References and Notes

(1) K. B. Wiberg, *Adv. Alicyclic Chem.*, **2**, 185 (1968); P. G. Gassman and G. D. Richmond, *J. Am. Chem. Soc.*, **92**, 2090 (1970); H. K. Hall, Jr., E. P. Blanchard, Jr., S. C. Cherkofsky, J. B. Sieja, and W. A. Sheppard, *ibid.*, **93**, 110 (1971); H. K. Hall, Jr., C. D. Smith, E. P. Blanchard, Jr., S. C. Cherkofsky, and J. B. Sieja, *ibid.*, **93**, 121 (1971); L. A. Paquette, G. R. Allen, Jr., and M. J. Broadhurst, *ibid.*, **93**, 4503 (1971).

(2) M. Pomerantz and E. W. Abrahamson, *J. Am. Chem. Soc.*, **88**, 3970 (1966); M. D. Newton and J. M. Schulman, *ibid.*, **94**, 767 (1972).

(3) M. D. Newton and J. M. Schulman, *J. Am. Chem. Soc.*, **98**, 6295 (1974); J. M. Schulman and T. J. Venanzi, *Tetrahedron Lett.*, 1461 (1976); M. Pomerantz, R. Fink, and G. A. Gray, *J. Am. Chem. Soc.*, **98**, 291 (1976).

(4) K. B. Wiberg, G. M. Lampman, R. P. Ciula, D. S. Connor, P. Schertler, and J. Lanavish, *Tetrahedron*, **21**, 2749 (1965).

(5) G. Szeimies, University of Munich, paper at Chemiedozententagung, Regensburg on April 30, 1976, and private communication.

(6) M. Horner and S. Hünig, *J. Am. Chem. Soc.*, preceeding paper in this issue.

(7) Voltammetry and UV spectroscopy of **1c** and **1d** points to the same reaction cycle. However, preparative results[6] were not conclusive.

(8) DMF/tetrabutylammonium tetrafluoroborat (TBA·BF_4)/Pt vs. Ag/AgCl/AN.

(9) This reagent reduces even benzene, which is reduced at −3.3 V; cf. F. Gerson, H. Ohya-Nishiguchi, and C. Wydler, *Angew. Chem.*, **88**, 617 (1976); *Angew. Chem., Int. Ed. Engl.*, **15**, 552 (1976).

(10) W. R. Moore, S. S. Hall, and C. Largman, *Tetrahedron Lett.*, 4353 (1969).

(11) M. R. Rifi, *J. Am. Chem. Soc.*, **89**, 4442 (1967); *Tetrahedron Lett.*, 1043 (1969); A. J. Fry, *Topics Curr. Chem.*, **34**, 14 (1972).

(12) ECE: electron transfer/chemical step/electron transfer. Evaluation of $i_p v^{-1/2}/c^{-1}$ vs. *v* in DMF, AN, and DCM according to R. S. Nicholson and I. Shain, *Anal. Chem.*, **37**, 178 (1965). Peak potentials of **1a** and **2a** are independent of concentration. Slope of the Tafel plot is 113–125 mV. On reduction of **2a**, 2.0 and, by oxidation of **1c**, 1.9 electrons are transferred (DC comparison with **8c** (1.0 electron transfer)).

(13) AN = acetonitrile; DMF = dimethylformamide; DCM = dichloromethane; TBA·BF_4 = tetrabutylammonium fluoroborate.

(14) Proof of disproportionations by concentration dependent CV; cf. M. Mastragostino and J. M. Saveant, *Electrochim. Acta*, **13**, 751 (1968).

(15) S. Hünig, *Justus Liebigs Ann. Chem.*, **676**, 32 (1964); S. Hünig, H. Balli, H. Conrad, H. Friedrich, J. Gross, G. Kiesslich, G. Ruider, G. Sauer, and D. Scheutzow, *Pure Appl. Chem.*, **15**, 109 (1967).

(16) S. Hünig, J. Gross, and W. Schenk, *Justus Liebigs Ann. Chem.*, 324 (1973).

(17) D. Seebach in "Methoden der Organischen Chemie", Houben-Weyl-Müller, Vol. IV/4, Thieme, Stuttgart, 1971, p 1, and literature cited therein.

(18) Symmetry b_2, orbital coefficient at position 4 = 0.56 (HMO type calculations).

(19) S. Masamune, *Tetrahedron Lett.*, 945 (1965).

(20) S. Masamune, *J. Am. Chem. Soc.*, **86**, 735 (1964).

(21) R. B. Woodward and D. L. Dalrymple, *J. Am. Chem. Soc.*, **91**, 4612 (1969).

(22) M. Frank-Neumann, *Angew. Chem.*, **79**, 98 (1967); *Angew. Chem., Int. Ed. Engl.*, **6**, 79 (1967).

(23) Estimated from ionisation potentials: γ-picoline, 10.0 eV (D. W. Turner, C. Baker, A. D. Baker, and C. R. Brundle, "Molecular Photoelectron Spectroscopy", Wiley-Interscience, London, New York, Sidney, Toronto, 1970 pp 297, 334); bicyclobutane, 9.14 eV;[24] toluene, 8.82 eV.

(24) P. Bischof, R. Gleiter, and E. Müller, *Tetrahedron*, **32**, 2769 (1976); H.-D. Martin, unpublished results.

(25) Detailed discussion see M. Horner, Dissertation, University of Würzburg, 1977.

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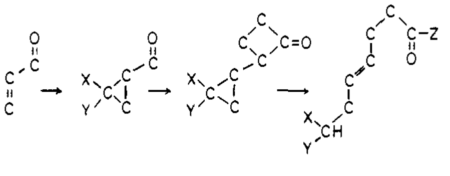
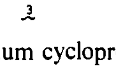
New Synthetic Reactions. Double Chain Extension

Sir:

We wish to report that carbon can function as a nucleofugal atom in the Grob fragmentation and consequently can allow chain extension of an α,β-unsaturated carbonyl system at both the carbonyl group and the β carbon as outlined in eq 1. Nucleophilically triggered ring opening of doubly activated cyclopropanes has generated a number of useful reagents and novel synthetic strategy.[1-4] The driving force provided by cleavage of cyclobutanone rings in secoalkylation,[5,6] when combined with the cyclopropanation of olefins, offers a unique opportunity to extend both termini of an α,β-unsaturated system where the two ends are differentially functionalized and the double bond is introduced stereo- and regioselectively between the carbonyl carbon and the α carbon of the starting enone.


(1)

In a fragmentation such as illustrated in eq 1, ~55 kcal/mol of strain energy is released. To ascertain how much of a driving force this provided, we attempted to cleave cyclobutanone (**1**) unsuccessfully by refluxing in methanolic sodium methoxide for 3.5 days. For comparison, epoxycyclobutanone (**2**) fragments in 10 min at room temperature.[7] On the other hand, the presence of a second substituent on the cyclopropane ring does lead to success.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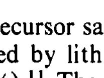
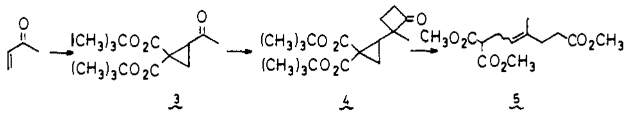
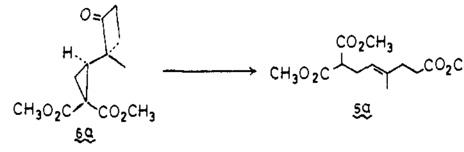
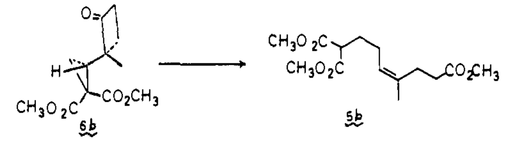

2

Addition of di-*tert*-butyl bromomalonate[8,9] to methyl vinyl ketone (KOC_4H_9-*t*, *t*-C_4H_9OH, 15 °C) gave the crystalline cyclopropane **3**, mp 51–53 °C.[10] Cyclobutanation to **4**[9] used diphenylsulfonium cyclopropylide (precursor salt, KOC_4H_9-*t*, Me_2SO, room temperature) followed by lithium fluoroborate) (PhH, room temperature, 82%).[11] The mixture of diastereomers of **4** was directly subjected to sodium methoxide in refluxing methanol which cleanly produced the *E* and *Z* isomers of fragmented product **5**[9] in 74% yield in which transesterification accompanied fragmentation.

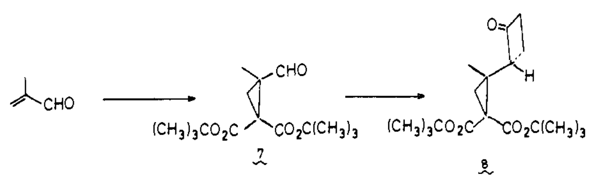

3 4 5

To determine the stereospecificity of the reaction, **4** was converted to its methyl esters (CF_3CO_2H, 0 °C, then CH_2N_2, ether) **6a**[9,12] and **6b**[9,12] which were separated by VPC.[13] Subjection of each pure isomer to the fragmentation reaction led to the correspondingly isomerically pure olefins **5a**[9,12] and **5b**[9,12] in 80 and 84% yields, respectively. The stereochemistry of the olefins follows from the higher field position of the protons and carbon of the vinyl methyl group in the *E* isomer **5a** (^1H NMR δ 1.64, ^{13}C NMR δ 15.9) compared to the *Z* isomer **5b** (^1H NMR δ 1.68, ^{13}C NMR δ 22.9).


6a 5a

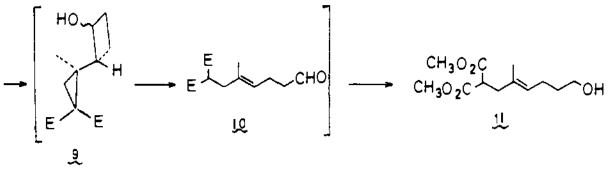

6b 5b

Having established the stereospecificity of the fragmentation, we endeavored to find a simple system in which cyclobutanone formation was highly stereocontrolled. Indeed, a single cyclobutanone was obtained from 2-methacrolein by first cyclopropanating ($BrCH(CO_2C_4H_9$-*t*$)_2$,$(CH_3)_2NC(=NH)N(CH_3)_2$, DMF, room temperature) to **7**,[9,14] mp 99–101.5 °C and then cyclobutanating with diphenylsulfonium cyclopropylide (precursor salt, KOH, Me_2SO, room temperature, then $LiBF_4$, PhH, room temperature) to **8**,[9,12] Both ^1H and ^{13}C NMR[12] and chromatography establish the stereo-

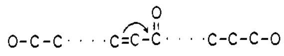


homogeneity of the cyclobutanone. Since use of different reaction conditions produced a mixture of cyclobutanones, we confirmed that these spectral tools do differentiate the isomers. The stereochemical assignment of **8** is based upon the stereochemistry of the olefin produced upon fragmentation and assuming the normal anti stereochemical course.

Direct treatment of **8** with methanolic base led to elimination via the enolate rather than fragmentation.[15] Reduction of ketone to the alcohol (i.e., **9**) precludes such problems. Indeed, treatment of **8** with a methanolic solution of recrystallized sodium borohydride and magnesium methoxide at 0 °C for 30 min and reflux for 40 h (to ensure complete transesterification) led cleanly (85%) to **11**.[9,12] The intermediate aldehyde **10** underwent reduction to the alcohol under these conditions. Spectral data[12] establishes the homogeneity of this compound and allows assignment of the *E* configuration as depicted (^{1}H NMR δ 1.60 (3H, s), 2.59 (2 H, d); ^{13}C NMR δ 15.6), whereas the mixture of olefin isomers obtained by fragmentation of the isomeric mixture of cyclobutanones shows the presence of the *Z* isomer (^{1}H NMR δ 1.68 (s), 2.66 (d); ^{13}C NMR δ 22.7) in addition to the *E* isomer. The ability of the alcohol to fragment cleanly bespeaks of the driving force provided by strain release.



This methodology allows the addition of a two carbon and three carbon unit both terminating in an oxygen functionality

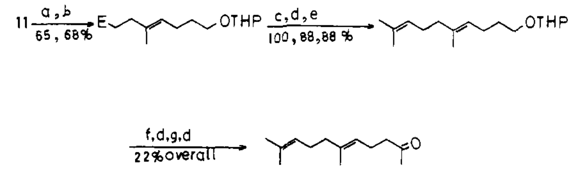


$$\mathrm{O{-}C{-}C \cdots C{=}C{-}\overset{O}{\overset{\|}{C}} \cdots C{-}C{-}C{-}O}$$

to the β and carbonyl carbons of an α,β-unsaturated system with regiospecific migration of the double bond to the position between the α and carbonyl carbons. Furthermore, this double bond can be formed with complete stereochemical control and the oxygen functionality at the two termini can be easily differentiated for selective manipulation. A flexible intermediate such as **11** can serve as a precursor to many acyclic terpene units (Scheme I). By standard methods, it can be elaborated at either end as was performed for conversion of **11** to pure (*E*)-geranylacetone. The comparison of our synthetic compound to an authentic sample further confirmed the stereochemical assignment of **11** as well as its stereohomogeneity.

Carbon leaving groups are relatively rare. As pointed out by Stirling,[16] leaving group ability decreases according to group of the periodic table to which the connecting atom belongs in the order group 6 > group 5 ≫ group 4. Indeed, in the comparison of fragmentation of **2**, **4**, and **1**, the relative rates of $\sim$1, $10^{-2.2}$, and $<10^{-4}$ verify this trend. On the basis of energetics in which the difference in pK_A of the conjugate acid of the leaving group is taken into account, fragmentation of **1** would be expected to be about 10 kcal/mol less exothermic than that of **2** in accord with their relative rates. In contrast, fragmentation of **4** could be expected to be 4 kcal/mol *more* exothermic than that of **2** in opposition to their relative rates. Thus, strain and stability of the resulting anion do not alone determine transition-state energies. One rationalization is the differential hydrogen bonding of the solvent to the nucleofuge. We believe this represents the first case of carbon serving as the nucleofugal group in a Grob fragmentation.[17] While the generality of such an observation remains to be established, these results do establish an upper limit to the type of carbon leaving group that is required. The possibility of this new type of leaving group has the potential of expanding the scope of Grob fragmentations in synthesis.[18]

Scheme I



(a) NaOH, H_2O, reflux, then CH_2N_2, ether. (b) DHP, TsOH, ether, 0 °C to room temperature. (c) Vitride, PhH, 5 °C. (d) NCS, $(CH_3)_2S$, $PhCH_3$, −25 °C, $(C_2H_5)_3N$. (e) $(CH_3)_2CPPh_3$, THF, −40 °C to room temperature. (f) TsOH, CH_3OH, room temperature. (g) CH_3Li, ether, 0 °C.

Acknowledgment. We wish to thank the National Science Foundation and the National Institutes of Health, General Medical Sciences, for their generous support of our programs.

References and Notes

(1) For a few recent references to the work of Danishefsky et al., see (a) R. K. Singh and S. Danishefsky, *J. Org. Chem.*, **41**, 1668 (1976); (b) *J. Am. Chem. Soc.*, **97**, 3239 (1975); (c) *J. Org. Chem.*, **40**, 3807 (1975); (d) S. Danishefsky and G. Rovnyak, *ibid.*, **40**, 114 (1975); (e) S. Danishefsky and J. Dynak, *ibid.*, **39**, 1979 (1974); (f) S. Danishefsky, J. Dynak, E. Hatch, and M. Yamamoto, *J. Am. Chem. Soc.*, **96**, 1256 (1974).

(2) (a) O. H. Mattsson, G. Sundström, and C. A. Wachtmeister, *Acta Chem. Scand.*, **25**, 206 (1971); (b) **24**, 2219 (1970); (c) O. H. Mattsson and G. Sundstrom, *ibid.*, **24**, 1454, 3563 (1970).

(3) P. L. Fuchs, *J. Am. Chem. Soc.*, **96**, 1607 (1974).

(4) J. P. Marino and R. C. Landick, *Tetrahedron Lett.*, 4531 (1975).

(5) For reviews, see B. M. Trost, *Acc. Chem. Res.*, **7**, 85 (1974); B. M. Trost, *Pure Appl. Chem.*, **43**, 563 (1975); B. M. Trost, *Top. Curr. Chem.*, **41**, 1 (1973).

(6) B. M. Trost and M. Bogdanowicz, *J. Am. Chem. Soc.*, **94**, 4777 (1972).

(7) (a) B. M. Trost and W. J. Frazee, manuscript in preparation. (b) W. J. Frazee, Ph.D. Thesis, University of Wisconsin, 1977.

(8) This reagent has not heretofore been reported. It is prepared in analogy to di-*tert*-butyl 2-methyl-2-bromomalonate (B. M. Trost and L. S. Melvin, Jr., *J. Am. Chem. Soc.*, **98**, 1204 (1976)): bp 66–74 °C (0.2 mm); IR (CCl_4) 1765, 1740 cm^{-1}; NMR (CCl_4) δ 1.49 (s, 18 H), 4.52 (s, 1 H). The choice of *tert*-butyl esters is essential for the success of the cyclopropylide reaction.

(9) (a) This compound has spectral properties in full accord with the assigned structure. (b) A satisfactory combustion analysis or high resolution mass spectrum confirmed the elemental composition.

(10) Cf. (a) C. R. Engel, A. F. de Krassny, A. Bélanger, and G. Dionne, *Can. J. Chem.*, **51**, 3263 (1973); (b) F. Gaudemar-Bardone and M. Gaudemar, *Bull. Soc. Chim. Fr.*, 4188 (1971); (c) Y. C. Kim and H. Hart, *J. Chem. Soc. C*, 2409 (1969); (d) Y. Inouye, S. Inamasu, M. Horiike, M. Ohno, and H. M. Walborsky, *Tetrahedron*, **24**, 2907 (1968); (e) L. L. McCoy, *J. Am. Chem. Soc.*, **84**, 2246 (1962); (f) D. T. Warner, *J. Org. Chem.*, **24**, 1536 (1959).

(11) B. M. Trost and M. J. Bogdanowicz, *J. Am. Chem. Soc.*, **95**, 5321 (1973); B. M. Trost, M. Preckel, and L. M. Leichter, *ibid.*, 97, 2224 (1975).

(12) **5a**: IR (CCl_4) 1740 cm^{-1}; NMR δ 1.64 (3 H, s), 2.59 (2 H, t, J = 8 Hz), 3.36 (1 H, t, J = 8 Hz), 3.64 and 3.73 (two s, 9 H), 5.09 (1 H, t, J = 8 Hz); ^{13}C NMR δ 15.9, 27.4, 32.7, 34.4, 51.3, 51.6, 52.2, 119.9, 136.5, 168.8, 172.9. **5b**: IR (CCl_4) 1745 cm^{-1}; NMR δ 1.68 (3 H, s), 2.61 (2 H, t, J = 7 Hz), 3.37 (1 H, t, J = 7 Hz), 3.67 and 3.74 (two s, 9 H), 5.11 (1 H, t, J = 7 Hz); ^{13}C NMR δ 22.9, 27.0, 27.2, 32.4, 51.4, 51.7, 52.3, 121.1, 136.3, 168.8, 172.9. **6a**: IR (CCl_4) 1780, 1740 cm^{-1}; NMR δ 1.25 (3 H, s), 3.68 (6 H, s). **6b**: IR (CCl_4) 1785, 1740 cm^{-1}; NMR δ 1.38 (3 H, s), 3.65 and 3.69 (3 H each, two s). **8**: IR ($CHCl_3$) 1785, 1720 cm^{-1}; NMR δ 1.15 (3 H, s), 1.47 (9 H, s), 3.66 (1 H, broad t, J = 9 Hz); ^{13}C NMR δ 14.1 (t), 16.2 (q), 26.8 (t), 28.1 (q), 29.3 (s), 39.3 (s), 44.9 (t), 64.4 (d), 81.3 (s), 81.7 (s), 167.3 (s), 168.2 (s), 209.5 (s). **11**: IR (ccl_4) 1740 cm^{-1}; NMR δ 1.60 (3 H, broad s), 2.08 (2 H, q, J = 7 Hz), 3.70 (s, 6 H), 5.21 (1 H, t, J = 7 Hz); ^{13}C NMR δ 15.6 (q), 24.2 (t), 32.4 (t), 38.5 (t), 50.4 (d), 52.2 (q), 62.1 (t), 126.5 (d), 130.9 (s), 168.8 (s).

(13) An 8 ft by ¼ in. 10% DC 710 on Chromosorb W, 60–80 mesh, at 200 °C was employed.

(14) Satisfactory combusion analysis was obtained on the oxime of 7, mp 87–88.5 °C, rather than the aldehyde itself.

(15) The following fragmentation is observed if the ketone is not reduced.

(16) D. R. Marshall, P. J. Thomas, and C. J. M. Stirling, *J. Chem. Soc., Chem. Commun.*, 940 (1975); P. J. Thomas and C. J. M. Stirling, *ibid.*, 829 (1976).

(17) C. A. Grob, private communication.

(18) For a review of one aspect of this important subject, see J. A. Marshall, *Synthesis*, 229 (1971).

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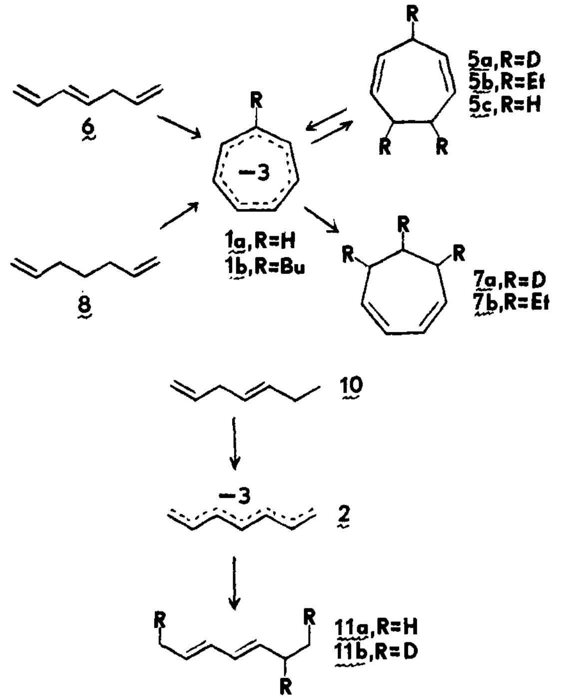
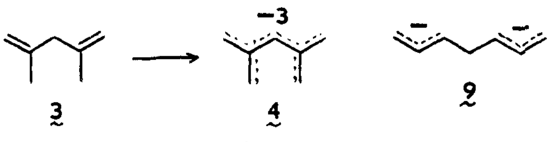
Cycloheptatrienyl and Heptatrienyl Trianions

Sir:

The third member in the series of 10π aromatic anions that begins with cyclononatetraenyl anion[1] and cyclooctatetraene dianion[2] is cycloheptatrienyl trianion (**1a**). Its heptaphenyl derivative was a possible reaction intermediate;[3] reduction of cycloheptatrienyl dianion radical with potassium and sodium gave "no unambiguous evidence" for trianion **1a** itself.[4] We wish to report metalation routes to the trilithium salts of **1a**, its *n*-butyl derivative **1b**, and its linearly conjugated analogue, i.e., heptatrienyl trianion (**2**).



As reported earlier,[5] allylic metalation of diene **3** gave, along with larger amounts of dianion, up to 18% yield of cross-conjugated trianion **4** (simple Hückel MO total π energy, $E_\pi = 10\alpha + 6.8\beta$), and this led us to try to similarly prepare cyclic trianion **1a** ($E_\pi = 10\alpha + 7.2\beta$). Either 1,4-cycloheptadiene (**5c**) or 1,3,6-heptatriene (**6**)[6] on standing with 3 mol of *n*-BuLi (1.8 M in hexane) and 3 mol of tetramethylethylenediamine (TMEDA) at room temperature for 3–10 days gave a black precipitate which apparently contained the trilithium salt of **1a** solvated by TMEDA, in ~70% yield as indicated by the following evidence: (a) quenching with D$_2$O gave a 70% yield of a mixture of **5a** and **7a** with the latter predominating, the degree of deuterium incorporation being indicated by mass spectrometry and the location of the deuteriums by ^{1}H NMR; (b) quenching with diethyl sulfate[7] gave a 70% yield of triethylcycloheptadienes **5b** and **7b** (not separated, but mass spectrum and ^{1}H NMR consistent with these structures); (c) between 2 and 12 h after mixing the reactants, a singlet at δ 4.55 ± 0.15 is observed in the ^{1}H NMR (Figure 1) and a singlet at δ 66.0 in the ^{13}C NMR, after which time the tube was clogged with black precipitate (these values are close to those predicted for **1a** by extrapolation from the cyclononatetraenyl anion[1] and cyclooctatetraene dianion[2] values); (d) the appearance of the ESR signal expected for cycloheptatrienyl dianion radical dilithium ($a_{\mathrm{H}} = 3.52$ and $a_{\mathrm{Li}} = 0.83$ G[8]), highest concentration estimated at 10^{-5} M, accompanies the development of the black color (this species is most likely formed in this system by loss of an electron from trianion **1a**).[9]



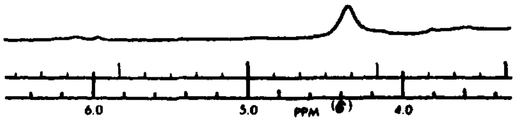


Figure 1. 60-MHz ^{1}H NMR spectrum of cycloheptatrienyl trianion (**1a**, peak at δ 4.4) in hexane–TMEDA; other peaks visible are due to cycloheptadienyl monoanion.

Surprisingly, attempts to prepare acyclic trianion **2** ($E_\pi = 10\alpha + 6.5\beta$) by metalating 1,6-heptadiene (**8**) gave instead cyclic trianion **1a**, as indicated by its D$_2$O quench products **5a** and **7a**. This requires an oxidation, which apparently occurs by the expulsion of lithium hydride[10] by an anionic intermediate which is most likely dianion **9**; the resulting heptatrienyl anion then proceeds to **1a** as above.[11] On the other hand, metalation of 1,4-heptadiene (**10**) with a large excess of *n*-BuLi-TMEDA followed by quenching with water gave an essentially quantitative yield of a heptadiene mixture consisting (GC and ^{1}H NMR comparison with an authentic sample) almost entirely of 2,4-heptadienes (**11a**); when the quench was with D$_2$O, this product was 35% monodeuterated, 45% dideuterated, and 20% trideuterated, indicating the formation of some of the trilithium salt of linearly conjugated trianion **2**.[12]

Monoalkyl derivatives of **1a**, e.g., **1b**, can be prepared in one step by mixing cycloheptatriene with 3 mol of the appropriate alkyllithium and 3 mol of TMEDA; the initial addition[6] is followed by two metalations.

Thus, of the three trianions **1a**, **2**, and **4**, the former, cyclic and aromatic, is as expected the most easily prepared. Like other aromatic anions, it may prove to be an interesting ligand.

Acknowledgment. Financial support from the National Science Foundation (GP-38070X) is gratefully acknowledged.

References and Notes

(1) T. J. Katz and P. J. Garratt, *J. Am. Chem. Soc.*, **86**, 5194 (1964).

(2) T. J. Katz, *J. Am. Chem. Soc.*, **82**, 3784 (1960).

(3) R. Breslow and H. W. Chang, *J. Am. Chem. Soc.*, **87**, 2200 (1965).

(4) N. L. Bauld and M. S. Brown, *J. Am. Chem. Soc.*, **89**, 5417 (1967).

(5) R. B. Bates, W. A. Beavers, M. G. Greene, and J. H. Klein, *J. Am. Chem. Soc.*, **96**, 5640 (1974).

(6) This triene is known to metalate readily to heptatrienyl anion, which cyclizes above −30 °C to cycloheptatrienyl anion (R. B. Bates, W. H. Deines, D. A. McCombs, and D. E. Potter, *J. Am. Chem. Soc.*, **91**, 4608 (1969)).

(7) When methyl and ethyl bromides and iodides were used, up to 25% yield of 7-methyl- or 7-ethylcycloheptatrienes were formed along with trialkylcycloheptadienes **5** and **7**. These products probably result from a sequence which starts with attack of the trianion **1a** on the halogen of the alkyl halide, and is almost completely avoided with diethyl sulfate (W. Priester, R. West, and T. L. Chwang, *J. Am. Chem. Soc.*, **98**, 8413 (1976)).

(8) This dilithium salt has not been described before, but the disodium salt was found to have $a_{\mathrm{H}} = 3.52$ and $a_{\mathrm{Na}} = 1.76$ G.[4]

(9) ESR signals were not found during the preparations of acyclic trianions **2** and **4**.

(10) Evidence for the formation of lithium hydride was vigorous reaction with