references therein. A similar 1,2-MeS shift via an episulfonium ion intermediate has been reported in the hydration of α-hydroxy dithioacetals under acidic conditions: G. A. Russell and L. A. Ochrymowycz, *J. Org. Chem.*, **35**, 764 (1970).



(14) For earlier preparative methods for cinnamates see: (a) Reference 2; (b) J. R. Johnson, *Org. React.*, **1**, 235 (1942). For α-alkylcinnamates see: (c) Reference 2; (d) Reference 14b; (e) R. F. Heck, *J. Am. Chem. Soc.*, **91**, 6707 (1969); (f) M. T. Bogert and D. Davidson *Ibid.*, **54**, 334 (1932); (g) H. Kasiwagi, N. Nakagawa, and J. Niwa, *Bull. Chem. Soc. Jpn.*, **36**, 410 (1963); (h) W. J. Gensler and E. Berman, *J. Am. Chem. Soc.*, **80**, 4949 (1958).

Scheme VII



20-21a, Ar = $C_6H_5$; R = H
b, Ar = p-$ClC_6H_4$; R = H
c, Ar = p-$MeC_6H_4$; R = H
d, Ar = $C_6H_5$; R = Me

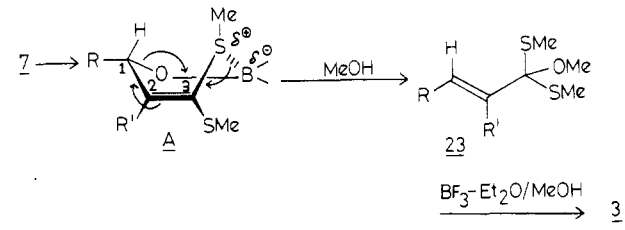
the products formed were all *E* isomers. Other possible isomeric mixtures containing either α,β-unsaturated esters from **7e–g** and **7i–k** or the β,γ-unsaturated esters from **7f–g** and **7i–k** were also not formed. These transformations confirm the stereo- and regiospecificity of the reactions.

Entries 12–16 represent the conversion of the cyclic ketones to the corresponding ene esters **3l-p**. It is interesting to note that **3l** is an intermediate in the synthesis of nornepatilinic acid,[5b] which has previously been prepared through the dehalogenation and decarboxylation of α-chloro-β-oxocyclohexane-1-carboxylate[16] and by the methyl cyanohydrin method.[17] The present method provides an alternative shorter route for **3l** and **3m**.

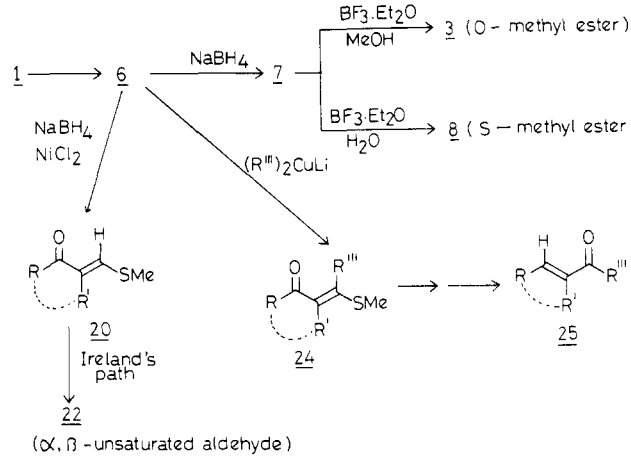
As an example of a synthetic application of the present method, the preparations of **17** and **19**, which are key intermediates in anthracyclinones synthesis,[18] were achieved in good yields. The sequence of the reactions is described in the Scheme VI, wherein the ene ester **16** (72%) gave, on hydrolysis, the desired acid **17** in 95% yield. It may be noted that the formation of **19** was accomplished from **14** by first subjecting it to 1,4-reduction with a mixture of sodium borohydride and nickel chloride in ethanol as per our reported method[8a] to yield the corresponding **18** followed by its conversion to the desired **19**. The dithioacetals can, therefore, be useful common intermediates for the synthesis of both α,β-unsaturated esters and aldehydes. The formation of **19** is identical with that reported by Ireland and co-workers.[10] Some of the (methylthio)methylene ketones derived from **6** were similarly converted to their corresponding aldehydes to test the generality of the method. Here again the products **22a–d** (Scheme VII) were all *E* isomers.

Incidentally, when **7a** was refluxed in boron trifluoride etherate and water, the corresponding *S*-methyl thiocinnamate (**8a**) was obtained in 55% yield with the *E* geometry (Scheme III). The thio esters **8b–g** which were prepared similarly are described in Table II.[19] The α,β-unsaturated *S*-alkyl thio esters were prepared earlier by

Scheme VIII



Scheme IX



condensation of lithium (trimethylsilyl)acetate[20] or α-halogeneted thio esters[21] (under Reformatsky conditions) with aldehydes and ketones, which required prior preparation of the thio esters.

**Mechanism.** The mechanism governing the exclusive formation of stereoselective and regiospecific α,β-unsaturated esters appears to be interesting but not unusual. The fact that the carbinols **7** failed to yield the desired esters either in the presence of mineral acids or under the conditions of Thuillier's experiments indicates that possibly a free carbonium ion is formed in the initial step, directing the course of the reactions to mixtures of the several products described. On the other hand, when the carbinol acetals **7** were treated with boron trifluoride in methanol, probably a boatlike six-membered transition state, A, as shown in Scheme VIII, is more likely to be formed rather than a free carbonium ion. In such a conformation, the substituent R at C-1 will occupy the less sterically hindered exo position rather than facing a severe nonbonded interaction as found in the alternate endo position, while the substituent at C-2 will occupy the sterically neutral position. The proposed mechanism is similar to one suggested by Katzenellenbogen for dehydration of β-hydroxy esters with aluminum isopropoxide. The ketene dithioacetal group appears to function more efficiently through participation of divalent sulfur than the corresponding ester group in controlling the stereoelectronic features toward exclusive stereoselectivity. The cyclic transition state A on concomitant addition of methanol and solvolysis of ortho ester **23** produces the *E* isomers **3** (Scheme VIII).

## Summary and Conclusion

In conclusion, a new general method for the conversion of easily available ketones to the corresponding stereoselective and regiospecific α,β-unsaturated *O*-methyl/*S*-

(15) For preparation of α-alkylcrotonates see: (a) Reference 5d; (b) J. Prejzner, *Rocz. Chem.*, **49**, 1953 (1975); *Chem. Abstr.*, **84**, 104672 (1976); (c) P. Miginiac and G. Zamlouty, *J. Organomet. Chem.*, **96**, 163 (1975).

(16) G. Büchi, V. Hochstrasser, and W. Pawlak, *J. Org. Chem.*, **38**, 4348 (1973).

(17) O. H. Wheeler and I. Lerner, *J. Am. Chem. Soc.*, **78**, 63 (1956).

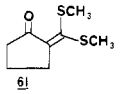
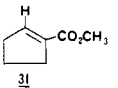
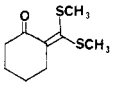
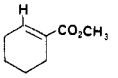
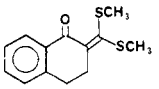
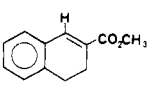
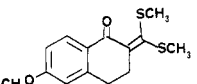
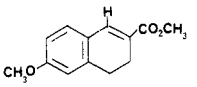
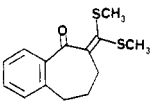
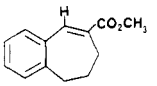
(18) (a) S. Terashima, S. Subjew, and K. Koga, *Tetrahedron Lett.*, 4937 (1978); (b) S. Subjew, S. Terashima, and K. Koga, *Chem. Pharm. Bull.*, **27**, 2351 (1979); (c) M. P. Reddy and G. S. Krishna Rao, *Tetrahedron Lett.*, **22**, 3549 (1981); (d) A. V. Rama Rao, V. N. Deshpande, *ibid.*, 1116 (1982).

(19) Interestingly while **8b–d** are *E* isomers, **8e** was found to be exclusively the *Z* isomer. The reason for this stereospecificity is, however, not clear and requires further study.

(20) D. H. Lucast and J. Wemple, *Tetrahedron Lett.*, 1103 (1977).

(21) (a) J. F. Arens and D. A. VanDorp, *Recl. Trav. Chim. Pays-Bas*, **66**, 407 (1947); *Chem. Abstr.*, **42**, 1213 (1948); (b) N. V. Organon, Dutch Patent 65 696; *Chem. Abstr.*, **44**, 7350 (1950).

Table I. Preparation of α,β-Unsaturated Methyl Esters

| entry | ketene dithioacetals | reaction time, h | products[a,b] unsaturated esters | isolated yield, % | mp [bp (mmHg)], °C | lit. mp [bp (mmHg)], °C |
|---|---|---|---|---|---|---|
| 1 | $C_6H_5C(O)CH=C(SMe)_2$ (6a) | 24 | $C_6H_5CH=CHCO_2Me$ ((E)-3a) | 70 | 37 | [36.5][26a] |
| 2 | $p$-$ClC_6H_4C(O)CH=C(SMe)_2$ (6b) | 18 | $p$-$ClC_6H_4CH=CHCO_2Me$ ((E)-3b) | 68 | 73-74 | [72-73][27] |
| 3 | $p$-$MeC_6H_4C(O)CH=C(SMe)_2$ (6c) | 15 | $p$-$MeC_6H_4CH=CHCO_2Me$ ((E)-3c) | 75 | 57-58 | [55-56][27] |
| 4 | $p$-$EtOC_6H_4C(O)CH=C(SMe)_2$ (6d) | 24 | $p$-$EtOC_6H_4CH=CHCO_2Me$ ((E)-3d) | 72 | 68-69 | [68-69][28] |
| 5 | $C_6H_5C(O)(Me)C=C(SMe)_2$ (6e) | 24 | $C_6H_5CH=C(Me)CO_2Me$ ((E)-3e) | 67 | 38-39 | [38-39][c,14e,g] |
| 6 | $C_6H_5C(O)(Et)C=C(SMe)_2$ (6f) | 24 | $C_6H_5CH=C(Et)CO_2Me$ ((E)-3f) | 75 | yellow viscous liquid | acid known,[14f] 103-104 |
| 7 | $C_6H_5C(O)(n$-$Pr)C=C(SMe)_2$ (6g) | 20 | $C_6H_5CH=C(n$-$Pr)CO_2Me$ ((E)-3g) | 75[d] | yellow viscous liquid | acid known,[14f] 93 |
| 8 | $MeC(O)CH=C(SMe)_2$ (6h) | 16 | $MeCH=CHCO_2Me$ ((E)-3h) | 50[d] | [121] | [121][c,26b,32] |
| 9 | $MeC(O)(Me)C=C(SMe)_2$ (6i) | 16 | $MeCH=C(Me)CO_2Me$ ((E)-3i) | 54[d] | [140] | [139.4][c,26b,32] |
| 10 | $MeC(O)(n$-$Bu)C=C(SMe)_2$ (6j) | 18 | $MeCH=C(n$-$Bu)CO_2Me$ ((E)-3j) | 75[d] | [91-93 (25)] | Et ester known[15c] |
| 11 | $MeC(O)(n$-$C_5H_{11})C=C(SMe)_2$ (6k) | 24 | $MeCH=C(n$-$C_5H_{11})CO_2Me$ ((E)-3k) | 80[d] | [98-100 (25)] | |
| 12 |  6l | 15 |  3l | 70[d] | [65-68 (15)] | [57 (10)][c,16,29] |
| 13 |  6m | 15 |  3m | 75[d] | [87-88 (15)] | [100 (30)][c,29,30] |
| 14 |  6n | 15 |  3n | 73 | 68 | ref. 31[c] (only IR, NMR) no mp |
| 15 |  6o | 16 |  3o | 67 | 50-51 | [51-20][5c] |
| 16 |  6p | 16 |  3p | 70 | yellow viscous liquid | |

[a] All the known esters were characterized by comparison of boiling point/melting point and IR/NMR spectral data with those reported in the literature. [b] $^1H$ NMR spectra of all products indicated >98% purity. [c] Literature references for IR and NMR spectra. [d] GLC showed >98% purity; column 10% DC-200 (2 m × 1/8 in.).

methyl esters and aldehydes via oxoketene dithioacetals has been developed.

The overall transformation can be viewed as the homologation of ketones **1** at α-position through intermolecular 1,3-carbonyl transposition (**1** → **6** → **7** → **3**).[22]

The ketene dithioacetal group is shown to be an excellent precursor as a masked alkoxycarbonyl group with better selectivity during reduction and solvolysis than the corresponding alkoxycarbonyl group.

Scheme IX depicts the transformations accomplished in the present studies (**6** → **7** → **3** or **8** and **6** → **20** → **22**) and their further potential synthetic applications to the corresponding α,β-unsaturated ketones (**6** → **24** → **25**),[10c] which are currently under investigation.

## Experimental Section

**General Methods.** Melting points were determined on Boetius (German) apparatus and are uncorrected. $^1H$ NMR spectra were recorded on a Varian EM-390 90-MHz spectrometer with $Me_4Si$ as an internal reference. Infrared spectra were obtained on Perkin-Elmer model 297 instrument.

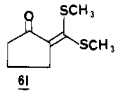
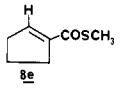
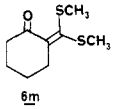
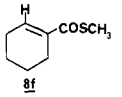
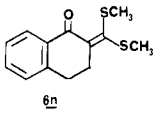
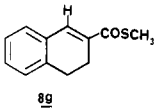
**Starting Materials.** All the acetophenones, acetone, ethyl methyl ketone, cyclopentanone, cyclohexanone, α-tetralone, and 6-methoxytetralone were available commercially, while propiophenone, butyrophenone,[23] valerophenone,[23] methyl $n$-butyl ketone,[23] 5,8-dimethoxytetralone,[24] and benzosuberone[25] were pre-

(22) For dicussions on inter- and intramolecular 1,3-carbonyl transpositions, see: (a) B. M. Trost and J. L. Stanton, *J. Am. Chem. Soc.*, **97**, 4018 (1975); (b) W. G. Dauben and D. M. Michno, *J. Org. Chem.*, **42**, 682 (1977); (c) T. Nakai, T. Mimura, and A. Ari-Izumi, *Tetrahedron Lett.*, 2425 (1977).

(23) A. I. Vogel, "A Textbook of Practical Organic Chemistry", 4th ed, ELBS and Longman, New York, 1978.

(24) J. A. Moore and M. Rahur, *J. Org. Chem.*, **26**, 1109 (1961).

Table II. Preparation of *S*-Methyl α,β-Unsaturated Thio Esters 4a-e

| entry | ketene dithioacetals | reaction time, h | products: *S*-methyl ester[a] | products: isolated yield, % | products: mp [bp (mmHg)], °C |
|---|---|---|---|---|---|
| 1 | $C_6H_5C(O)CH=C(SMe)_2$ (6a) | 36 | $C_6H_5CH=CC(O)SMe$ ((*E*)-8a) | 55 | 50-51, lit.[21a] 49-50 |
| 2 | $p$-$ClC_6H_4C(O)CH=C(SMe)_2$ (6b) | 16 | $p$-$ClC_6H_4CH=CC(O)SMe$ ((*E*)-8b) | 60 | 95-96 |
| 3 | $p$-$EtOC_6H_4C(O)CH=C(SMe)_2$ (6c) | 14 | $p$-$EtOC_6H_4CH=CC(O)SMe$ ((*Z*)-8c) | 75 | viscous liquid |
| 4 | $p$-$MeC_6H_4C(O)CH=C(SMe)_2$ (6d) | | $p$-$MeC_6H_4CH=CC(O)SMe$ ((*E*)-8d) | 75 | [150-152] |
| 5 |  6l | 15 |  8e | 55 | [71-73] |
| 6 |  6m | 16 |  8f | 70 | [51 (10)] |
| 7 |  6n | 18 |  8g | 65 | [160] |

[a] NMR spectra of all products show >98% purity.

pared according to the reported procedures. All the known ketene dithioacetals **6a-p** and the unknown **14** were prepared by the standard procedure reported earlier.[6] Similarly, (methylthio)-alkenyl ketones **20a-d** and **18** were prepared by sodium borohydride/nickel chloride reduction[8a] of the respective ketene dithioacetals **6a-b,d,e** and **14**.

**2,2-[Bis(methylthio)methylene]-5,8-dimethoxy-1-tetralone (14)**: 70% yields; yellow crystals; mp 56 °C; IR (KBr) $\nu_{max}$ 1670, 1620 $cm^{-1}$; NMR ($CDCl_3$) δ 2.33 (s, 6 H, 2 $SCH_3$), 2.55-3.10 [m, 4 H, $(CH_2)_2$], 3.73 (s, 6 H, 2 $OCH_3$), 6.70 (d, 2 H, arom). Anal. Calcd for $C_{15}H_{18}O_3S_2$: C, 58.06; H, 5.80. Found: C, 58.10; H, 5.78.

**2,2-[(Methylthio)methylene]-5,8-dimethoxy-1-tetralone (18)** was obtained in 70% yield by $NaBH_4/NiCl_2$ reduction of **14**: mp 61 °C; IR (Nujol) $\nu_{max}$ 1667, 1618 $cm^{-1}$; NMR ($CCl_4$) δ 2.47 (s, 3 H, $SCH_3$), 2.81 [$A_2B_2$, 4 H, $(CH_2)_2$], 3.75 (s, 6 H, 2 $OCH_3$), 6.75 (m, 2 H, arom), 7.86 (s, 1 H, vinylic). Anal. Calcd for $C_{14}H_{16}O_3S$: C, 63.63; H, 6.06. Found: C, 63.95; H, 6.32.

**Reduction of α-Oxoketene Dithioacetals 6 to Carbinols 7. General Procedure. 3,3-Bis(methylthio)-1-phenyl-2-propenol (7a).** To a well-stirred suspension of ketene dithioacetal **6a** (6.72 g, 0.03 mol) in absolute ethanol (70 mL) was added excess $NaBH_4$ (3.8 g, 0.1 mol), and the mixture was refluxed with stirring for 2 h. The cooled reaction mixture was poured into water (150 mL) and extracted with chloroform (2 × 35 mL). The chloroform extract was washed twice with saturated salt solution (10 mL), dried ($Na_2SO_4$), and evaporated under vacuum to give the carbinol **3a** (6.8 g, 100%) as an undistillable, thick viscous liquid. The IR and NMR spectra of **7a** were identical with the reported data.[9]

The ketene dithioacetals **6b-d,n-p** and **14** were reduced by a similar procedure, and the resulting carbinols **7b-d,n-p** and **15** were obtained as unstable, thick, viscous liquids in nearly quantitative yields and used as such for the preparation of α,β-unsaturated esters without further purification.

The ketene dithioacetals **6e-m**, which were soluble in methanol were reduced by a slightly different procedure. To a stirring solution of ketene dithioacetals **6e** (7.14 g, 0.03 mol) in absolute methanol (70 mL) was added excess of $NaBH_4$ (5.7 g, 0.15 mol) in small lots. A fresh addition was made only when evolution of hydrogen had subsided. The solution was further stirred for 0.5 h at room temperature after complete addition of $NaBH_4$, and the reaction mixture was worked up as described above.

The infrared spectra of all the carbinols **7a-p** and **15** showed a strong band between 3100 and 3600 $cm^{-1}$ due to OH group.

**Solvolysis of 7a in 10% Methanolic HCl.** A solution of **3a** (3.89 g, 0.015 mol) in methanol (75 mL) and 10% HCl (15 mL) was stirred at room temperature for 24 h. It was then poured over water (150 mL) extracted with chloroform (2 × 35 mL), washed with saturated sodium bicarbonate solution and finally with water, dried ($Na_2SO_4$), and concentrated to give dark brown liquid which was chromatographed over silica gel. Elution with hexane gave *S*-methyl 3-(methylthio)-3-phenylopropanethioate (**11**: 1.75 g, 45%) as a colorless viscous liquid (TLC single spot). The IR and NMR spectral data of **11** were identical with the reported data.[9]

**Solvolysis of 7a in Refluxing Methanol and Concentrated $H_2SO_4$. Methyl 3-(Methylthio)-3-phenylpropionate (12).** A solution of **3a** (3.89 g, 0.015 mol) in absolute methanol (35 mL) and concentrated $H_2SO_4$ (3 mL) was refluxed for 14 h. The workup of the reaction mixture as described in the above experiment yielded a dark viscous residue which was column chromatographed over silica gel. Elution with hexane yielded **12** as a colorless viscous liquid: 1.55 g (43%); TLC single spot; IR (neat) $\nu_{max}$ 1740 (ester CO) $cm^{-1}$; NMR ($CCl_4$) δ 1.8 (s, 3 H, $SCH_3$), 2.75 (d, 2 H, $CH_2$), 3.5 (s, 3 H, $OCH_3$), 4.07 (t, 1 H, CH), 7.2 (br s, 5 H, arom); MS, *m/e* 210 ($M^+$). Anal. Calcd for $C_{11}H_{14}SO_2$: C, 62.85; H, 6.66. Found: C, 62.58; H, 6.85.

**Preparation of *O*-Methyl α,β-Unsaturated Esters (3). General Procedure. Preparation of Methyl Cinnamate (3a).** To the crude carbinol **7a** (6.80 g, 0.03 mol) obtained by reduction of 6.72 g (0.03 mol) of **6a** was added 17 mL of boron trifluoride etherate, and the reaction mixture was stirred at room temperature for 5 min. It was then diluted with 70 mL of absolute methanol, and the solution was refluxed for 8-24 h (Table I). The cooled reaction mixture was poured over water (200 mL) and extracted with chloroform (2 × 50 mL); and the chloroform extract was washed successively with saturated sodium bicarbonate solution

(25) P. C. Gilmore, Jr., and W. J. Horton, *J. Am. Chem. Soc.*, **73**, 1411 (1951).
(26) "Dictionary of Organic Compounds", Vol. 4, Eyre and Spottiswoode, London, 1965: (a) p 2158, (b) p 2161.
(27) G. P. Schiemenz and J. Thobe, *Chem. Ber.*, **99**, 2663 (1966).
(28) R. Stoermer and F. Wodarg., *Chem. Ber.*, **61**, 2326 (1928).
(29) S. J. Rhoads, J. K. Chattopadhyaya, and E. E. Waali, *J. Org. Chem.*, **35**, 3352 (1970).
(30) W. J. Bailey and R. A. Bayloung, *J. Am. Chem. Soc.*, **81**, 2127 (1959).
(31) Y. Ito, K. Yonezawa, and T. Seegusa, *J. Org. Chem.*, **39**, 2769 (1974).
(32) (a) R. R. Fraser, *Can. J. Chem.*, **38**, 549 (1960); L. M. Jackman and R. H. Wiley, *J. Chem. Soc.*, 2886 (1960).

(200 mL), saturated sodium chloride solution (100 mL), and water (100 mL), dried ($Na_2SO_4$), and evaporated to give crude cinnamate **3a**, which was purified by passing it through a short column of silica gel; mp 35.8–36.5 °C (lit. 36.5 °C). The NMR and IR spectra of **3a** were identical with the reported values.

The esters **3a–q,n–p** and **16** were purified by passing them through silica gel column, with hexane as the eluent, while the esters **3e,f,h–m** were purified by distillation under reduced pressure. All the known esters were characterized by comparison of their boiling point/melting point and NMR/IR spectral data (Table I) with those of reported data and of authentic samples. The spectral and analytical data for the unknown esters and for those esters whose spectral data is not reported in the literature are given below.

**(*E*)-Methyl 2-ethylcinnamate (3f)**: IR (neat) $\nu_{max}$ 1715, 1640 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.15 (t, 3 H, $CH_3CH_2$), 2.45 (q, 2 H, $CH_3CH_2$), 3.72 (s, 3 H, $OCH_3$), 7.28 (s, 5 H, arom), 7.52 (s, 1 H, olefinic). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.77; H, 7.37. Found: C, 75.98; H, 7.73.

**(*E*)-Methyl 2-*n*-propylcinnamate (3g)**: IR (neat) $\nu_{max}$ 1720, 1635 $cm^{-1}$, NMR $CCl_4$) $\delta$ 0.92 [t, 3 H, $CH_3(CH_2)_2$], 1.1–1.6 (m, 2 H, $CH_3CH_2CH_2$), 2.40 (t, 2 H, $CH_3CH_2CH_2$), 3.72 (s, 3 H, $OCH_3$), 7.25 (br s, 5 H, arom), 7.52 (s, 1 H, olefinic). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.47; H, 7.84. Found: C, 76.75; H, 7.53.

**(*E*)-Methyl 2-*n*-butylcrotonate (3j)**: IR (neat) $\nu_{max}$ 1730, 1600 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 0.91 [br t, $CH_3(CH_2)_2CH_2$], 1.20–1.55 [br m, 4 H, $CH_3(CH_2)_2CH_2$], 1.79 (d, $J$ = 6 Hz, $CH_3CH$=), 2.18–2.40 [br t, 2 H, $CH_3(CH_2)_2CH_2$], 3.61 (s, 3 H, $OCH_3$), 6.71 (q, J = 6 Hz, 1 H, olefinic). Anal. Calcd for $C_9H_{16}O_2$: C, 69.23; H, 10.25. Found: C, 69.48; H, 10.47.

**(*E*)-Methyl 2-*n*-amylcrotonate (3k)**: IR (neat) $\nu_{max}$ 1731, 1600 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 0.9 [br t, 3 H, $CH_3(CH_2)_3CH_2$], 1.15–1.55 [br m, 6 H, $CH_3(CH_2)_3CH_2$], 1.8 (d, 3 H, $CH_3CH$=), 2.28 [br t, 2 H, $CH_3(CH_2)_3CH_2$], 3.65 (s, 3 H, $OCH_3$), 6.70 (q, $J$ = 6 Hz, olefinic). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.58; H, 10.58. Found: C, 70.83; H, 10.91.

**Methyl 7-methoxy-3,4-dihydronaphthalene-2-carboxylate (3o)**: IR (Nujol) $\nu_{max}$ 1715, 1640 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 2.42–2.90 [m, 4 H, $(CH_2)_2$], 3.71 (s, 3 H, $OCH_3$), 3.76 (s, 3 H, $OCH_3$), 6.56–7.15 (m, 3 H, arom), 7.35 (s, 1 H, olefinic). Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.55; H, 6.42. Found: C, 71.83; H, 6.70.

**Methyl 3,4,5-hexahydrobenzocycloheptene-2-carboxylate (3p)**: IR (neat) $\nu_{max}$ 1715, 1640 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 0.80 (m, 2 H, $CH_2$) 1.80–2.15 (t, 2 H, $CH_2$), 2.55 (t, 2 H, $CH_2$), 3.70 (s, 3 H, $OCH_3$), 7.20 (m, 4 H, arom), 7.55 (s, 1 H, olefinic). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.22; H, 6.93. Found: C, 77.61; H, 7.25.

**Methyl 5,8-dimethoxy-3,4-dihydronaphthalene-2-carboxylate (16)**: mp 57–59 °C; 80% isolated yield; IR (Nujol) $\nu_{max}$ 1716, 1640 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 2.25–2.80 [m, 4 H, $(CH_2)_2$], 3.70 (s, 3 H, $OCH_3$), 3.73 (s, 3 H, $OCH_3$), 3.77 (s, 3 H, $OCH_3$), 6.72 (d, 2 H, arom), 7.78 (s, 1 H, olefinic). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.74; H, 6.45. Found: C, 67.90; H, 6.28.

The ester **16** was hydrolyzed with 2 N NaOH according to the procedure reported for the ethyl ester to give the acid **17**: 95% yield; mp >230 °C (lit.[18a] >220 °C). The IR and NMR spectra of **17** were identical with those reported.[18a]

**Preparation of *S*-Methyl α,β-Unsaturated Thiocarboxylates (8). General Procedure. Preparation of *S*-Methyl Thiocinnamate (8a).** The carbinol **7a** (6.80 g, 0.03 mol) obtained by reduction of 6.72 g (0.03 mol) of **6a** was dissolved in 100 mL of dry ether, 25 mL of boron trifluoride etherate was added, and the mixture was stirred at room temperature for 5 min. The reaction mixture was then diluted with 20 mL of water, and after being refluxed for 12–16 h (Table II) it was poured over water (150 mL) and extracted with benzene (2 × 75 mL). The benzene layer was washed with saturated bicarbonate solution (250 mL) and then with water (200 mL), dried ($Na_2SO_4$), and evaporated to give a dark colored residue, which on column chromatography over silica gel with hexane as the eluent gave **8a** (2.94 g, 55%) as a low-melting solid: mp 48 °C (lit.[21] mp 48–49); IR (Nujol) $\nu_{max}$ 1660 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 2.35 (s, 3 H, $SCH_3$), 6.6 (d, $J$ = 15 Hz, 1 H, olefinic), 7.1–7.65 (m, 6 H, arom and olefinic). Anal. Calcd for $C_{10}H_{10}OS$: C, 67.41; H, 5.61. Found: C, 67.72; H, 5.93.

The *S*-methyl esters **8b–g** were prepared by the above general procedure. The spectral and analytical data of **8b–g** are given below.

***S*-Methyl *p*-chlorothiocinnamate (8b)**: IR (Nujol) $\nu_{max}$ 1665 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 2.32 (s, 3 H, $SCH_3$), 6.55 (d, $J$ = 16 Hz, 1 H, olefinic), 7.1–7.65 (m, 5 H, aromatic and olefinic). MS, $m/e$ 212.5 ($M^+$). Anal. Calcd for $C_{10}H_9ClOS$: C, 56.47; H, 4.23. Found: C, 56.21; H, 4.63.

***S*-Methyl *p*-ethoxythiocinnamate (8c).** IR (Neat) $\nu_{max}$ 1660 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.35 (t, 3 H, $CH_3CH_2O$), 2.28 (s, 3 H, $SCH_3$), 3.93 (q, 2 H, $CH_3CH_2O$), 5.05 (d, $J$ = 9 Hz, 1 H, olefinic), 5.93 (d, $J$ = 9 Hz, 1 H, olefinic), 6.55–7.31 (dd, $A_2B_2$, 4 H, aromatic).[19] Anal. Calcd for $C_{12}H_{14}O_2S$: C, 64.86; H, 6.30. Found: C, 65.08; H, 6.61.

***S*-Methyl *p*-methyl-2-methylthiocinnamate (8d)**: IR (neat) $\nu_{max}$ 1655 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 2.15 (s, 3 H, $SCH_3$), 2.20 (s, 3 H, $CH_3$) 2.22 (s, 3 H, $CH_3$), 7.01–7.32 (q, $A_2B_2$, 4 H, aromatic), 7.51 (br s, 1 H, olefinic); MS, $m/e$ 206 ($M^+$). Anal. Calcd for $C_{12}H_{14}OS$: C, 69.90; H, 6.79. Found: C, 69.67; H, 6.46.

***S*-Methyl cyclopentene-1-thiocarboxylate (8e)**: IR (neat) $\nu_{max}$ 1660 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.70–2.72 [m, 6 H, $(CH_2)_3$], 2.28 (s, 3 H, $SCH_3$), 6.85 (br s, 1 H, olefinic). Anal. Calcd for $C_7H_{10}OS$: C, 59.15; H, 7.04. Found: C, 59.45; H, 7.36.

***S*-Methyl cyclohexene-1-thiocarboxylate (8f)**: IR (neat) $\nu_{max}$ 1662 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 1.61–1.84 [m, 4 H, $(CH_2)_2$], 2.25 (s, 3 H, $SCH_3$), 2.05–2.41 [m, 4 H, $(CH_2)_2$], 6.85 (br s, 1 H), olefinic). Anal. Calcd for $C_8H_{12}OS$: C, 61.53; H, 7.69. Found: C, 61.83; H, 7.95.

***S*-Methyl 3,4-dihydronaphthalene-2-thiocarboxylate (8g)**: IR (neat) $\nu_{max}$ 1658 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 2.30 (s, 3 H, $SCH_3$), 2.40–2.92 (m, 4 H, $(CH_2)_2$, 6.85–7.15 (m, 4 H, aromatic), 7.36 (s, 1 H, olefinic); MS, $m/e$ 204 ($M^+$). Anal. Calcd for $C_{12}H_{12}OS$: C, 70.58; H, 5.88. Found: C, 70.85; H, 5.95.

**Preparation of Substituted Cinnamaldehydes 15a–d and 19. General Procedure. Preparation of 19.** To a stirring suspension of **18** (6.6 g, 0.025 mol) in 100 mL of absolute ethanol was added 3.0 g (0.78 mol) of sodium borohydride, and the reaction mixture was refluxed for 2 h. The workup of the reaction mixture, as described in the general procedure for the reduction of ketene dithioacetal **6a**, yielded the carbinol (6.60 g, 99%) as thick viscous liquid: IR (neat) $\nu_{max}$ 3100–3600 (OH). The carbinol **19** was dissolved in 150 mL of ethanol and 22 mL of 10% HCl, and the solution was stirred at room temperature for 48 h. It was then poured over water (150 mL), extracted with benzene (3 × 50 mL), washed with saturated sodium bicarbonate (2 × 100 mL) and water (2 × 100 mL), dried, and evaporated to yield crude **19**, which was purified by passage through a silica gel column. Elution with hexane gave 3.24 g (60%) of **19**, mp 91.5–92.8 (lit.[18d] mp 91–92 °C). Its IR and NMR spectra were identical with the reported values.

The following cinnamaldehydes were also prepared according to above general procedure. The NMR and IR spectra of **21a–d** were identical with those of anthentic samples of cinnamaldehyde (**21a**; bp 130 °C (20 mm)],[33a] *p*-methylcinnamaldehyde (**21b**; mp 42 °C),[33b] *p*-chlorocinnamaldehyde (**21c**; mp 62–63 °C),[33c] and 2-methylcinnamaldehyde [**21d**; bp 131 °C (16 mm)].[33d]

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(33) (a) "Dictionary of Organic Compounds", Vol. 2, Eyre and Spottiswoode, London, 1963, p 710; (b) *ibid.*, 1966, Vol. 5, p 3081; (c) *ibid.*, Vol. 2, p 610; (d) *ibid.*, 1965, Vol. 4, p 2292.