Oxidative Seco Rearrangement. A Novel Carbon-Carbon Bond Cleavage

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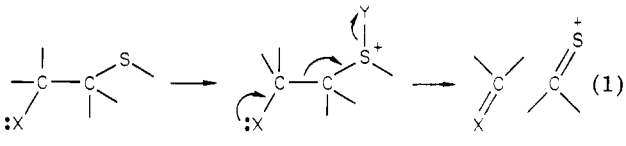
Cycloalkanones can be converted to 2,2-(trimethylenedithio)cycloalkanones and, by reduction or addition of an organometallic reagent, to the corresponding alcohols. These hydroxydithianes undergo a novel ring cleavage with concomitant rearrangement of the oxidation pattern to produce 3-(ω-oxoalkyl)-1,4-dithiacycloheptan-2-ones upon treatment with lead tetraacetate. In this way the oxidation level of C(1), C(2), and C(3) of the original cycloalkanone has been adjusted. Six-, nine-, and twelve-membered rings have been cleaved in 65–95% yields. The regiocontrol of the method was illustrated with a 2- and a 3-substituted cyclohexanone in which only the oxidation pattern of C(5), C(6), and C(1) were adjusted. The 1,4-dithiacycloheptan-2-ones are simultaneously a β-keto sulfide and a thioester. The β-keto sulfide was subjected to oxidation–elimination to illustrate the versatility of these substances, giving (after methanolysis) pure (*E*)-α,β-unsaturated methyl esters. This process extended the adjustment of the oxidation level to C(4) of the original cycloalkanone. Application of this sequence to cyclononanone allowed a synthesis of the queen's substance that is found in several species of insects. The utility of the thioester unit was illustrated by a ketone synthesis upon treatment with organocuprates. The resultant α-thioketones were subjected to oxidation–elimination to give (*E*)-α,β-unsaturated enones. Possible mechanistic pathways for this unusual oxidative rearrangement are discussed. In this connection, it was found that treatment of a ketene thioacetal with lead tetraacetate at 55 °C smoothly effected acetoxylation.

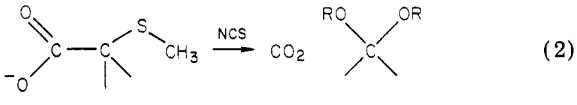
The cleavage of C–C bonds constitutes an important reaction for degradation and for development of synthetic strategy. The stereodefined synthesis of acyclic or large ring compounds frequently entails the synthesis of simple cyclic or bicyclic systems followed by ring cleavage. Cleavage of olefins is very well-known. Carbonyl compounds can be treated as a problem in olefin cleavage by converting the carbonyl group into an enol derivative.[1] Direct cleavage of carbonyl compounds is relatively rare and presumably involves enol (or enolate) formation in most cases.[2] Cleavage of α-hydroxy compounds proceeds under mild conditions but suffers from the difficulty of obtaining such compounds from simple carbonyl systems.[3] More recently, the cleavage of α-halo compounds with superoxide has been reported.[4] The ready availability of α-sulfenylated carbonyl compounds suggested that they would be excellent substrates if mild chemoselective ways could be found for their cleavage.[5] We have previously reported the chemoselective oxidative cleavage of β-keto sulfides with hydrogen peroxide, which appears to be a very general reaction.[6a] Since it did not maintain differentiation of the two newly created functional groups at the opposite ends of the chain, we sought yet other approaches. Cleavage of α,α-disulfenylated ketones with mild base in the case of strained cycloalkanones[6b] or "naked hydroxide" in the case of unstrained cycloalkanones[6c] maintains the differentiation but is restricted in its scope.

Oxidation of sulfur compounds normally focuses on conversion of sulfur to its higher oxidation states. Oxidation of the carbon attached to sulfur invokes Pummerer-type processes and has found utility in synthesis.[7] On the other hand, weakening of C–C bonds by attack of an electrophile at sulfur is not generally recognized as a potential C–C cleavage reaction. As shown in eq 1, such



(1)

a process should be particularly facilitated by the presence of an electron-donating group on the carbon β to sulfur. Indeed, we found that fragmentation overwhelmed direct oxidation of sulfur and oxidation at the α carbon upon treatment of α-sulfenylated carboxylates with NCS (eq 2)[8]



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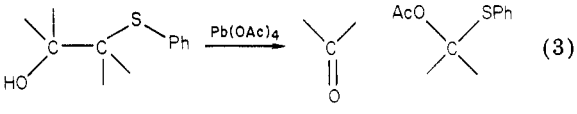

(3)

or of β-hydroxy sulfides with lead tetraacetate (eq 3).[9] The latter reaction was limited to strained ring systems until recently when we discovered a more general set of conditions.[8b] As part of this investigation, we explored the

(1) Carter, R. H.; Colyer, R. M.; Hill, R. A.; Staunton, J. *J. Chem. Soc., Perkin Trans. 1* **1976**, 438. Heathcock, C. H.; Clark, R. D. *J. Org. Chem.* **1976**, *41*, 1396. Grieco, P. A.; Reap, J. J.; Noguez, J. A. *Synth. Commun.* **1975**, *5*, 155. Champagne, J.; Favre, H.; Vocelle, D.; Zbikowski, I. *Can. J. Chem.* **1964**, *42*, 212.

(2) Rogic, M. M.; Vitrone, J.; Swerdloff, M. D. *J. Am. Chem. Soc.* **1977**, *99*, 1156.

(3) For some recent methods see: Vedejs, E.; Engler, D. A.; Telschow, J. E. *J. Org. Chem.* **1978**, *43*, 188, and references therein. Volkmann, R.; Danishefsky, S.; Eggler, J.; Solomon, D. M. *J. Am. Chem. Soc.* **1971**, *93*, 5576. Büchi, G.; Matsumoto, K. E.; Nishimura H. *Ibid.* **1971**, *93*, 3299. For some examples of oxidative cleavage of ketones with oxygen and base see: Doering, W. V. E.; Haines, R. M. *Ibid.* **1954**, *76*, 482. Siddall, J. B.; Baddeley, G. V.; Edwards, J. A. *Chem. Ind. (London)* **1966**, 25. Richardson, W. H.; Smith, R. S. *J. Am. Chem. Soc.* **1967**, *89*, 2230. Barton, D. H. R.; Werstiuk, N. H. *J. Chem. Soc. C* **1968**, 148. Bordwell, F. G.; Knipe, A. C. *J. Am. Chem. Soc.* **1971**, *93*, 3416. Cocker, W.; Crowley, K. J.; Srinivasan, K. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1971. Adam, W.; Liu, J.-C. *J. Am. Chem. Soc.* **1972**, *94*, 2894. Richardson, W. H.; Hodge, V. F.; Stiggall, D. L.; Yelvington, M. B.; Montgomery, F. C. *Ibid.* **1974**, *96*, 6652. Sawaki, Y.; Ogata, Y. *Ibid.* **1975**, *97*, 6983; *J. Org. Chem.* **1976**, *41*, 2340.

(4) San Filippo, J., Jr.; Chern, C.-I.; Valentine, J. *J. Org. Chem.* **1976**, *41*, 1077.

(5) For reviews see: Trost, B. M. *Acc. Chem. Res.* **1978**, *11*, 453; *Chem. Rev.* **1978**, *78*, 363.

(6) (a) Trost, B. M.; Massiot, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 4405. (b) Trost, B. M.; Rigby, J. *J. Org. Chem.* **1976**, *41*, 3217. Trost, B. M.; Preckel, M.; Leichter, C. M. *J. Am. Chem. Soc.* **1975**, *97*, 2224. Cossement, E.; Biname, R.; Ghosez, L. *Tetrahedron Lett.* **1974**, 997. (c) Marshall, J. A.; Seitz, D. E. *J. Org. Chem.* **1974**, *39*, 1814; **1975**, *40*, 534.

(7) For a few illustrations see: Iriuchijima, S.; Maniwa, K.; Tsuchihashi, G. *J. Am. Chem. Soc.* **1975**, *97*, 596. Bakuzis, P.; Bakuzis, M. L. F. *J. Org. Chem.* **1977**, *42*, 2362.

(8) Trost, B. M.; Tamaru, Y. *J. Am. Chem. Soc.* **1975**, *97*, 3528; *Tetrahedron Lett.* **1975**, 3797; *J. Am. Chem. Soc.* **1977**, *99*, 3101. For an electrolytic approach see: Nokami, J.; Kawada, M.; Okawara, R.; Torii, S.; Tanaka, H. *Tetrahedron Lett.* **1979**, 1045.

(9) (a) Trost, B. M.; Hiroi, K. *J. Am. Chem. Soc.* **1975**, *97*, 6911. (b) Trost, B. M.; Ochiai, M.; McDougal, P. *Ibid.* **1978**, *99*, 7103. (c) For an application of this method see: Caine, D.; Frobese, A. S. *Tetrahedron Lett.* **1977**, 3107.

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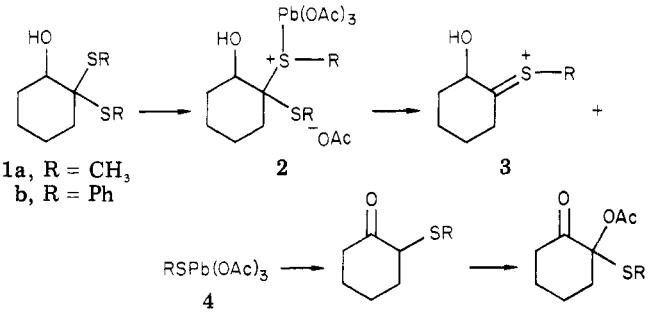
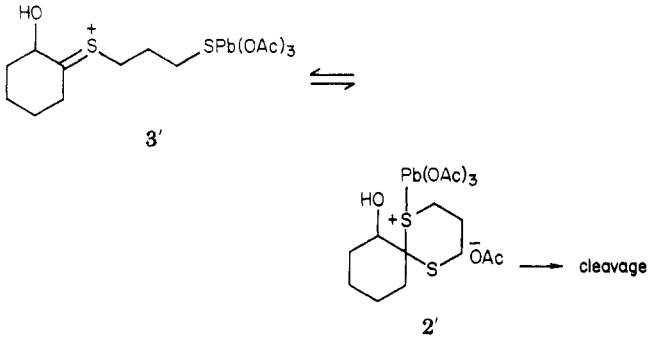
effect of geminal sulfur substitution β to a hydroxyl group on the cleavage reaction. In this paper, we detail the results of this study[10] and the application of this new cleavage reaction to the synthesis of the queen's substance,[11] methyl 9-oxodec-(*E*)-2-enoate, from cyclononanone.

The inability to effect cleavage of 1-hydroxy-2-(methylthio)- (or (phenylthio)) cyclohexane led us to explore the bissulfenylated compounds **1a** and **1b**. Treatment of these

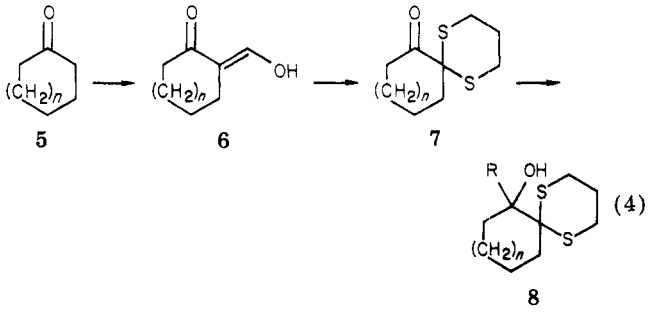


compounds with lead tetraacetate under many different conditions led to no detectable ring cleavage. We were able to isolate 2-acetoxy-2-(methylthio)- (or (phenylthio)) cyclohexanone. Reasoning that the initial attack occurred at sulfur to give **2** but that C–C bond cleavage was too slow relative to sulfur serving as a leaving group to give **3** and **4**, we felt we might achieve ring cleavage if the ionization of the sulfur substituent could be made reversible by tying **3** and **4** together. In this way, **2** has a chance to undergo the energetically less favorable C–C bond cleavage.

We chose the β-hydroxydithiane system since (1) such systems were readily available from cycloalkanones[12] and (2) the fact that reversion of **3′** and **2′** involves six-membered-ring formation might facilitate this process.

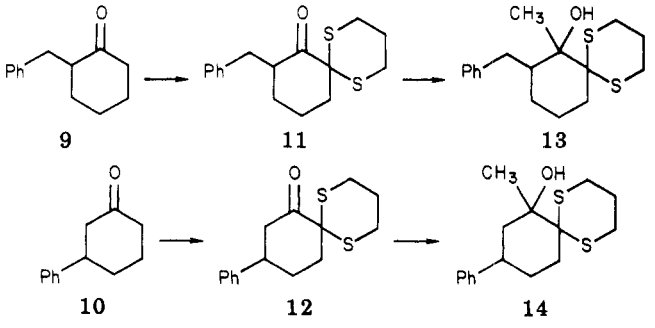


Preparation of 1-Hydroxy-2,2-(trimethylenedithio)cycloalkanes. The introduction of the dithianyl group into a cycloalkanone followed the method of Woodward et al. (eq 4).[12] Choice of cycloalkanones of six or more members stemmed from the fact that such ring systems failed to cleave in the simple β-hydroxy sulfide series. Hydroxymethylenation was performed under standard conditions (NaH, PhH, $HCO_2C_2H_5$, CH_3OH, room temperature) and the crude **6** (~90% crude yield) directly subjected to 1,3-propanedithiol ditosylate (KOAc, C_2H_5OH, reflux) to give **7** in 66–82% yield, normally as crystalline solids.



a, $n = 1$; b, $n = 4$; c, $n = 7$

To demonstrate the regiocontrol of the oxidative cleavage method, we converted two unsymmetrically substituted cycloalkanones, **9** and **10**, to their dithianyl de-



rivatives **11** and **12**. While only a single dithiane is possible for **9**, two are possible for **10** but only the expected less hindered one is observed. Conversion of **8a–c**, **11**, and **12** to hydroxy derivatives was accomplished either by reduction or by addition of an organolithium. For minimization of desulfenylation, reduction was performed with either sodium borohydride or diisobutylaluminum hydride. In the cases of **7a**, **9**, and **10**, methyllithium added in >90% yields; on the other hand, neither of the medium-ring compounds, **7b** and **7c**, gave good conversions upon treatment with organometallic reagents; recovered starting material greatly predominated. Steric hindrance cannot account for such an observation since **11** which gives **13** in 98% yield is certainly more congested than either **7b** or **7c**. Presumably, the ring conformations enhance the rate of enolization in **7b** and **7c**, which leads to recovered starting material after workup.

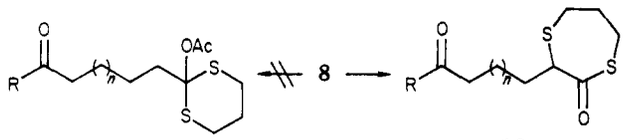
Both **13** and **14** appeared to be single stereoisomers. Both showed only one absorption for the methyl group (**13**, δ 1.38; **14**, δ 1.54), and **13** was sharp melting, mp 130–131 °C. The data did not allow an exact stereochemical assignment. Since such stereochemical questions were deemed irrelevant for the ring cleavage, they were not pursued further.

Ring Cleavage. Lead tetraacetate (from G. Frederick Smith & Co., stabilized with acetic acid) was washed free of acetic acid with benzene. To a suspension of 2–3 equiv of lead tetraacetate in benzene was added 1 equiv of the hydroxydithiane and the mixture was heated at 55–60 °C. After the solution was cooled and excess lead tetraacetate destroyed with ethylene glycol, the product was isolated either by chromatography or by direct crystallization. Examination of the spectral data immediately ruled out the expected cleavage product **15**. Mass spectroscopy ruled out dimeric products (such as disulfides which might arise by hydrolysis of **15** and oxidative coupling). IR and NMR spectroscopy revealed the absence of acetate. The IR spectrum suggested the presence of a thioester (1669 ± 3 cm^{-1}) in addition to the aldehyde (1728 cm^{-1}) or ketone (1718 cm^{-1}) absorptions. Most revealing was the presence of a deshielded distorted triplet at δ 3.68 ± 0.05 which

(10) A preliminary report of a portion of this work has appeared: Trost, B. M.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4313.

(11) Sannasi, A.; George, C. J. *Nature (London)* **1972**, *237*, 457. Gary, N. E. *Science* **1962**, *136*, 773. Callow, R. K.; Johnston, N. C. *Bee World* **1960**, *41*, 152. Barbier, M.; Lederer, E. *C. R. Hebd. Seances Acad. Sci., Ser. B* **1960**, *250*, 4467. Blum, M. S.; Boch, R.; Doolittle, R. E.; Tribble, M. T.; Traynham, J. G. *J. Insect Physiol.* **1971**, *17*, 349.

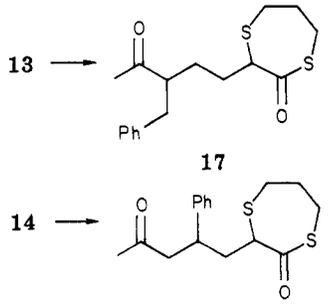
(12) Woodward, R. B.; Pachter, I. J.; Scheinbaum, M. L. *J. Org. Chem.* **1971**, *36*, 1137.



15 16

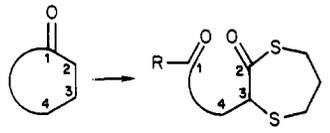
a, $n = 1$; b, $n = 4$; c, $n = 7$

suggested a proton on carbon bearing both sulfur and a carbonyl group with only a CH_2 as a near neighbor. In addition, there remained four protons on carbon bearing sulfur at δ 3.0–3.2. In conjunction with the elemental composition as determined by mass spectroscopy and/or combustion analysis, we assigned structure **16** to the cleavage products. All substrates, **8a–c** (R = H), **8a** (R = CH_3), **13**, and **14**, cleaved in 65–95% yields.[13,14] This ring



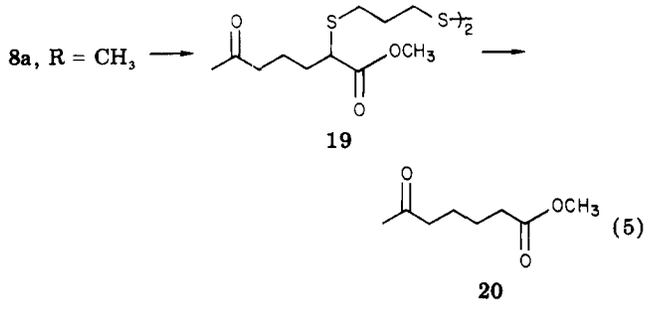
17 18

cleavage appears independent of ring size (6-, 9-, and 12-membered rings all cleave), steric hindrance (cf. **13**), and the nature of the alcohol (i.e., secondary or tertiary). In one step, not only has ring cleavage been accomplished but also the oxidation level of C(3) of the original cycloalkanone had been modified simultaneously with C(1) and C(2). The fact that the 1,4-dithiacycloheptan-2-one si-



multaneously is an acylating agent in the form of the thioester and is activated at the α position in the form of the β-keto sulfide moiety gives great versatility to this particular ring cleavage (vide infra).

On the other hand, if simple ring cleavage is desired, the products can be converted to a saturated keto ester (see eq 5). For example, **8a** (R = CH_3) was transesterified with

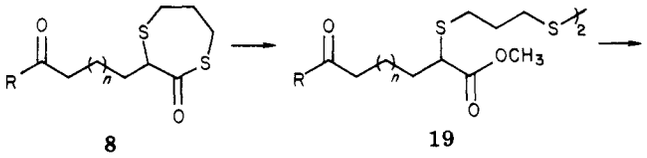


19 20 (5)

methanol in the presence of iodine to give presumably **19**.

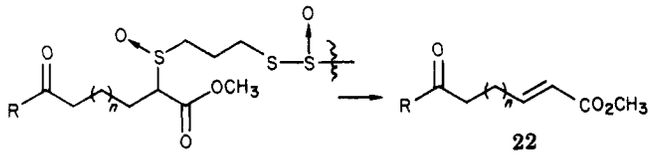
Without isolation, the latter was directly subjected to desulfurization with W-2 Raney Ni to give keto ester **20**.

Elaboration via Sulfoxide Pyrolysis. The creation of a β-keto sulfide as a consequence of the ring-cleavage reaction offered the opportunity for yet further adjustment of the oxidation pattern. Two methods were employed. In the first, the 1,4-dithiacycloheptan-2-ones **8a–c** (R = H) and **8a** (R = CH_3) were treated, sequentially and without isolation of any intermediates, with iodine in hot methanol (to give presumably **19**), 2 equiv of sodium me-



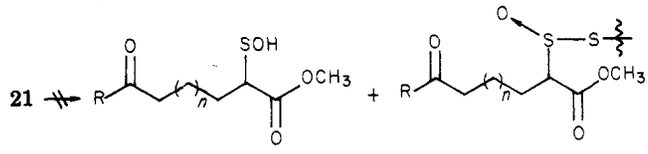
8 19

a, $n = 1$; b, $n = 4$; c, $n = 7$

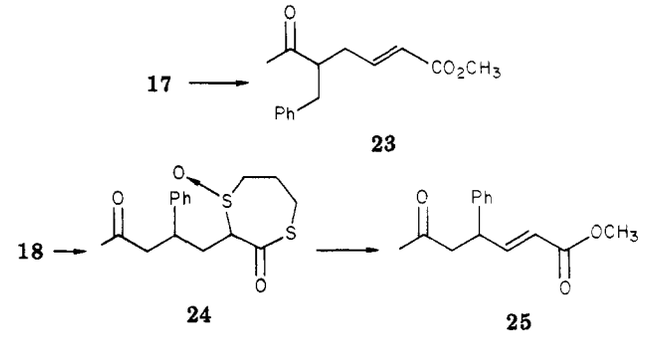


21 22

taperiodate to give **21**, and then thermolyzed in refluxing toluene to give the (*E*)-enoates **22** in 51–58% overall yield. The assignment of *E* stereochemistry is based upon the J = 15–17 Hz values for the vinyl protons in the NMR spectra and analogy with other sulfoxide pyrolyses.[15] Since sulfoxide pyrolyses frequently involve statistical eliminations in terms of the number of β hydrogens with consequently little regiochemical control, it is interesting to note that, by far, the major (if not exclusive) product arose by elimination in the chain bearing the ester group rather than in the trimethylene chain. This regiochemical control presumably reflects the activating influence of the carbonyl group.



The same sequence applied to **17** led to **23** in 46% overall yield. An alternative sequence was employed for



23 24 25

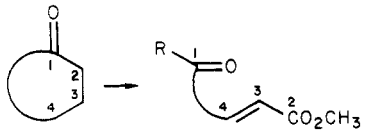
18. Here, the 1,4-dithiacycloheptan-2-one was chemoselectively oxidized with MCPBA, thermolyzed in hot toluene, and then solvolyzed in methanolic iodine to give **25** in 43% overall yield. The ring cleavage combined with the sulfoxide pyrolysis provides a method for selectively ad-

(13) A recent study by another group has just appeared. Lottenbach; Graf, W. *Helv. Chim. Acta* **1978**, *61*, 3087.

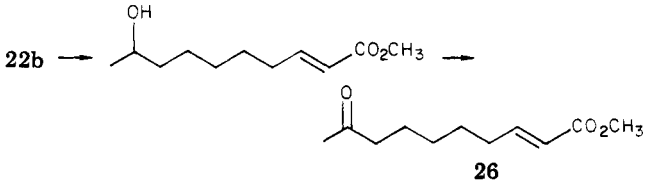
(14) Lottenbach and Graf report a rather low yield of **16a** (R = H) from **8a** in addition to other products. In the hands of two independent investigators in these laboratories, cleavages of six-membered rings proceeded in 75–95% yields to give 1,4-dithiacycloheptan-2-ones. We cannot account for the discrepancy except for noting different sources of lead tetraacetate.

(15) Trost, B. M.; Salzmann, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887.

justing the oxidation level of C(1), C(2), C(3), and C(4) of a cycloalkanone.



With the formation of **22b** from cyclononanone, a synthesis of the queen's substance was virtually in hand.[15,16] Chemoselective addition of methylmagnesium chloride (ether, −40 °C) followed by Jones oxidation of the crude alcohol gave the queen's substance of insects (**26**) in 53% overall yield.



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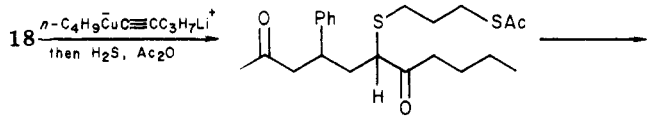
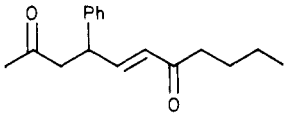
Elaboration via Acylation. Thioesters are more reactive acylating agents than their corresponding esters. Their utilization in lactonization has been particularly noteworthy.[17] A striking report was the reaction with stoichiometric quantities of organocuprates to give the corresponding ketones.[18] Attempts to react lithium di-*n*-butylcuprate (made from cuprous iodide and *n*-butyllithium) followed by aqueous workup led to a small amount of recovered starting material, with the majority of material being unaccounted for. Use of organocuprates generated from Grignard reagents and cuprous halides led to similar results, whereas, the mixed cuprate from *n*-butyllithium and 1-pentynylcopper in the presence of hexamethylphosphorus triamide did give some of the desired product but in low (<10%) yields. The fact that the reaction mixture contained voluminous amounts of precipitate which did not dissolve upon aqueous workup suggested that part of the problem may be formation of copper salts of our desired product. Indeed, bubbling H_2S into the reaction mixture followed by treatment with acetic anhydride–pyridine gave the expected product **27a** in 30% yield



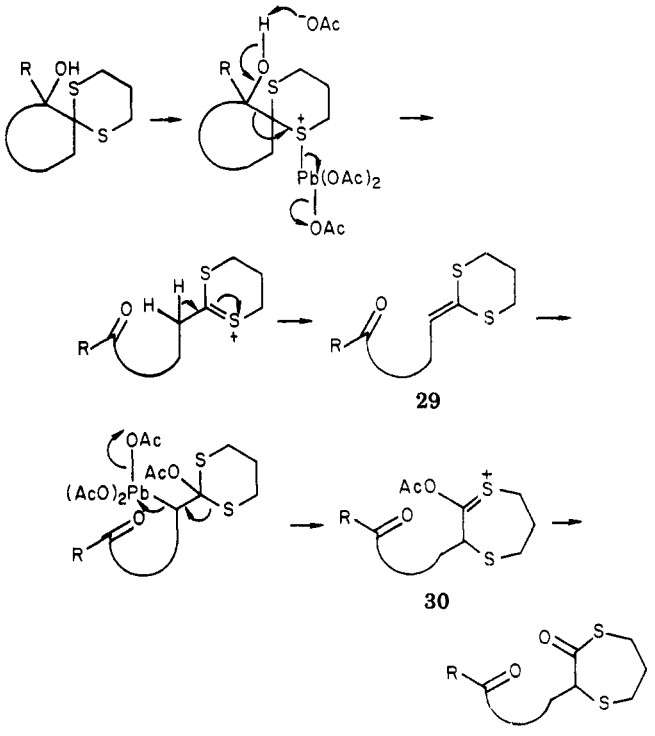
27a



28a

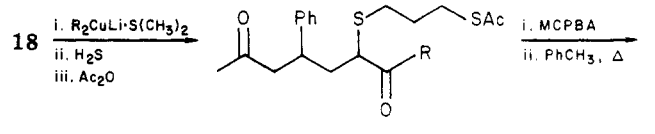
as a diastereomeric mixture. The mass spectrum indicated

Scheme I. Mechanistic Rationale for Oxidative Seco Rearrangement



a formula of $C_{22}H_{32}O_3S_2$. IR absorptions at 1705 and 1640 cm^{-1} indicated the presence of a normal ketone and a thioester. The NMR spectrum showed H_a at δ 3.5, a singlet at 2.28 for SAc, and two singlets (total 3 H) at 2.0 and 1.96 for the remaining acetyl group.

Feeling that copper complexation with the sulfurs of the starting material and/or product was responsible for the low yield, we generated the organocuprate from dimethyl sulfide–cuprous bromide[19] and worked up the reaction as described above. Indeed, the yield jumped to 58% with 1 mol of cuprate/mol of thioester. To eliminate the problem of dealing with a diastereomeric mixture as well as to illustrate the utility of retaining an α-thio substituent in the product, we oxidized **27a** with 1 equiv of MCPBA and thermolyzed the resulting sulfoxide in hot toluene to give the (*E*)-enone **28a**. We briefly explored the generality



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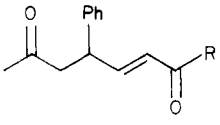


28

b, R = CH_3; **c**, R = Ph; **d**, R = $(CH_2)_3CCH_3$

of this sequence with a range of organocuprates including methyl, phenyl, and 4,4-ethylenedioxypentyl cuprates. The yields normally ranged between 55–65% for the cuprate

(16) For some alternatives see: (a) Tsuji, J.; Masaoka, K.; Takahashi, T. *Tetrahedron Lett.* **1977**, 2267. (b) Reference 15. (c) Kyskina, A. S.; Gankina, L. V.; Ivanov, L. L.; Pyatonova, Yu. B.; Evstigneeva, R. P. *Zh. Org. Khim.* **1971**, *7*, 51. (d) Kovalev, B. G.; Vaskan, R. N.; Lavrinenko, E. S. *Ibid.* **1971**, *7*, 667. (e) Bestmann, H. J.; Kunstmann, R.; Schulz, H. *Justus Liebigs Ann. Chem.* **1966**, *699*, 33. (f) Eiter, K. *Ibid.* **1962**, *658*, 91. (g) Barbier, M.; Hügel, M. F. *Bull. Soc. Chim. Fr.* **1961**, 951. (h) Callow, R. K.; Johnston, N. C. *Bee World* **1960**, *41*, 152. (i) Hase, T. A.; McCoy, K. *Synth. Commun.* **1979**, *9*, 63.

(17) Gerlach, H.; Kunzler, P.; Oertle, K. *Helv. Chim. Acta* **1978**, *61*, 1226. Minato, H.; Kodama, H.; Muira, T.; Kobayashi, M. *Chem. Lett.* **1977**, 413. Masamune, S.; Hayase, Y.; Schilling, W.; Chan, W. K.; Bates, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 6756. Corey, E. J.; Brunelle, D. J. *Tetrahedron Lett.* **1976**, 3409, and earlier ref.

(18) Anderson, R. J.; Henrick, C. A.; Rosenblum, L. D. *J. Am. Chem. Soc.* **1974**, *96*, 3654.

(19) House, H. O.; Chen, C.-Y.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, *40*, 1460.

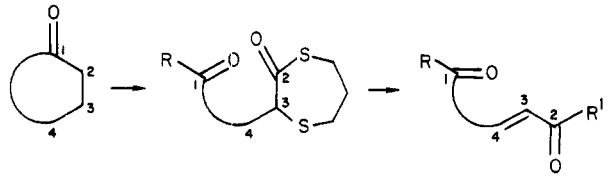
(20) Yoshion, H.; Kawazoi, Y.; Taguchi, T. *Synthesis* **1974**, 713. Also see: Chen, C. H. *Tetrahedron Lett.* **1976**, 25.

(21) Wilson, G. E., Jr. *J. Am. Chem. Soc.* **1965**, *87*, 3785.

reaction and 70–80% for the oxidation–elimination. Attempts to generate an anion at C(3) of the 1,4-dithiacycloheptan-2-ones for alkylation have been unsuccessful thus far.

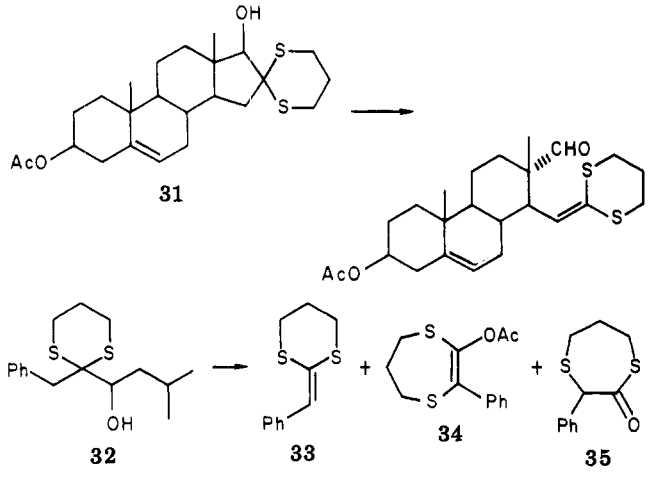
Discussion

An unusual ring cleavage reaction has been uncovered. Accompanying the C–C bond cleavage is oxidation at an unactivated position—C(3) of the original ketone. The



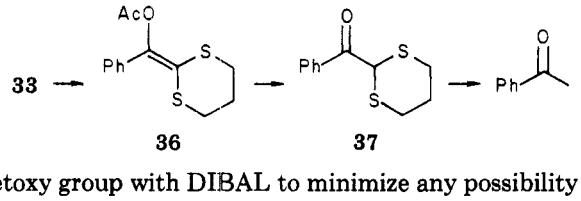
fact that rearrangement of the oxidation pattern accompanies ring cleavage led us to refer to this process as oxidative seco rearrangement.

The dramatic structural changes accompanying the C–C bond scission implicate a multistep process. Scheme I presents our original suggestion.[10] In support of this scheme is the recent report by Lottenbach and Graf[13] who isolated the ketoketene thioacetals corresponding to **29** in the oxidative seco rearrangement of a number of steroids such as **31**. In simpler cases, such as **32**, these workers



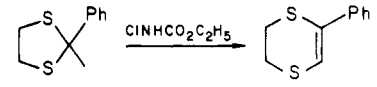
reported the isolation of not only the ketene acetal **33** but also a second compound which would arise by deprotonation of the equivalent of **30** (Scheme I), i.e., **34**, in addition to 3-phenyl-1,4-dithiacycloheptan-2-one (**35**). The isolation of products corresponding to **34** and **35** was also reported from **8a** (R = H). We never observed products corresponding to **34** which should have survived our workup according to Lottenbach and Graf. It is interesting to note that the hydrolysis of **34** to **35** (or of any of the related compounds in their other series) was not reported.

This discrepancy led us to attempt the proposed conversion of the ketene thioacetal **33** to the acetoxy-1,4-dithiacyclohept-2-ene **34**. Treatment of **33** under the cleavage reaction conditions generated a product of formula $C_{13}H_{14}O_2S_2$ in virtually quantitative yield whose spectral data agreed with that published for **34**. Since the data did not distinguish between **34** and **36**, we cleaved the



acetoxy group with DIBAL to minimize any possibility of rearrangements to give a product of formula $C_{11}H_{12}OS_2$, mp 94–95 °C (unrecrystallized), whose properties corresponded closely to those reported for **35**. The infrared carbonyl frequency at 1690 cm^{-1} was considerably higher than we had normally observed for the 1,4-dithiacycloheptan-2-ones (1669 ± 3 cm^{-1}). It was in good accord with a benzoyl group as present in **37**. That the structure was indeed **37** and not **35** was proven by Raney nickel desulfurization which gave a quantitative conversion to acetophenone. Thus, some of the structures reported by Lottenbach and Graf appear to be incorrect.[13] The structures of the compounds obtained from ring cleavage and assigned as 1,4-dithiacycloheptan-2-ones appear to be correct since the NMR spectral data rule out the alternative although it is not possible to conclude anything about the correctness of the structures assigned as 2-acetoxy-1,4-dithiacyclohept-2-enes.

The failure of ketene thioacetal **33** to undergo oxidative rearrangement when subjected to the conditions of the cleavage reaction raises some questions about the original mechanistic scheme presented. The validity of this control experiment can be questioned on the grounds that other lead species which may be responsible for the rearrangement are present during the course of the ring cleavage. The fact that ketene thioacetals can be isolated in some cases lends credence to that argument. Furthermore, very recently it was found that *alkyl*-substituted ketene dithioacetals do undergo the oxidative rearrangement postulated in Scheme I.[22] However, an alternative proposal involving two competing pathways, one leading to ketene thioacetals and one leading to 1,4-dithiacycloheptan-2-ones, may be invoked. In this latter scheme (see Scheme II), the oxidative rearrangement occurs first and ring cleavage second. The branching point between the two pathways is **38**, which is common to both schemes. If sufficient ring strain exists, **38** apparently prefers to ring cleave via Scheme I to account for the steroid results of Lottenbach and Graf. Our cases involve relatively nonstrained ring systems and thus **38** is drained off via Scheme II. Analogy for the formation of **39** arises in the conversion of ethylene dithioketals to 1,4-dithiines[20] and of oxathiolanes to 1,4-oxathiines[21] (eq 6 and 7).



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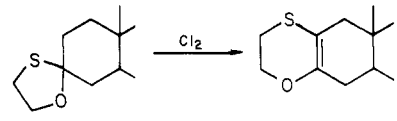
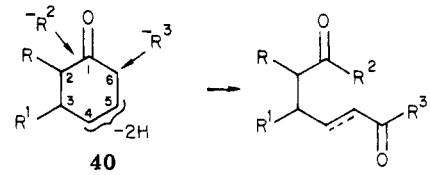


(7)

While the mechanistic pathway must yet be refined, the process outlined is a novel and potentially very versatile approach for structural elaboration. Regio- and chemodifferentiation between the two ends of the chain is fully maintained. As summarized in **40**, the process allows the



equivalent of the addition of nucleophiles to C(1) and C(6) and removal of 2 H from C(4) and C(5). The enone is obviously capable of further elaboration such as conjugate addition and regioselective alkylation which represents the

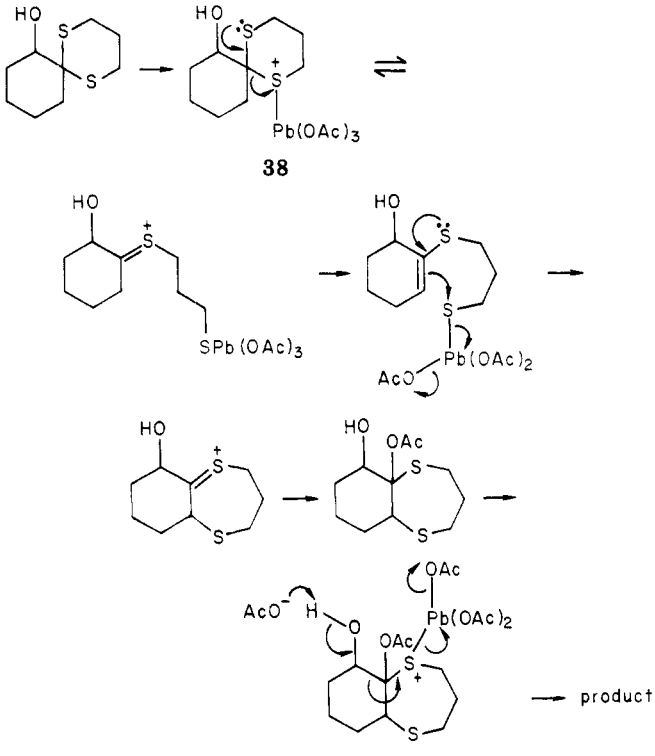
(22) Hiroi, K.; Sato, S. *Chem. Lett.* **1979**, 923.

Table I. Experimental Details for Preparation of α,α-(Trimethylenedithio)cycloalkanones

ketone wt, mmol	NaH % dispersion, mmol	PhH, mL	time, h	6[a] wt, % yield[b] (wt, mmol)[b]	TsS wt, mmol	KOAc wt, mmol	C_2H_5OH, mL	time, h	7 wt, % yield	mp, °C
5a (1.96 g, 20.0)	57, 22.0	20	16	1.77 g, 70 (756 mg, 6.00)	2.08 g, 5.00	1.96 g, 20.0	40	15	670 mg, 66[i]	53–54[g,h]
5b	see text									
5c (3.64 g, 20.0)	57, 22.0	30	22	3.13 g, 75 (630 mg, 3.00)	1.25 g, 3.00	735 mg, 7.50	30[j]	20	683 mg, 80[k]	88[e]
9 (940 mg, 5.00)	57, 5.50	20	24	673 mg, 96[c] (335 mg, 1.60)	645 mg, 1.60	456 mg, 470	12	16	340 mg, 73[d]	84[e]
10 (6.0 g, 34.5)	50, 68.9	100	24	5.54, 79 (5.5, 27.2)	11.3 g, 27.2	8.0 g, 8.6	80	16	3.35 g, 44[f]	112.5–113.5[e]

[a] 6 refers to the hydroxymethylene derivatives in all cases even though it is not specifically indicated for ketones 9 and 10 in the text. [b] The first weight and % yield refer to that isolated from the formylation reaction. The weight and millimole given in parentheses represent the amount used for the preparation of the dithiane. [c] The yield given is based upon recovery of 330 mg (35%) of starting ketone. [d] Purified by preparative TLC by eluting with 30% ether in hexane. [e] Recrystallized from ethanol. [f] Purified by column chromatography by utilizing 330 g of Grace silica gel 60 in a 5.3 × 38 cm column and eluting with 9:1 hexane–ether. [g] Lit.[6c] mp 54–55 °C. [h] Recrystallized from hexane. [i] Purified by preparative TLC by eluting with 20% ethyl acetate in hexane. [j] Methanol employed for this reaction. [k] Purified by preparative TLC by eluting with 25% ether in hexane.

Scheme II. Alternative Mechanistic Rationale



addition of an R^- to C(4) and R^+ to C(5).

Experimental Section

General Procedures. All reactions were run under a positive pressure of dry nitrogen. Infrared spectra were obtained as solutions in the indicated solvent on a Beckman IR-8 or a Perkin-Elmer 267 spectrophotometer and are reported in cm^{-1}. NMR spectra were determined in the indicated solvent on a Jeolco MH-100 or a Bruker WH270 instrument; chemical shifts are reported in parts per million downfield from tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; addition of br indicates a broadened pattern. Coupling constants are given in hertz. Mass spectra were recorded on an AEI-MS-902 high-resolution mass spectrometer at an ionizing voltage of 70 eV and an ionizing current of 100 mA unless otherwise specified. Melting points were obtained on a Thomas-Hoover apparatus and are uncorrected. Boiling points are uncorrected. Micronanalyses were performed by Spang Microanalytical Laboratories, Ann Arbor, MI. In cases where elemental composition was determined by high-resolution mass spectroscopy, chemical purity was established by spectral and chromatographic criteria with details regarding the spectral data and chromatographic conditions reported in each case. Thin-layer or preparative thick-layer (1.5 mm) plates were made of Merck AG Darmstadt silica gel PF-254 or Brinkmann silica gel P/UV-254 no. 66 and activated by drying at 140 °C for 2 h. Eluting solvents are indicated in the text. Removal of material from the silica gel was accomplished by successive washings with ether or ethyl acetate.

In experiments requiring dry solvents, ether, tetrahydrofuran, dioxane, and dimethoxyethane were distilled from sodium benzophenone ketyl.

Preparation of α,α-(Trimethylenedithio)cycloalkanones. 2,2-(1,3-Propanedithio)cyclononanone (7b). To a suspension of 700 mg (5.00 mmol) of cyclononanone and 232 mg (57% dispersion, 5.50 mmol) of sodium hydride in 20 mL of benzene were added 4 mL of ethyl formate and 40 mg of methanol. After the mixture was stirred for 20 h at room temperature, 20 mL of water was added. The aqueous layer was washed with ether (from which any recovered ketone could be reisolated), acidified with concentrated aqueous hydrochloric acid at 0 °C, and extracted with ether. The latter ether layer was washed with brine, dried over $MgSO_4$, and evaporated in vacuo to give 760 mg (90%) of a pale yellow oil which was used directly: IR ($CHCl_3$) 1705, 1625, 1590 cm^{-1}; NMR (CCl_4) δ 1.2–2.0 (11 H, m), 2.2–2.6 (4 H, m), 8.42 (1 H, s).

A mixture of 760 mg (4.50 mmol) of (hydroxymethylene)-cyclononanone, 1.872 g (4.50 mmol) of 1,3-propanedithiol bis(*p*-toluenesulfonate), and 1.323 g (13.5 mmol) of anhydrous potassium acetate in 15 mL of ethanol was refluxed for 17 h. The reaction mixture was concentrated in vacuo and the residue diluted with ether. The ether layer was washed with 10% aqueous sodium hydroxide and brine, dried, and evaporated in vacuo. Purification by preparative TLC (30% ether in hexane) gave 900 mg (82%) of colorless prisms: mp 66 °C (ethanol); IR ($CHCl_3$) 1690 cm^{-1}; NMR ($CDCl_3$) δ 1.1–2.1 (14 H, m), 2.1–3.3 (6 H, m); exact mass calcd for $C_{12}H_{20}OS_2$ 244.0956, found 244.0977.

Experimental details for the remaining examples are summarized in Table I.

7a: IR ($CHCl_3$) 1710 cm^{-1}; NMR ($CDCl_3$) δ 1.6–2.3 (8 H, m), 2.4–2.8 (4 H, m), 3.0–3.3 (2 H, m); exact mass calcd for $C_9H_{14}OS_2$ 202.0486, found 202.0487.

7c: IR ($CHCl_3$) 1707 cm^{-1}; NMR ($CDCl_3$) δ 1.1–2.1 (20 H, m), 2.3–2.9 (6 H, m); exact mass calcd for $C_{15}H_{26}OS_2$ 286.1425, found 286.1420.

11: IR ($CHCl_3$) 1700 cm^{-1}; NMR ($CDCl_3$) δ 1.2–2.7 (12 H, m), 3.1–3.7 (3 H, m), 7.1–7.4 (5 H, m); exact mass calcd for $C_{16}H_{20}OS_2$ 292.0956, found 292.0968.

12: IR ($CHCl_3$) 1705, 1600, 1520, 1500 cm^{-1}; NMR ($CDCl_3$) δ 1.6–3.2 (11 H, m), 3.2–3.8 (2 H, m), 7.1–7.6 (5 H, m); exact mass calcd for $C_{15}H_{18}OS_2$ 278.0799, found 278.0802.

Reduction of α,α-(Trimethylenedithio)cycloalkanones. 2-Hydroxy-1,1-(1,3-propanedithio)cyclohexane (8a, R = H). A mixture of 220 mg (1.09 mmol) of **7a** and 41 mg (1.09 mmol)

Table II. Experimental Details for Preparation of 1,4-Dithiacycloheptan-2-ones

hydroxydithiane (wt, mmol)	$Pb(OAC)_4$, wt, mmol	PhH, mL	time, h	product (wt, % yield)	mp,[a] °C (recrystallization solvent)
8a, R = CH_3 (120 mg, 0.55)	611 mg, 1.38	10.5	16	**16a**, R = CH_3[b] (122 mg, 95)	62 (CCl_4)
8b, R = H (580 mg, 2.36)	2.72 g, 6.14	20	17	**16b**, R = H[c] (405 mg, 66)	oil
8c, R = H (230 mg, 0.80)	921 mg, 2.08	20	15	**16c**, R = H[c] (157 mg, 65)	115–116 (CCl_4-hexane)
13 (178 mg, 0.58)	669 mg, 1.51	10	19	**17**[c] (150 mg, 80)	oil
14 (2.5 g, 8.5)	9.8 g, 22.1	150	16	**18**[d] (1.96 g, 73)	gum

[a] Uncorrected. [b] The residue, after initial evaporation, was triturated with hexane and deposited as colorless prisms. [c] Isolated by preparative TLC by utilizing 50% ether in hexane. [d] Isolated by preparative TLC by utilizing 40% ethyl acetate in hexane.

of sodium borohydride in 2 mL of ethanol was stirred at room temperature for 2 h. After evaporation of solvent and dilution of the residual oil with ether, the resulting solution was washed with 10% aqueous sodium hydroxide and brine, dried ($MgSO_4$), and evaporated in vacuo to give 222 mg (quantitative) of alcohol **8a** which was pure by TLC (20% ethyl acetate in hexane): IR ($CHCl_3$) 3450 cm^{-1}; NMR (CCl_4) δ 1.1–2.2 (10 H, m), 2.4–3.2 (5 H, m), 3.96 (1 H, m); exact mass calcd for $C_9H_{16}OS_2$ 204.0643, found 204.0640.

2-Hydroxy-1,1-(1,3-propanedithio)cyclononane (8b, R = H). Method A. As for the preparation of **8a** (R = H), 215 mg (0.881 mmol) of 2,2-(1,3-propanedithio)cyclononanone (**7b**) was reduced with 66 mg (1.76 mmol) of sodium borohydride in 4 mL of ethanol to give after preparative TLC (30% ether in hexane) 165 mg (76%) of **8b** (R = H): IR ($CHCl_3$) 3520 cm^{-1}; NMR ($CDCl_3$) δ 1.1–2.2 (16 H, m), 2.3–3.1 (5 H, m), 4.00 (1 H, m); exact mass calcd for $C_{12}H_{22}OS_2$ 246.1112, found 246.1120.

Method B. A 3.80-mL aliquot of a 1.4 M solution of DIBAL in hexane (5.32 mmol) was added to a −78 °C solution of 650 mg (2.66 mmol) of ketone **7b** in 10 mL of toluene. After the solution was stirred for 2 h at −78 °C, addition of 0.3 mL of ethanol quenched the reaction. The reaction was warmed to room temperature, 0.6 mL of a saturated aqueous sodium sulfate solution added, and the mixture stirred for 4 min. After the organic layer was separated and dried, the solvent was removed in vacuo and the residue purified by preparative TLC (30% ether in hexane) to give 590 mg (90%) of **8b** (R = H), identical with the sample prepared by method A.

2-Hydroxy-1,1-(1,3-propanedithio)cyclododecane (8c, R = H). As for the conversion of **7a** to **8a**, 250 mg (0.87 mmol) of **7c** in 3 mL of ethanol and 2 mL of THF was reduced with 66 mg (1.75 mmol) of sodium borohydride to give after 22 h 240 mg (95%) of **8c** as colorless prisms, mp 104–105 °C (hexane), after preparative TLC and elution with benzene: IR ($CHCl_3$) 3500 cm^{-1}; NMR ($CDCl_3$) δ 1.1–2.5 (23 H, m), 2.90 (4 H, m), 3.90 (1 H, m); exact mass calcd for $C_{15}H_{28}OS_2$ 288.1582, found 288.1573.

Reaction of α,α-(Trimethylenedithio)cycloalkanones with Methyllithium. 2-Hydroxy-2-methyl-1,1-(1,3-propanedithio)cyclohexane (8a, R = CH_3). A 1.82-mL aliquot (2.73 mmol) of a 1.5 M solution of methyllithium in hexane was added to 370 mg (1.82 mmol) of oxodithiane **7a** in 6 mL of dry THF at 0 °C. After the mixture was stirred for 4 h at 0 °C, the reaction was quenched with water and diluted with ether. The organic layer was washed with brine, dried ($MgSO_4$), and evaporated in vacuo. Preparative TLC (20% ether in hexane) gave 364 mg (92%) of hydroxydithiane **8a** (R = CH_3): IR ($CHCl_3$) 3450 cm^{-1}; NMR (CCl_4) δ 1.42 (3 H, s), 1.44–2.40 (12 H, m), 2.64–2.90 (3 H, m); exact mass calcd for $C_{10}H_{18}OS_2$ 218.0799, found 218.0792.

3-Benzyl-2-hydroxy-2-methyl-1,1-(1,3-propanedithio)-cyclohexane (13). As above, 1.25 mmol of a solution of methyllithium in hexane was added to 182 mg (0.62 mmol) of oxodithiane **11** to give, after preparative TLC, 187 mg (98%) of hydroxydithiane **13** as colorless prisms (hexane): mp 130–131 °C; IR ($CHCl_3$) 3520, 1600 cm^{-1}; NMR ($CDCl_3$) δ 1.38 (3 H, s), 1.4–2.5 (10 H, m), 2.6–3.4 (6 H, m), 7.0–7.4 (5 H, m); exact mass calcd for $C_{16}H_{20}OS_2$ 292.0956, found 292.0968.

2-Hydroxy-2-methyl-4-phenyl-1,1-(1,3-propanedithio)-cyclohexane (14). As above, an 8.7-mL (15.7 mmol) aliquot of a 1.81 M solution of methyllithium in ether was added to 2.19 g (7.87 mmol) of oxodithiane **12** to give, after preparative TLC (20% ethyl acetate in hexane), 2.23 g (96%) of hydroxydithiane **14**: IR ($CHCl_3$) 3540, 1600, 1500 cm^{-1}; NMR ($CDCl_3$) δ 1.54 (3 H, s), 1.4–3.0 (14 H, m), 7.1–7.4 (5 H, m); exact mass calcd for $C_{16}H_{22}OS_2$ 294.1112, found 294.1132.

Preparation of 1,4-Dithiacycloheptan-2-ones. Cleavage of 2-Hydroxy-1,1-(1,3-propanedithio)cyclohexane 8a (R = H). To 1.245 g (2.81 mmol) of lead tetraacetate, washed free of acetic acid with benzene, suspended in 22 mL of benzene was added 220 mg (1.08 mmol) of **8a** (R = H). The reaction was heated at 50–55 °C for 15 h, cooled to room temperature, quenched by the addition of 900 mg of ethylene glycol, and diluted with ether. The solution was washed with brine, dried ($MgSO_4$), and evaporated in vacuo. The residue, after preparative TLC (33% hexane in ether), gave 189 mg (80%) of **16a** (R = H) as colorless needles (CCl_4): mp 61 °C; IR ($CHCl_3$) 1727, 1668 cm^{-1}; NMR ($CDCl_3$) δ 1.5–2.3 (6 H, m), 2.3–2.6 (2 H, m), 2.7–3.4 (4 H, m), 3.70 (1 H, t, J = 6 Hz), 9.76 (1 H, br s); exact mass calcd for $C_9H_{14}O_2S_2$ 218.0435, found 218.0421.

Experimental details for the remaining examples are summarized in Table II.

16a (R = CH_3): IR 1719, 1679 cm^{-1}; NMR ($CDCl_3$) δ 1.4–2.1 (6 H, m), 2.13 (3 H, s), 2.3–2.6 (2 H, m), 2.8–3.4 (4 H, m), 3.70 (1 H, t, J = 6 Hz); exact mass calcd for $C_{10}H_{16}O_2S_2$ 232.0592, found 232.0581. Anal. ($C_{10}H_{16}O_2S_2$) C, H, S.

16b (R = H): IR ($CHCl_3$) 1723, 1666 cm^{-1}; NMR ($CDCl_3$) δ 1.1–2.6 (14 H, m), 2.6–3.4 (4 H, m), 3.70 (1 H, t, J = 6 Hz), 9.78 (1 H, br s); exact mass calcd for $C_{12}H_{20}O_2S_2$ 260.0905, found 260.0899.

16c (R = H): IR ($CHCl_3$) 1722, 1667 cm^{-1}; NMR ($CDCl_3$) δ 1–1.7 (16 H, m), 2.3–2.7 (2 H, m), 2.8–3.4 (4 H, m), 3.76 (1 H, t, J = 6 Hz), 9.90 (1 H, br s); exact mass calcd for $C_{15}H_{26}O_2S_2$ 302.1374, found 302.1375.

17: IR (CCl_4) 1715, 1673, 1605, 1500 cm^{-1}; NMR ($CDCl_3$) δ 1.3–2.2 (6 H, m) with 2.0 (3 H, s) superimposed, 2.4–3.4 (7 H, m), 3.62 (1 H, t, J = 5 Hz), 7.0–7.4 (5 H, m); exact mass calcd for $C_{17}H_{22}O_2S_2$ 322.1061, found 322.1069.

18: IR (CCl_4) 1715, 1670, 1590 cm^{-1}; NMR ($CDCl_3$) δ 1.6–2.6 (3 H, m) with 2.05 (3 H, s) superimposed, 2.6–3.0 (6 H, m), 3.0–3.8 (3 H, m), 7.1–7.45 (5 H, m); exact mass calcd for $C_{16}H_{20}O_2S_2$ 308.0905, found 308.0896.

Preparation of Methyl 6-Oxoheptanoate (20). A solution of 125 mg (0.54 mmol) of **8a** (R = CH_3) and 137 mg (0.54 mmol) of iodine in 10 mL of methanol was refluxed for 3 h. After evaporation of the solvent, the residue was diluted with chloroform. The resultant solution was washed with 10% aqueous sodium thiosulfate, dried ($MgSO_4$), and evaporated in vacuo to give 130 mg of crude product. This compound was taken up in 6 mL of methanol and refluxed with 1.4 mL of W-2 Raney nickel for 5 h. The reaction mixture was filtered and evaporated in vacuo, and the residue was purified by preparative TLC (25% ether in benzene) to give 58 mg (68%) of keto ester **20**: IR ($CHCl_3$) 1730, 1715 cm^{-1}; NMR (CCl_4) δ 1.4–1.7 (4 H, m), 2.08 (3 H, s), 2.1–2.6 (4 H, m), 3.64 (3 H, s); exact mass calcd for $C_8H_{14}O_3$ 158.0943, found 158.0946.

Preparation of Enoates. Methyl 3-Oxohept-(*E*)-2-enoate (22a, R = CH_3). A solution of 110 mg (0.47 mmol) of **8a** (R = CH_3) and 119 mg (0.47 mmol) of iodine in 8 mL of methanol was refluxed for 3 h. The solvent was evaporated and the residue diluted with chloroform. The organic layer was washed with 10% aqueous sodium thiosulfate and brine, dried ($MgSO_4$), and evaporated in vacuo. The crude product (120 mg) in 3 mL of methanol was stirred at room temperature for 20 h with 201 mg (0.94 mmol) of sodium metaperiodate. The solvent was evaporated in vacuo and the residue triturated with chloroform. After evaporation of the chloroform in vacuo, the crude product (~125 mg) in 2 mL of toluene was refluxed for 3.5 h. The solvent was

evaporated in vacuo. After purification by TLC (50% ether in hexane), there was obtained 37 mg (51%) of **22a**, R = CH_3: IR ($CHCl_3$) 1715, 1658 cm^{-1}; NMR (CCl_4) δ 2.07 (3 H, s), 2.2–2.7 (4 H, m), 3.62 (3 H, s), 5.66 (1 H, d, J = 15 Hz), 6.76 (1 H, dt, J = 15, 7 Hz); exact mass calcd for $C_8H_{12}O_3$ 156.0803, found 156.0811.

Methyl 6-Oxohex-(*E*)-2-enoate. As above, methanolysis of 80 mg (0.37 mmol) of **8a** (R = H) with 93 mg (0.37 mmol) of iodine followed by conversion to the sulfoxide with 158 mg (0.74 mmol) of sodium metaperiodate in 6 mL of methanol (20 h) gave, after thermolysis (3 mL, 4 h), 28 mg (54%) of **22a** (R = H): IR ($CHCl_3$) 1720, 1660 cm^{-1}; NMR (CCl_4) δ 2.54 (4 H, m), 3.68 (3 H, s), 5.76 (1 H, d, J = 17 Hz), 6.80 (1 H, dt, J = 17, 7 Hz), 9.74 (1 H, br s).

Methyl 9-Oxonon-(*E*)-2-enoate. As above, methanolysis of 430 mg (1.65 mmol) of **8b** (R = H) with 419 mg (1.65 mmol) of iodine followed by oxidation to the sulfoxide with 706 mg (3.30 mmol) of sodium metaperiodate in 10 mL of methanol gave, after thermolysis in 10 mL of toluene, 165 mg (54%) of enoate **22b**: IR ($CHCl_3$) 1724, 1712, 1658 cm^{-1}; NMR (CCl_4) δ 1.2–1.8 (6 H, m), 2.0–2.4 (4 H, m), 3.66 (3 H, s), 5.72 (1 H, d, J = 16 Hz), 6.84 (1 H, d, J = 16 Hz), 9.70 (1 H, br s); exact mass calcd for $C_{10}H_{16}O_3$ 184.1099, found 184.1095.

Methyl 12-Oxododec-(*E*)-2-enoate. As above, methanolysis of 88 mg (0.29 mmol) of **8c** (R = H) with 74 mg (0.29 mmol) of iodide followed by oxidation with 124 mg (0.58 mmol) of sodium metaperiodate in 5 mL of methanol gave, after thermolysis in 2 mL of toluene, 38 mg (58%) of **22c** (R = H): IR ($CHCl_3$) 1720, 1658 cm^{-1}; NMR (CCl_4) δ 1.1–1.6 (12 H, m), 2.0–2.4 (4 H, m), 3.64 (3 H, s), 5.70 (1 H, d, J = 17 Hz), 6.04 (dt, J = 17, 7 Hz), 9.68 (1 H, br s); exact mass calcd for $C_{13}H_{22}O_3$ 226.1569, found 226.1562.

Methyl 5-Benzyl-6-oxohept-(*E*)-2-enoate (23). As above, methanolysis of 69 mg (0.21 mmol) of **17** followed by oxidation with 90 mg (0.42 mmol) of sodium metaperiodate in 3:1 methanol–THF gave, after thermolysis in 3 mL of toluene, 24 mg (46%) of **23** after preparative TLC (50% ether in hexane): IR ($CHCl_3$) 1725, 1619 cm^{-1}; NMR (CCl_4) 1.92 (3 H, s), 1.8–3.5 (5 H, m), 3.65 (3 H, s), 5.77 (1 H, d, J = 16 Hz), 6.79 (1 H, dt, J = 16, 7 Hz), 7.0–7.4 (5 H, m); exact mass calcd for $C_{15}H_{18}O_3$ 246.1256, found 246.1263.

Methyl 4-Phenyl-6-oxohept-(*E*)-2-enoate (25). To a −78 °C solution of 156 mg (0.506 mmol) of **18** in 2 mL of methylene chloride was added 100 mg (0.50 mmol, 85% pure) of *m*-chloroperbenzoic acid. After 30 min, the reaction mixture was warmed to room temperature, diluted with methylene chloride, washed with saturated aqueous sodium carbonate and brine, dried (Na_2SO_4), and evaporated in vacuo to give 165 mg: IR ($CHCl_3$) 1710, 1660, 1650, 1355, 1155 cm^{-1}; NMR ($CDCl_3$) δ 1.6–3.6 (11 H, m) with 2.08 (3 H, s) superimposed, 3.6–4.2 (1 H, m), 7.0–7.4 (5 H, m). A solution of 65 mg (0.20 mmol) of crude sulfoxide in 2 mL of toluene was refluxed for 4 h and then concentrated in vacuo. The residue was refluxed for 3 h in 2 mL of methanol containing 51 mg (0.20 mmol) of iodine. The solvent was evaporated in vacuo. The residue was dissolved in chloroform, washed with 10% aqueous sodium bisulfite and brine, dried ($MgSO_4$), and evaporated in vacuo to give, after preparative TLC (50% ether in hexane), 21 mg (45%) of **25**: IR (CCl_4) 1725, 1650, 1600, 1490 cm^{-1}; NMR (CCl_4) δ 2.0 (3 H, s), 2.80 (2 H, d, J = 8 Hz), 3.64 (3 H, s), 3.96 (1 H, q, J = 8 Hz), 5.64 (1 H, d, J = 16 Hz), 6.9 (1 H, m), 7.0–7.4 (5 H, m); exact mass calcd for $C_{14}H_{16}O_3$ 232.1099, found 232.1094.

Preparation of Methyl 9-Oxodecan-(*E*)-2-enoate (Queen's Substance). At −40 °C (aqueous $CaCl_2$–dry ice), 0.65 mmol of methylmagnesium chloride (3 M in ether) was added dropwise to 80 mg (0.43 mmol) of aldehydo enoate **22b** in 2.5 mL of ether. After 3 h at −40 °C, the reaction mixture was quenched by addition of 0.2 mL of methanol, warmed to room temperature, diluted with ether, washed with brine, dried ($MgSO_4$), and evaporated in vacuo to give 83 mg of colorless oil. The crude alcohol was dissolved in 2 mL of acetone and 0.10 mL of Jones reagent added dropwise at 0 °C. The reaction mixture was stirred at 0 °C for 15 min and then quenched with sufficient 2-propanol to change the color from brown to blue. The solvent was evaporated in vacuo and the residue diluted with ether. The ether layer was washed with brine, saturated aqueous sodium bicarbonate, and brine again, dried ($MgSO_4$), and concentrated in vacuo to give after subjection to preparative TLC (1:1 ether/hexane) 45 mg (53%) of queen's substance **26**. It was identical by IR and NMR spectral comparisons and by TLC with an authentic sample.[14]

Cuprate Couplings. 4-Phenylundec-(*E*)-5-ene-2,7-dione (28a). To a −78 °C slurry of $CuBr{\cdot}S(CH_3)_2$ (54 mg, 0.266 mmol) in 3 mL of dry ether was added *n*-butyllithium in hexane (0.34 mL, 0.532 mmol). After the mixture was kept for 1 h at −40 °C (at which time the mixture became a clear yellow solution) and cooled to −78 °C, a solution of 3-(4-oxo-3-phenylpentyl)-1,4-dithiacycloheptan-2-one (**18**) (77 mg, 0.25 mmol) in 2 mL of ether was added and stirring continued at −78 °C for 2 h. Hydrogen sulfide was then bubbled through the solution for several minutes. The dark reaction mixture was diluted with ether and washed with 1% hydrochloric acid, saturated aqueous sodium bicarbonate, and brine. The aqueous washes were back-extracted with ethyl acetate, the combined organic extracts were dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo.

The residual oil was dissolved in pyridine (2 mL) and ether (2 mL). Acetic anhydride (0.1 mL) was added and the mixture was stirred at 0 °C for 1 h. The mixture was then diluted with ether and washed with 1% hydrochloric acid solution, saturated aqueous sodium bicarbonate, and brine. The organic extracts were dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo to give a yellow oil. TLC on silica gel with 3:2 hexane/ethyl acetate gave 59 mg (58%) of **27a** as a yellow oil (R_f 0.6): IR (CCl_4) 1705, 1640, 1600, 1500, 945 cm^{-1}; NMR (CCl_4) δ 0.92 (3 H, t, J = 6 Hz), 1.96 and 2.00 (total 3 H, 2 s), 2.28 (3 H, s), 1.0–3.1 (17 H, m), 3.5 (1 H, m), 7.0–7.4 (5 H, m); exact mass calcd for $C_{22}H_{32}O_3S_2$ 408.1784, found 408.1792.

To a −78 °C solution of **27a** (55 mg, 0.134 mmol) in 2 mL of methylene chloride was added MCPBA (31.2 mg, 0.156 mmol). The mixture was stirred at −78 °C for 3 min and then −20 °C for 90 min. The mixture was poured into saturated sodium carbonate solution and extracted with ether (2 × 30 mL). The ether extracts were washed with brine, dried ($MgSO_4$), and filtered, and the solvent was removed in vacuo.

The residue was dissolved in toluene (2 mL), placed in a preheated (120 °C) oil bath to reflux for 2.5 h, and then cooled, and the solvent was removed in vacuo. TLC with 3:2 hexane/ethyl acetate gave 27 mg (78%) of **28a** (R_f 0.47): IR (CCl_4) 1720, 1690, 1630, 1590 cm^{-1}; NMR (CCl_4) δ 0.88 (3 H, t, J = 6 Hz), 1.0–1.8 (4 H, m), 2.02 (3 H, s), 2.4 (3 H, q, J = 6 Hz), 2.84 (2 H, d, J = 7 Hz), 4.0 (1 H, q, J = 7 Hz), 5.96 (1 H, d, J = 16 Hz), 6.8 (1 H, dd, J = 16, 8 Hz), 7.0–7.4 (5 H, m); exact mass calcd for $C_{17}H_{22}O_2$ 258.1620, found 258.1609.

4-Phenyloct-(*E*)-5-ene-2,7-dione (28b). As above, 154 mg (0.5 mmol) of the 1,4-dithiacycloheptan-2-one **18** was reacted with (1) lithium dimethylcuprate in 4 mL of ether prepared from 1.08 mmol of methyllithium and 111 mg (0.541 mmol) of cuprous bromide–dimethyl sulfide and (2) 0.15 mL of acetic anhydride in 3 mL of pyridine and 2 mL of ether to give, after TLC (3:2 hexane/ethyl acetate), 119 mg (65%) of **27b**: IR (CCl_4) 1710, 1680, 1600, 1495 cm^{-1}; NMR (CCl_4) δ 1.96 (3 H, s), 2.0 (3 H, s), 2.28 (3 H, s), 1.2–3.6 (12 H, m), 7.0–7.4 (5 H, m); exact mass calcd for $C_{19}H_{26}O_3S_2$ 366.1323, found 366.1326.

Oxidation of 115 mg (0.314 mmol) of **27b** with 69 mg (0.345 mmol) of MCPBA in 4 mL of methylene chloride followed by elimination at 120 °C in 3 mL of toluene gave 46 mg (69%) of **28b** after TLC (3:2 hexane/ethyl acetate): IR (CCl_4) 1720, 1680, 1625, 1495 cm^{-1}; NMR (CCl_4) δ 2.03 (3 H, s), 2.14 (3 H, s), 2.85 (2 H, d, J = 6 Hz), 4.04 (1 H, m), 5.94 (1 H, d, J = 16 Hz), 6.80 (1 H, dd, J = 16, 6 Hz), 7.0–7.4 (5 H, m); exact mass calcd for $C_{14}H_{16}O_2$ 216.1150, found 216.1146.

1,4-Diphenylhept-(*E*)-2-ene-1,6-dione (28). As above, 154 mg (0.500 mmol) of 1,4-dithiacycloheptan-2-one **18** was reacted with (1) lithium diphenylcuprate in 4 mL of ether prepared from 1.13 mmol of phenyllithium (in 7:3 benzene/ether from Alfa Ventron Co.) and 116 mg (0.565 mmol) of cuprous bromide–dimethyl sulfide and (2) 0.3 mL of acetic anhydride in 3 mL of pyridine and 3 mL of ether to give, after TLC (3:2 hexane/ethyl acetate), 127 mg (59%) of **27c**: IR ($CHCl_3$) 1710, 1670, 1590, 1490 cm^{-1}; NMR ($CDCl_3$) 1.2–4.0 (12 H, m), 2.0 (3 H, s), 2.23 (3 H, s), 7.0–8.0 (10 H, m); exact mass calcd for $C_{24}H_{28}O_3S_2$ 428.1480, found 428.1466.

Oxidation of 110 mg (0.257 mmol) of **27c** with 60 mg (0.300 mmol) of MCPBA in 3 mL of methylene chloride followed by elimination at 120 °C in 3 mL of toluene gave after TLC (3:2

hexane/ethyl acetate) 50 mg (70%) of **28c**: IR (CCl_4) 1720, 1670, 1620, 1595, 1490 cm^{-1}; NMR (CCl_4) δ 2.0 (3 H, s), 2.84 (2 H, d, J = 8 Hz), 4.04 (1 H, q, J = 6 Hz), 6.68 (1 H, d, J = 16 Hz), 6.75–7.8 (11 H, m); exact mass calcd for $C_{19}H_{18}O_2$ 278.1307, found 278.1312.

4-Phenyl-11,11-(ethylenedioxy)dodec-(*E*)-5-ene-2,7-dione (28d). To 3 mL of dry THF containing 2.45 mmol of *tert*-butyllithium in pentane at −78 °C was added dropwise 320 mg (1.25 mmol) of 2,2-(ethylenedioxy)-5-iodopentane in 4 mL of THF. After 1 h, the clear solution was added to a −40 °C slurry of 125 mg (0.600 mmol) of cuprous bromide–dimethyl sulfide in 7 mL of ether. After the black mixture was stirred at −40 °C for 1 h and cooled to −78 °C, a solution of 154 mg (0.500 mmol) of 1,4-dithiacycloheptan-2-one in 4 mL of ether was added and the resultant mixture was stirred for 2 h. After workup as described for **28a**, acetylation with 0.2 mL of acetic anhydride in 3 mL of pyridine and 3 mL of ether, and purification by TLC (3:2 hexene/ethyl acetate), 111 mg (46%) of **27d** was isolated: IR ($CHCl_3$) 1700, 1660, 1600, 1490 cm^{-1}; NMR ($CDCl_3$) δ 1.28 (3 H, s), 2.0 (3 H, s), 2.18 (3 H, s), 1.2–3.6 (18 H, m), 3.88 (4 H, s), 7.0–7.4 (5 H, m); exact mass calcd for $C_{25}H_{36}O_5S_2$ 480.2004, found 480.1986.

Oxidation of 80 mg (0.17 mmol) of **27d** with 36 mg (0.18 mmol) of MCPBA in 3 mL of methylene chloride and elimination at 120 °C in 3 mL of toluene generated, after TLC (3:2 hexane/ethyl acetate), 22 mg (40%) of **28d**: IR (CCl_4) 1710, 1680, 1620, 1490 cm^{-1}; NMR (CCl_4) 1.2 (3 H, s) 1.92 and 2.0 (3 H, 2 s), 1.4–2.5 (6 H, m), 2.58 and 2.80 (2 H, 2 d, J = 7 Hz), 3.8 (4 H, s), 3.9 (1 H, m), 5.88 (1 H, d, J = 16 Hz), 6.72 (1 H, dd, J = 16, 6 Hz), 6.9–7.3 (5 H, m).

Treatment of 2-Benzylidene-1,3-dithiane with Lead Tetraacetate. A solution of 208 mg (1 mmol) of 2-benzylidene-1,3-dithiane in 4 mL of benzene was added to 576 mg (1.3 mmol) of lead tetraacetate which had been washed free of acetic acid. After the mixture was heated at 55 °C for 5 min, a white powdery precipitate formed. Stirring continued for 1 h at 55 °C. The mixture was diluted with ether, washed with 5% aqueous sodium thiosulfate and brine, dried ($MgSO_4$), and evaporated in vacuo to give 264 mg (99%) of 2-(1′-acetoxybenzylidene)-1,3-dithiane **36**, pure by TLC and spectroscopy: IR (CCl_4) 1765, 1600 cm^{-1}; NMR (CCl_4) δ 1.96–2.3 (2 H, m), 2.12 (3 H, s), 2.82 (2 H, t, J = 6.5 Hz), 2.92 (2 H, t, J = 7 Hz), 7.16–7.54 (5 H, m); exact mass calcd for $C_{13}H_{14}O_2S_2$ 266.0435, found 266.0436.

To a solution of 264 mg (0.992 mmol) of **36** in 4 mL of toluene at −78 °C was added 1.1 mmol of a solution of DIBAL in hexane. After 6.5 h at −78 °C, 1 mL of methanol was added and the reaction allowed to warm to ambient temperature. A 1-mL aliquot of saturated aqueous sodium sulfate solution followed by 30 mL of ether was added, and the mixture was stirred 10 min. Excess solid sodium sulfate was added for drying, and the mixture was filtered and evaporated in vacuo. Purification by preparative TLC (7:3 hexane/ethyl acetate) gave 156 mg (70%) of **37** as an amorphous solid: mp 94–95 °C; IR (CCl_4) 1690, 1595, 1580 cm^{-1}; NMR ($CDCl_3$) δ 1.96–2.32 (2 H, m), 2.56–2.84 (2 H, m), 3.24–3.56 (3 H, m), 5.17 (1 H, s), 7.3–7.7 (3 H, m), 7.9–8.1 (2 H, m); exact mass calcd for $C_{11}H_{12}OS_2$ 224.0329, found 224.0330.

A solution of 35 mg (0.16 mmol) of **37** in 1 mL of absolute ethanol was refluxed for 4 h with 1 mL of W-2 Raney nickel. The solution was analyzed by TLC and VPC and showed only a single compound corresponding to acetophenone. The mixture was filtered through Celite and the filter cake washed with pentane. The filtrate was washed with water and dried, and the solvent was removed by distillation to give 16 mg (85%) of acetophenone, identical by NMR and IR spectroscopy, VPC, and TLC with an authentic sample.

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Registry No. 5a, 108-94-1; **5b**, 3350-30-9; **5c**, 830-13-7; **6a**, 823-45-0; **6b**, 1009-12-7; **6c**, 949-07-5; **7a**, 51310-03-3; **7b**, 73194-43-1; **7c**, 73194-44-2; **8a** (R = H), 60450-09-1; **8a** (R = CH_3), 60450-20-6; **8b** (R = H), 60450-12-6; **8c** (R = H), 60450-13-7; **9**, 946-33-8; **10**, 20795-53-3; **11**, 73194-45-3; **12**, 73194-46-4; **13**, 60450-11-5; **14**, 73194-47-5; **16a** (R = H), 60450-07-9; **16a** (R = CH_3), 60450-08-0; **16b** (R = H), 60450-14-8; **16c** (R = H), 60450-15-9; **17**, 60450-10-4; **18**, 73194-48-6; **20**, 2046-21-1; **22a** (R = H), 2018-74-8; **22a** (R = CH_3), 60450-18-2; **22b** (R = H), 60450-16-0; **22b** (R = CH_3), 1189-64-6; **22c** (R = H), 60450-17-1; **23**, 60450-19-3; **24**, 73194-49-7; **25**, 73194-50-0; **26**, 1189-64-6; **27a**, 73194-51-1; **27b**, 73194-52-2; **27c**, 73194-53-3; **27d**, 73194-54-4; **28a**, 73194-55-5; **28b**, 73194-56-6; **28c**, 73194-57-7; **28d**, 73194-58-8; **33**, 17590-58-8; **36**, 72019-01-3; **37**, 21504-07-4; 1,3-propanedithiol bis(*p*-toluenesulfonate), 3866-79-3; methyl 9-hydroxy-2-decenoate, 40979-98-4; 2,2-(ethylenedioxy)-5-iodopentane, 3695-28-1; acetophenone, 98-86-2.

Synthesis of 1,8-(6′,7′-Dioxododecamethylene)phenanthrene[1]

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The synthesis of the title compound (1) is described starting from *o,o′*-stilbenedicarboxylic acid which was converted to *o,o′*-bis[(carbomethoxy)pentyl]stilbene which underwent acyloin cyclization and oxidation to give 1 in 9.5% overall yield. Spectroscopic properties of 1 are presented.

α-Diketones possess a variety of desirable properties for study of photophysical and photochemical phenomena.[2] The most extensively investigated member of this family of compounds is biacetyl, which has weak ($\epsilon \sim 30$), solvent-dependent, absorption maxima at about 275 and 420 nm (cf. Figure 1), exhibits both fluorescence and phosphorescence in fluid solution at room temperature, and undergoes a variety of photochemical reactions. It thus seemed that substances incorporating both an α-diketone moiety and an additional chromophore would be good candidates for investigation of intramolecular energy transfer[3] and might also exhibit photochromic properties.

(1) From the D.Sc. dissertation of S. Welner, Technion, 1978.
(2) For review articles see M. B. Rubin, *Top. Curr. Chem.*, 13, 257 (1969); B. M. Monroe, *Adv. Photochem.*, 8, 77 (1971).
(3) For a general discussion see D. O. Cowan and R. L. Drisko, "Elements of Organic Photochemistry", Plenum, New York, 1976, Chapter 6.

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