THE JOURNAL OF Organic Chemistry

VOLUME 47, NUMBER 15

JULY 16, 1982

Use of Protected β-Bromocyclopentenones and β-Bromocyclohexenones as β-Acylvinyl Anion Equivalents

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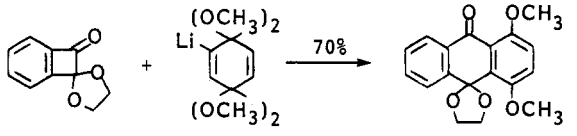
Received January 27, 1982

Ethylene glycol ketals of the 3-bromocyclohex-2-en-1-one as well as its 2-methyl, 2-*n*-propyl, and 5,5-dimethyl derivatives have been prepared, and their reactions with butyllithium were studied. The organolithium reagents derived from the above compounds react with a variety of electrophiles to afford after acid hydrolysis the corresponding 3-substituted cyclohexenones. Attempts to prepare the ethylene glycol ketal of 2-methyl-3-bromocyclopent-2-en-1-one gave a low yield of the bromoketal. However, dithioketals of 3-bromocyclopent-2-en-1-one and its 2-methyl derivative could be prepared in good yield. The metalation chemistry of the dithioketals in both the five- and six-membered-ring series was examined. The functionalization chemistry of the resulting organolithium compounds afforded after dithioketal hydrolysis 3-functionalized cyclohex-2-en-1-ones and cyclopent-2-en-1-ones. Several limitations of the chemistry using allyl bromide and cyclohexenone as electrophiles are noted.

The utilization of organometallic reagents wherein a carbonyl group in the compound is present in protected form is a commonly used technique in organic chemistry. Our interest in this area arose in 1976 when we reported that **2** served as a useful intermediate for obtaining functionalized quinone systems.[1] An interesting annelation reaction of **1** was subsequently developed (**1** + **2** → **3**) and successfully applied to anthracyclinone synthesis.[2]

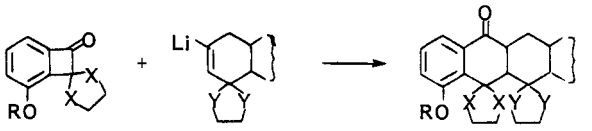


1 **2** **3**

Not only did this chemistry allow the preparation of an anthraquinone system under mild nonacidic conditions but it also formed **3**, in which the two anthraquinone carbonyls were differentiated chemically.

Since the above chemistry permits a convergent approach to polycyclic natural products possessing labile functionalities, we were interested in exploring this chemistry further. In particular, the reaction of a β-acylvinyl anion equivalent with an appropriate benzocyclobutenedione derivative would afford three rings of a potential tetracycline wherein all three carbonyl groups could be differentiated chemically (Scheme I). In recent years two basic strategies have been employed to generate β-acylvinyl anion equivalents. In one, the β-position of a latent carbonyl system is activated toward proton abstraction by an electron-withdrawing group (cyano,[3] nitro,[4] phenylthio,[5] sulfonyl[6]), the resulting carbanion reacted with an electrophile, and the activating group eliminated to introduce the required unsaturation. The second method involves lithiation of a vinyl substituent (bromo,[7] trialkylstannyl[8]) β to a latent carbonyl group followed by reaction of the resulting organometallic compound with electrophiles. While these studies have employed some

Scheme I. Reaction of a β-Acylvinyl Anion Equivalent with a Benzocyclobutenedione Derivative



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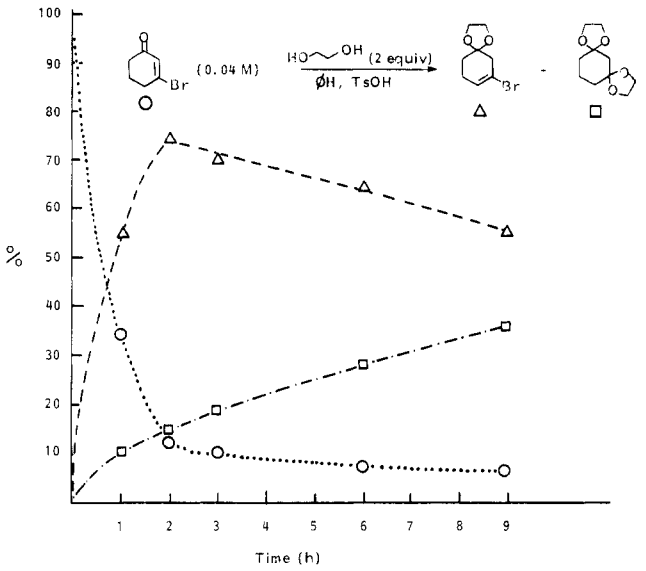
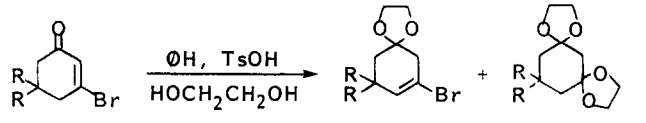


Figure 1. Ketalization of β-bromocyclohexenone.

novel methods, utilization of these reagents on a moderate-scale reaction is often inconvenient and/or expensive.

This need, together with our experience with lithiated ketals as metalated quinone[1,2] and α-acylvinyl anion[9,10] equivalents, suggested examination of ketals of β-bromocycloalkenones. The conspicuous absence of such compounds as β-acylvinyl anion equivalents suggested that they either were difficult to prepare or else did not react properly in either the metal–halogen exchange or the alkylation step. We report here that ethylene glycol and ethanedithiol ketals can be prepared for a number of β-bromo enones and that these compounds serve as viable β-acylvinyl anion equivalents of cyclohexenones[11] and cyclopentenones.

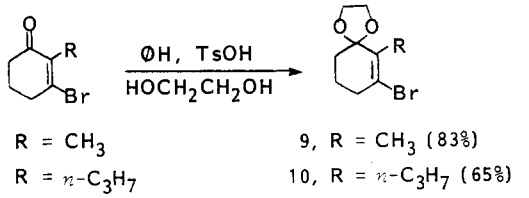
Ethylene Glycol Ketals of β-Bromo Enones. When β-bromocyclohexenone (**4a**) was ketalized under standard



azeotropic conditions by employing an excess of ethylene glycol, the bisketal **6a** was formed almost exclusively. However, it was found that the ratio of the monoketal **5a** to the bisketal **6a** when using 2 equiv of ethylene glycol was time dependent (Figure 1), and by careful monitoring of the reaction, the monoketal **5a** could be obtained in 68% yield. The reason for the time dependence of the product ratio was established when it was shown that **5a** under the reaction conditions was cleanly converted to **6a**. The structure of **5a** was assigned primarily on the basis of its NMR spectrum and decoupling studies [NMR (CCl_4/200 MHz) δ 6.05 (seven-line m, 1 H), 3.98 (s, 4 H), 2.64 (d, J = 1.8 Hz, 2 H) 2.24 (m, 2 H), 1.74 (t, J = 6.5 Hz, 2 H)]. Irradiation of the vinyl hydrogen changed the doublet at δ 2.64 to a barely discernible triplet ($J \simeq 1.0$ Hz) and markedly simplified the multiplet at δ 2.24. Irradiation of the δ 2.24 signal collapsed the triplet at δ 1.74 to a singlet and the vinyl multiplet to a triplet (J = 1.8 Hz) while irradiation at δ 2.64 simplified the multiplet at δ 2.24 and changed the vinyl multiplet to a triplet (J = 4.0 Hz). These decoupling data and the chemistry described herein are only consistent with structure **5a**. The structure of **5b** has been assigned by analogy with that of **5a**: NMR (CCl_4/90 MHz) δ 5.73 (poorly resolved t, $J \simeq 1.0$ Hz, 1 H), 3.92 (s, 4 H), 2.54 (br s, 2 H), 2.59 (s, 2 H), 1.12 (s, 6 H).

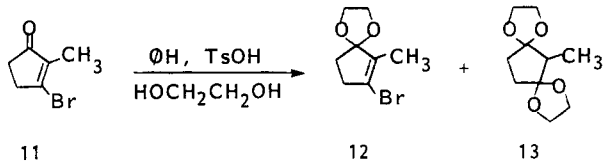
Since for some of our projected studies (e.g., Scheme I) we desired the ketal in which double-bond migration did not occur, the recent ketalization procedure of Noyori et al.[12] was examined. These workers reported that the use of the disilyl derivative of ethylene glycol and trimethylsilyl triflate ketalized cyclohex-2-en-1-one without double-bond isomerization. When **4a** was ketalized in the above fashion, **5a** was obtained in 75% yield, with only a very small amount of **6a** being formed. Apparently, even under these mild conditions, the double-bond isomerization of **4a** could not be suppressed.

As expected, substituents at C_2 of the cyclohexenone stabilize the carbon–carbon double bond. Thus, the ketalization of **7** and **8** proceeded smoothly under our azeo-

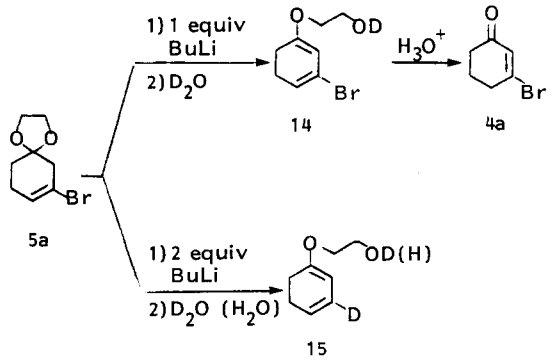


tropic conditions to furnish the ketals **9** and **10** in which double-bond isomerization did not occur. In both **7** and **8**, formation of bisketals akin to **6** was barely detectable.

All attempts to extend these ketalization reactions to β-bromocyclopentenones met with very limited success even when the number of equivalents of ethylene glycol was controlled and the progress of the reaction carefully monitored. For example, even at partial conversion, ketalization of **11** gave only 18% of **12** in addition to **13**.



Functionalization Reactions of β-Bromocycloalkenone Ketals. Initial metal–halogen exchange reactions of **5a** were disappointing. The reaction of **5a** with 1 equiv of n-butyllithium followed by addition of deuterium oxide did not give the expected deuterio ketal but rather a product assigned as **14**.[13] Acid hydrolysis of **14**



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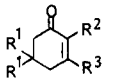
(11) For a preliminary report describing the cyclohexenone functionalizations, see: Shih, C.; Swenton, J. S. *Tetrahedron lett.* **1981**, *22*, 4217–4220.
(12) Tsunoda, Y.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1357–1358.

Table I. Summary of Functionalizations of β-Bromocycloalkenone Ketals



entry	starting compd	electrophile	R^1	R^2	R^3	yield, %
1	5a	methyl iodide	H	H	CH_3	82
2	5a	ethyl iodide	H	H	C_2H_5	71
3	5a	trimethylsilyl chloride	H	H	$Si(CH_3)_3$	79
4	5a	cyclohexanone	H	H		80
5	5a	cyclopentanone	H	H		76
6	5a	benzaldehyde	H	H		75
7	5a	carbon dioxide	H	H	CO_2H	66
8	5a	cyclohexenone	H	H		77
9	5b	methyl iodide	CH_3	H	CH_3	86
10	5b	cyclohexanone	CH_3	H		82
11	9	methyl iodide	H	CH_3	CH_3	80
12	9	cyclohexanone	H	CH_3		80
13	9	cyclopentanone	H	CH_3		65
14	9	cyclohexenone	H	CH_3		78
15	10	cyclohexanone	H	n-C_3H_7		60

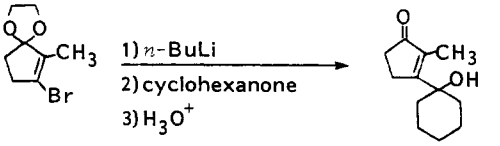
produced the starting β-bromo enone **4a**. However, reaction of **5a** with 2 equiv of *n*-butyllithium followed by addition of deuterium oxide gave **15** whose structure is assigned on the basis of spectroscopic data, the most meaningful being its ultraviolet spectrum: λ_{max} (hexane) 267 nm (ε 3720); calcd[14] λ_{max} 260 nm. With this information **5a** was reacted with 2 equiv of *n*-butyllithium at −78 °C followed by addition of the electrophile. Acidic workup of the reaction mixture gave the functionalized cycloalkenones listed in Table I. The functionalization chemistry of **9** and **10** was performed similarly except only 1.1 equiv of *n*-butyllithium was utilized for the metal–halogen exchange reaction. The structures in Table I were assigned on the basis of spectroscopic data. The ^{13}C NMR spectra were especially useful in establishing structure and purity in selected systems.

Several points should be noted concerning the reactions summarized in Table I. First, these organolithium compounds react with a modest range of alkyl iodides and simple ketones to give products easily purified by direct recrystallization or filtration through a short silica gel column. Especially noteworthy is the reaction of the lithium reagents with cyclopentanone (entries 5 and 13), a ketone often showing a tendency to undergo predominantly enolization with some organolithium reagents.[1] Furthermore, steric hindrance from a methyl group at the 2-position (entries 11–13) does not give any dramatic reduction in yield. Even **10** (entry 15), in which a methyl group is at the 6-position relative to attack at the cyclohexanone carbonyl, affords the product in acceptable yield.

(13) Apparently, β elimination is more rapid than metal–halogen exchange. For cases when deprotonation is competitive with metal–halogen exchange, see the discussion of ref 2b.

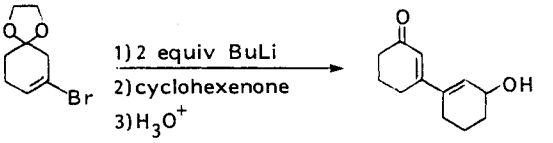
(14) Silverstein, R. M.; Bassler, G. C. "Spectrometric Identification of Organic Compounds", 2nd ed.; Wiley: New York, 1967; p 244.

Finally, while the cyclopentane system **12** is formed in poor yield from the β-bromo enone, its organolithium chemistry proceeds very satisfactorily. Thus, **12** reacts with cyclohexanone to afford **16** in 68% yield.



12 16 (68%)

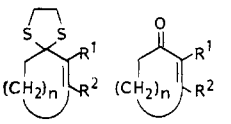
In general, no rearrangements were noted under the mild acid hydrolysis conditions employed in the work except for entry 8. In this reaction, spectroscopic data and chemical transformations as outlined later establish that **5a** gives with cyclohexenone the rearranged adduct **17**.



5a 17

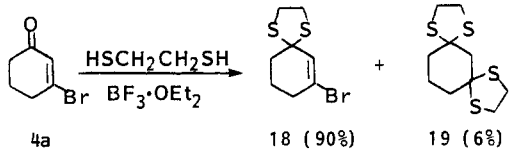
Formation and Functionalization of β-Bromocycloalkenone Dithioketals. The chemistry presented thus far has established that ethylene glycol ketals of β-bromo enones are viable β-acylvinyl anion equivalents. Two limitations on the chemistry did emerge from the studies thus far. First, for the parent system, double-bond isomerization accompanies ketalization. While this does not impose a serious limitation on its use as a β-acylvinyl anion equivalent, it cannot be used in the projected annelation chemistry in Scheme I. Second, due to severe problems in the ketalization of β-bromocyclopentenones,

Table II. Summary of Functionalizations of β-Bromocycloalkenone Dithioketals

entry	starting material	electrophile	n	R^1	R^2	% yield 
1	18	methyl iodide	2	H	CH_3	85 85
2	18	cyclohexanone	2	H		80 85
3	18	cyclopentanone	2	H		80 80
4	18	benzaldehyde	2	H		82 84
5	18	cyclohexenone	2	H		92 78
6	21	methyl iodide	1	H	CH_3	81
7	21	ethyl iodide	1	H	CH_2CH_3	79
8	21	cyclohexanone	2	H		90 86
9	21	cyclopentanone	1	H		75 81
10	21	benzaldehyde	1	H		82 81
11		methyl iodide	1	CH_3	CH_3	89
12		cyclohexanone	1	CH_3		79 79

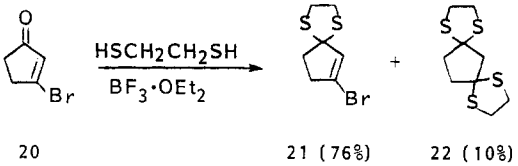
the chemistry (vide supra) does not serve to functionalize cyclopentenones.

Dithioketals can be formed under mild conditions, and it was hoped that β-bromocycloalkenones protected in this manner could partially alleviate the two problems noted above. When **4a** was treated with 1 equiv of ethanedithiol with boron trifluoride etherate as a catalyst, **18** was formed



4a 18 (90%) 19 (6%)

in 90% yield. This dithioketal is a colorless liquid which is stable for months when stored at 5 °C. The unrearranged structure **18** was assigned because the vinyl hydrogen appeared as a triplet (J = 1.5 Hz) instead of a heptet as was the case for **5a**. Furthermore, β-bromocyclopentenone **20** underwent smooth formation of the dithioketal **21** under standard conditions. In contrast to

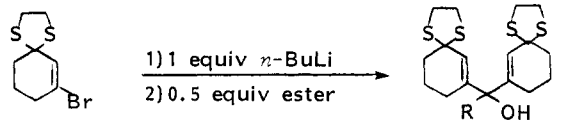


20 21 (76%) 22 (10%)

18, this material decomposes slowly at room temperature but can be stored without appreciable decomposition under nitrogen at 0 °C for days. Thus, the use of the dithioketal makes accessible two types of potential β-acylvinyl anion equivalents not available from the work described above.

The functionalization chemistry of the β-bromocycloalkenone dithioketals was carried out in the standard fashion: metal–halogen exchange at −78 °C followed by addition of the electrophile. The hydrolysis of the dithioketal function was performed by using a mixture of mercuric chloride and mercuric oxide in methanol/water or acetonitrile/water. The reactions of these lithiated dithioketals with our standard set of electrophiles showed good yields of products for both the five- and six-membered-ring systems (Table II).

Two functionalization reactions merit comment. First, when allyl bromide was used as the electrophile with the lithium reagent generated from **18**, the starting material **18** was the major dithioketal product. Apparently, allyl bromide suffers metal–halogen exchange rather than alkylation. Second, the bis addition reactions of the organolithium compound from **18** with ethyl formate and methyl benzoate were examined. In these cases, respectable yields of adducts **23** and **24** were formed. Nazarov-

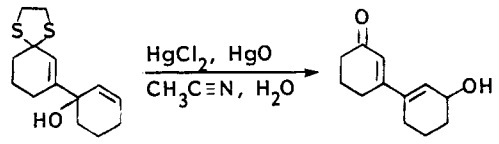


18

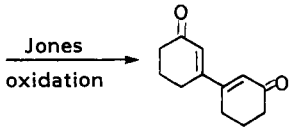
23, R = H (71%)
24, R = Ø (65%)

type cyclization of these systems could afford an entry into tricyclic systems of either the 6,5,6 or 5,5,5 arrangement.

As noted earlier, the hydrolysis product from the reaction of **5a** with cyclohexenone was assigned the rearranged structure **17**. Likewise, from the dithioketal **25**, hydrolysis afforded **17**. The structure **17** was supported by its UV [λ_{max} (CH_3OH) 278 nm] and ^{13}C NMR data which showed the hydroxyl-bearing carbon at 66.6 ppm as a doublet in its off-resonance spectrum. The other absorptions and their multiplicities which where discernible were 200.6 (s), 158.6 (s), 138.4 (s), 132. 8 (d), 124.4 (d), 37.5, 31.7, 26.0, 25.3, 22.6, and 19.4 ppm. That no basic skeletal rearrangement had occurred was established by oxidation of **17** to **26**. The diketone **26** showed, in addition to standard spectroscopic data, only six ^{13}C resonances indicative of a symmetrical structure.



25 17



26

Summary

The chemistry presented herein establishes that the organolithium species from protected β-bromocyclopentenones and cyclohexenones are viable equivalents of the corresponding β-acylvinyl anions. The parent β-bromocyclohexenone can be prepared on a reasonable scale (20–30 g) from commerically available 1,3-cyclohexanedione via a modification of the literature procedure.[15] Alkylation of the dione followed by conversion to the bromide makes 2-substituted systems such as **7** and **8** easily available also. In the five-membered-ring series, both 1,3-cyclopentanedione[16] and 2-methyl-1,3-cyclopentanedione[17] can be prepared via literature procedures. Conversion of these diones to the corresponding β-bromocyclopentenones and then to the dithioketals proceeds acceptably, making these systems available for preparation of functionalized cycloalkenones. The chemistry reported here affords an alternative to more conventional methods of β-substituted enone syntheses involving nucleophilic attack on a 1,3-diketone precursor. The problem of obtaining the required β-bromocycloalkenone regiospecifically from an unsymmetrical 1,3-dione has not been addressed and serves as a limitation in the use of this chemistry.

Experimental Section[18]

3-Bromocyclohex-2-en-1-one (4a). A 2-L, three-necked flask equipped with a mechanical stirrer and pressure-equalized dropping funnel was charged with 74.8 g (0.285 mol) of triphenylphosphine in 800 mL of benzene. To this cooled solution (ca. 5 °C) was added 46 g (0.285 mol) of bromine in 50 mL of benzene over a period of 1.5 h followed by the addition of 28.8 g (0.285 mol) of triethylamine. To this cooled solution was added 20.6 g (0.178 mol) of 1,3-cyclohexanedione (97%) in 250 mL of chloroform over a 1-h period. The resulting reaction mixture was stirred for 4 h at room temperature and then filtered through Celite. The filtrate was washed with water (100 mL), brine (100 mL), and dried (calcium sulfate). Removal of the solvent in vacuo gave a red-brown viscous liquid which was distilled to give 28 g (90%) of 3-bromocyclohexenone as a colorless liquid [bp 67–70 °C (0.5 mm)] which showed spectroscopic properties in agreement with those reported.[15]

Ketalization of 4a. A solution of 10 g (0.06 mol) of **4a**, 7.08 g (0.11 mol) of ethylene glycol, and 200 mg of *p*-toluenesulfonic acid monohydrate in 800 mL of benzene was refluxed for 4 h with azeotropic removal of water. The reaction was conveniently monitored by VPC (6 ft × 1/8 in. column of 5% SE-30 on 60/80 Chromosorb G at 120 °C) with the retention times in the following order: **4a**, **5a**, and then **6a**. The solution was washed with 5% sodium bicarbonate (100 mL) and brine (50 mL) and dried over calcium sulfate. Concentration gave 14 g of colorless liquid which was chromatographed on Activity II neutral alumina (5 × 20 cm column, 8–10% E/PE as eluant). Elution proceeded as follows: 0–125 mL, nil; 125–450 mL, 8.5 g (68%) of **5a** as a colorless liquid [IR (neat) 2955 (m), 2930 (m), 2882 (m), 1362 (m), 1337 (m), 1145 (m), 1118 (s), 1060 (s), 1023 (s), 950 (m), 852 (m)].

Elution was continued as follows: 450–750 mL, nil; 750–1000 mL, 2.1 g (17%) of **6a** as long needles, mp 62–63 °C [IR (KBr) 2955 (s), 2879 (s), 1232 (s), 1187 (s), 1108 (s), 1082 (vs), 1035 (s) 950 (s), 825 (s); NMR (CCl_4) 3.82 (s, 8 H), 1.72 (s, 2 H), 1.55 (br s, 6 H)].

Alternatively, the product can be distilled through a 5-in. Vigreux column [bp 80–83 °C (2.5 mm)] to give a 51% yield of a 95:5 mixture of **5a** and **6a** on a 20-g-scale ketalization.

Formation of 15. To a −78 °C solution of 200 mg (0.91 mmol) of **5a** in 10 mL of dry tetrahydrofuran was added dropwise 1.31 mL of 1.57 M *n*-butyllithium. The resulting solution was stirred at −78 °C for 0.5 h before quenching with 0.5 mL of deuterium oxide (99.8 atom % of D). A usual workup gave 120 mg of pale yellow liquid. This diene has a very short lifetime (~0.5 h) and decomposes on the silica gel column; thus, purification was carried no further: UV (CH_3OH) λ_{max} 267 nm (ε 3720); IR (neat) 3380 (s), 1636 (s), 1584 (s); NMR 5.34 (br s, 1 H), 4.87 (s, 1 H), 3.76 (s, 4 H), 3.03 (s, 1 H, OH), 2.24 and 2.21 (2 s, 4 H).

Functionalization of 5a (Table I). To a −78 °C solution of 1.44 g (6.6 mmol) of **5a** in 75 mL of dry tetrahydrofuran was added dropwise 9.1 mL of 1.59 M *n*-butyllithium (2.2 equiv). The resulting solution was stirred at −78 °C for 0.5 h (the color changed from a clear pink to brown and finally to a cloudy pale yellow suspension). The cyclohexanone (0.96 g, 9.8 mmol) was added, and the reaction mixture was stirred at −78 °C for 1 h and at room temperature for 1 h. After the reaction mixture was poured into 30 mL of 5% hydrochloric acid and after a standard workup, the crude product was filtered through a short silica gel column (2 × 15 cm column, 30% E/PE as eluant) to give after concentration 1.02 g (80%) of product alcohol, mp 50–51 °C.

For the remaining functionalizations of **5a**, the data below are given in the following order: electrophile (number of equivalents); eluant used in silica gel chromatography; physical state; spectroscopic data. Where no spectroscopic properties are given, they were identical with those previously reported.

Methyl iodide (2); 8% E/PE; liquid.[19]

Ethyl iodide (2.2); 8% E/PE; liquid.[20]

Trimethylsilyl chloride (2); 7% E/PE; liquid.[21]

Cyclohexanone (1.5); 30% E/PE; mp 50–51 °C (from ether/hexane); IR (KBr) 3450 (m, br), 2935 (m), 1650 (s); NMR (90 MHz, $CDCl_3$) 6.18 (s, 1 H), 2.77–1.33 (17 H with str m at 2.35 and br s at 1.62); ^{13}C NMR 200.8, 171.4, 123.2, 73.7, 37.6, 35.3, 25.5, 25.4, 23.2, 21.5.

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(18) All melting points were taken with a Thomas-Hoover capillary melting point apparatus and are uncorrected. Measurements of standard samples indicated that the observed melting points were probably 1–2 °C lower than the corrected value. Infrared spectra were recorded on a Perkin-Elmer Model 283B grating spectrometer and are reported in reciprocal centimeters. ^1H NMR spectra were taken at 60 MHz in CCl_4 with a Varian EM-360 and are reported in δ units unless noted otherwise. ^{13}C NMR spectra (Me_4Si reference) were recorded on a Bruker HX-90 instrument at 20 MHz in $CDCl_3$ by Mr. Carl Engelman. Mass spectra and exact mass measurements were obtained by Mr. C. R. Weisenberger on a Consolidated Electronic MS-9 double-focusing mass spectrometer. Analytical samples were determined by Scandinavian Microanalytical Laboratory. Aluminum oxide and silica gel were from E. Merck Co. Butyllithium in hexane (Ventron) was titrated in tetrahydrofuran with 1,10-phenanthroline as the indicator. A workup as usual refers to extraction with ether, washing of the ether layers with saturated brine solution, drying over calcium sulfate, and concentration in vacuo. In chromatography, E referes to ether and PE refers to petroleum ether, bp 35–50 °C. For the functionalization, the reaction flask was dried with a flame for approximately 1 min while being flushed with a stream of dry nitrogen. The system was then placed under a static nitrogen atmosphere, and reagents were introduced in dry tetrahydrofuran via syringe. All new compounds showed correct exact mass measurements (±0.0005) or acceptable combustion analyses.
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Cyclopentanone (1.1); 20–40% E/PE; viscous oil; IR (neat) 3500 (br, s), 2970 (s), 1658 (s); NMR 6.07 (s, 1 H), 2.62–1.47 (15 H with br s at 2.15 and s at 1.6); ^{13}C NMR 200.6, 169.4, 123.1, 83.7, 39.0, 37.6, 26.3, 24.1, 23.2.

Benzaldehyde (1.1); 20–50% E/PE; viscous oil; IR (neat) 3400 (s, br), 1660 (vs); NMR (90 MHz) 7.24 (s, 5 H), 6.13 (s, 1 H), 5.06 (br s, 1 H), 4.51 (OH, br s, 1 H), 2.38–1.61 (m, 6 H).

Carbon dioxide (excess); crystallized directly from methanol/water; mp 123–125 °C (lit.[22] mp 127–129 °C).

Cyclohex-2-enone (1.1); 2% methanol/chloroform; viscous oil; IR (neat) 3400 (br s), 2940 (s), 1660 (vs), 1584 (s), 1263 (s), 1187 (s), 750 (s); NMR (90 MHz) 6.21 (m, 1 H), 5.93 (s, 1 H), 4.23 (br s, 1 H), 3.64 (OH, br s, 1 H), 2.67–1.33 (highly structured m, 12 H); UV (CH_3OH) λ_{max} 278 nm (ϵ 28 560); ^{13}C NMR 200.6, 158.6, 138.4, 132.8, 124.4, 66.6, 37.5, 31.7, 26.0, 25.3, 22.6, 19.4.

3-Bromo-5,5-dimethylcyclohex-2-en-1-one (4b). In a manner similar to that described for the parent system, 5 g (35.7 mmol) of 5,5-dimethyl-1,3-cyclohexanedione (50 mL of chloroform), 14.9 g (57 mmol) of triphenylphosphine (200 mL of benzene), 9.13 g (57 mmol) of bromine, and 5.76 g (57 mmol) of triethylamine were reacted to give 6.03 g (83%) of the title compound, bp 83–85 °C (0.2 mm).[15]

Ketalization of 4b. A solution of 1.2 g (5.9 mmol) of **4b**, 0.73 g (11.4 mmol) of freshly distilled ethylene glycol, and 25 mg of *p*-toluenesulfonic acid monohydrate in 150 mL of benzene was heated to reflux for 23 h in an apparatus equipped with a Dean–Stark trap. The cooled reaction mixture was washed with 5% sodium bicarbonate (20 mL) and brine (10 mL), dried, and concentrated. The crude product was chromatographed on Fisher neutral alumina (Activity I) by using a 2 x 18 cm column with 8% E/PE as the eluant. Elution proceeded as follows: 0–100 mL, nil; 100–500 mL, 1.05 g (72%) of **5b** as a colorless liquid [IR (neat) 2957 (s,), 2920 (s), 2880 (s), 1355 (s), 1095 (s), 1032 (s); NMR (90 MHz) 5.73 (t, J = 1 Hz, 1 H), 3.91 (s, 4 H), 2.54 (s, 2 H), 1.59 (s, 2 H), 1.12 (s, 6 H)]. The reaction, when performed on a 5-g scale, gave a slightly lower yield (68%) of **5b**.

Functionalization of 5b (Table I). Methyl Iodide. To a solution of 500 mg (2.0 mmol) of **5b** in 15 mL of tetrahydrofuran was added dropwise 2.8 mL of 1.59 M *n*-butyllithium (2.2 equiv). The resulting solution was stirred at −78 °C for 2 h (solution turned cloudy), and then 0.63 g (2.2 equiv) of methyl iodide was added. A workup as for **5a** functionalization gave 400 mg of crude product which was filtered through a 2 × 15 cm silica gel column with 15% E/PE as the eluant to give 240 mg (86%) of 3,5,5-trimethylcyclohex-2-en-1-one, isophorone, as a colorless liquid which was identical with authentic sample.

Cyclohexanone. The reaction was performed as above by using 1.5 equiv of cyclohexanone to give the pure product by direct recrystallization: mp 94–95 °C; IR (KBr) 3420 (s), 2942 (s), 2920 (s), 1644 (vs), 1613 (s); NMR ($CDCl_3$, 90 MHz) 6.19 (s, 1 H), 2.28 and 2.20 (2 s, 4 H), 1.64 (br s with sh, 11 H), 1.04 (s, 6 H); ^{13}C NMR 200.9, 168.9, 122.2, 73.6, 51.2, 39.9, 35.0, 33.7, 28.1, 25.4, 21.4.

3-Bromo-2-methylcyclohex-2-en-1-one (7). A suspension of 5 g (39.6 mmol) of 2-methyl-1,3-cyclohexanedione and 2.50 mL of phosphorus tribromide (26.4 mmol) in 30 mL of chloroform was heated to reflux under nitrogen for 19 h. The resulting cooled reaction mixture was poured into 100 mL of ice–water and extracted with ether (2 × 75 mL). Workup and vacuum distillation gave 4.84 g (65%) of colorless liquid: bp 62–64 °C (0.2 mm);[15] IR (neat) 2947 (m), 1676 (s), 1620 (s), 1429 (m), 1334 (s), 1326 (s), 1279 (s), 1190 (m), 1037 (m), 967 (m), 896 (m); NMR 2.84 (m, 2 H), 2.59–2.00 (m, 4 H), 1.88 (t, J = 1.5 Hz, 3 H); ^{13}C NMR 195.4, 146.9, 136.7, 37.7, 37.4, 23.0, 15.7.

Ketalization of 7. A solution of 2 g (10.6 mmol) of **7**, 1.31 g (22.2 mmol) of ethylene glycol, and 45 mg of *p*-toluenesulfonic acid monohydrate in 300 mL of benzene was heated to reflux under a Dean–Stark trap. The reaction, monitored by VPC (7 ft × $^1/_8$ in. column, 5% SE-30 on Chromosorb G at 150 °C), showed only **7** and **9**. A peak corresponding to a bisketal was barely discernible. After 21 h of reaction (~5% **7** remaining), the cooled reaction mixture was washed with saturated sodium bicarbonate (20 mL) and brine (20 mL) and worked up as usual. The resulting crude product was purified by passage through a 3.5 × 28 cm column of silica gel with 6% E/PE as the eluant to give 2.04 g (83%) of **9** as a colorless liquid: IR (neat) 2947 (s), 2879 (s), 1292 (s), 1177 (s), 1147 (s), 1102 (s), 1071 (s), 1048 (s), 1018 (s), 947 (s), 926 (s); NMR 3.98 (s, 4 H), 2.48 (m, 2 H), 1.72 (m, 7 H); ^{13}C NMR 134.0, 127.4, 108.1, 65.3, 36.6, 33.5, 21.6, 16.3.

Functionalization of 9 (Table I). Cyclohexanone. To a solution of 400 mg (1.72 mmol) of **9** in 10 mL of tetrahydrofuran at −78 °C was added dropwise 1.19 mL of 1.58 M *n*-butyllithium (1.88 mmol). This solution was stirred for 30 min, and then 252 mg (2.6 mmol) of cyclohexanone was added. The resulting solution was stirred at −78 °C for 2 h and then at room temperature for 1 h. The reaction mixture was quenched with 10 mL of 5% hydrochloric acid and extracted with ether (2 × 50 mL). A workup as usual gave a viscous oil which was filtered through a 2.5 × 17 cm column of silica gel with 15% E/PE as the eluant to give 283 mg (80%) of white solid: mp 74–76 °C (recrystallized from ether/petroleum ether); IR (KBr) 3374 (s, br), 2948 (s), 2930 (s), 1649 (vs), 1308 (m); NMR (90 MHz) 2.75 (br s, 1 H), 2.1–2.6 (m, 4 H), 2.05–1.40 [1.96 (s) and 1.72 (br s) in a broad absorption, 15 H]; ^{13}C NMR 200.7, 162.5, 131.7, 75.6, 37.6, 34.8, 28.3, 25.4, 22.4, 21.4, 13.4.

The other functionalizations summarized below were performed similarly. The data are summarized in the following order: electrophile (number of equivalents); eluant used in silica gel chromatography; physical state; spectroscopic properties or literature reference if compound is known.

Methyl iodide (2); 5% E/PE liquid.[23]

Cyclopentanone (1.5); 20% E/PE; mp 33–35 °C (petroleum ether); IR (KBr) 3440 (m, br), 2957 (m), 1652 (s); NMR ($CDCl_3$) 2.82–2.15 (str m, 6 H), 1.88 (m, 12 H); ^{13}C NMR 200.6, 160.5, 132.4, 84.8, 39.7, 37.5, 29.9, 23.8, 22.5, 13.2.

Cyclohex-2-en-1-one (1.5); 20% E/PE; mp 89–91 °C (hexane); IR (KBr) 3492 (s, br), 1654 (vs); NMR ($CDCl_3$) 5.83 (m, 2 H), 2.76–1.56 (m, 16 H); ^{13}C NMR (multiplicity in off-resonance spectrum) 200.5 (s), 162.5 (s), 131.6 (d), 130.7 (s), 130.0 (d), 72.5 (s), 37.8 (t), 33.8 (t), 28.0 (t), 24.6 (t), 22.7 (t), 18.1 (t), 12.5 (q).

2-*n*-Propyl-1,3-cyclohexanedione. A mixture of 5.0 g of 2-allyl-1,3-cyclohexanedione[24] and 0.2 g of 5% Pd/C in 100 mL of methanol at 30 psi for 15 min gave an uptake of 1 equiv of hydrogen. The reaction mixture was filtered through Celite, and the filtrate was concentrated in vacuo. Recrystallization of the residue from ether/methanol gave 4.5 g (89%) of white flakes, mp 131–133 °C (lit.[24] mp 135–137 °C).

3-Bromo-2-*n*-propylcyclohex-2-en-1-one (8). A mixture of 4.3 g (28 mmol) of the dione from above and 7.56 g (28 mmol) of phosphorus tribromide in 40 mL of chloroform was refluxed under nitrogen for 2 h. A workup as for **7** gave 3.90 g (65%) of **8** as a colorless liquid: bp 85–90 °C (1 mm); IR (neat) 2957 (s), 1677 (vs), 1613 (s), 1286 (s), 1276 (s); NMR 2.88 (t, J = 5.4 Hz, 2 H), 2.60–1.87 (m, 6 H), 1.73–1.17 (m, 2 H), 0.92 (t, J = 6.5 Hz, 3 H).

Ketalization of 8. A solution of 2 g (9.2 mmol) of **8**, 2.28 g (36.9 mmol) of ethylene glycol, and 150 mg of *p*-toluenesulfonic acid monohydrate was refluxed under a Dean–Stark trap for 36 h. The VPC analysis (7 ft × $^1/_8$ in. column of 5% SE-30 on Chromosorb G, 150 °C) showed the presence of 10% unreacted starting bromoenone and ~13% of bisketal. A standard workup procedure gave ca. 2 g of crude product which was chromatographed on a 2.5 × 30 cm silica gel column (6% E/PE). Elution proceeded as follows: 0–150 mL, nil; 150–250 mL, 1.45 g (65%) of bromo ketal **10** as colorless liquid; IR (KBr) 2955 (s), 2870 (m), 1177 (m), 1108 (s), 1072 (s), 1022 (s), 832 (s); NMR 3.93 (s, 4 H), 2.53 (m, 2 H), 2.28–1.20 (m, 8 H), 0.90 (t, J = 6 Hz, 3 H).

Functionalization of 10. To a solution of 400 mg (1.53 mmol) of **10** in 5 mL of tetrahydrofuran at −78 °C was added 1.07 mL of 1.58 M *n*-butyllithium. The clear solution was stirred at −78 °C for 1 h and then warmed to 0 °C for 5 min. After the mixture was recooled to −78 °C, 189 mg (1.9 mmol) of cyclohexanone was added. The reaction mixture was stirred at −78 °C for 3 h and at room temperature for 1 h and then worked up as for the

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functionalization of **9**. The crude oil was chromatographed on a 2.5 × 18 cm silica gel column with 15% E/PE as the eluant. Elution proceeded as follows: 0–150 mL, nil; 150–230 mL, 0.06 g of an unidentified compound; 230–450 mL, nil; 450–730 mL, 218 mg (60%) of product alcohol as a white solid, mp 56.5–57.5 °C (recrystallized from hexane) [IR (KBr)[25,26] 3418 (s), 2950 (s), 2930 (s), 2863 (m), 2855 (m), 1660 (s), 1642 (s), 1586 (m), 970 (m); NMR 2.67–2.07 (m, 6 H), 2.07–0.83 (m, 18 H); ^{13}C NMR 200.4, 161.9, 136.9, 75.7, 38.0, 35.3, 29.3, 28.4, 25.2, 23.9, 23.3, 22.4, 21.3, 14.6].

Ketalization of 11. A solution of 1 g (5.7 mmol) of **11**,[15] 0.17 g (11.4 mmol) of ethylene glycol, and 25 mg of *p*-toluenesulfonic acid monohydrate in 150 mL of benzene was heated to reflux under a Dean–Stark trap for 45 h. VPC analysis (7 ft × $^1/_8$ in. column, 5% SE-30 on 60/80 Chromosorb G at 120 °C) showed only ca. 25% reaction to monoketal with the peak presumed to be the corresponding bisketal increasing with time. A usual workup (e.g., **7**) gave 0.80 g of an oil which was chromatographed on a 2.5 × 20 cm silica gel column with 8% E/PE as the eluant. Elution proceeded as follows: 0–50 mL, nil; 50–130 mL, 226 mg (18%) of **12** as a colorless liquid [IR (neat) 2952 (m), 2920 (m), 2882 (m), 1317 (s), 1281 (m), 1259 (m), 1152 (s), 1060 (s), 1035 (m), 1012 (m), 980 (m), 972 (m), 947 (m), 913 (s); NMR 3.90 (s, 4 H), 2.58 (m, 2 H), 2.03 (m, 2 H), 1.62 (t, J = 2 Hz, 3 H)].

Functionalization of 12 with Cyclohexanone. In a manner similar to that used for **7**, 100 mg (0.46 mmol) of **12** was reacted with cyclohexanone to afford after filtration through silica gel (2 × 10 cm column, 20–50% E/PE as eluant) 60.3 mg (68%) of **16** as a white solid: mp 65–66 °C (recrystallized from ether/hexane); IR (KBr) 3368 (m, br), 2950 (m), 2938 (m), 2850 (m), 1682 (s), 1621 (m), 1174 (m); NMR 2.93 (br s, 1 H), 2.48 (m, 2 H), 2.18 (m, 2 H), 1.67 (m, 13 H).

Thioketalization of 4a. A mixture of 5.48 g (31.3 mmol) of **4a**, 3.24 g (34.4 mmol) of 1,2-ethanedithiol, 1.0 mL of boron trifluoride etherate, and 5 g of 4A molecular sieves in 250 mL of chloroform was stirred at room temperature under nitrogen for 4 h. The reaction mixture was filtered, and the filtrate was washed with saturated sodium bicarbonate (2 × 50 mL) and brine (20 mL) and dried over calcium sulfate. Removal of the solvent in vacuo left ca. 8 g of crude liquid which was chromatographed on a 5 × 17 cm silica gel column. Elution with 4% E/PE gave 0–150 mL, nil; 150–490 mL, 7.10 g (90.3%) of bromo dithioketal **18** as colorless liquid which solidified on standing in the freezer: IR (neat) 2922 (s), 1631 (s), 1427 (s), 1349 (m), 1276 (s), 1002 (s), 844 (s), 710 (s), 620 (s); NMR (90 MHz) 6.11 (t, J = 1.5 Hz, 1 H), 3.32 (s, 4 H), 2.42 (m, 2 H), 2.02 (m, 4 H).

Elution was continued as follows: 490–550 mL, nil; 550–750 mL, 0.49 g (6%) of bisthioketal as white needles, mp 154–155 °C [IR (KBr) 2930 (s), 2916 (sh, s), 1440 (m), 1423 (m, br), 1274 (m); NMR ($CDCl_3$) 3.28 (s, 4 H), 2.72 (s, 2 H), 1.93 (br s, 4 H)].

In a larger run (10 g, 0.057 mol of **4a**), the crude product was directly distilled [135–137 °C (0.7 mm)] to give 11 g (77%) of colorless bromo dithioketal. The bisthioketal remained in the pot as the residue.

Functionalization of 18 (Table II). Methyl Iodide. To a solution of 400 mg (1.6 mmol) of **18** in 10 mL of tetrahydrofuran at −78 °C was added dropwise 1.1 mL of 1.58 M *n*-butyllithium. The reaction mixture was stirred at −78 °C for 30 min, and then 340 mg (2.4 mmol) of methyl iodide was added. The resulting reaction mixture was stirred for 2 h at −78 °C and at room temperature for 1 h before it was quenched with 10 mL of brine solution. A usual workup gave 280 mg of pale yellow oil which was filtered through silica gel (2.5 × 10 cm column, 3% E/PE as the eluant) to give 251 mg (85%) of product as a colorless liquid: IR (neat) 2921 (s), 2858 (s), 2817 (s), 1450 (s), 1435 (s), 1426 (s), 1274 (s), 1168 (m), 881 (s), 831 (s); NMR ($CDCl_3$) 5.60 (br s, 1 H), 3.35 (s, 4 H), 2.38–1.5 (2 s at ~1.85 and 1.68 in a broad absorption, 9 H).

A mixture of 200 mg (1.08 mmol) of the dithioketal, 1.19 g (4.3 mmol) of mercuric chloride, 350 mg (1.62 mmol) of mercuric oxide in 20 mL of methanol, and 5 mL of water was refluxed for 3 h. The cooled reaction mixture was filtered, the filtrate concentrated, and then the reaction mixture worked up as usual. The crude product was filtered through silica gel (5% E/PE as the eluant) to give 101 mg (85%) of 3-methylcyclohex-2-en-1-one as a colorless liquid which showed spectroscopic properties identical with those of an authentic sample.[19]

The remaining functionalizations and hydrolyses were performed in a manner similar to that above. The pertinent data are summarized in the following form: electrophile (number of equivalents); purification method for dithioketal; spectroscopic properties; hydrolysis conditions for dithioketal; purification method of functionalized ketone; spectroscopic properties or reference of functionalized ketone.

Cyclohexanone (1.5); crystallization from E/PE at low temperature, mp 61–63 °C; IR (KBr) 3450 (m, br), 2941 (s), 2921 (s), 2848 (m); NMR ($CDCl_3$) 5.90 (br s, 1 H) 3.33 (s, 4 H), 2.35–1.33 (m, overlapping with s at 1.58, 17 H); stirred at room temperature for 24 h; crystallized from E/PE to give product identical with that reported earlier.

Cyclopentanone (1.5); silica gel chromatography (8% E/PE as the eluant), oil; IR (neat) 3404 (m, br), 2936 (s), 2870 (m), 2837 (m), 1452 (m), 1436 (m), 1429 (m), 1275 (m), 999 (m), 837 (m); NMR 5.75 (s, 1 H) 3.28 (s, 4 H), 2.4–1.51 (m, with s at 1.8, 15 H); heated at reflux for 3 h; preparative TLC on silica gel (50% E/PE as the eluant) to give a product identical with that reported earlier.

Benzaldehyde (1.5); silica gel chromatography (8% E/PE as the eluant), oil; IR (neat) 3495 (s, br), 2918 (s), 1452 (m), 1275 (m), 1037 (s), 1020 (s), 700 (s); NMR ($CDCl_3$) 7.29 (s, 5 H), 6.05 (s, 1 H), 5.02 (s, 1 H), 3.33 (s, 4 H), 2.49 (br s, 1 H), 2.11 (m, 2 H), 1.74 (m, 4 H); heated at reflux for 3 h; silica gel chromatography as previously described, showing properties identical with those of an authentic sample.

Cyclohex-2-enone (1.2); low-temperature crystallization, mp 77–79 °C (this adduct is quite acid labile and must be stored in a base-washed flask at 0 °C); IR (KBr) 3435 (s, br), 2930 (s), 1050 (m), 1035 (m); NMR ($CDCl_3$, 90 MHz) 5.82 (m, 2 H), 5.53 (appears to be the higher field half of an AB q, $J \approx 7$ Hz, 1 H), 3.33 (s, 4 H), 2.43–1.43 (str m, 13 H); ^{13}C NMR 143.5, 131.5, 130.8, 126.8, 72.5, 65.7, 41.5, 40.0, 35.1, 25.1, 23.3, 23.1, 19.0; stirred at room temperature (CH_3CN/H_2O) for 12 h; preparative TLC on silica gel (10% $CH_3OH/CHCl_3$) to give a product identical with that reported earlier.

Methyl benzoate (0.5); recrystallization from petroleum ether, mp 133–135 °C; IR (KBr) 3508 (br, m), 2926 (s), 2860 (m), 2840 (m), 1446 (m), 1280 (m), 1156 (m), 1016 (m), 892 (m), 758 (m), 704 (s), 611 (m); NMR ($CDCl_3$) 7.28 (s, 5 H), 5.65 (br s, 2 H), 3.30 (s, 8 H), 2.3–1.7 (m, 13 H).

Ethyl formate (0.5); recrystallization from petroleum ether, mp 129–131 °C dec; IR (KBr) 3442 (s, br), 2960 (s), 2890 (m), 2867 (m), 1448, (m), 1430 (m), 1285 (m), 1069 (m), 1042 (m), 894 (m); NMR ($CDCl_3$, 90 MHz) 5.86 (s, 2 H), 4.31 (s, 1 H), 3.35 (s, 8 H), 2.24 (m, 4 H), 1.82 (s, 9 H); ^{13}C NMR 138.4, 128.4, 78.2, 65.1, 41.8, 41.4, 40.0, 23.3, 22.7.

3-Bromocyclopent-2-en-1-one (20). A mixture of 3.4 g (34.7 mmol) of 1,3-cyclopentanedione and 18.8 g (69.4 mmol) of phosphorus tribromide in 50 mL of chloroform was heated to reflux under nitrogen for 22 h. A workup as for **7** gave 3.20 g (57%) of **20** as colorless liquid; IR (neat) 3932 (m), 1718 (vs), 1584 (vs), 1436 (s), 1405 (m), 1253 (s), 1236 (s), 1164 (s), 966 (s), 846 (s), 810 (s); NMR 6.38 (t, J = 2 Hz, 1 H), 2.98 (m, 2 H), 2.58 (m, 2 H).

Dithioketalization of 20. A mixture of 2 g (12.4 mmol) of 3-bromocyclopent-2-en-1-one, 1.46 g (15.5 mmol) of 1,2-ethanedithiol, 0.3 mL of boron trifluoride etherate, and 4 g of 4A molecular sieves in 50 mL of chloroform was stirred under nitrogen for 2 h. The reaction mixture was filtered, and the filtrate was worked up as for **18**. Chromatography on a 3.5 × 25 cm column of silica gel with 6% E/PE as the eluant gave in the first 210 mL 2.24 g (76%) of **21** as a white solid: mp 64–65 °C dec (recrystallized from ether/petroleum ether); IR (KBr) 2922 (w), 1599 (s), 1439 (m), 1415 (s), 1313 (m), 1273 (m), 1234 (m), 1204 (m), 1095 (m), 1020 (m), 965 (m), 857 (s), 842 (s), 768 (m); NMR 5..83 (t, J = 1.5 Hz, 1 H), 3.27 (s, 4 H), 2.65 (br s, 4 H).

Continued elution gave 0.30 g (10%) of the bisdithioketal **22** as a white solid: mp 62–63 °C (recrystallized from ether); IR (KBr) 2958 (s), 2918 (s), 2835 (w), 1420 (s), 1274 (s), 1241 (w), 1215 (w), 1190 (w), 1172 (w), 970 (m), 950 (m), 847 (m), 838 (m); NMR 3.25 (s, 8 H), 2.82 (s, 2 H), 2.35 (s, 4 H).

(25) The splitting of the carbonyl absorption of some simple cyclic cycloalkenones in the IR spectrum has been discussed.[26]

(26) Noack, K.; Jones, R. N. *Can. J. Chem.* **1961**, *39*, 2201–2213.

Functionalization of 21 (Table II). This chemistry and the subsequent hydrolyses were performed as described for 8. The pertinent data are summarized in the following form: electrophile (equivalents); purification method for dithioketal; spectroscopic properties; hydrolysis conditions for dithioketal; purification method for functionalized ketone; spectroscopic properties or reference of functionalized ketone.

Methyl iodide (2); preparative TLC on silica gel (10% E/PE as the eluant), liquid; IR (neat) 2963 (s), 2920 (s), 2842 (s), 1648 (m), 1446 (m, br), 1275 (m), 986 (m), 968 (m), 840 (m), 822 (m); NMR 5.33 (m, 1 H), 3.22 (s, 4 H), 2.43 (m, 4 H), 1.75 (s, 3 H).

Ethyl iodide (1.5); chromatography on silica gel with 5% E/PE as the eluant, liquid; IR (neat) 2967 (s), 2924 (s), 2877 (s), 2822 (s), 1640 (m), 1460 (m), 1444 (m), 1430 (m), 1422 (m), 1274 (m), 845 (m); NMR ($CDCl_3$) 5.43 (m, 1 H), 3.30 (s, 4 H), 2.48 (m, 4 H), 2.08 (q, J = 7 Hz, 2 H), 1.05 (t, J = 7 Hz, 3 H).

Cyclohexanone (1.2); chromatography on silica gel with 15% E/PE as the eluant, mp 72–74 °C (ether/petroleum ether); IR (KBr) 3475 (s, br), 2937 (s), 2918 (s), 1447 (m), 1439 (m), 1271 (m), 1260 (m), 1180 (m), 1173 (m), 1133 (m), 983 (m), 964 (m); NMR ($CDCl_3$, 90 MHz) 5.64 (dist t, $J \approx 1.5$ Hz, 1 H), 3.33 (s, 4 H), 2.53 (s, 4 H), 1.72 (m, 11 H); ^{13}C NMR 151.8, 128.9, 74.1, 71.1, 45.0, 40.5, 36.3, 30.6, 25.6, 21.8; heated under reflux for 3 h; low-temperature recrystallization from ether/petroleum ether, mp 75–76 °C dec; IR (KBr) 3477 (s, br), 2942 (s), 2922 (s), 1701 (s, sh), 1675 (vs), 1600 (vs), 1178 (s), 1155 (s), 862 (s); NMR ($CDCl_3$) 6.12 (t, J = 1.5 Hz, 1 H), 2.68 (m, 2 H), 2.42 (m, 2 H), 2.08 (s, 1 H), 1.67 (br, s, 10 H); ^{13}C NMR 210.0, 187.8, 127.9, 72.5, 36.1, 35.4, 27.3, 25.3, 21.4.

Cyclopentanone (1.5); preparative TLC with 30% E/PE as the eluant, mp 58–60 °C (ether/hexane); IR (KBr) 3285 (s, br), 2963 (s, br), 2938 (s, br), 2862 (m), 2844 (m), 1275 (m), 1200 (m), 1190 (m), 1102 (m), 1021 (m), 862 (m), 845 (m); NMR ($CDCl_3$, 90 MHz) 5.66 (br s, 1 H), 3.34 (s, 4 H), 2.56 (s, 4 H), 1.78 (br s, 9 H); heated under reflux for 3 h; preparative TLC on silica gel with 50% E/PE as the eluant, liquid; IR (CCl_4) 3400 (m, br), 2952 (m), 1710 (s), 1680 (s), 1607 (m), 1438 (m), 1213 (m), 1176 (m); NMR (90 MHz) 5.83 (t, $J \approx 1.5$ Hz, 1 H), 3.54 (br s, 1 H), 2.76 (m, 2 H), 2.31 (m, 2 H), 1.83 (br s, 8 H).

Benzaldehyde (1.5); chromatography on silica gel with 15% E/PE as the eluant, oil; IR (neat) 3490 (s, br), 2918 (s), 2842 (m), 1494 (m), 1454 (m), 1423 (m), 1275 (m), 1211 (m), 1022 (m), 908 (m), 730 (m), 698 (s); NMR 7.25 (s, 5 H), 5.77 (m, 1 H), 5.17 (br s, 1 H), 3.27 (s, 4 H), 2.7–2.0 (m, 5 H); heated under reflux for 3 h; low-temperature recrystallization from ether/petroleum ether; mp 72–74 °C; IR (KBr) 3440 (s, br), 3400 (s, br), 1700 (sh, s), 1672 (vs), 1616 (s), 1607 (s), 1240 (m), 1182 (m), 1126 (m), 690 (s); NMR ($CDCl_3$) 7.25 (s, 5 H), 6.20 (m, 1 H), 5.45 (br s, 1 H), 3.30 (br s, 1 H), 2.37 (m, 4 H); ^{13}C NMR 209.4, 181.6, 140.5, 129.1, 128.8, 126.7, 74.9, 35.2, 27.9.

Dithioketalization of 3-Bromo-2-methylcyclopent-2-en-1-one. This was performed as for **20** except the reaction time was 46 h. Purification by silica gel chromatography gave the dithioketal (81%) as a colorless liquid: IR (neat) 2960 (m), 2916 (s), 2847 (m), 1649 (s), 1449 (m), 1432 (s), 1420 (s), 1373 (s), 1306 (s), 1277 (s), 1227 (m), 973 (s), 953 (s), 773 (m); NMR 3.26 (s, 4 H), 2.76 (s, 4 H), 1.83 (br s, 3 H).

Functionalization of 3-Bromo-2-methylcyclopent-2-en-1-one Dithioketal. The functionalization and hydrolyses were performed similarly to those of **18**. The data are summarized as for **18**.

Methyl iodide (1.3); molecular distillation at 0.8 mm with a bath temperature of 60 °C, liquid; IR (neat) 2957 (s), 2917 (s), 2845 (s), 1445 (m), 1430 (m), 1420 (m), 1376 (m), 1274 (m), 956 (m); NMR 3.21 (s, 4 H), 2.34 (m, 4 H), 1.67 (br s, 6 H).

Cyclohexanone (1.5); chromatography on silica gel with 20% E/PE as the eluant, mp 83–85 °C (ether/petroleum ether); IR (KBr) 3427 (m, br), 2920 (s), 2843 (m), 958 (m); NMR ($CDCl_3$) 3.31 (s, 4 H), 2.40 (s, 4 H), 2.02 (s, 3 H), 1.58 (br s, 11 H); heated under reflux for 3 h; crystallization with ether/petroleum ether to give a white solid showing spectra identical with those reported (vide supra).

Conversion of 25 to 26. A mixture of 130 mg (0.48 mmol) of **25**, 585 mg (1.94 mmol) of mercuric chloride, and 157 mg (0.73 mmol) of mercuric oxide in 15 mL of acetonitrile and 10 mL of water was stirred under nitrogen at room temperature for 3 h. A usual workup afforded 75 mg (80%) of viscous oil **26** (NMR spectrum is identical with that of the authentic sample obtained from the ethylene glycol route). This oil was then dissolved in 10 mL of acetone, treated with 2 equiv of Jones reagent, and stirred at room temperature for 30 min. The reaction mixture was then filtered, and the filtrate was concentrated. The crude product was purified by preparative TLC (10% $CH_3OH/CHCl_3$) to give 60 mg (81%) of **26** as a white solid: mp 88–90 °C; IR (KBr) 2950 (m), 1661 (vs), 1636 (m), 1575 (m), 1416 (m), 1329 (m), 1262 (m), 1187 (m), 1145 (m); ^1H NMR ($CDCl_3/Me_4Si$, 90 MHz) 6.26 (t, J = 2 Hz, 2 H), 2.44 (m, 8 H), 2.08 (m, 4 H); ^{13}C NMR 199.6, 156.6, 128.0, 37.5, 29.5, 22.3; UV (CH_3OH) λ_{max} 285 nm (ϵ 2874), calcd[14] λ_{max} 293 nm.

Registry No. 4a, 56671-81-9; **4b**, 13271-49-3; **5a**, 81036-84-2; **5b**, 81036-85-3; **6a**, 177-77-5; **6b**, 24770-68-1; **7**, 56671-83-1; **8**, 81770-68-5; **9**, 81770-69-6; **10**, 81770-70-9; **11**, 56671-87-5; **12**, 81770-71-0; **13**, 81770-72-1; **15**, 81770-73-2; **16**, 81770-74-3; **17**, 81770-75-4; **18**, 81770-76-5; **19**, 7490-36-0; **20**, 51865-32-8; **21**, 81770-77-6; **22**, 81770-78-7; **23**, 81770-79-8; **24**, 81770-80-1; **25**, 81770-81-2; **26**, 76995-53-4; 1,3-cyclohexanedione, 504-02-9; methyl iodide, 74-88-4; ethyl iodide, 75-03-6; trimethylsilyl chloride, 75-77-4; cyclohexanone, 108-94-1; cyclopentanone, 120-92-3; benzaldehyde, 100-52-7; carbon dioxide, 124-38-9; cyclohex-2-enone, 930-68-7; 5,5-dimethyl-1,3-cyclohexanedione, 126-81-8; 2-methyl-1,3-cyclohexanedione, 1193-55-1; 2-allyl-1,3-cyclohexanedione, 42738-68-1; methyl benzoate, 93-58-3; ethyl formate, 109-94-4; 1,3-cyclopentanedione, 3859-41-4; 3-bromo-2-methylcyclopent-2-en-1-one dithioketal, 81770-82-3; 3-methyl-2-cyclohexen-1-one, 1193-18-6; 3-ethyl-2-cyclohexen-1-one, 17299-34-2; 3-(trimethylsilyl)-2-cyclohexen-1-one, 66085-04-9; 3-(1-hydroxycyclohexane-1-yl)-2-cyclohexen-1-one, 81036-89-7; 3-(1-hydroxycyclopentone-1-yl)-2-cyclohexen-1-one, 81036-90-0; 3-(α-hydroxybenzyl)-2-cyclohexen-1-one, 81036-91-1; 3-oxo-1-cyclohexene-1-carboxylic acid, 24079-79-6; 3,5,5-trimethyl-2-cyclohexen-1-one, 78-59-1; 5,5-dimethyl-3-(1-hydroxycyclohexane-1-yl)-2-cyclohexen-1-one, 81036-93-3; 2,3-dimethyl-2-cyclohexen-1-one, 1122-20-9; 2-methyl-3-(1-hydroxycyclohexane-1-yl)-2-cyclohexen-1-one, 81770-83-4; 2-methyl-3-(1-hydroxycyclopentane-1-yl)-2-cyclohexen-1-one, 81770-84-5; 2-methyl-3-(1-hydroxy-2-cyclohexen-1-yl)-2-cyclohexen-1-one, 81770-85-6; 2-propyl-3-(1-hydroxycyclohexane-1-yl)-2-cyclohexen-1-one, 81770-86-7; 7-methyl-1,4-dithiaspiro[4.5]dec-6-ene, 76793-92-5; 7-(1-hydroxycyclohexane-1-yl)-1,4-dithiaspiro[4.5]dec-6-ene, 81770-87-8; 7-(1-hydroxycyclopentane-1-yl)-1,4-dithiaspiro[4,5]dec-6-ene, 81770-88-9; 7-(α-hydroxybenzyl)-1,4-dithiaspiro[4.5]dec-6-ene, 81770-89-0; 7-methyl-1,4-dithiaspiro[4.4]non-6-ene, 76793-90-3; 7-ethyl-1,4-dithiaspiro[4.4]non-6-ene, 81770-90-3; 7-(1-hydroxycyclohexane-1-yl)-1,4-dithiaspiro[4.4]non-6-ene, 81770-91-4; 7-(1-hydroxycyclopentane-1-yl)-1,4-dithiaspiro[4.4]non-6-ene, 81770-92-5; 7-(α-hydroxybenzyl-1,4-dithiaspiro[4.4]non-6-ene, 81770-93-6; 6,7-dimethyl-1,4-dithiaspiro[4.4]non-6-ene, 81770-94-7; 6-methyl-7-(1-hydroxycyclohexane-1-yl)-1,4-dithiaspiro[4.4]non-6-ene, 81770-95-8; 3-(1-hydroxy-2-cyclohexen-1-yl)-2-cyclohexen-1-one, 81770-96-9; 3-(1-hydroxycyclohexane-1-yl)-2-cyclopenten-1-one, 81770-97-0; 3-(1-hydroxycyclopentane-1-yl)-2-cyclopentane-1-one, 81770-98-1; 3-(α-hydroxybenzyl)-2-cyclopenten-1-one, 81770-99-2; 2-propyl-1,3-cyclohexanedione, 54244-73-4.