

made for differences in the stabilization energies of the organic radicals that are produced. Thus, the activation energy for desulfonation of $\text{CH}_3\dot{\text{S}}\text{O}_2$ is reported to be ca. 22.4 kcal/mol in the gas phase,^{23,24} which is consistent with our limiting value of ≤ 5 kcal/mol for $\text{C}_6\text{H}_5\text{CH}_2\dot{\text{S}}\text{O}_2$ since the methane-based stabilization energy^{26,27} of benzyl [$E_s^{\text{Me-H}}(\text{C}_6\text{H}_5\text{CH}_2\cdot) = D[\text{Me-H}] - D[\text{C}_6\text{H}_5\text{CH}_2\text{-H}]$] is 19 kcal/mol. Some additional activation energies which have been reported for $\text{R}\dot{\text{S}}\text{O}_2$ desulfonations also appear to be consistent with our result,²⁸ but others are clearly in error. We also note that a value of 12.0 ± 3.2 kcal/mol which has been estimated²⁹ for $D[\text{C}_6\text{H}_5\text{CH}_2\text{-}\dot{\text{S}}\text{O}_2]$ is both inconsistent with our present data and with a failure to detect this radical by EPR spectroscopy in solution at temperatures as low as 130 K.^{30,31} The rapid disulfonation of $\text{C}_6\text{H}_5\text{CH}_2\dot{\text{S}}\text{O}_2$ makes it a useful probe for laser flash photolytic investigation of various reactions which generate sulfonyl radicals from sulfonyl halides.³³

Finally, rate constants for the self-reactions of $\text{CH}_3\dot{\text{S}}\text{O}_2$, $\text{C}_2\text{H}_5\dot{\text{S}}\text{O}_2$, $\text{C}_6\text{H}_5\dot{\text{S}}\text{O}_2$, and the (2,5-dichlorophenyl)sulfonyl radical³⁴ were measured by kinetic EPR spectroscopy. The sulfonyl radicals, which were generated in an $\text{R}\text{SO}_2\text{Cl}/\text{Me}_3\text{COOCMe}_3/\text{Et}_3\text{SiH}/c\text{-C}_6\text{H}_6$ mixture (1:1:1:5, v/v) with the pulse from a nitrogen laser, decayed with clean second-order kinetics (reaction 6). At 223 K the values found



for $2k_6$ were in the range $(4.5 \pm 1.5) \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ for all four $\text{R}\dot{\text{S}}\text{O}_2$ radicals. Reaction 6 is clearly a diffusion-controlled process. Previous measurements of $2k_6$ in solution by time-resolved optical absorption spectroscopy^{9,35,36} have given rate constants which would imply that reaction 6 might be slightly slower than diffusion controlled. We attribute this discrepancy to uncertainties in the values used for the sulfonyl radicals' extinction coefficients in the optical kinetic work.

Experimental Section

All materials were commercial products that were carefully purified by standard procedures before use. The experimental procedures for the kinetic measurements by laser flash photolysis were identical with those employed to study other reactions of triethylsilyl radicals.¹⁰⁻¹² These radicals were generated by photolysis of di-*tert*-butyl peroxide in the presence of Et_3SiH ,

(22) Horowitz, A. *Int. J. Chem. Kinet.* 1976, 8, 709-723.

(23) Good, A.; Thynne, J. C. *J. Trans. Faraday Soc.* 1967, 63, 2708-2719.

(24) The data from which this activation energy was derived have been severely criticized.²⁵

(25) Calvert, J. G.; Slater, D. H.; Gall, J. W. In "Chemical Reactions in Urban Atmospheres"; Tuesday, C. S., Ed.; Elsevier: New York, 1971; pp 133-158.

(26) Davies, A. G.; Griller, D.; Ingold, K. U.; Lindsay, D. A.; Walton, J. C. *J. Chem. Soc., Perkin Trans. 2* 1981, 633-641.

(27) Dewar, M. J. S.; Fox, M. A.; Nelson, D. J. *J. Organomet. Chem.* 1980, 185, 157-181.

(28) See, e.g.: Good, A.; Thynne, J. C. *J. Trans. Faraday Soc.* 1967, 63, 2720-2727. Thoi, H. H.; Iino, M.; Matsuda, M. *Macromolecules* 1979, 12, 338-339.

(29) Busfield, W. K.; Ivin, K. J.; Mackle, H.; O'Hare, P. A. G. *Trans. Faraday Soc.* 1961, 57, 1064-1069.

(30) Chatgililoglu, C.; Gilbert, B. C.; Gill, B.; Sexton, M. D. *J. Chem. Soc., Perkin Trans. 2* 1980, 1141-1150.

(31) A radical, purported to be $\text{C}_6\text{H}_5\text{CH}_2\dot{\text{S}}\text{O}_2$ but with uncharacteristically large α -H hyperfine splitting, has been observed by EPR in the solid phase at room temperature.³²

(32) Geoffroy, M.; Lucken, E. A. C. *J. Chem. Phys.* 1971, 55, 2719-2723.

(33) Nazran, A. S.; Chatgililoglu, C.; Ingold, K. U., unpublished results.

(34) Chosen because the SO_2 moiety in this radical is in a locked conformation,⁵ whereas it rotates freely in the other three $\text{R}\dot{\text{S}}\text{O}_2$ radicals.^{5,6}

(35) Bjellqvist, B.; Reitberger, T. *Nucl. Sci. Abstr.* 1971, 30, 12.

(36) Komissarov, V. D.; Safiullin, P. L. *React. Kinet. Catal. Lett.* 1980, 14, 67-72.

and rate constants were determined at ambient temperatures (300 ± 3 K) in deoxygenated $\text{Me}_3\text{COOCMe}_3/\text{Et}_3\text{SiH}$ (1:1 v/v) as the solvent with benzil as the probe. The experimental procedures for the kinetic measurements by EPR spectroscopy were similar to those employed in the study of other bimolecular radical-radical self-reactions³⁷ except that the intermittent light source was the pulse from a nitrogen laser, rather than a mechanically chopped light beam from a high-pressure mercury lamp. Rate constants for sulfonyl radical decay were measured at 223 ± 1 K in a degassed mixture of the sulfonyl chloride, $\text{Me}_3\text{COOCMe}_3$, Et_3SiH , and cyclopropane (1:1:1:5 v/v), the radicals being generated in the cavity of a Varian E-4 EPR spectrometer.

Acknowledgment. We thank Drs. D. Griller, A. S. Nazran and J. C. Scaiano for helpful discussions.

Registry No. $\text{CH}_3\text{SO}_2\text{Cl}$, 124-63-0; $\text{C}_6\text{H}_5\text{SO}_2\text{Cl}$, 98-09-9; $\text{C}_6\text{H}_5\text{CH}_2\text{SO}_2\text{Cl}$, 1939-99-7; $\text{CH}_3\text{SO}_2\text{F}$, 558-25-8; *p*- $\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{F}$, 455-16-3; Et_3Si , 24669-77-0.

Supplementary Material Available: Tables II-VI giving detailed kinetic data for Table I (6 pages). Ordering information is given on any current masthead page.

(37) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* 1980, 13, 193-200 and references cited therein.

Preparative Reversed-Phase Flash Chromatography, a Convenient Method for the Workup of Reaction Mixtures

Thomas C. Kähler* and Göran R. Lindsten

Department of Organic Chemistry, Chalmers University of Technology and University of Gothenburg, S-41296 Gothenburg, Sweden

Received March 16, 1983

In this paper we describe a convenient chromatographic technique for routine purification of polar as well as of nonpolar organic compounds.

Reversed-phase high-performance liquid chromatography (HPLC) has found widespread application, and results are often satisfactory on an analytical scale. Preparative reversed-phase HPLC is more seldom used and often involves tedious and time consuming repetitive fraction collection.

In the course of the synthetic work we needed preparative reversed-phase HPLC. A few such systems have been described in the literature,^{1,2} while others are commercially available.³⁻⁵ However, these are often designed for special purposes and are slow or quite expensive.

Evans and co-workers have developed a method for the preparation of chemically bonded phases, especially *n*-octadecyldimethylsilyl modified phases suitable for HPLC.⁶ We have designed a convenient system for preparative separations on this type of stationary phases and observed factors of importance for the performance of reversed-phase flash chromatography (RPFC).⁷

(1) Gesellchen, P. D.; Tafur, S.; Shields, J.-E. *Pept., Struct. Biol. Funct., Proc. Am. Pept. Symp.*, 6th, 1979, 117.

(2) Crane, L. J.; Zeif, M.; Horvath, J. *Am. Lab. (Fairfield, Conn.)* 1981, 5, (13), 128.

(3) Ehlert, K.; Engler, R. *GIT Fachz. Lab.* 1979, 7, 659.

(4) Rabel, F. M. *Am. Lab. (Fairfield, Conn.)* 1980, 12 (10), 126.

(5) Baker, J. T. Chemical Co., Phillipsburg, NJ.

(6) Evans, M. B.; Dale, A. D.; Little, C. J. *Chromatographia* 1980, 13 (1), 5.

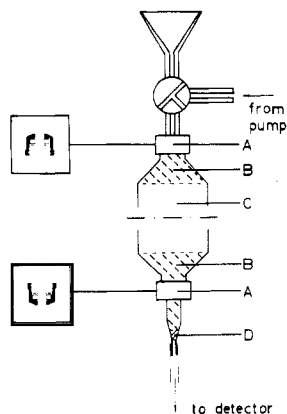


Figure 1. Column and injector of the RPFC system: A, Quickfit 13-mm screw-thread tube with screw cap, silicone rubber sealing ring, and PTFE washer; B, washed sea sand; C, reversed-phase packing material; D, cotton; injector, a 2-mm-bore three-way stopcock with a PTFE key; column diameter, 34 mm; column length (modified phase part), 125 mm; weight of packing material, 70 g.

The RPFC system consists mainly of three parts, a solvent pump,⁸ a column and injector, and a detector with recorder.⁹ The column-injector system¹⁰ (Figure 1) was designed with inexpensive, easily available components. The column was made from two ordinary screw-thread tubes, which were fused to a piece of glass tubing. The injector was made by fusing one outlet of a three-way stopcock to a small glass funnel. The two other outlets of the stopcock were connected to the column and to the pump with a solvent reservoir. The samples were applied by gravity flow.

The RPFC system has been investigated by regarding particle size¹¹ and the flow rate by studying the resolution (R),¹² the selectivity factor (α),¹² and the capacity factor (k').¹² Only *n*-octadecyl-modified phases were studied since they have been claimed to be the most useful.¹³

To check the quality of the prepared phases, conventional HPLC columns¹⁴ were dry packed, and their separating ability was measured with two different test mixtures,¹⁵ using a suitable water/methanol mixture as the eluting agent at a constant flow rate. On a preparative scale, columns were also dry packed⁷ and their efficiency studied by using the same test mixtures¹⁶ and eluents at different flow rates. New columns were conditioned with 200–300 mL of eluent,¹⁷ preferably 60–80% methanol in

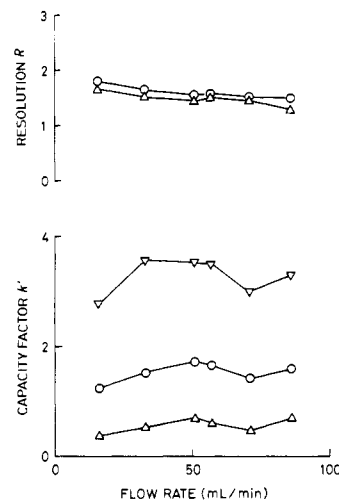


Figure 2. Plot of R and k' for the hydrophilic test mixture separated on the preparative column (40–63 μm). k' : Δ , 1,3,5-trihydroxybenzene; \circ , 1,2-dihydroxybenzene; ∇ , phenol. R : Δ , 1,3,5-trihydroxybenzene and 1,2-dihydroxybenzene; \circ , 1,2-dihydroxybenzene and phenol.

water. The pressure drops were typically between 0.2 and 1.3 MPa. All runs were performed at ambient temperature, e.g., 20 °C.

The 63–200- μm modified phase, though giving good peak shapes, yielded quite broad peaks and poor resolution on the analytical column and was thus omitted from the rest of the study.

On the analytical as well as on the preparative scale, the 40–63- μm modified phase yielded not only good peak shapes but also good resolution with both the hydrophilic and lipophilic test mixtures. As expected the 15–40- μm modified phase gave the best resolution and the narrowest peaks. It separated the components of both the mixtures with good peak shapes.

For each test mixture and modified phase the selectivity factor α was approximately constant throughout the whole flow-rate interval of 10–90 mL/min. The coefficient of variation¹⁸ for repeated measurements of α was less than 5%. For the 40–63- μm modified phase with the hydrophilic test mixture it was as high as 12%. The stability of the α value shows the robustness and reproducibility of the system.

In all cases the resolution obtained on the analytical columns was maintained on the preparative ones. A typical plot of R and k' against the flow rate is shown in Figure 2.

The system separated test mixtures up to a total weight of 500 mg. The maximum sample amount will be dependent on the α value, and gram quantities have been separated in some applications.

The capacity factor k' has two minima, the first at the lowest flow rate and the other at about 68 mL/min, corresponding to total eluting times of about 25 and 6 min, respectively.

The decrease in R with increasing flow rate is negligible. R is more influenced by a change in the mobile phase; e.g., R is increased with a higher water content in the eluent. This also applies to the k' value. The loss in speed at a higher k' value is outweighed by the gain in speed by the higher flow rate. In practical applications we used a flow rate of about 68 mL/min, corresponding to a linear flow rate of 7.5 cm/min, which is the same as in the analytical case. Hence, a complete preparative separation will be as

(7) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* 1978, 43 (14), 2923.

(8) Pump, Nikkiso Chemical Feeder BZ-10 equipped with a stainless-steel pump head and PTFE membrane; Puls dampener, 1-m PTFE tubing (i.d. 8 mm), NKS Kemipumpar, Kungsbacka, Sweden.

(9) Detector: LKB Uvicord, 254 nm, operating in transmittance.

(10) The cost of the column and injector was less than \$50.

(11) Particle sizes: 15–40, 40–63, and 63–200 μm ; Kieselgel 60, Merck, Germany.

(12) Defined as follows:

$$k' = (V_R - V_{\text{void}}) / V_{\text{void}} \quad \alpha = k'_{i+1} / k'_i$$

$$R = 2(V_{R_{i+1}} - V_{R_i}) / (w_i + w_{i+1})$$

where V_R = retention volume at peak maximum, V_{void} = void volume determined by eluting 1,3-dihydroxybenzene with methanol, and w = peak broadness at base line.

(13) Little, C. J.; Dale, A. D.; Evans, M. B. *J. Chromatogr.* 1978, 153, 381.

(14) Stainless steel, length 100 mm, and i.d. 4 mm.

(15) Lipophilic test mixture: benzene, naphthalene, and biphenyl. Hydrophilic test mixture: 1,3,5-trihydroxybenzene, 1,2-dihydroxybenzene, and phenol.

(16) The preparative runs were performed with 80, 30, and 30 mg, respectively, of the substances in a test mixture.

(17) Void volumes were between 70 and 90 mL.

(18) Defined as (standard deviation/mean value) \times 100%.

fast as an analytical HPLC analysis and is completed within 5-15 min.

Experimental Section

The *n*-octadecyl-modified phases were prepared on a 100-g scale mainly according to ref 6. Thus 100 g of silica gel¹¹ was added to a solution of 10 g of *n*-octadecyltrichlorosilane¹⁹ 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 trimethylchlorosilane¹⁹ 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- μ m 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).

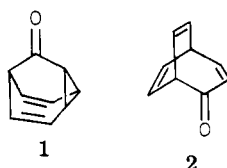
Short Synthesis of Bicyclo[3.2.2]nona-3,6,8-trien-2-one

James H. Rigby* and Jean-Marc Sage

Department of Chemistry, Wayne State University, Detroit,
Michigan 48202

Received January 25, 1983

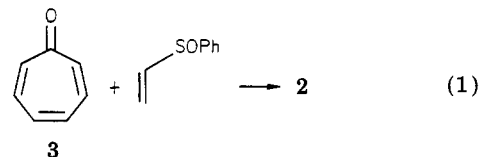
Compounds possessing the bicyclo[3.2.2]nonatrienyl skeleton continue to attract attention because they are important precursors for a wide range of theoretically interesting reactive intermediates¹ and provide access to a number of unique polycyclic molecules such as barbaralone (1) which exhibit fluxional behavior.^{2,3}



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

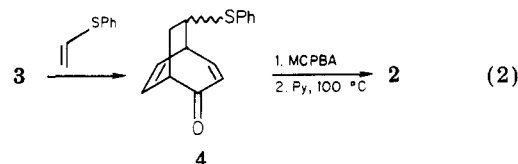
for the construction of several substituted bicyclo[3.2.2]nonatrienone derivatives⁴ but apparently has not been employed for preparation of the parent compound itself. The limited utility of acetylene as a dienophile is a major obstacle to such a strategy.

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 sulfoxide⁵ with 2,4,6-cycloheptatrien-1-one (3)⁶ (eq 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



of phenyl vinyl sulfide⁷ 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 pyridine⁵ 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 contaminant reported in previous preparations of trienone 2.

Experimental Section

All reactions were performed under an atmosphere of dry N₂. 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 Me₄Si 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 sulfide⁷ (36 g) was heated at 140-150

(4) (a) Ciabattoni, J.; Crowley, J. E.; Kende, A. S. *J. Am. Chem. Soc.* 1967, 89, 2778. (b) Kinstle, T. H.; Carpenter, P. D. *Tetrahedron Lett.* 1969, 3943. (c) Uyehara, T.; Funamizu, M.; Kitahara, Y. *Chem. Ind. (London)* 1970, 1500.

(5) Paquette, L. A.; Moerck, R. E.; Harirchian, B.; Magnus, P. D. *J. Am. Chem. Soc.* 1978, 100, 1597.

(6) Radlick, P. *J. Org. Chem.* 1964, 29, 960.

(7) (a) Boehme, H.; Bentler, H. *Chem. Ber.* 1956, 89, 1464. (b) Kirner, W. R.; Richter, G. H. *J. Am. Chem. Soc.* 1929, 51, 3409. (c) Ohno, A.; Ohnishi, Y.; Tsuchihashi, G. *Ibid.* 1969, 91, 5038.

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

(1) (a) Grutzner, J. B.; Winstein, S. *J. Am. Chem. Soc.* 1972, 94, 2200. (b) Freeman, P. K.; Swenson, K. E. *J. Org. Chem.* 1982, 47, 2040.

(2) Barborak, J. C.; Chari, S.; Schleyer, P. v. R. *J. Am. Chem. Soc.* 1971, 93, 5275.

(3) Goldstein, M. J.; Odell, B. G. *J. Am. Chem. Soc.* 1967, 89, 6356.