(d), 51.93 (d), 53.41 (d), 90.49 (d), 115.42 (d), 120.48 (d), 129.30 (d), 158.10 (s); mass spectrum (70 eV), m/e (relative intensity) 368 (molecular ion, 23.9), 275 (100.0).

Anal. Calcd for $C_{26}H_{24}O_2$: M_r 368.1776. Found (high-resolution mass spectrometry): M_r 368.1771.

Further elution of the chromatography column afforded dimer ketone **5a** as a colorless microcrystalline solid. Repeated recrystallization from hexane afforded pure **5a** (885 mg, 11%) as a colorless microcrystalline solid: mp 138 °C; IR (KBr) 1714 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 2.0–2.2 (m, 2 H), 2.8–3.6 (m, 6 H), 4.1 (s, 1 H), 4.2 (s, 1 H), 6.0–6.3 (m, 4 H), 6.7–7.4 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 42.44 (d), 45.13 (d), 48.29 (d), 49.29 (d), 49.95 (d), 50.93 (d), 57.35 (d), 58.51 (d), 86.00 (d), 89.32 (d), 114.66 (d), 115.43 (d), 121.15 (d), 121.29 (d), 129.37 (d), 129.55 (d), 133.20 (d), 133.91 (d), 134.19 (d), 136.28 (d), 156.29 (d), 156.73 (d), 220.29 (s); mass spectrum (70 eV), m/e (relative intensity) 396 (molecular ion, 1.6), 303 (18.8), 275 (3.0), 91.0 (100.0).

Anal. Calcd for $C_{27}H_{24}O_3$: M_r 396.1726. Found (high-resolution mass spectrometry): M_r 396.1711.

Reaction of 3a with $Fe_2(CO)_9$. To a solution of **3a** (3.5 g, 19 mmol) in dry benzene (100 mL) under nitrogen was added iron enneacarbonyl (6.9 g, 19 mmol). The resulting mixture was refluxed under nitrogen with stirring for 72 h and then was cooled to room temperature, and a solution of ferric chloride hexahydrate (10.5 g, 39 mmol) in acetone (75 mL) was added. The resulting mixture was stirred under nitrogen at room temperature for 7 days and then was concentrated in vacuo. The residue was partitioned between ether (100 mL) and water (100 mL). The aqueous layer was extracted sequentially with ether (3 × 100 mL) and ethyl acetate (3 × 100 mL). The combined extracts were dried (anhydrous magnesium sulfate) and filtered, and the filtrate was concentrated in vacuo. The residue was purified via elution chromatography on Florosil by using a 3%–30% ethyl acetate–hexane gradient elution scheme. Cage dimer **4a** (44 mg, 13%) and dimer ketone **5a** (1.10 g, 31%) were thereby obtained.

Reaction of 3b with $Fe_2(CO)_9$. To a solution of **3b** (1.7 g, 8 mmol) in dry benzene (50 mL) under nitrogen was added iron enneacarbonyl (2.9 g, 8 mmol). The resulting mixture was refluxed under nitrogen with stirring for 72 h and then was cooled to room temperature, and a solution of ferric chloride hexahydrate (4.6 g, 17 mmol) in acetone (30 mL) was added. The resulting mixture was stirred under nitrogen at room temperature for 7 days and then was concentrated in vacuo. Workup was performed in the manner described above for the corresponding reaction of **3a** with $Fe_2(CO)_9$. The crude product was purified via elution chromatography on Florisil by using a 3%–30% ethyl acetate–hexane gradient elution scheme. After a forerun of unreacted **3b** (950 mg, 56%), cage dimer **4b** (50 mg, 2.9%) was collected as a colorless microcrystalline solid: mp 246–248 °C; IR (KBr) 2210 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 2.60 (br s, 6 H), 2.73 (s, 2 H), 2.87 (br s, 4 H), 4.96 (s, 2 H), 6.90–6.95 (m, 6 H), 7.57–7.65 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 48.45 (d), 49.12 (d), 50.88 (d), 51.12 (d), 51.77 (d), 53.11 (d), 90.63 (d), 103.62 (s), 115.79 (d), 119.30 (s), 133.91 (d), 161.74 (s).

Anal. Calcd for $C_{26}H_{24}O_2$: M_r 418.1681. Found (high-resolution mass spectrometry): M_r 418.1666.

Further elution of the chromatography column afforded dimer ketone **5b** (105 mg, 6.2%) as a colorless microcrystalline solid. Repeated recrystallization from ethyl acetate–hexane afforded pure **5b** as a colorless microcrystalline solid: mp 197–199 °C; IR (KBr) 2200 (m), 1710 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 2.05–2.25 (m, 2 H), 2.73–2.80 (m, 1 H), 3.05–3.14 (m, 2 H), 3.23–3.32 (m, 2 H), 3.38–3.45 (m, 1 H), 4.15 (s, 1 H), 4.20 (s, 1 H), 6.06–6.30 (m, 4 H), 6.70–7.60 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 42.15 (d), 44.90 (d), 48.05 (d), 48.99 (d), 49.76 (d), 50.43 (d), 56.84 (d), 58.10 (d), 86.10 (d), 89.20 (d), 104.71 (s), 104.98 (s), 115.43 (d), 115.65 (d), 118.82 (s), 118.88 (s), 131.34 (d), 133.15 (d), 133.84 (d), 134.09 (d), 134.16 (d), 136.18 (d), 159.54 (s), 160.19 (s), 219.09 (s).

Anal. Calcd for $C_{27}H_{24}O_3$: M_r 446.1631. Found (high-resolution mass spectrometry): M_r 446.1653.

Reaction of 3b with $Fe(CO)_5$. To a solution of **3b** (3.0 g, 14 mmol) in freshly distilled di-*n*-butyl ether (30 mL) under nitrogen was added $Fe(CO)_5$ (5.6 g, 28 mmol), and the mixture was refluxed under nitrogen with stirring for 72 h. The reaction mixture was cooled to room temperature, and a solution of ferric chloride hexahydrate (15 g, excess) in acetone (75 mL) was added. The resulting mixture was stirred at room temperature for 7 days. Distilled water (100 mL) was added, and the mixture was extracted with ethyl acetate (7 × 100 mL). The combined extracts were washed with water (100 mL), dried (anhydrous magnesium sulfate), and filtered, and the filtrate was concentrated in vacuo. The residue was purified via elution chromatography on Florisil by using a 3%–30% ethyl acetate–hexane gradient elution scheme. The only products thereby obtained were *p*-cyanophenol (mp 110–112 °C, undepressed upon admixture with authentic *p*-cyanophenol, 600 mg, 36%) and a small amount of cage dimer **4b** (40 mg, 1.3%).

Control Experiment. Reaction of 2b with $FeCl_3$–Acetone. To a solution of **2b** (60 mg, 0.28 mmol) in acetone (20 mL) was added ferric chloride hexahydrate (300 mg, excess), and the resulting mixture was stirred at room temperature for 7 days. The progress of the reaction was monitored periodically by thin-layer chromatographic (TLC) analysis. The reaction mixture was concentrated in vacuo, and the residue was partitioned between ethyl acetate (25 mL) and water (25 mL). The layers were separated, and the organic layer was extracted with 10% aqueous sodium hydroxide solution (25 mL). The aqueous layer then was extracted with ethyl acetate (25 mL), and the organic layer was discarded. The aqueous layer was acidified by gradual addition of concentrated hydrochloric acid solution and then was extracted with ethyl acetate (25 mL). The organic layer was dried (anhydrous magnesium sulfate) and filtered, and the filtrate was concentrated in vacuo. The residue was purified by passage through a short silica gel column and eluted with 20% ethyl acetate–hexane mixed solvent. Pure *p*-cyanophenol (8 mg, 24%), identical in all respects with a sample of authentic material, was thereby obtained as colorless needles: mp 108–109 °C.

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Improved Synthesis of 3,4-Disubstituted Furans: Use of Phase-Transfer Conditions

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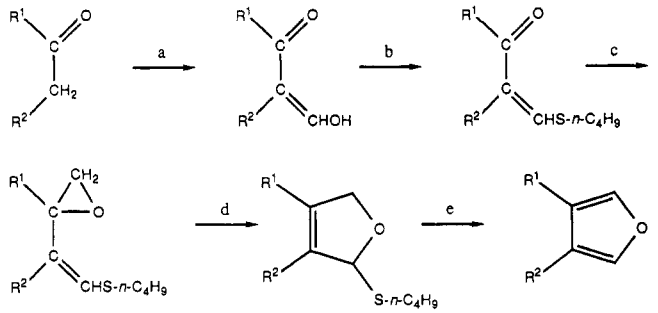
In the course of work toward the total synthesis of a natural product containing a 3,4-disubstituted furan, we have realized the utility of a new reagent and reaction conditions for the preparation of this type of compound. This methodology advances the general method for the preparation of 3,4-disubstituted furans reported by Garst in 1973.[1] The methodology described herein is cheaper, does not necessitate the use of anhydrous solvents and strong organic bases, and does not require low reaction temperatures.

The central step in the Garst sequence (Scheme I) is formation of a vinyl oxirane from treatment of an *S*-butyl-α-thiomethylene ketone with a nonstabilized sulfur ylide prepared from trimethylsulfonium fluoroborate[2] and *n*-butyllithium in dimethoxyethane at −78 °C. Trimethylsulfonium iodide under similar conditions was described as unsuitable; this was found to be the case in our hands as well.[3] However, formation of simple oxiranes

(1) Garst, M. E.; Spencer, T. A. *J. Am. Chem. Soc.* **1973**, *95*, 250.
(2) The fluoroborate salt is not commercially available and requires expensive precursors for its preparation.

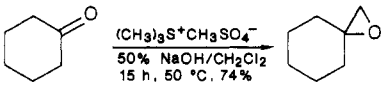
0022-3263/89/1954-2777$01.50/0

Scheme I[a]



[a] (a) $NaOCH_3$, C_2H_5OCHO, THF; (b) n-C_4H_9SH, p-TsOH, C_6H_6, Δ; (c) $CH_2{=}S(CH_3)_2$, DME; (d) 24 h, room temperature; (e) $HgSO_4$, Et_2O.

under much more convenient phase-transfer conditions using trimethylsulfonium methylsulfate (**1**) was the subject of a recent publication by Mosset (eq 1).[4]



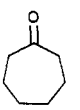
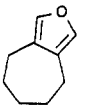
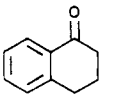
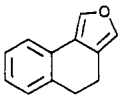
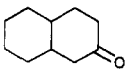
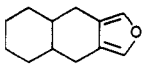
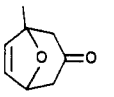
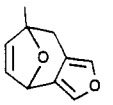
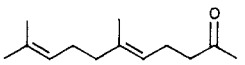
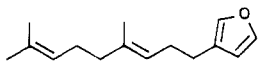
(1)

Our interest was sparked concerning the utility of these conditions for making oxiranes of α-thiomethylene ketones. Our only concern was the possible hydrolysis of the α-thiomethylene function with strong inorganic base, although we felt that base-catalyzed hydrolysis was much less likely to occur under phase-transfer conditions than might otherwise be the case.[5]

Our initial reactions were performed on the α-thiomethylene derivative of cycloheptanone. After workup and concentration, NMR analysis showed the presence of the oxirane, which rearranged upon standing at room temperature. After 24 h the material was stirred with dilute hydrochloric acid in THF to induce aromatization to the furan. The latter was obtained essentially free of side products; the only other major component of the mixture was unreacted starting material, as was the case in Garst's work. Similar observations with several additional ketones gave comparable results, with one exception. The α-thiomethylene derivative of geranylacetone, which is converted satisfactorily to 3-geranylfuran upon reaction with the sulfonium tetrafluoroborate,[1] gives only low yields of furan via the phase-transfer procedure. The poor mass balance in this case is consistent with increased sensitivity of the substrate to the potentially hydrolytic reaction conditions.

Yields of various furans prepared under these phase transfer conditions are listed in Table I. In general the reaction involves reflux of a solution of 1 mmol of the α-thiomethylene ketone in 1 mL dichloromethane in the presence of 1.4 mmol of **1** and 0.5 mL of 50% sodium hydroxide for 42 h.[6] After workup the crude oil is left at room temperature for 24 h and then dissolved in 1.0 mL of THF and stirred with 0.5 mL of 2 N HCl for 3 h at room temperature. After standard workup the furan is isolated by column chromatography on silica gel. Starting material is also recovered in this fashion. In the case of α-tetralone, the low conversion to product is substantially improved by addition of excess sulfonium salt (five 0.3-equiv portions) over a 30-h period beginning 4 h after the start of the reaction.

Table I

ketone	furan	yields,[a] %
		35 (65)
		26 (84), 56[b]
		59 (69)
		42 (53)
		21 (29)

[a] Yields are for conversion of S-butyl-α-thiomethylene ketone to furan. Values in parentheses corrected for recovered starting material. [b] $(CH_3)_3S^+CH_3SO_4^-$ (**1**) added in portions (see text).

Experimental Section

General. Solvents were used as received; all reactions were carried out under an argon atmosphere. Preparation of the S-butyl-α-thiomethylene ketones corresponding to cycloheptanone, α-tetralone, 2-decalone, geranylacetone, and 1-methyl-8-oxabicyclo[3.2.1]oct-6-en-3-one[7] followed the Garst procedures.[1]

Representative Procedure for Transformation of *S*-Butyl-α-thiomethylene Ketones into 3,4-Disubstituted Furans. To a solution of 1.0 mmol of ketone in 1.0 mL of dichloromethane was added 0.27 g (1.4 mmol) of **1** and 0.5 mL of 50% aqueous NaOH. The stirred mixture was heated to 48 °C for 42 h. The layers were separated, and the aqueous layer was extracted with 3 × 1 mL of diethyl ether. The organic layers were combined, washed with water and brine, dried over Na_2SO_4, and evaporated giving a yellow oil, which was allowed to stand at room temperature for 24 h. The material was taken up into 1 mL of tetrahydrofuran and stirred with 0.5 mL of 2 N HCl for 3 h at room temperature. The mixture was saturated with $CaCO_3$, the layers were separated, and the aqueous portion was extracted with 3 × 1 mL of ether. The organic layers were combined, washed with water and brine, dried over Na_2SO_4, and evaporated to give a mixture of product and unreacted starting material. Separation by flash chromatography (5:95 ether/hexane) yielded the pure materials (Table I).

4,5-Dihydronaphtho[1,2-*c*]furan. To 0.22 g (0.90 mmol) of 2-[(butylthio)methylene]-3,4-dihydro-1(2*H*)-naphthalenone in 2 mL of dichloromethane was added 0.17 g (0.90 mmol) of **1** and 1 mL of 50% aqueous NaOH, and the rapidly stirred two-phase mixture was heated to reflux. At the following times after start of reaction the indicated portions of **1** were added: 4 h, 0.053 g (0.28 mmol); 9.5 h, 0.044 g (0.26 mmol); 19 h, 0.052 g (0.28 mmol); 25 h 0.042 g (0.25 mmol); and 33 h, 0.042 g (0.25 mmol). At 19 h and at 33 h two to three additional drops of 50% aqueous NaOH were added. After a total reaction time of 43 h the mixture was cooled and worked up as above. Yield of purified furan: 0.086 g (56%). Only traces of unreacted starting material were isolated from later chromatographic fractions.

Acknowledgment. This work was supported by a grant from the National Institutes of Health (GM 26294).

(3) Tochterman reports use of trimethylsulfonium iodide under conditions first described by Corey. See: Tochterman, W.; Jessen, J. L.; Schröder, G. *Chem. Ber.* **1985**, *118*, 3287.

(4) Mosset, P.; Gree, R. *Synth. Commun.* **1985**, 749.

(5) Conditions for removal of the α-thiomethylene group when it is used to protect the α-carbon involve treatment with strong inorganic base in refluxing diethylene glycol: Ireland, R. E.; Marshall, J. A. *J. Org. Chem.* **1962**, *27*, 1615.

(6) The longer reaction times than those originally reported by Mosset (ref 4) are presumably the result of greater steric hindrance in these α-thiomethylene ketones.

(7) Sato, T.; Watanabe, M.; Noyori, R. *Tetrahedron Lett.* **1979**, 2897.