Table I. ΔH_f and IE for Keto and Enol Radical Cations and Neutrals

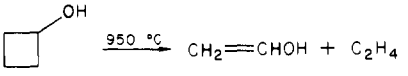
species	ΔH_f(ion), kcal mol^{-1}	ΔH_f(neutral), kcal mol^{-1} lit.	ΔH_f(neutral), kcal mol^{-1} this work	ionization energy, eV lit.	ionization energy, eV this work
CH_3CHO	196	−39.7[6]		10.23[5]	
CH_2=CHOH	183.5[2]	−28.0[2]		(9.17)[2 a]	
	181[3]	−26.5[3]	−29.8[b]	(9.0)[3 a]	9.14
CH_3COCH_3	172	−51.9[6]		9.70[5]	
CH_2=C(OH)CH_3	158[4]	−38[10]	−38[b]	8.2[7]	8.48
				9.1–9.4[8]	
				8.75[9]	

[a] From ΔH_f(ion) − ΔH_f(neutral). [b] From ΔH_f(ion) − IE.

variance; ΔH_f for the neutral enol of acetone derived from these estimates and the value of 158 kcal mol^{-1} for ΔH_f of $[CH_2$=C-$(CH_3)OH]^{+\cdot}$, with the relationship ΔH_f(neutral) = ΔH_f(ion) − IE, will of course show the same uncertainty. A direct experimental measurement of the IE of these two enols would permit more reliable values for the heats of formation of the neutral molecules to be obtained.

Vinyl alcohol is a transient species in the gas phase; it has been prepared[11] by the pyrolysis of ethylene glycol in a quartz tube at 1000 °C. The half-life was about 30 min. The apparent ease with which gas-phase vinyl alcohol rearranged to acetaldehyde in spite of a calculated activation energy barrier of 85 kcal mol^{-1} has been commented upon.[1] We report here a better pyrolytic source for vinyl alcohol and one for the enol of acetone, together with ionization energies measured by impact of a monoenergetic electron beam.[12]

Almost complete pyrolysis of cyclobutanol to vinyl alcohol plus ethene was obtained at 950 °C and 10^{-3} torr in a tubular quartz furnace[13] which leads directly into the ionization chamber.



The threshold for the ionization efficiency curve for m/z 44 (C_2H_4O) was 9.14 ± 0.05 eV. The cross section for ionization was quite small over the initital portion of the curve, suggesting that the Franck–Condon factors for the adiabatic transition are small. As pointed out by Bouma et al.,[2] the hydroxyl hydrogen in the lowest energy configuration of the ion is anti, in contrast with the syn position in the neutral molecule. A low probability for the adiabatic transition is therefore possible. The observed IE, 9.14 eV, is close to the 9.17-eV value derived in the theoretical study,[1,2] but the agreement is partly fortuitous because our experimental $\Delta H_f(\text{vinyl alcohol})^{+\cdot}$ from dissociative ionizations[3] is 2.5 kcal mol^{-1} lower than the value of 183.5 kcal mol^{-1} from the theoretical calculations. Our experimental IE, taken with ΔH_f(ion) = 181 kcal mol^{-1}, leads to $\Delta H_f[CH_2$=CHOH] = −29.8 kcal mol^{-1}, with a probable error of ±2 kcal mol^{-1}.

The neutral enol of acetone, CH_2=C(CH_3)OH, was obtained in good yield from the pyrolysis of 1-methylcyclobutanol at 950 °C in the same apparatus. The threshold for the ionization efficiency curve for m/z 58 was 8.48 ± 0.05 eV. At temperatures above 950 °C the yield of enol decreased and ketene and methane were produced. From the ΔH_f for the enol of acetone,[4] 158 kcal mol^{-1}, and the experimental IE for the enol, 8.48 eV, ΔH_f[neutral CH_2=C(CH_3)OH] = −38 kcal mol^{-1}. This is identical with the value obtained by Pollack and Hehre[10] from ion cyclotron resonance experiments.

It is noteworthy that the substitution of CH_3 for H in vinyl alcohol decreases the ΔH_f(neutral) by 8.2 kcal mol^{-1}. The corresponding substitution for the isoelectronic species CH_3CH=CH_2 to give $(CH_3)_2C$=CH_2 decreases ΔH_f by a similar amount,[6] 9.1 kcal mol^{-1}. It is possible to derive from these results a useful new additivity term in the thermochemical scheme of Benson et al.,[14] for the group O–$(C_d)(H)$. Combining the presently accepted additivity terms [C–$(H)_3(C)$ = −10.08, C_d–(H_2) = 6.26, C_d–(O)(H) = 8.6, and C_d–(O)(C) = 10.3 kcal mol^{-1}] with the heats of formation for neutral vinyl alcohol and for the enol of acetone reported above yields values for this additivity term of −44.7 and −44.5 kcal mol^{-1}, respectively. The satisfactory agreement between these figures leads us to propose the adoption of O–$(C_d)(H)$ = −44.6 ± 2 kcal mol^{-1}. With use of this term heats of formation of other enols may now be calculated.

Registry No. CH_3CHO radical cation, 36505-03-0; CH_2=CHOH, 557-75-5; CH_2=CHOH radical cation, 57239-63-1; CH_3COCH_3 radical cation, 34484-11-2; CH_2=C(OH)CH_3, 29456-04-0; CH_2=C(OH)CH_3 radical cation, 34507-14-7.

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Use of D-[$^{13}C_6$]Glucose Together with ^{13}C-Depleted Glucose and Homonuclear ^{13}C Decoupling To Identify the Labeling Pattern by This Precursor of the "*m*-C_7N" Unit of Geldanamycin

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A "*m*-C_7N unit", consisting of a benzenoid ring plus one carbon atom and a nitrogen attached meta to each other, has recently been identified as a metabolic unit in a number of antibiotics including pactamycin,[1] geldanamycin,[2] mitomycin,[3] porfiromycin,[4] rifamycin,[5] and actamycin[6] and is presumably found in a number of related compounds[7] such as maytansine and streptovaricin.[8]

(1) (a) Rinehart, K. L., Jr.; Potgieter, M.; Delaware, D. L.; Seto, H. *J. Am. Chem. Soc.* **1981**, *103*, 2099–2101. (b) Weller, D. D.; Rinehart, K. L., Jr. *Ibid.* **1978**, *100*, 6757–6760.
(2) (a) Haber, A.; Johnson, R. D.; Rinehart, K. L., Jr. *J. Am. Chem. Soc.* **1977**, *99*, 3541–3544. (b) Johnson, R. D.; Haber, A.; Rinehart, K. L., Jr. *Ibid.* **1974**, *96*, 3316–3317.
(3) (a) Hornemann, U.; Eggert, J. H.; Honor, D. P. *J. Chem. Soc., Chem. Commun.* **1980**, 11–13. (b) Hornemann, U. In "Antibiotics. IV. Biosynthesis"; Corcoran, J. W., Ed.; Springer-Verlag: Berlin, 1981; pp 295–312. (c) Hornemann, U.; Kehrer, J. P.; Numez, C. S.; Ranieri, R. L. *J. Am. Chem. Soc.* **1974**, *96*, 320–322.
(4) Anderson, M. G. Kibby, J. J.; Rickards, R. W.; Rothschild, J. M. *J. Chem. Soc., Chem. Commun.* **1980**, 1277–1278.
(5) (a) Ghisalba, O.; Nüesch, J. *J. Antibiot.* **1981**, *34*, 64–71. (b) White, R. J.; Martinelli, E.; Gallo, G. G.; Lancini, G.; Beynon, P. *Nature (London)* **1973**, *243*, 273–277. (c) White, R. J.; Martinelli, E. *FEBS Lett.* **1974**, *49*, 233–236.
(6) Kibby, J. J.; McDonald, I. A.; Rickards, R. W. *J. Chem. Soc., Chem. Commun.* **1980**, 768–769.
(7) Rinehart, K. L., Jr.; Shield, L. S. *Fortschr. Chem. Org. Naturst.* **1976**, *33*, 231–307. The most recent addition to the group is apparently ansatrienin (Damberg, M.; Russ, P.; Zeeck, A., submitted for publication).

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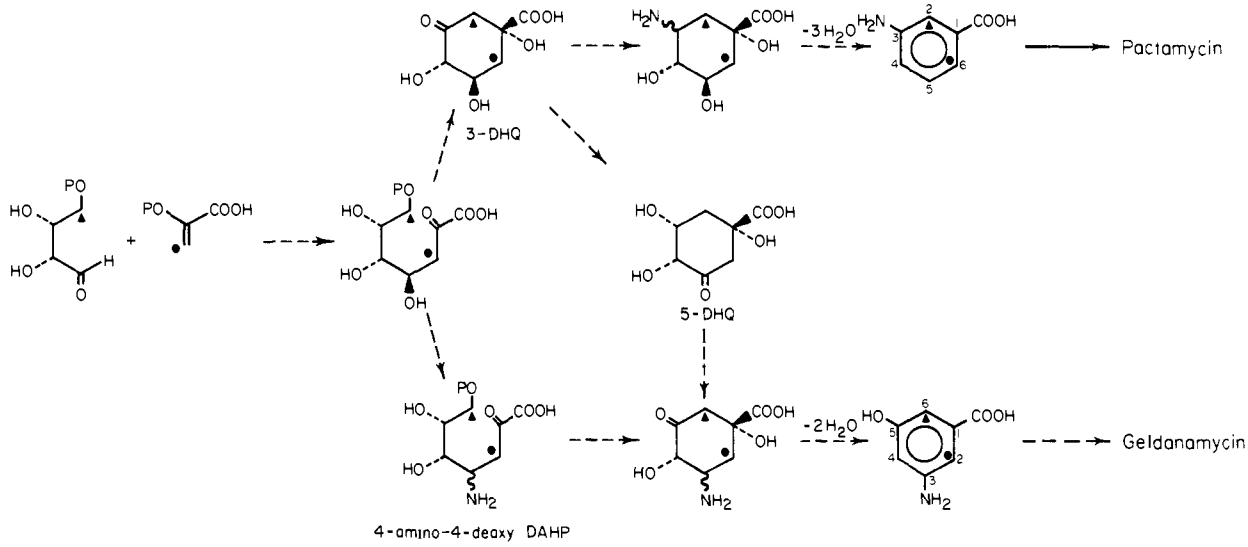
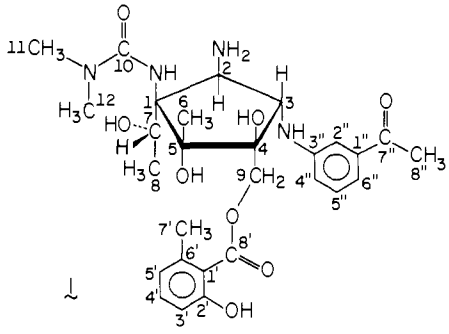
Scheme I

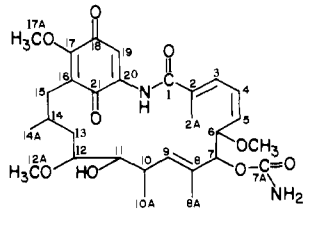


The precursor to the "*m*-C_7N unit" has been shown in the case of pactamycin to be *m*-aminobenzoic acid[1a] and in the case of porfiromycin,[4] actamycin,[6] and rifamycin[5a] to be 3-amino-5-hydroxybenzoic acid. The origin of *m*-aminobenzoic and 3-amino-5-hydroxybenzoic acids has been proposed to involve either transamination of dehydroshikimate or dehydroquinate[1a] or cyclization of a C_7 amino sugar acid.[3a]

We recently demonstrated that the labeling pattern of the *m*-aminoacetophenone ring of pactamycin (**1**) could be well ac-



counted for by phosphoenol pyruvate giving C-1″, C-6″, and C-7″ and erythrose 4-phosphate giving C-2″–C-5″, the pattern expected from the dehydroquinate (shikimate) transamination option (Scheme I).[1a] The study involved administering [$^{13}C_6$]glucose to *Streptomyces pactum* in the presence of excess unlabeled glucose and interpreting the resulting ^{13}C–^{13}C coupling pattern in the isolated pactamycin (actually its dimethylamine elimination product, pactamyçate). When we attempted to employ the same procedure to study the biosynthetic labeling pattern of the benzoquinone ring of geldanamycin (**2**) by *Streptomyces hygroscopicus* var. *geldanus* var. *nova*, we were unable to interpret the ^{13}C–^{13}C labeling pattern due to low enrichment of the geldanamycin carbons by [$^{13}C_6$]glucose relative to labeling by naturally abundant ^{13}C.



We report here that we have now solved the latter problem by carrying out the same experiment but diluting with ^{13}C-depleted glucose (99.9% ^{12}C) rather than with ordinary glucose. This gave a labeled geldanamycin sample possessing a readily interpretable ^{13}C spectrum that demonstrates that phosphoenol pyruvate labels carbons 15, 16, and 21 of geldanamycin, while erythrose 4-phosphate labels carbons 17–20, a pattern opposite to that found earlier for pactamycin.[1]

Nutrient agar slants were inoculated with *S. hygroscopicus*, incubated for 3.0 days, then transferred to 100 mL of vegetative medium [glucose, 1.0%; bacto-peptone, 1.0%; yeast extract 0.25%], and incubated for 2.0 days. The production medium [four flasks, each with 100 mL of medium consisting of 1.5% of [$^{12}C_6$]glucose (0.12% ^{13}C at each carbon), 0.25% of bacto-peptone; 0.25% of bacto-tryptone, 0.25% of yeast extract, 0.5% of oatmeal, and 1.0% of molasses] was seeded and incubated at 30 °C for 36 h, when 550 mg of [$^{13}C_6$]glucose (84% ^{13}C), together with 2.45 g of [$^{12}C_6$]glucose (0.12% ^{13}C) and 31 μCi of [U-^{14}C]glucose as a tracer, was divided and added in equal protions to the fermentation flasks. After another 60 h of incubation, the mycelia were harvested, blended, filtered, and extracted with chloroform. The dried extract was chromatographed (10 g of silica gel, MeOH/$CHCl_3$, 1:99), and geldanamycin was recrystallized from ether–chloroform to give 162 mg of pure antibiotic (0.56 μCi) employed for ^{13}C NMR spectroscopy. The incorporation of [U-^{14}C]glucose into geldanamycin was thus 1.8%.

The results found in Table I clearly demonstrate that carbons 15, 16, and 21 of geldanamycin are derived from a C_3 unit from [$^{13}C_6$]glucose (phosphoenol pyuvate) and that carbons 17–20 are derived from a C_4 unit from [$^{13}C_6$]glucose (erythrose 4-phosphate).[9] The splitting patterns for C-20 and C-21 both indicate coupling to only one other carbon; each pattern consists of a doublet due to coupling with one adjacent carbon, accompanied by a singlet due to randomization of the label as well as to a contribution from the 0.12% of residual ^{13}C at each carbon of [$^{12}C_6$]glucose. For C-20 this can only be the case if it is not coupled to C-21 and vice versa; thus, C-21, C-16, and C-15 must constitute a C_3 unit. The splitting patterns for carbons 16 and 18, on the other hand, indicate strong coupling to two other carbons. That for C-18 consists of a doublet sandwiched between the three peaks of a triplet; the triplet (which should probably

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(9) The labeling patterns for the remaining carbons of geldanamycin isolated from this experiment are in agreement with those expected from the earlier reports[2] and will be discussed in detail in a full paper. Carbons of special interest due to their coupling patterns and/or heavy labeling are the C-5, C-6 and C-11, C-12 pairs, earlier shown to be derived from glycerate as well as glycolate,[2a] and C-3, C-4, the pair derived from acetate.[2b]

Table I. ^{13}C NMR Signals[a] for the Benzoquinone (*m*-C_7N) Unit of Geldanamycin

C_x	δ[b]	pattern[c]	J_{C-C}, Hz	change(s) on irradiating C_x
C-16 (1)	127.5	dd + d + d + s	57.5, 43.5	C-21 → s C-15 → s
(2)	128.0	m		
C-17 (1)	157.4	dd + d + d + s	53.5, 16.6	C-18 → d + s C-19 → w dd + d + s
(2)	156.3	dd + d + d + s	56.1, 17.5	
C-18 (1)	183.9	t + d	~52.4, ~56.6	C-17 → d + s C-19 → w dd + d + s
(2)	183.4	t + d	55.7, 56.4	
C-19 (1)	111.6	w ddd + w dd + dd + d + d + s	70.2, 58.7, 16.5	C-18 → d + s C-20 → s
(2)	110.7	w ddd + w dd + dd + d + d + s	75.4, 55.8, 15.6	
C-20 (1)	138.0	w d + s	70.5	C-19 → loss of w sidebands
(2)	139.4	w d + s	73.9	
C-21 (1)	184.7	d + s	57.3	C-16 → d + s
(2)	183.0	d + s	57.4	
C-15 (1)	32.5	d + s	41.0	
(2)	31.7	d + s	44.1	

[a] Conditions: (1) $CDCl_3$ solution, University of Illinois Regional Instrumentation Facility NSF-250 spectrometer; (2) Me_2SO-d_6 solution, Nicolet NT 360 spectrometer. [b] From Me_4Si, values determined by comparing to ^{13}C of $CHCl_3$. [c] s = singlet, d = doublet, t = triplet, w = weak; see text.

be a doublet of doublets but is unresolved) is due to coupling of C-18 to two other carbons. The doublet and a singlet superimposed on the center peak of the triplet are signals presumably due to some combination of randomization of label and incomplete labeling in the starting glucose. The triplet for C-18 is especially significant, since C-18 must then be coupled to C-17 and C-19 and thus must be part of the C_4 unit (C-17–C-20). The pattern for C-16 consists of the expected doublet of doublets (J = 57.5, 43.5 Hz) plus doublets (J = 56.9, 45.7 Hz) due to labeling at only one adjacent carbon, plus a singlet due to complete randomization of label. The coupling pattern for C-17 also consists of a doublet of doublets (J = 53.5, 16.6 Hz) plus two doublets plus a singlet due to strong coupling to C-18 plus long-range coupling to C-19. The pattern for C-19 is the most complicated since it also shows long-range coupling (J = 16 Hz) with C-17; the other two coupling constants for C-19 differ from one another (J = 70, 59 Hz), and the intensity of the label in C-20 is quite low (due to extensive randomization) so that the outer lines of C-19 due to C-19, C-20 coupling are weak. Without the long-range coupling C-17 would show a d + s pattern and C-19 a dd (w) + d + d + s pattern. Figure 1 shows the coupling patterns for the six carbons of the benzoquinone ring.

The conclusions drawn from the coupling patterns were fully confirmed by homonuclear decoupling (Table I). Thus, irradiation of C-16 collapsed C-21 to a broad singlet but did not alter the C-17 pattern, while irradiation of C-18 collapsed C-17 to a doublet plus a singlet and irradiation of C-20 eliminated the weak sidebands for C-19 but did not alter the C-21 pattern.

To the extent that coupling constants could be determined, they agreed with the conclusions derived by homonuclear decoupling. For example, neither C-16 nor C-17 shows a coupling constant corresponding to alkene coupling (ca. 70 Hz), and the coupling constant of C-21 does not match that of C-20 (Table I).

From the results described it is clear that the C_3 portion of geldanamycin's benzoquinone "*m*-C_7N" unit is composed of C-15, C-16, and C-21 and the C_4 portion of C-17–C-20, the opposite grouping of carbons from that found in the *m*-aminoacetophenone unit of pactamycin.[1a,10] In the latter antibiotic *m*-amino[*ring*-U-^{14}C]benzoic acid was incorporated into pactamycin to the extent of 11.5%. In the present study, administering *m*-amino[*ring*-U-^{14}C]benzoic acid to cultures of *S. hygroscopicus*, however, gave

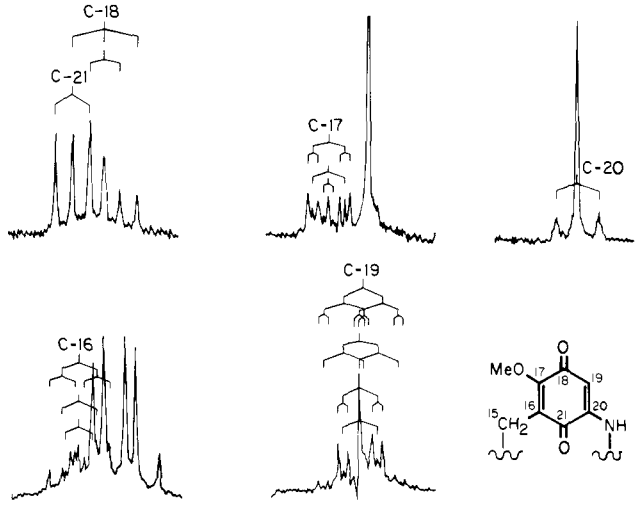

Figure 1. Coupling patterns for the six benzoquinone carbons of geldanamycin prepared biosynthetically with [$^{13}C_6$]glucose diluted with [$^{12}C_6$]glucose (^{13}C-depleted glucose): top left, C-18 and C-21; top center, C-17 (singlet to right, C-7A); top right, C-20; bottom left, C-16 (intense AB quartet to right, C-3 and C-4); bottom center, C-19. The numbering scheme for quinone is at the bottom right, with the complete numbering scheme in text (**2**).

geldanamycin containing only minimal label (<0.25%) in three experiments. Thus, although uptake of *m*-aminobenzoic acid by the streptomycete has not been specifically investigated, it does not appear to be a precursor of geldanamycin. The recent results of Rickards[4,6] and Nüesch[5a] suggest the intermediacy of 3-amino-5-hydroxybenzoic acid, but we have not yet substantiated that argument for geldanamycin.

While the *m*-aminobenzoic acid unit of pactamycin and the apparent 3-amino-5-hydroxybenzoic acid unit of geldanamycin are both labeled by C_3 and C_4 units derived from glucose, arguing for a similar biosynthetic pathway, clearly at some point the biosyntheses diverge, since the units label different carbons of the two acids. One possible branch point is 3-dehydroquinic acid (3-DHQ). As shown in Scheme I, transamination of 3-DHQ (conversion of keto group to amino group) followed by loss of 3 mol of water would lead to 3-aminobenzoic acid with a labeling pattern like that found in pactamycin. On the other hand, reduction of 3-dehydroquinate to quinate, oxidation of the 5-hydroxyl to a keto group (to 5-DHQ), followed by transamination and elimination of 2 mol of water would lead to 3-amino-5-

(10) The labeling pattern found for geldanamycin agrees with that proposed earlier for rifamicin,[5c] based on relative labeling levels at the two carbons ortho to the exocyclic carbon of the "C_7N" unit by D-[1-^{13}C]glucose. It is of interest that this argument (relative labeling at the ortho carbons) has now been borne out in two cases—pactamycin (by D-[6-^{13}C]- and D-[1-^{13}C]-glucose)[1a] and the ansamycins (in the rifamicin experiment cited above).[5c]

hydroxybenzoic acid with the observed labeling pattern. The alternative proposal of Hornemann,[3a] involving transamination at the acyclic heptulosonic acid stage to form 4-amino-3,4-dideoxy-D-*arabino*-heptulosonic acid 7-phosphate (4-amino-4-deoxy DAHP), followed by cyclization, also remains a viable possibility. A distinction among these and other possible intermediates must await labeling results with those intermediates.

Acknowledgment. This work was supported in part by a research grant (AI 04769) from the National Institute of Allergy and Infectious Diseases and by a Procter & Gamble Fellowship to M.P. (1981-1982). We thank the Stable Isotopes Resource at Los Alamos Scientific Laboratories, jointly supported by the Energy Research and Development Administration and the Division of Research Resources, NIH (Grant No. 1 P07 RR-00962-01), for providing [$^{13}C_6$]glucose and ^{13}C-depleted glucose and the University of Illinois NSF Regional Instrumentation Facility (NSF CHE 79-16100) for ^{13}C NMR spectra.

Registry No. 2, 30562-34-6; phosphoenol pyruvate, 138-08-9; erythrose 4-phosphate, 19234-99-2; [$^{13}C_6$]glucose, 19030-38-7; glucose, 50-99-7.

Calixarenes. 6. Synthesis of a Functionalizable Calix[4]arene in a Conformationally Rigid Cone Conformation

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Received January 11, 1982

The calixarenes[1] when in the "cone" conformation, are members of a small group of organic compounds that are basketlike in shape and possess the potential for forming guest-host complexes in which the guest resides in a cavity completely within a single host molecule. Calixarenes have been synthesized by two fundamentally different methods. One is a rather lengthy multistep process originally devised by Hayes and Hunter[2] and recently improved and exploited by Kämmerer and co-workers[3]; the other is a simple, one-flask, base-catalyzed condensation of a *p*-substituted phenol with formaldehyde. The latter method was first reported by Zinke and co-workers[4] and subsequently, with modifications, by Cornforth and co-workers,[5] Buriks, Fauke, and Munch,[6] Gutsche and co-workers[7] and Patrick and Egan.[8] As our recent work[1] has shown, however, this procedure affords mixtures of cyclic oligomers that are difficult to separate; to date, good yields of pure products have been obtained *only* from the *p-tert*-butylphenol condensation in which, by appropriate choice of reaction conditions, it is possible to prepare *p-tert*-butylcalix[4]arene (**1a**), *p-tert*-butylcalix[6]arene (**1b**), and *p*-tert-butylcalix[8]arene (**1c**). This communication describes the conversion of **1a** to a calixarene that is conformationally fixed in the "cone" conformation and which carries the potentially functionalizable allyl group in the para positions.

p-tert-Butylcalix[4]arene (**1a**) was obtained in ca. 35% yield, mp 344-346 °C, by using the Zinke method[4] as modified by Cornforth,[5] and the *tert*-butyl groups were then removed by an aluminum chloride catalyzed alkyl group transfer.[9] From 5.00 g of the toluene complex of **1a** calix[4]arene (**2**) was obtained in 66% yield as opaque, trapezoidal plates after recrystallization first from $CHCl_3/CH_3OH$ and then from acetone: mp 315-318 °C; IR (KBr) 3120 cm^{-1} (OH stretching); ^1H NMR (Me_4Si, $CDCl_3$) δ 10.19 (s, 4, OH), 7.22-6.64 (m, 12, ArH), 3.63-3.48 (br d, 8, CH_2); ^{13}C NMR (Me_4Si, $CDCl_3$) δ 148.4 (25%, Ar), 129.0 (100%, Ar), 128.2 (53%, Ar), 122.2 (60%, Ar), 31.7 (42%, CH_2); osmometric M_r ($CHCl_3$, 37 °C), 452 (calcd for **2** with $^1/_4$ mol of acetone, 439); mass spectrum M_r, 424 (calcd 424). Anal. Calcd for $C_{28}H_{24}O_4 \cdot {}^1/_4C_3H_6O$: C, 78.67; H, 5.81. Found: C, 78.68; H, 5.88.

The allyl ether **3** was prepared by the method of Stoochnoff and Benoiton[10] and obtained in 74% yield as colorless needles after recrystallization from 95% ethanol: mp 183-184 °C; IR (KBr) 1645 and 930 cm^{-1} (vinyl group); ^1H NMR (Me_4Si, $CDCl_3$) δ 7.4-5.9 (m, 16, ArH and HC=), 5.5-4.8 (m, 8, H_2C=), 4.5-2.9 (m, 16, $ArCH_2Ar$ and OCH_2CH=CH_2); mass spectrum M_r, 584 (calcd, 584). Anal. Calcd for $C_{40}H_{40}O_4$: C, 82.16; H, 6.90. Found: C, 82.43; H, 6.97.

A Claisen rearrangement of **3** was effected[11] by refluxing a solution of 1.66 g (2.84 mmol) of **3** in 25 mL of *N,N*-diethylaniline in an atmosphere of N_2 for 4 h. The crude product was recrystallized from isopropyl alcohol to yield 1.22 g (74%) of off-white needles, mp 245-248 °C. An analytical sample was obtained by a second recrystallization as colorless needles: mp 250.5-252 °C; IR (KBr) 3150 (OH stretching), 1635, and 905 cm^{-1} (vinyl group); ^1H NMR (Me_4Si, $CDCl_3$) δ 10.1 (s, 4, OH), 6.8 (s, 8, ArH), 6.1-5.5 (m, 4, vinyl H), 5.2-5.0 (m, 4, vinyl H), 5.0-4.8 (m, 4, vinyl H), 4.1-3.3 (br d, 8, $ArCH_2Ar$), 3.17 (d, 8, CH_2CH=CH_2); ^{13}C NMR (Me_4Si, $CDCl_3$) δ 137.5 (46%, vinyl), 133.4 (37%, Ar), 128.9 (100%, Ar), 128.2 (65%, Ar), 115.5 (50% vinyl), 39.3 (49%, CH_2CH=CH_2), 31.7 (34%, $ArCH_2Ar$); osmometric M_r ($CHCl_3$, 37 °C), 590 (calcd, 585). Anal. Cacld for $C_{40}H_{40}O_4$: C, 82.16; H, 6.90. Found: C, 82.25; H, 7.02.

All of the analytical and spectral data for **4** support the fact that the macrocyclic ring survives the Claisen rearrangement intact. Of particular significance in this respect is the temperature-dependent ^1H NMR spectrum, which displays a singlet resonance for the $ArCH_2Ar$ methylene hydrogens at temperatures above 60 °C and a pair of doublets at temperatures below 20 °C. This behavior is best interpreted in terms of a "cone" conformation that is interconverting rapidly on the NMR time scale above room temperature and slowly below room temperature.[12-14] Among the four possible conformations ("cone", "partial cone", "1,2-alternate", "1,3-alternate"), the "cone" is favored (especially in nonpolar solvents[14]) because of the very strong intramolecular hydrogen bonding between the four OH groups at the "bottom" of the calix. Thus, in spite of this conformational mobility, appropriately functionalized calixarenes may have the capacity to serve as catalysts via host-guest complexation that requires the "cone" conformation. Nevertheless, it is of interest to prepare a conformationally rigid calixarene that exists at all times in the "cone" conformation. This has been accomplished by conversion to the tetrakis(trimethylsilyl) derivative (**5**). The ^1H NMR pattern for each of the four conformations is distinctive, allowing a definitive characterization of the conformation on this basis. For example, the pattern that would be expected for the tetrakis-(trimethylsilyl) ether of *p-tert*-butylcalix[4]arene (**5a**) in the "cone"

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