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Conformations of the Acyl Esters of *p*-Tert-butylcalix[4]arene and Calix[4]arene

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Tetra acyl esters of *p*-tert-butylcalix[4]arene and calix[4]arene, including acetyl, propionyl, butyryl and isobutyryl, are synthesized and their conformations are inferred from $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectra. The conformer distribution is affected by the presence of *t*-butyl group, whereas the acylation products of *p*-*t*-butylcalix[4]arene are the cone conformers, those of calix[4]arene are mostly partial cone and/or 1,3-alternate conformers. The conformational outcome is also affected by the method of preparation, the NaH-induced reaction is preferred to the acid-induced reaction for cone and partial cone. Interestingly, 1,2-alternate conformer was isolated in 14% yield from the butyrylation of calix[4]arene.

Introduction

Calixarenes are cavity containing macrocyclic compound made up of phenol and formaldehyde building blocks, and have received a great deal of attention in recent years because of their basket shape and their ability to be functionalized in various ways^{1,2}. The cavity of calixarene is conformationally mobile³ and exists four possible conformational isomers; cone, partial cone, 1,2-alternate and 1,3-alternate as shown on Figure 1.

Shaping the cavity plays a potentially vital role in the design of calixarenes as enzyme mimics, for host-guest interactions depend on complementarity in shape as well as functionality. Upon replacement of the phenolic hydrogens with larger than ethyl group, the calix[4]arenes become conformationally inflexible, existing as discrete entities in one or another of the conformations^{4,5}. However, considerable confusion still exists in the conformer distribution on the alkylation or acylation of calixarene. In a study of the arylation of calix[4]arenes, Gutsche⁶ reported that the products partition principally between the cone and 1,3-alternate conformers and the particular conformation in which a calix[4]arene is fixed upon derivatization is dependent on the temperature, the solvent, the para substituent of the calix[4]arene, and the reactivity of the arylation agent. He also reported that the products of arylmethylation partition principally between the cone and partial cone conformers⁷. The conformation of

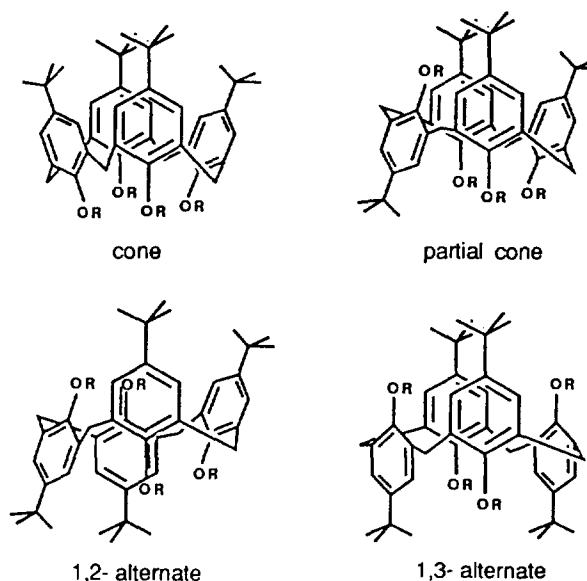
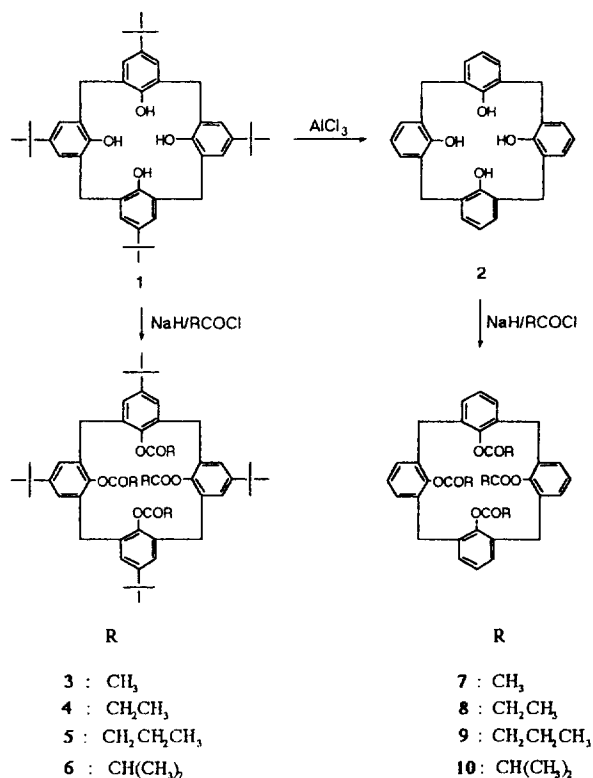


Figure 1. Conformations of calix[4]arene.

a derivatized calix[4]arene can be readily established on the bases of its $^1\text{H-NMR}$ spectrum, particularly from the patterns arising from the methylene protons joining the aromatic rings of the cyclic array, the cone conformer shows



Scheme 1. Syntheses of tetra acyl esters of *p*-*tert*-butylcalix[4]arene and calix[4]arene.

one pair of doublets, the partial cone conformer two pairs of doublets or a pair of doublets and a singlet, the 1,2-alternate conformer one singlet and two doublets, and the 1,3-alternate conformer one singlet. ¹³C-NMR spectrum also can be utilized for the conformational assignment of calix[4]arene⁸, shows resonances at around 38 and 31 ppm for the bridge methylene carbons, the down field resonance is characteristic of a methylene carbon carrying adjacent aromatic moieties 'anti' to one another, the upfield one is characteristic of a methylene carbon carrying these groups 'syn' to one another. The present paper deals with the investigation of conformation of tetra acyl esters of *p*-*tert*-butylcalix[4]arene and calix[4]arene.

Results and Discussions

Tetra acyl esters of *p*-*tert*-butylcalix[4]arene **3-10** were prepared as shown on Scheme 1.

p-*Tert*-butylcalix[4]arene **1** was treated with corresponding acid chloride and NaH in dry THF. After refluxing 2 h, solvent was evaporated. Excess NaH was decomposed with water, and the product was extracted with chloroform. The organic layer was washed with water, dried, and then evaporated to afford the crude products, which were purified by recrystallization or flash chromatography⁹. The tetra acetate of *p*-*tert*-butylcalix[4]arene **3** shows three sharp singlets and a pair of doublets in ¹H-NMR spectrum. ¹³C-NMR spectrum shows a single resonance each for the carbonyl carbons, methyl and quaternary carbons of *t*-butyl groups, and methylene carbons (at 30.99 ppm) of the 'calix' along with four lines for the aryl carbons. Only the cone conformation is commensurated with these spectral data. Gutsche⁴ reported the synthesis of compound **3** by the treatment of **1** with refluxing acetic anhydride in the presence of conc. sulfuric acid. Based on the ¹H-NMR spectrum they interpreted the conformation of this compound as a partial cone¹⁰ and which was confirmed by Andreotti¹¹ via X-ray crystallographic structure determination. In the preparation of propionyl ester, two products were isolated based on the solubility difference in acetone. The ¹H-NMR spectrum of the acetone less soluble compound **4a** (high melting, 9% yield) shows a singlet for the ArCH₂Ar protons and one set of triplet and quartet for the methyl and methylene protons of ethyl groups. The ¹³C-NMR spectrum of **4a** shows single peak each for carbonyl carbons and bridging methylene carbons and four peaks from aromatic carbons, particularly significant is the position of methylene carbons at 38.47 ppm which is commensurated with the 1,3-alternate conformation. ¹H-NMR spectrum of the acetone more soluble compound **4b** (lower melting, 75% yield) shows four doublets for the ArCH₂Ar protons, three sets of quartet and triplet in the ratio of 1 : 2 : 1 for the methylene and methyl protons of ethyl groups. The ¹³C-NMR spectrum of **4b** shows three peaks for carbonyl carbons, two peaks at 38.53 and 31.00 ppm for ArCH₂Ar carbons and twelve peaks from the aromatic carbons. Therefore it is a partial cone conformer. ¹H-NMR spectra of **5** and **6** were commensurated with the cone conformation respectively; singlet for aromatic protons, one pair of doublet for ArCH₂Ar protons and one singlet for *t*-butyl protons. ¹³C-NMR spectra also supports the cone conformation; one peak for carbonyl carbons, four peaks for aromatic carbons, and one peak at 30.47 ppm from the ArCH₂Ar carbons. Table 1 shows the ¹H and ¹³C-NMR spectral data of the esters of *p*-*tert*-butyl-calix[4]arene.

In the arylation of *p*-substituted calix[4]arene. Gutsche and coworkers⁶ reported that there is a considerably greater

Table 1. ¹H- and ¹³C-NMR Spectral Peaks of the Conformers of *p*-*tert*-butylcalix[4]arene Tetra Acyl Esters

Compound	¹ H-NMR			¹³ C-NMR					Conformation
	ArH	CH ₂	<i>t</i> Bu	C=O	Ar	CH ₂	C(CH ₃) ₃	C(CH ₃) ₃	
3	One singlet	One pair of doublets	One singlet	1	4	1 (30.99)	1	1	Cone
4a	One singlet	One singlet	One singlet	1	4	1 (38.47)	1	1	1,3-alternate
4b	Multiplet	One pair of AB quarters	3 singlets (1 : 1 : 2)	3	14	2 (38.53) (31.00)	3	3	Partial cone
5	One singlet	One pair of doublets	One singlet	1	4	1 (30.56)	1	1	Cone
6	One singlet	One pair of doublets	One singlet	1	4	1 (30.47)	1	1	Cone

Table 2. Effect of Method of Acylation on the Conformer Distribution

Compound	NaH-induced reaction		Acid-induced reaction	
	conformation	yield	conformation	yield
3	Cone	89%	Partial cone ¹⁰	42%
7	Cone	25%	Partial cone	34%
	Partial cone	50%	1,3-alternate	41%
10	Partial cone	74%	Partial cone	55%
			1,3-alternate	13%

preference for the formation of the cone conformer in the case of *p*-*tert*-butylcalix[4]arene than in the case of *p*-allylcalix[4]arene or calix[4]arene. They interpreted this in terms of a competition between the rate of conformational interconversion and the rate of derivatization, *viz.* if the rate of conformational inversion is slow relative to the rate of derivatization, the cone or partial cone conformer will be formed. Studies of the conformational behavior of the calixarene¹² have shown that the rate of conformational inversion, as measured by the coalescence temperature obtained from ¹H-NMR spectral measurements, in which *p*-*tert*-butyl group is particularly effective in maintaining the cone conformation. To investigate the effect of *p*-*tert*-butyl group on the conformational outcome of acylation reaction, esterification were carried out with calix[4]arene. Calix[4]arene **2** in THF was treated with NaH and the appropriate acyl chloride to yield products whose conformations were established by inspection of their ¹H and ¹³C-NMR spectra.

Treatment of calix[4]arene with acetyl chloride yields tetraacetate **7** as a 2 : 5 mixture of cone and partial cone conformers based on ¹H-NMR spectrum. Isolation of pure conformers was tried, but was not successful. Gutsche and coworkers¹¹ prepared the same compound by treatment of **2** with acetic anhydride and *p*-toluenesulfonic acid and, based on the ¹H and ¹³C-NMR spectra, they assigned the conformation as 1,3-alternate. Compound **7** was also prepared in our labo-

ratory¹³ by treatment of **2** with acetic anhydride and conc sulfuric acid. The product was a 6 : 5 mixture of 1,3-alternate and partial cone conformers. From the results of preparation of **3**, **7** and **10**, it is evident that the NaH-induced reaction is preferred to the acid-induced reaction for cone and partial cone conformer as shown on Table 2.

The propionyl ester of calix[4]arene **8a** shows ¹H and ¹³C-NMR spectra whose patterns are best interpreted in terms of a 1,3-alternate conformation. When the propionyl chloride was mixed with calix[4]arene and NaH simultaneously instead of dropping of acylating agent in THF into the pre-mixture of **2** and NaH in THF, a different conformer **8b** was obtained as the only isolable product, whose ¹H and ¹³C-NMR spectra were commensurated with the partial cone conformation.

When the calix[4]arene **2** was reacted with butyryl chloride, two products were isolated based on the solubility difference in acetone. In ¹H-NMR spectrum of the acetone insoluble compound **9a** (high melting, 14% yield), aromatic protons give two sets of multiplet in 2 : 1 ratio, those of bridge methylene shows a singlet and two pairs of doublets in 2 : 1 : 1 ratio. This pattern is commensurated with 1,2-alternate conformation. ¹³C-NMR spectrum, which shows single peak from carbonyl carbons and two peaks from the bridge methylene carbons at 38.02 and 29.33 ppm, also supports the result of ¹H-NMR spectrum. Substitution at all four phenolic oxygen atoms of a calix[4]arene generally leads to conformationally rigid products, which exist in the cone, the partial cone, the 1,3-alternate conformation or mixture of these, depending on the substituent and on the reaction conditions. The 1,2-alternate conformation seems to be excluded as a product of tetra substitution except only one case. Gutsche and coworkers^{14,15} published that the tetrakis (dimethylthiocarbamate) of *p*-*tert*-butylcalix[4]arene is identified as 1,2-alternate conformer by X-ray crystallography. However, the existence of 1,2-alternate conformer in a solution of conformationally flexible calix[4]arene tetra ether are reported by Shinkai and Reinhoudt. Shinkai and coworkers^{16,17} reported that the tetra ethylether of **1** is flexible. They claimed that

Table 3. ¹H- and ¹³C-NMR Spectral Peaks of the Conformers of Calix[4]arene Tetra Acyl Esters

Compound	¹ H-NMR		¹³ C-NMR			Conformation
	ArH	CH ₂	C=O	Ar	CH ₂	
7a	Multiplet	One pair of doublets	1	4	1 (30.60)	Cone
7b	Multiplet	One doublet	3	12	2 (37.53)	Partial cone
		One pair of doublets (2 : 1 : 1)			(30.92)	
7c ^d	Singlet	Singlet	1	4	1 (37.67)	1,3-alternate
8a	Singlet	Singlet	1	4	1 (37.77)	1,3-alternate
8b ^b	Multiplet	One doublet	3	14	2 (37.03)	Partial cone
		One pair of doublets (2 : 1 : 1)			(30.43)	
9a	Multiplet	One singlet	1	6	2 (38.02)	1,2-alternate
		One pair of doublets (2 : 1 : 1)			(29.33)	
9b	Singlet	Singlet	1	4	1 (37.49)	1,3-alternate
10a	Multiplet	One doublet	3	14	2 (38.36)	Partial cone
		One pair of doublets (2 : 1 : 1)			(31.68)	
10b ^c	Singlet	Singlet	1	4	1 (37.86)	1,3-alternate

^aPrepared by cone sulfuric acid catalyzed esterification, ^bPrepared by the modified NaH-induced esterification.

the partial cone, when dissolved in 1,1,2,2-tetrachloroethane and heated to temperature above 100°C, isomerized to a 1,2-alternate conformation until equilibrium was reached. Reinhoudt¹⁸ reported that in solution tetra substituted calix[4]arenes adopt all four possible conformation, including 1,2-alternate, when these are in the thermodynamic equilibrium, and sometimes the 1,2-alternate is even in the thermodynamically most stable conformation depending on the substituent. A 1,2-alternate conformation has been reported by Atwood¹⁹ for the adduct of *p*-tert-butylcalix[4]arene methyl ether with two molecules of AlMe₃ in the solid state, but in this case the conformation is determined by the steric demands of the binding of AlMe₃ moieties. ¹H and ¹³C-NMR spectra of acetone soluble product **9b** (low melting, 73% yield) supports the 1,3-alternate conformation. When the calix[4]arene **2** was reacted with isobutyryl chloride, partial cone conformer **10a** was isolated in 74% yield. On the preparation of the same compound by the treatment of **2** with isobutyric anhydride in the presence of conc sulfuric acid and additional isomer was produced. The major isomer, isolated in 55% yield, was the partial cone. The spectral data of the minor isomer **10b**, isolated in 13%, was interpreted as 1,3-alternate conformation. Table 3 shows the ¹H and ¹³C-NMR spectral data of the esters of calix[4]arene.

The data in Table 1 and 3 support the idea that *p*-tert-butyl group is effective in maintaining the cone conformation on acylation of calix[4]arene.

Experimental

Melting points of all compounds were taken in sealed and evacuated capillary tubes on a syblon thermolyne apparatus with polarizing microscope and were not corrected. IR spectra were determined on a Nicolet Impact 400 FT-IR spectrometer as KBr pellet. ¹H-NMR and ¹³C-NMR spectra were recorded on Varian Gemini 300 (300 and 75 MHz) instrument. Chemical shifts are recorded as values in parts per million relative to TMS (δ 0.0) as an internal standard. TLC analyses were carried out on silica gel plates (absorbent thickness 250 μm). Flash chromatography was carried out with E. Merck silica gel (230-400 mesh ASTM). Elution rate were 2 in./min.

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrahydroxycalix[4]arene 1 was prepared in 52% yield from *p*-tert-butylphenol and formaldehyde as described elsewhere²⁰; mp. 344-346°C (lit²⁰ 344-346°C).

25,26,27,28-Tetrahydroxycalix[4]arene 2 was prepared in 74% yield by AlCl₃-catalyzed removal of the *tert*-butyl groups from the compound **1** following the published procedure²¹; mp. 315-317°C (lit²¹ 314-318°C).

Preparation of tetra-acylesters via NaH-induced esterification of *p*-tert-butylcalix[4]arene. A solution of *p*-tert-butylcalix[4]arene **1** (1.00 g, 1.35 mmole) in 40 mL of dry THF was placed in an oil bath, treated with NaH (4 mole equivalent per OH group, 60% oil dispersion), and stirred for 30 min. A solution of the corresponding acid chloride (5 mole equivalent per OH group) in 10 mL of dry THF was added dropwise, and the reaction mixture was refluxed an additional 2 h. The solvent was removed on a rotary evaporator, and the residue was treated with water. The product was extracted with 20 mL portions of CHCl₃ twice,

the combined organic layer was washed with water three times, dried, concentrated, and treated with 20 mL of methanol to yield the crude product, which was purified as follows;

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetraacetyoxycalix[4]arene 3. The crude product (980 mg, 89%) was recrystallized from CHCl₃/methanol to afford 870 mg (79%) of crystalline solid; mp. 336-338°C; IR (KBr) 1758 cm⁻¹ (C=O); ¹H-NMR (CDCl₃) δ 7.27 (s, 8, ArH), 3.75 (d, 4, CH₂, *J*=13.2 Hz), 3.30 (d, 4, CH₂, *J*=13.2 Hz), 2.51 (s, 12, CH₃), 1.11 (s, 36, *t*Bu); ¹³C-NMR (CDCl₃) δ 171.40 (C=O), 148.55, 144.08, 133.24, 126.02 (Ar), 34.27 (C(CH₃)₃), 31.14 (C(CH₃)₃), 30.99 (ArCH₂Ar), 21.63 (CH₃).

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetrapropionyoxycalix[4]arene. 4a and 4b. The crude product (1.40 g, 88%) was boiled with 15 mL of acetone to leave 110 mg (9%) of **4a** (1,3-alternate) as crystalline solid; mp > 360°C; IR (KBr) 1743 cm⁻¹ (C=O); ¹H-NMR (CDCl₃) δ 6.99 (s, 8, ArH), 3.71 (s, 8, CH₂), 1.61 (q, 8, CH₂, *J*=7.4 Hz), 1.27 (s, 36, *t*Bu), 0.95 (t, 12, CH₃, *J*=7.4 Hz); ¹³C-NMR (CDCl₃) δ 172.20 (C=O), 147.86, 147.77, 133.06, 126.20 (Ar), 38.47 (ArCH₂Ar), 34.39 (C(CH₃)₃), 31.59 (C(CH₃)₃), 26.01 (CH₂), 8.24 (CH₃). The acetone filtrate and washing were combined, concentrated and then treated with methanol to yield 890 mg (75%) of **4b** (partial cone) as crystalline solid; mp. 340-342°C; IR (KBr) 1781 cm⁻¹ (C=O); ¹H-NMR (CDCl₃) δ 7.27-6.81 (m, 8, ArH), 3.67 (d, 2, CH₂, *J*=15.9 Hz), 3.60 (d, 2, CH₂, *J*=12.9 Hz), 3.59 (d, 2, CH₂, *J*=15.9 Hz), 3.28 (d, 2, CH₂, *J*=12.9 Hz), 2.61 (q, 2, CH₂, *J*=7.5 Hz), 2.37 (q, 4, CH₂, *J*=7.5 Hz), 1.71 (q, 2, CH₂, *J*=7.5 Hz), 1.40 (s, 9, *t*Bu), 1.30 (s, 9, *t*Bu), 1.25 (t, 6, CH₃, *J*=7.5 Hz), 1.14 (s, 18, *t*Bu), 0.95 (t, 3, CH₃), 0.40 (t, 3, CH₃); ¹³C-NMR (CDCl₃) δ 174.70, 173.60, 172.29 (C=O), 149.08, 147.89, 144.77, 147.40, 144.80, 144.44, 134.15, 133.17, 133.06, 131.84, 126.98, 126.72, 126.19, 125.85 (Ar), 38.53, 31.00 (ArCH₂Ar), 34.53, 34.45, 34.22 (C(CH₃)₃), 31.76, 31.64, 31.43 (C(CH₃)₃), 27.15, 26.87, 26.22 (CH₂), 9.04, 8.87, 7.93 (CH₃).

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetra-*n*-butyloxycalix[4]arene 5. The crude product (1.14 g, 91%), which was 98 : 2 mixture of cone and partial cone conformer by the HPLC analysis, was recrystallized from methylene chloride and methanol to afford 940 mg (75%) of the desired product as crystalline solid; mp. 325-326°C; IR (KBr) 1751 cm⁻¹ (C=O); ¹H-NMR (CDCl₃) δ 6.96 (s, 8, ArH), 3.73 (d, 4, CH₂, *J*=13 Hz), 3.27 (d, 4, CH₂, *J*=13 Hz), 2.84 (t, 8, CH₂, *J*=7.5 Hz), 1.82 (sextet, 8, CH₂, *J*=7.5 Hz), 1.30 (s, 36, *t*Bu), 1.10 (t, 12, CH₃, *J*=7.5 Hz); ¹³C-NMR (CDCl₃) δ 173.51 (C=O), 147.38, 142.48, 132.96, 125.56 (Ar), 35.47 (CH₂), 33.88 (C(CH₃)₃), 31.07 (C(CH₃)₃), 30.56 (ArCH₂Ar), 18.01 (CH₂), 13.40 (CH₃).

5,11,17,23-Tetra-tert-butyl-25,26,27,28-tetra(2-methylpropanoxy)calix[4]arene 6. The crude product (1.18 g, 94%) was purified by flash chromatography (eluent was 9 : 1 mixture of hexane and acetone) to afford 940 mg (75%) of the desired product as crystalline solid; mp. 317-318°C; IR (KBr) 1751 cm⁻¹ (C=O); ¹H-NMR (CDCl₃) δ 6.93 (s, 8, ArH), 3.83 (d, 4, CH₂, *J*=12 Hz), 3.27 (d, 4, CH₂, *J*=12 Hz), 3.15 (septet, 4, CH, *J*=7 Hz), 1.36 (d, 24, CH₃, *J*=7 Hz), 1.11 (s, 36, *t*Bu); ¹³C-NMR (CDCl₃) δ 178.02 (C=O), 148.02, 143.80, 133.29, 125.96 (Ar), 34.22 (C(CH₃)₃), 33.11 (CH(CH₃)₂), 31.46 (C(CH₃)₃), 30.47 (ArCH₂Ar), 20.20 (CH(CH₃)₂).

Preparation of tetra-acylestere via NaH-induced esterification of calix[4]arene. A solution of calix[4]arene **2** (650 mg, 1.53 mmole) in 30 mL of dry THF was placed in an oil bath, treated with NaH (4 mole equivalent per OH group, 60% oil dispersion), and stirred for 30 min. A solution of the corresponding acid chloride (5 mole equivalent per OH group) in 10 mL of dry THF was added dropwise, and the reaction mixture was refluxed an additional 2 h. The reaction mixture was treated by the same procedure as describe above for the preparation of *p*-*tert*-butylcalix[4]arene tetra esters.

25,26,27,28-Tetraacetoxycalix[4]arene 7a and 7b.

The crude product (860 mg, 88%), which showed 2 spots on TLC, was tried to purify by recrystallization and flash chromatography, however, the isolation of pure product was not successful. A recrystallization from chloroform and methanol affords 730 mg (75%) of product as a 1:2 mixture of cone and partial cone conformers; mp softening at 350°C then dose not melt up to 360°C; IR (KBr) 1750 cm⁻¹ (C=O); **7a** (cone conformer); ¹H-NMR (CDCl₃) δ 7.13-6.93 (m, 12, ArH), 3.81 (d, 4, CH₂, *J*=13.5 Hz), 3.34 (d, 4, CH₂, *J*=13.5 Hz), 2.50 (s, 12, CH₃); ¹³C-NMR (CDCl₃) δ 171.09 (C=O), 146.53, 134.06, 129.19, 126.26 (Ar), 30.06 (ArCH₂Ar), 21.56 (CH₃). **7b** (partial cone conformer); ¹H-NMR (CDCl₃) δ 7.27-7.06 (m, 6, ArH), 6.90-6.71 (m, 6, ArH), 3.65 (d, 4, CH₂, *J*=3.3 Hz), 3.54 (d, 2, CH₂, *J*=13.6 Hz), 3.26 (d, 2, CH₂, *J*=13.6 Hz), 2.35 (s, 6, CH₃), 2.05 (s, 3, CH₃), 1.77 (s, 3, CH₃); ¹³C-NMR (CDCl₃) δ 170.79, 169.42, 168.88 (C=O), 146.59, 135.45, 134.61, 131.96, 130.66, 130.06, 129.95, 129.56, 126.64, 125.19 (Ar), 37.53, 30.92 (ArCH₂Ar), 21.61, 21.16, 20.44 (CH₃). The mixture of **7b** and **7c** (1,3-alternate) was prepared by the published procedure¹⁴. Calix[4]arene **2** (1.00 g, 2.36 mmole) was treated with 20 mL of acetic anhydride and one drop of conc sulfuric acid. The reaction mixture was heated under reflux for 1.5 h and poured into 100 mL of ice-water. The resulting precipitate was collected by filtration, washed with dilute NaHSO₃ solution and water several times, and then dried to afford the crude product (1.25 g, 89%). A recrystallization from benzene affords 1.05 g (75%) of a 5:6 mixture of partial cone conformer **7b** and 1,3-alternate conformer **7c**. The separation of the pure isomer was not tried. **7c**; mp¹⁰ 399-402°C; IR (KBr) 1735 cm⁻¹ (C=O); ¹H-NMR (CDCl₃) δ 7.07 (s, 12, ArH), 3.76 (s, 8, CH₂), 1.55 (s, 12, CH₃); ¹³C-NMR (CDCl₃) δ 168.88 (C=O), 148.83, 133.62, 129.56, 125.85 (Ar), 37.67 (ArCH₂Ar), 20.44 (CH₃).

25,26,27,28-Tetra(*propanoyloxy*)calix[4]arene 8a.

The crude product (960 mg, 97%) was recrystallized from ether and hexane to afford 770 mg (78%) of **8a** (1,3-alternate) as crystalline solid; mp. 310-312°C (dec); IR (KBr) 1735 cm⁻¹ (C=O); ¹H-NMR (CDCl₃) δ 7.02 (s, 12, ArH), 3.72 (s, 8, ArCH₂Ar), 1.69 (q, 8, CH₂, *J*=7.5 Hz), 1.01 (t, 12, CH₃, *J*=7.5 Hz); ¹³C-NMR (CDCl₃) δ 172.01 (C=O), 148.98, 133.73, 129.49, 125.56 (Ar), 37.77 (ArCH₂Ar), 26.41 (COCH₂), 8.36 (CH₃). The partial cone conformer **8b** was prepared by refluxing the mixture of **2** (0.65 g, 1.53 mmole), NaH (4 mole equiv. per OH group, 60% oil dispersion), and propionyl chloride (5 mole equiv. per OH group) in 40 mL THF for 2 h followed by usual treatment. The crude product (1.81 g, 91%), which showed 2 spots on TLC (**8a** and **8b**), was recrystallized from chloroform and methanol to produce 0.74 g (74%) of compound **8b** as a crystalline solid; mp. 286-288°C; IR (KBr)

1750 cm⁻¹ (C=O); ¹H-NMR (CDCl₃) δ 7.26-7.13 (m, 6, ArH), 6.88-6.64 (m, 6, ArH), 3.60 (d, 4, CH₂, *J*=4.8 Hz), 3.48 (d, 2, CH₂, *J*=13.8 Hz), 3.22 (d, 2, CH₂, *J*=13.8 Hz), 2.58 (q, 2, CH₂, *J*=7.5 Hz), 2.55 (q, 2, CH₂, *J*=7.5 Hz), 2.37 (q, 2, CH₂, *J*=7.5 Hz), 2.24 (q, 2, CH₂, *J*=7.5 Hz), 1.30 (t, 6, CH₃, *J*=7.5 Hz), 1.28 (t, 6, CH₃, *J*=7.5 Hz), 1.09 (t, 6, CH₃, *J*=7.5 Hz); ¹³C-NMR (CDCl₃) δ 174.17, 172.70, 172.20 (C=O), 146.19, 135.17, 134.31, 132.77, 131.44, 130.32, 129.53, 129.45, 129.18, 128.76, 125.98, 124.84, 124.54 (Ar), 37.03, 30.43 (ArCH₂Ar), 27.38, 27.20, 25.09 (CH₂), 8.89, 8.55, 7.65 (CH₃).

25,26,27,28-Tetra(*butanoyloxy*)calix[4]arene 9a and 9b.

The crude product (990 mg, 92%) was triturated with 15 mL of acetone at room temperature to leave 150 mg (14%) of **9a** (1,2-alternate) as acetone insoluble crystalline solid; mp. 309-310°C; IR (KBr) 1735 cm⁻¹ (C=O); ¹H-NMR (CDCl₃) δ 7.27-7.26 (m, 4, ArH), 7.12-7.06 (m, 8, ArH) 3.82 (s, 4, CH₂), 3.65 (d, 2, CH₂, *J*=13.5 Hz), 3.34 (d, 2, CH₂, *J*=13.5 Hz), 1.86 (t, 2, COCH₂, *J*=7.5 Hz), 1.80 (t, 2, COCH₂, *J*=7.5 Hz), 1.43 (sextet, 8, CH₂, *J*=7.5 Hz), 1.29 (t, 2, COCH₂, *J*=7.5 Hz), 1.23 (t, 2, COCH₂, *J*=7.5 Hz), 0.87 (t, 12, CH₃, *J*=7.5 Hz); ¹³C-NMR (CDCl₃) δ 171.66 (C=O), 147.38, 133.68, 132.15, 129.74, 129.30, 125.34 (Ar), 38.02 (ArCH₂Ar), 34.34 (CH₂), 29.33 (ArCH₂Ar), 17.36 (CH₂), 13.33 (CH₃). The acetone filtrate and washing were combined, concentrated and then treated with methanol to yield 0.79 g (73%) of **9b** (1,3-alternate) as crystalline solid; mp. 224-225°C; IR (KBr) 1740 cm⁻¹ (C=O); ¹H-NMR (CDCl₃) δ 7.04 (s, 12, ArH), 3.74 (s, 8, ArCH₂Ar), 1.64-1.51 (m, 16, COCH₂ and CH₂), 0.92 (t, 12, CH₃, *J*=6.9 Hz); ¹³C-NMR (CDCl₃) δ 170.76 (C=O), 148.63, 133.30, 129.22, 125.14 (Ar), 37.49 (ArCH₂Ar), 34.63 (COCH₂), 17.08 (CH₂), 13.49 (CH₃).

25,26,27,28-Tetra(*2-methylpropanoyloxy*)calix[4]arene 10a.

The crude product (940 mg, 87%) was recrystallized from ether and hexane to yield 800 mg (74%) of the desired product **10a** (partial cone) as crystalline solid; mp. 286-287°C; IR (KBr) 1735 cm⁻¹ (C=O); ¹H-NMR (CDCl₃) δ 7.18-6.94 (m, 12, ArH), 3.84 (d, 2, CH₂, *J*=13.5 Hz), 3.74 (d, 4, CH₂, *J*=13.5 Hz), 3.39 (d, 2, CH₂, *J*=13.5 Hz), 2.55 (septet, 2, CH, *J*=7.2 Hz), 2.26 (septet, 1, CH, *J*=7.2 Hz), 2.10 (septet, 1, CH, *J*=7.2 Hz), 1.34 (d, 6, CH₃, *J*=7.2 Hz), 1.28 (d, 6, CH₃, *J*=7.2 Hz), 0.96 (d, 6, CH₃, *J*=7.2 Hz), 0.35 (d, 6, CH₃, *J*=7.2 Hz); ¹³C-NMR (CDCl₃) δ 175.13, 174.96, 174.10 (C=O), 146.71, 134.18, 133.80, 133.53, 133.29, 130.66, 130.46, 130.12, 129.47, 128.91, 128.38, 128.65, 125.58, 120.51 (Ar), 38.36 (ArCH₂Ar), 34.09, 33.64, 33.49 (CH), 31.68 (ArCH₂Ar), 19.57, 18.83, 18.52, 17.35 (CH₃). The 1,3-alternate conformer **10b** was prepared by the published procedure¹⁴. Calix [4]arene **2** (1.00 g, 2.36 mmole) was treated with 20 mL of isobutyric anhydride and one drop of conc sulfuric acid. The reaction mixture was heated under reflux for 3 h and poured into 100 mL of ice-water. The resulting precipitate was collected by filtration, washed with dilute NaHSO₃ solution and water several times, and then dried to afford the crude product which was triturated with 15 mL of acetone at room temperature to leave 140 mg (13%) of **10b** (1,3-alternate) as acetone insoluble crystalline solid; mp. 315-317°C (dec); IR (KBr) 1735 cm⁻¹ (C=O); ¹H-NMR (CDCl₃) δ 7.08-7.02 (m, 12, ArH), 3.71 (s, 8, CH₂), 2.26 (septet, 4, CH, *J*=6.9 Hz), 0.96 (d, 24, CH₃, *J*=6.9 Hz); ¹³C-NMR (CDCl₃) δ 174.79 (C=O), 149.02, 133.83, 130.11, 125.44 (Ar), 37.86 (ArCH₂Ar), 33.14 (CH), 18.49 (CH₃). In this preparation **10a** was obtained

in 55% yield.

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A Nonlinear Theory for the Oregonator Model with an External Input

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An approximate nonlinear theory of the Oregonator model is obtained with the aid of an ordinary perturbation method when the system is perturbed by some kinds of external input. The effects of internal and external parameters on the oscillations are discussed in detail by taking specific values of the parameters. A simple approximate solution for the Oregonator model under the influence of a constant input is obtained and the result is compared with the numerical result. For other types of external inputs the approximate solutions up to the fourth order expansion are compared with the numerical results. For a periodic input, we found that the entrainment depends crucially on the difference between the internal and external frequencies near the bifurcation point.

Introduction

With the aid of the star expansion method, originally proposed by Houard and his coworkers¹⁻³, two⁴ of us have obtained approximate nonlinear solutions for the Schlögl models⁵ under the influence of some kinds of external input and compared the numerical predictions with the exact solution available for some cases and also with the linearized solutions and the approximate ones obtained by the Feynman method. Although the approximate solution based on the star

expansion method and that obtained by the Feynman method numerically agree well with each other, the former is more systematic and simpler. We also have extended the star expansion method to the Lotka-Volterra model, which is the two-component chemical reaction model exhibiting the sustained oscillation and then discussed the effects of nonlinearity, amplitude and frequency of the external input on the chemical oscillations in the model by taking specific values of the model parameters⁶.

The purpose of the present paper is to discuss the effects