Acknowledgment. This research was supported by the National Science Foundation, to whom the authors express grateful appreciation.

Registry No.—2, Ar = p-C_6H_4F, 67711-71-1; 1-chlorocycloheptatriene, 32743-66-1; 2-chlorocycloheptatriene, 34896-79-2; 3-chlorocycloheptatriene, 55619-05-1.

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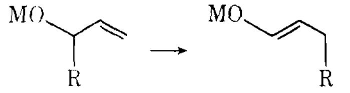
(6) The validity of this equation depends on the constancy of the ratio S_H/S_X. This was checked indirectly by weighing the final products, calculating the total amounts of styrenes consumed in the reaction (assuming all of the products were spirocyclopropanes, **2**), and determining the net change in the S_H/S_X ratio at the end of the reaction. In no case was the change >3%.
(7) This is barring the coincidence that **3** and **7** give two different intermediates that have the same ρ value, which cannot be excluded.

Communications

Potassium Alkoxide Promoted 1,3 Shifts of Dithianes

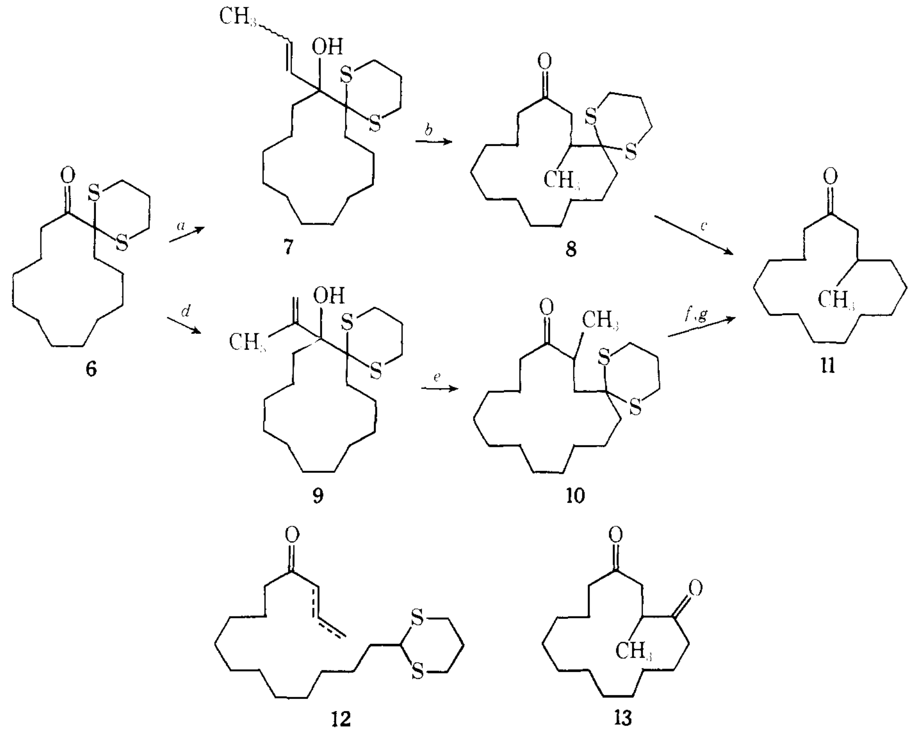
Summary: Applications of alkoxide-promoted 1,3 shifts to 1,4-dicarbonyl synthesis gives a new ring expansion route to *d,l*-muscone.

Sir: Sigmatropic rearrangements have found a wide variety of uses in organic synthesis.[1] Therefore, the report by Evans[2] that the oxy-Cope [3,3] sigmatropic rearrangement[3] can be strongly accelerated as the potassium salt appeared to us to have significant synthetic consequences. A number of subsequent reports on alkoxy counterparts to [3,3][4] and [1,3][5] rearrangement processes have since appeared. The [1,3] rearrangement depicted in eq 1 is of course a well-known process, the retro-1,2-carbonyl addition/1,4-Michael addition process.[6] Although not normally considered in these terms, the overall process is the result of a [1,3] sigmatropic shift. The alkoxide substituent on the crucial C–C bond which is breaking in the transition state can promote the requisite first step of the rearrangement process, i.e., reversal of the 1,2 addition.[7] Thus, the use of highly dissociated metal alkoxides in polar aprotic solvents should promote isomerization of 1,2 adducts, such as **1a** (mp 40–41 °C),[11,12] to the corresponding 1,4 adducts. This has proved to be the case. The *potassium salt* of **1a** isomerized to **2a** in 80% HMPA/THF solution (2 h, 25 °C) in 53% isolated yield.[13] The corresponding cyclohexenone adduct **1b** isomerized to **2b** in 23% yield,[14] whereas **1c** (mp 62–63 °C) gives none[14] of the desired **2c**, indicating steric hindrance at the newly forming C–C bond cannot be tolerated. The sodium and lithium salts of **1b** yielded mostly recovered starting material under similar conditions,[15,16] while the po-



(1)

Scheme I



[a] $CH_3CH{=}CHLi$ (3 recycles); 48% (+48% recovered **2**). [b] KH, TPPA/THF; 21%. [c] Ra-Ni/EtOH; 40%. [d] $CH_3C(Li){=}CH_2$ (5 recycles); 51%. [e] KH, HMPA/THF; 28%. [f] NH_2NH_2, KOH; 41%. [g] HgO, $BF_3 \cdot OEt_2$/aq THF; 72%.

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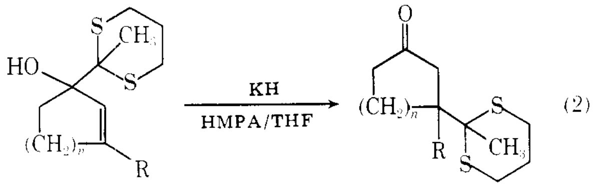
tassium salt in THF/18-crown-6 or refluxing DME and the sodium salt in refluxing DME resulted in only fragmentation.

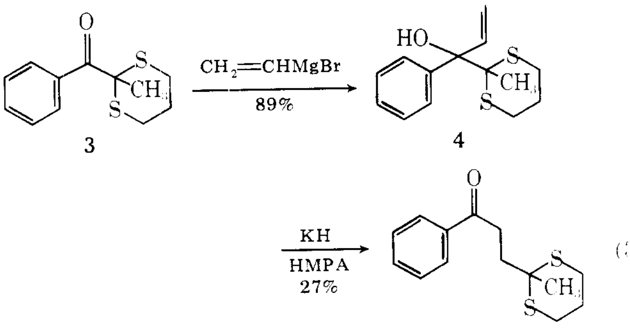
The overall [1,3] shift in eq 2 results in conjugate addition



1a, $n = 1$; R = H
b, $n = 2$; R = H
c, $n = 2$; R = CH_3

2a, $n = 1$; R = H
b, $n = 2$; R = H
c, $n = 2$; R = CH_3

of a masked acyl function and thus only extends present methodology[17] in this area. However, the availability of α-ketodithianes, such as **3**,[18] allows the generation of intermediates such as **4** upon treatment with a vinyl anion. *Subsequent isomerization "inserts" the two carbons of the vinyl group between two now differentiated carbonyls* (eq 3). This transformation then possesses unique features which are exemplified in a two-carbon ring expansion[19] route to muscone.



3

4

5

Macrocyclic compounds, such as muscone **11**,[20] have intrigued organic chemists for many years, and the substantial synthetic challenges posed by complex macrocyclic antibiotics have recently been reviewed.[21] One of the most interesting synthetic strategies is the "ring growing" reaction[22] which, in principal, allows successive ring enlargements. We wish to describe here our approach to macrocyclic ring expansion by [1,3] isomerizations of 1,3-dithianes (Scheme I). In the first step cyclotridecanone[23] is converted[24] to the crystalline α-ketodithiane derivative **6** (mp 51–53 °C, two steps 40%). Addition of 1-propenyllithium at 0 °C in ether to the hindered carbonyl of **6**,[25] after three recycles and short-column chromatography, results in 31% *trans*-**7**, 17% *cis*-**7**, and 48% recovered **6**. Direct isomerization of **7** with KH in 80% HMPA/THF (2 h, 25 °C) gave the ring-expanded ketone **8** (mp 82–84 °C) in 15% yield. The yield was improved to 21% (45 min, 25 °C) using tripyrrolidinylphosphoramide (TPPA),[26] a solvent *more polar than HMPA*. In addition, the ring-cleaved product **12** was isolated.[27] Raney nickel[28] desulfurization gave a 42% yield of *d,l*-muscone (**11**)[29] and a 34% yield of diketone **13**. Very facile hydrolysis of **8** can be explained as a result of participation by the neighboring carbonyl group. This type of participation has been observed previously.[30] To illustrate the flexibility of our approach an alternate route to **11** was investigated. Treatment of **6** with isopropenyllithium (0 °C in ether, 5 recycles) gave allylic alcohol **9** (in 51% yield). This was isomerized in 28% yield to ketone **10**. Wolff–Kishner reduction[31] (41%) followed by hydrolysis[10] (72%) again gives *d,l*-muscone (**11**).

In principle the "ring growing" process from ketone to ring-expanded ketone could be repeated. We are currently exploring the rearrangements of other sulfur-stabilized carbanions and methodology to the synthesis of more highly functionalized macrocycles.

Acknowledgment. We wish to thank the Research Corporation, the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Institutes of Health (GM 24438) for financial support.

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(15) It should be borne in mind that reversal of carbonyl additions is affected by the strength of the C–O double bond (175 kcal/mol vs. 85 kcal/mol for C–O) *and* the pK_a of the alkoxide. Ions in polar aprotic solvents have little source of stabilization other than ion pairing or aggregation so that RO^-K^+ is more basic in Me_2SO than 1,3-dithiane anion. For example, the fragmentation of the potassium salt of tri-*tert*-butylcarbinol in Me_2SO: E. M. Arnett, L. E. Small, R. T. McIver Jr., and J. S. Miller, *J. Org. Chem.*, **43,** 815 (1978).

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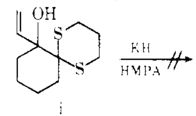
(17) Since the "classic" acyl anion equivalent[8] did not undergo conjugate addition, alternative methods have been devised: J. E. Baldwin, G. A. Höfle, and O. W. Lever, Jr., *J. Am. Chem. Soc.*, **96,** 7125 (1974), and references cited therein.

(18) E. J. Corey, D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **4,** 1077 (1965).

(19) The ring expansion methodology is probably only general for strain-free systems (cf. **1c**). The attempted expansion of i was unsuccessful.



i

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(29) Identity was based on comparison to spectral data previously reported: B. D. Mookherjee, R. W. Trenkle, and R. Patel, *J. Org. Chem.*, **36**, 3266 (1971).
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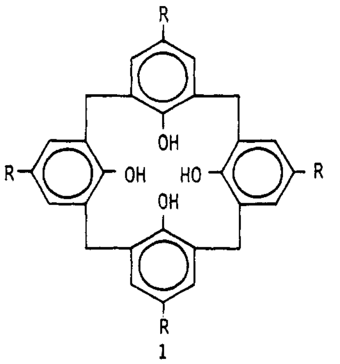
Calixarenes. 1. Analysis of the Product Mixtures Produced by the Base-Catalyzed Condensation of Formaldehyde with Para-Substituted Phenols

Summary: The products obtained from the base-catalyzed condensation of formaldehyde with several para-substituted phenols have been shown to be mixtures of two or more components which appear to be cyclic oligomers with five or more aromatic units in the cyclic array.

Sir: The recent publication[1] of a method for the preparation of compounds thought to have structure **1A–E** and the subsequent appearance of these compounds on the commercial market[2] prompts us to publish a preliminary account of our experiments with these materials to which we have given the name *calixarenes*.[3]



1
A (R = CH_3)
B (R = $C(CH_3)_3$)
C (R = C_6H_5)
D (R = OCH_3)
E (R = CO_2CH_3)

In 1944 Zinke and Ziegler[4] obtained high melting solids from the reaction of para-substituted phenols and formaldehyde, and they assigned a cyclic tetrameric structure (i.e., 1) to these compounds. This assignment has gained acceptance as the result of X-ray crystallographic data by Cornforth et al.[5] (who obtained crystal lattice constants that are not incommensurate with a cyclic tetramer) and the stepwise synthesis of Hayes and Hunter,[6] repeated and extended by Kämmerer and co-workers.[7] Data recently obtained in our laboratory, however, are difficult to reconcile with some of these earlier observations, and the structures of these compounds appear to be less well established than had been supposed.

The synthesis of calixarenes by the "direct" method by Zinke and Ziegler[4] involves treating para-substituted phenols in aqueous base with formaldehyde for 45 h at 50–55 °C, acidifying the reaction mixture with dilute acid, separating an oil which solidified on heating at 110–120 °C, and heating this solid in linseed oil at 200–220 °C. Cornforth and co-workers[5] used a similar procedure but substituted Dowtherm for linseed oil. A shorter method was worked out several years ago by J. H. Munch[8] in which the phenol and paraformaldehyde are dissolved in xylene and treated with a small amount of concentrated aqueous potassium hydroxide, and the mixture is refluxed for several hours to yield the product as an easily separable precipitate. The recently published method[1] represents only a slight modification of the Munch method, substituting tetralin for xylene and potassium *tert*-butoxide for potassium hydroxide.[9] However, a comparison of the products from these two methods has revealed some differences in yield, melting points, and IR spectra, and solvent extraction–partition procedures and TLC separations of trimethylsilyl derivatives have shown that the products from paraformaldehyde and *p*-cresol, *p*-*tert*-butylphenol, *p*-phenylphenol, or *p*-carbomethoxyphenol are mixtures of two or more compounds produced in somewhat different ratios by the two methods.

The product from *p*-*tert*-butylphenol and formaldehyde prepared by the "direct" method proved to be amenable to purification by simple recrystallization and, therefore, was selected for the initial experiments aimed at gaining further insight into the calixarene structures. The crude product, mp 361–372 °C, was twice recrystallized from chloroform to give colorless, fine needles: mp 400–401 °C; IR (KBr) 3230 cm^{-1}; IR ($CHCl_3$) 3200 cm^{-1}; ^{1}H NMR (Me_4Si, pyridine-d_5) δ 7.33 (br, 2, ArH), 4.18 (br, 2, CH_2), 1.28 (s, 9, $C(CH_3)_3$); ^{13}C NMR (Me_4Si, $CDCl_3$) δ 21 (89%, $C(CH_3)_3$), 24 (17.5%, $\mathbf{C}(CH_3)_3$), 26.5 (30%, $ArCH_2Ar$), 131.5 (92%, Ar), 141 (100%, Ar), 156 (25%, Ar), 162 (30%, Ar); osmometric molecular weight 1330 ($CHCl_3$ at 37 °C), 1400 (pyridine at 37 °C), 1225 (pyridine at 65 °C) (calcd for octamer, 1296). The trimethylsilyl derivative was obtained as colorless needles from hexane–acetone: mp 356–358 °C; IR (KBr) 1251 and 841 cm^{-1} (CSi); ^{1}H NMR (Me_4Si, CCl_4) δ 6.86 (m, 2, ArH), 3.83 (br s, 2, CH_2), 1.20 (s, 9, $C(CH_3)_3$), −0.02 (s, 3, $Si(CH_3)_3$); ^{13}C NMR (Me_4Si, $CDCl_3$) δ 0.8 (53%, $Si(CH_3)_3$), 30.3 (100%, $C(CH_3)_3$), ~31 (very weak, $\mathbf{C}(CH_3)_3$), 32.8 (15%, CH_2), 124.4 (28%, Ar), 128.8 (43%, Ar), 141.7 (19%, Ar), 148.2 (10%, Ar); mass spectrum (EI, 90 eV) *m/e* 1872 (100%, octamer), 936 (13%, tetramer).

From the mother liquors of the crystallization of the higher melting calixarene from *tert*-butylphenol a lower melting fraction was obtained. A sample of this material was converted to the trimethylsilyl derivative, purified by TLC, and hydrolyzed to yield a compound with mp 367–369 °C: IR (KBr)

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