fast as an analytical HPLC analaysis and is completed within 5–15 min.

Experimental Section

The *n*-octadecyl-modified phases were prepared on an 100-g scale mainly according to ref 6. Thus 100 g of silica gel[11] was added to a solution of 10 g of *n*-octadecyltrichlorosilane[19] in dry carbon tetrachloride.[20] The mixture was shaken to produce a suspension and reacted for 2 h at room temperature. The reaction mixture was occasionally shaken.

The product was filtered off on a dry filter funnel and washed three times with 200 mL of carbon tetrachloride, two times with 200 mL of methanol, and two times with 200 mL of dichloromethane. The product was dried at 40 °C overnight.

The reaction procedure was repeated with 10 g of trimethylchlorosilane[19] dissolved in dry carbon tetrachloride followed by four washings with 200 mL of dichloromethane. The packing material was dried at 40 °C.

For the 15–40-μm material 20 g of each reagent was used. This was necessary for obtaining sufficient bonding and capping.

Acknowledgment. We thank Prof. Martin Nilsson for encouraging us in our work. The work was supported by grants from Stiftelsen Bengt Lundqvists Minne and the Swedish Council for Planning and Coordination of Research (Grant No. 81/2140).

Registry No. Benzene, 71-43-2; naphthalene, 91-20-3; biphenyl, 92-52-4; 1,3,5-trihydroxybenzene, 108-73-6; 1,2-dihydroxybenzene, 120-80-9; phenol, 108-95-2.

(19) Merck, Germany, and Fluka, Switzerland.

(20) Approximately 200–300 mL. Carbon tetrachloride and dichloromethane were of redistilled purum quality (Kebo-Grave, Sweden), and methanol was of HPLC quality (Fison, UK).

Short Synthesis of Bicyclo[3.2.2]nona-3,6,8-trien-2-one

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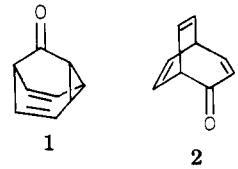
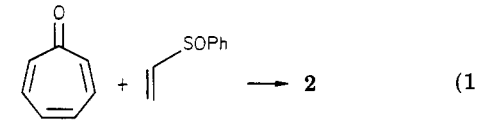
Compounds possessing the bicyclo[3.2.2]nonatrienyl skeleton continue to attract attention because they are important precursors for a wide range of theoretically interesting reactive intermediates[1] and provide access to a number of unique polycyclic molecules such as barbaralone (**1**) which exhibit fluxional behavior.[2,3]



1 **2**

To date, the parent bicyclo[3.2.2]nona-3,6,8-trien-2-one (**2**) has been most effectively prepared through a multistep sequence starting from tropylium fluoborate.[1a,3] An interesting alternative route to this valuable trienone is to exploit the well-established propensity of tropone for thermal [4 + 2] cycloaddition with a variety of dienophiles. This strategy has been previously used quite effectively for the construction of several substituted bicyclo[3.2.2]nonatrienone derivatives[4] but apparently has not been employed for preparation of the parent compound itself. The limited utility of acetylene as a dienophile is a major obstacle to such a strategy.

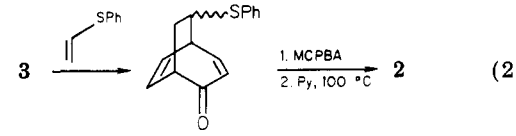
We report a short and relatively efficient synthesis of bicyclo[3.2.2]nona-3,6,8-trien-2-one (**2**) based on a variation of the thermal cycloaddition of the acetylene equivalent phenyl vinyl sulfoxide[5] with 2,4,6-cycloheptatrien-1-one (**3**)[6] (eq 1).



3 (1)

Initial attempts to affect the one-step cycloaddition–elimination reaction by using phenyl vinyl sulfoxide as the dienophilic partner with 2,4,6-cycloheptatrien-1-one (**3**) resulted in disappointingly low yields (10–12%) of trienone **2**. A variety of different conditions were examined in an effort to improve the yields of **2** but with little success.

Substantially better yields were realized when a sequential cycloaddition–oxidation–elimination protocol was employed (eq 2). Heating cycloheptatrienone in an excess



4 (2)

of phenyl vinyl sulfide[7] at 140 °C for several hours led in good yields to dienone **4**, which was then carefully oxidized to the corresponding sulfoxide with *m*-chloroperbenzoic acid (MCPBA). The resulting sulfoxide was heated at 100 °C in toluene containing 1.5 equiv of pyridine[5] for several hours to give the trienone **2** in overall yields as high as 32% from 2,4,6-cycloheptatrien-1-one.[8]

This sequence appears to be adaptable to reasonably large-scale runs. The product is easily isolated in its pure form since under these conditions there has been no evidence for the formation of 1-indanone, a major contaminent reported in previous preparations of trienone **2**.

Experimental Section

All reactions were performed under an atmosphere of dry N_2. Methylene chloride and toluene were freshly distilled from calcium hydride before use. The melting points were obtained on a Thomas-Hoover melting point apparatus and are uncorrected. The ^1H NMR spectra were obtained on a Varian T-60 (60 MHz) spectrometer with Me_4Si as the internal standard. The IR spectra were obtained on a Perkin-Elmer 283 B spectrophotometer and the mass spectra on a AEI MS-902 mass spectrometer. The C and H analyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, MI.

Preparation of 9-(Phenylthio)bicyclo[3.2.2]nona-3,6-dien-2-one (4). A mixture of 2,4,6-cycloheptatrien-1-one (**3**;[6] 9 g, 0.085 mol) and phenyl vinyl sulfide[7] (36 g) was heated at 140–150

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(8) Prolonged heating at higher temperatures resulted in substantially reduced yields of trienone **2**.

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°C for 12 h. The reaction mixture was cooled and the crude product isolated by flash chromatography on 300 g of silica gel 60 (230–400 mesh) first with hexane as the eluant to remove excess phenyl vinyl sulfide followed by 4:1 hexane/ether to isolate the product.[9] The resulting pale yellow oil was subsequently distilled (170 °C, 1 mm Hg,) to give a colorless oil: 12 g (70%); IR (CCl_4) 3050, 2950, 2860, 1675, 1640, 1580, 1450, 1260, 1150 cm^{-1}; NMR (CCl_4) δ 1.6–2.1 (m, 1 H), 2.3–2.8 (m, 1 H); 3.2–4.0 (m, 3 H), 5.6–7.2 (m, 4 H), 7.2–7.6 (m, 5 H); MS, *m/e* (relative intensity) 242 (17), 219 (4), 137 (4), 136 (100), 135 (52), 133 (55). Anal. Calcd for $C_{15}H_{14}OS$: C, 74.35; H, 5.82. Found: C, 74.44; H, 5.79.

Preparation of Bicyclo[3.2.2]nona-3,6,8-trien-2-one(1). To a solution of 9-(phenylthio)bicyclo[3.2.2]nona-3,6-dien-2-one (4; 12 g, 0.05 mol) in 50 mL of methylene chloride at −78 °C was added 80% *m*-chloroperbenzoic acid (10.7 g, 0.05 mol) in 50 mL of methylene chloride. The resulting mixture was stirred at this temperature for 45 min at which time the mixture was diluted with chloroform and washed with three 60-mL portions of saturated aqueous sodium bicarbonate solution and one 60-mL portion of saturated aqueous sodium chloride solution. The organic layer was dried over anhydrous sodium sulfate, and the solvent was removed in vacuo to give 16 g of crude sulfoxide which was used without further purification. The sulfoxide was dissolved in 25 mL of dry toluene containing 1.5 equiv of pyridine (10 mL), and the mixture was heated at 95–100 °C for 48 h. The resulting reaction mixture was cooled and purified by flash column chromatography on 150 g of silica gel 60 (230–400 mesh) with 10:1 pentane/ether as the eluant. The product was recrystallized from pentane to provide 3.5 g (32% from 2,4,6-cycloheptatrien-1-one) of pure trienone **2**; mp 43–44 °C (lit.[3] mp 44 °C). Alternatively, trienone **2** could be isolated in pure form by fractional distillation (75–80 °C, 1.5 mmHg) of the reaction mixture. The spectral and analytical properties of this material were shown to be identical in every respect (^1H NMR, IR, TLC, mixture melting point, mass spectrum) with those of trienone **2** prepared by known methods.[3]

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Institutes of Health (Grant GM-30771-01) for their support of this research.

Registry No. 1, 6006-24-2; 3, 539-80-0; 4, 86900-37-0; 4 sulfoxide, 86854-65-1; phenyl vinyl sulfide, 1822-73-7.

(9) Alternatively, the material could be purified by distillative removal of the excess phenyl vinyl sulfide followed by flash column chromatography of the residue on silica gel 60 with 4:1 hexane/ether as the eluant.

Improved Synthesis and Absolute Configuration of (+)- and (−)-2,2,4-Trimethyl-1,3-dioxolane-4-carboxaldehyde

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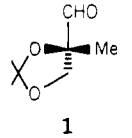
Received March 16, 1983

During the course of our ongoing investigations on the synthesis of bicyclomycin in optically active form,[1] it became necessary to prepare (*S*)-2,2,4-trimethyl-1,3-dioxolane-4-carboxaldehyde (**1**) as a means for introducing the C-1′–C-3′ polyoxo side chain with the correct absolute configuration. Preparation of (*R*)-**1** and racemic **1** has been



1

previously reported by two Hoffman-La Roche groups.[2,3] This protected aldehyde has been used in several total syntheses[4] and holds potential for being a useful chiral starting material for other synthetic targets.[5] Herein is reported a practical synthesis of both (+)- and (−)-**1**; the absolute configurations of which have been unambiguously confirmed by X-ray crystallographic analysis of a camphanyl ester derivative.

Results and Discussion

Our initial attempts to prepare useful quantities of both (*R*)- and (*S*)-**1** involved the resolution of the racemic alcohol precursor[6] **2**. Alcohol **2** was coupled with (−)-camphanyl chloride[7] (**3**) in pyridine to afford the diastereomeric esters **4** and **5** (Scheme I). These esters were separated by HPLC and hydrolyzed with $NaOCH_3$ in CH_3OH to afford the optically pure *R* and *S* alcohols **2**. Although large quantities of the esters **4** and **5** could be readily prepared, the separation proved to be feasible on a very small scale (HPLC) only; we were unable to find a practical large-scale chromatographic separation system.[8] Thus, for the purpose of preparing useful quantities of optically active **1**, we abandoned the resolution.

Both esters **4** and **5** were crystalline. A single-crystal X-ray structural determination was carried out on diastereomer **5**;[9] the structure thus established is exhibited in Figure 1. This structure unambiguously establishes the stereochemistry of the optically pure (−)-**2** as *S*.

We next turned our attention to an asymmetric synthesis of **1**. Sharpless'[10] asymmetric epoxidation of 2-methyl-2-propen-1-ol followed by the mercaptide ring opening/isopropylidination/oxidation sequence of Sharpless and Masamune[11] proceeded without incident to directly afford the optically pure aldehydes **1** (Scheme II). The aldehyde resulting from the (+)-tartrate-mediated epoxidation sequence possesses the expected *S*-configuration. Conversely, the (−)-tartrate-mediated epoxidation sequence provides (*R*)-**1**. The absolute configuration of the products was unambiguously correlated to the resolved alcohols **2** by $LiAlH_4$ reduction and comparison of optical rotation. From this data, it can be concluded that the

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(4) (a) Vitamin E, see ref 3. (b) Bicyclomycin rearrangement product, see ref 2. (c) *N,N,O*-trimethylbicyclomycin: Nakatsuka, S.; Yoshida, K.; Goto, T. *Tetrahedron Lett.* **1981**, *22*, 4973. (d) *N,N′*-Dimethyl-4-desmethylenebicyclomycin, see ref. 1a,b,d.

(5) The corresponding (*R*)- and (*S*)-glyceraldehyde acetonides have often been used as chiral intermediates in synthesis and are readily available from natural sources, see: Jung, M. E.; Shaw, T. J. *J. Am. Chem. Soc.* **1980**, *102*, 6304 and references cited therein.

(6) Calinaud, P.; Gelas, J. *Bull. Soc. Chim. Fr.* **1975**, 1228.

(7) The procedure used for the preparation of camphanyl chloride was furnished by Dr. Juergen Martens.

(8) Silica gel chromatography on column and PTLC did not effect separation. Small quantities (up to 50 mg) could be separated on an analytical HPLC but proved to be impractical on a preparative scale (see Experimental Section).

(9) A small (0.17 × 0.24 × 0.36 mm^3) crystal of **5** was orthorhombic (space group $p2_12_12_1$) with a = 7.458 (1) Å, b = 10.776 (2) Å, and c = 22.592 (5) Å. The 1015 observed ($I > 2\sigma(I)$) reflections (of 1408 unique reflections with 3.5° < 2θ < 45.0°) gave R = 0.047, R_w = 0.052, and the standard deviation in an observation of unit weight of 1.10 for a structural model that included anisotropic thermal parameters for all non-hydrogen atoms and hydrogen atoms included in idealized positions.

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