Selective Monocarbamoylation of Symmetrical Diols with Alkyl Halides and Potassium Cyanate Using Phase-Transfer Catalysis

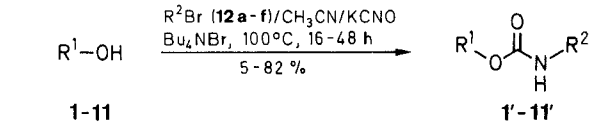
Mahavir Prashad,* John C. Tomesch, William J. Houlihan
Sandoz Research Institute, East Hanover, NJ 07936, USA

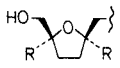
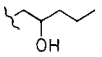
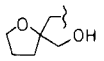
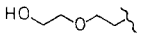
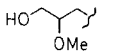
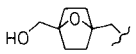
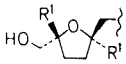
A convenient method for the selective monocarbamoylation of diols by reaction with alkyl isocyanates, generated *in situ* from alkyl halides and potassium cyanate under phase-transfer catalysis, is described. Under these conditions the ease of reaction shows the following order *cis*-diols > *trans*-diols and diols > monoalcohols. An increase in the number of methylene groups between two hydroxyl groups lead to a decrease in product yields. A plausible mechanism to explain these results is proposed.

(Alkylaminocarbonyloxy)-hydroxyalkanes, such as **1′–5′**, serve as important intermediates in the synthesis of Platelet Activating Factor (PAF) receptor antagonists.[1] In principle, these compounds can be prepared by the reaction of the corresponding diols with an appropriate alkyl isocyanate as reported[2] for the diol **4a**, however, in poor yield. The limited availability of commercial alkyl isocyanates with varying R^2 groups, necessary for structure-activity relationship studies, coupled with the toxicity[3] associated with these compounds restricting their direct use in large scale syntheses, prompted us to develop an alternative *in situ* generation method for the synthesis of these intermediates.

Direct displacement of an alkyl halide with cyanate anion to give an alkyl isocyanate is an attractive possibility. However, such a reaction in dimethylformamide has been reported to lead to trimerization or to a mixture of ureas and 1,3,5-trialkyl isocyanurates.[4] The use of phase-transfer catalysis (PTC) in this reaction is also described in the patent literature[5] to give high yields of trimeric products, i.e. trialkyl isocyanurates. In this paper we describe the *in situ* generation of alkyl isocyanates by the reaction of alkyl halides with potassium cyanate under PTC conditions and their reaction with diols to yield selectively monocarbamoylated products (Scheme A).

In our laboratories, octadecylcarbamate derivatives of 2,5-bis(hydroxymethyl)tetrahydrofurans were found to give rise to active PAF receptor antagonists.[1] Hence, octadecyl bromide was chosen as a representative case for the present study. Treatment of *cis*-2,5-bis(hydroxymethyl)tetrahydrofuran (**1a**) with potassium cyanate, octadecyl bromide, and tetrabutylammonium bromide in acetonitrile at 100 °C for 20 hours gave the



1-6, 1′-6′	R^1		7-11, 7′-11′	R^1	
1, 1′a		R = H	7, 7′a		
b		R = Me			
c		R = Ph	8, 8′a		n = 5
d		R = *t*-Bu	b		n = 8
2, 2′a			c		n = 16
3, 3′a			9, 9′a		
4, 4′a			10, 10′a		
5, 5′a					
6, 6′a		R = H	11, 11′a		n = 2
b		R = Me	b		n = 4

1′–11′, 12	R^2	1′–11′, 12	R^2
a	C_7H_{15}	d	$CH(CH_3)C_5H_{11}$
b	Bn	e	$(CH_2)_{14}C(CH_3)_3$
c	$C_{10}H_{21}$	f	$C_{18}H_{37}$

Scheme A

monocarbamate, *cis*-2-[octadecylaminocarbonyl)oxy]-methyl-5-hydroxymethyltetrahydrofuran (**1'af**) in 69% isolated yield (Table 1, entry 2). Under these conditions no bis-carbamate was isolated. The effect of the phase-transfer catalyst was evident since without it only 9% of the product was obtained (Table 1, entry 1). It is evident from Table 1 (entries 3 and 4) that benzyltriethylammonium bromide and methyltriphenylphosphonium bromide are as effective as tetrabutylammonium bromide, however, the later was chosen for further work.

To study their general applicability, these reaction conditions were tried on several symmetrical diols and one unsymmetrical diol. The results are listed in Table 1. As anticipated, most of the diols gave good yields of monocarbamates. Only in three cases were small amounts of bis-carbamate isolated (entries 5, 8 and 10). It was observed that an increase in the number of methylene groups between the two hydroxyl groups lead to a decrease in the yield of the product. Thus, 1,16-hexadecanediol (**8c**) (Table 1, entry 17) gave only a 5% yield of monocarbamate while 1,5-pentanediol (**8a**) afforded a 69% yield (entry 15). Also, *trans*-2,5-dimethyl-2,5-bis(hydroxymethyl)tetrahyrofuran (**6b**) (Table 1, entry 12) reacted more slowly than the corresponding *cis*-analog **1b** (Table 1, entry 5). Therefore, when a mixture of *cis*- and *trans*-diols (**1b** and **6b**, 6:4 ratio) was treated with one equivalent of alkyl halide only the corresponding *cis*-monocarbamate was obtained. Similar results were obtained when a mixture of *cis*- and *trans*-2,5-bis(hydroxymethyl)tetrahydrofuran (**1a** and **6a**) was used.

Table 1. Selective Monocarbamoylation of Diols with Octadecyl Bromide (**12f**) and Potassium Cyanate in the Presence of Phase-Transfer Catalysts

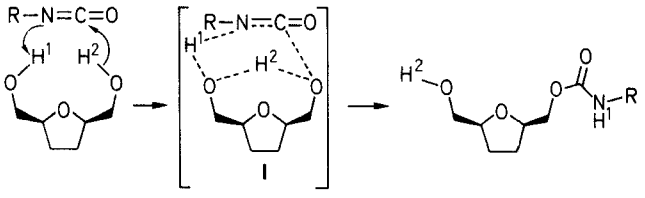
Entry	Substrate	Product	PT Catalyst[a] (molar equiv)	Time (h)	Yield[b] (%)
1	**1a**	**1'af**	none	20	9
2	**1a**	**1'af**	A (0.15)	20	69
3	**1a**	**1'af**	B (0.2)	20	66
4	**1a**	**1'af**	C (0.2)	20	67
5	**1b**	**1'bf**	A (0.15)	17	77
6	**1c**	**1'cf**	A (0.15)	24	65
7	**1d**	**1'df**	A (0.15)	24	65
8	**2a**	**2'af**	A (0.1)	23	82
9	**3a**	**3'af**	A (0.1)	16	62
10	**4a**	**4'af**	A (0.2)	24	69
11	**5a**	**5'af**	A (0.2)	20	62
12	**6b**	**6'bf**	A (0.2)	48	42
13	**7a**	**7'af**	none	22	10
14	**7a**	**7'af**	A (0.2)	22	71
15	**8a**	**8'af**	A (0.2)	22	69
16	**8b**	**8'bf**	A (0.2)	22	37
17	**8c**	**8'cf**	A (0.2)	24	5

[a] A = Tetrabutylammonium bromide,
B = Benzyltriethylammonium bromide,
C = Methyltriphenylphosphonium bromide.

[b] Yield of isolated product. In the cases of **1'bf**, **2'af** and **4'af**, the corresponding biscarbamates were obtained in 5, 8 and 5% yield respectively.

Reactions of diols with alkyl halides other than octadecyl bromide were also examined and are listed in Table 2. As expected, primary alkyl halides reacted faster and in good yields compared to secondary halides, which were sluggish and generally gave lower yields. It was noticed that the yield of monocarbamate did not vary greatly with chain length as they did with diols. This method was extended to some primary and secondary monoalcohols **9a–11b**, which gave satisfactory yields of the corresponding carbamates (Table 4).

In order to explain the observation that *cis*-diol **1b** reacts faster than the corresponding *trans*-diol **6b** and that the reactivity decreases on increasing the number of methylene groups between the two hydroxyl groups, we propose the mechanism depicted in Scheme **B**.



Scheme **B**

Table 2. Selective Monocarbamoylation of Diols with Primary and Secondary Alkylhalides and Potassium Cyanate in the Presence of Tetrabutylammonium Bromide (0.2 equiv)

Substrate Diol	R^2Br **12**	Product	Time (h)	Yield[a] (%)
1b	**e**	**1'be**	24	80
1b	**a**	**1'ba**	24	83
1b	**b**	**1'bb**	19	87
1b	**d**	**1'bd**	72	37
2a	**a**	**2'aa**	20	70
2a	**c**	**2'ac**	20	81
2a	**d**	**2'ad**	24	18

[a] Yield of the isolated product. In the cases of **1'ba**, **1'bb**, **2'aa** and **2'ac**, the corresponding bis-carbamate was isolated in 5, 7, 5 and 6%, respectively.

In this mechanism, a proton H^1 from one hydroxyl group of the diol is transferred directly[6] to the isocyanate nitrogen, and the oxygen of this hydroxyl group in turn shares the hydrogen atom H^2 from the other hydroxyl group of the diol via a cyclic transition state, e.g. **I**. Thus, in a *cis*- diol, where such a cyclic transition state is feasible, the reaction is faster than with the corresponding *trans*-diol where this transition state would be improbable. In fact, *trans*-diols may react by a different mechanism. Furthermore, an increase in the number of methylene groups between the two hydroxyl groups would also make such a mechanism less feasible since the ability of one oxygen to abstract a hydrogen atom from the other hydroxyl group is decreased.

This mechanism also explains the high selectivity towards monocarbamate formation, since the monocarbamate, when formed, should be less reactive towards the isocya-

nate than the diol. However, monocarbamate **1'bf** reacted under identical conditions to give 48% yield of *cis*-2,5-dimethyl-2,5-bis[octadecylaminocarbonyl)oxy]tetrahydrofuran, suggesting that monoalcohols can react with isocyanates but at a considerably slower rate and perhaps by a different mechanism, which normally is superceded by the mechanism proposed above for diols. A cyclic transition state for the reaction of monoalcohols with the isocyanates through their polymeric species has been proposed.[7]

In order to show that diols react faster than monoalcohols, which leads selectively to monocarbamoylation, some competitive experiments were performed. Thus,

Table 3. Analytical and Spectral Data of Monocarbamoyl Compounds Prepared

Product	mp (°C)	Molecular Formula[a] or Lit. mp (°C)	IR (neat/KBr) ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ, J (Hz)
1'af	79–80	$C_{25}H_{49}NO_4$ (427.7)	3345, 1684	0.88 (t, 3H, J = 6), 1.25 (br s, 30H), 1.4–1.6 (m, 2H), 1.6–1.8 (m, 1H), 1.81–2.1 (m, 3H), 2.75 (t, 1H, J = 5), 3.17 (q, 2H, J = 7.5), 3.39–3.57 (m, 1H), 3.66–3.84 (m, 1H), 3.9–4.3 (m, 4H), 4.81 (t, 1H, J = 5)
1'bf	45–47	$C_{27}H_{53}NO_4$ (455.7)	3440, 3344, 1697	0.88 (t, 3H, J = 6), 1.2 (s, 3H), 1.21–1.39 (br s, 33H), 1.4–1.58 (m, 2H), 1.6–2.07 (m, 3H), 2.11–2.31 (m, 1H), 3.06–3.55 (m, 5H), 3.71 (d, 1H, J = 11), 4.27 (d, 1H, J = 11), 4.85 (br t, 1H)
1'be	46–47	$C_{27}H_{53}NO_4$ (455.7)	3397, 3286, 1697	0.86 (s, 9H), 1.11–1.35 (m + s, 30H), 1.49–1.57 (m, 2H), 1.6–2.08 (m, 3H), 2.13–2.32 (m, 1H), 3.05–3.56 (m, 5H), 3.73 (d, 1H, J = 11), 4.29 (d, 1H, J = 11), 4.76 (br t, 1H)
1'ba	oil	$C_{16}H_{31}NO_4$ (301.4)	3341, 1704	0.87 (t, 3H, J = 6), 1.19 (s, 3H), 1.21–1.48 (br s, 11H), 1.49–1.58 (m, 2H), 1.61–2.07 (m, 3H), 2.12–2.31 (m, 1H), 3.06–3.56 (m, 5H), 3.72 (d, 1H, J = 12.5), 4.3 (d, 1H, J = 12.5), 4.79 (br s, 1H)
1'bb	oil	$C_{16}H_{23}NO_4$ (293.4)	3336, 1701	1.19 (s, 3H), 1.3 (s, 3H), 1.6–1.77 (m, 1H), 1.77–2.07 (m, 2H), 2.12–2.31 (m, 1H), 3.2 (br s, 1H), 3.4 (dd, 2H, J = 12), 3.76 (d, 1H, J = 11), 4.28–4.45 (m, 4H), 5.16 (br t, 1H), 7.28 (s, 5H)
1'bd	oil	$C_{16}H_{31}NO_4$ (301.4)	3340, 1701	0.9 (t, 3H, J = 6), 1.12 (d, 3H, J = 6), 1.2 (s, 3H), 1.23–1.4 (br s, 11H), 1.6–2.08 (m, 3H), 2.12–2.32 (m, 1H), 3.4 (dd, 2H, J = 11), 3.6–3.8 (m, 3H), 4.26 (dd, 1H, J = 5), 4.57 (d, 1H, J = 7)
1'cf	40–41	$C_{37}H_{57}NO_4$ (579.9)	3315, 1700	0.89 (t, 3H, J = 7), 1.25 (s, 30H), 1.49 (m, 2H), 2.05–2.26 (m, 2H), 2.35–2.55 (m, 1H), 2.64–2.86 (m, 1H), 3.2 (q, 2H, J = 7), 3.51–3.88 (m, 2H), 3.44–4.03 (m, 2H), 4.72 (d, 1H, J = 11), 4.81 (t, 1H, J = 5)
1'df	oil	$C_{33}H_{65}NO_4$ (539.9)	3343, 1701	0.89 (t, 3H, J = 6), 1.0, 1.23 (2s, 48H), 1.4–1.72 (m, 4H), 1.8–1.98 (m, 2H), 2.98 (d, 1H, J = 10), 3.15 (q, 2H, J = 7.5), 3.32 (d, 1H, J = 10), 3.77 (t, 1H, J = 10), 4.14 (q, 2H, J = 12.5), 4.9 (br m, 1H)
2'af	57–58	$C_{25}H_{49}NO_4$ (427.7)	3344, 1685	0.86 (t, 3H, J = 6), 1.21 (br s, 30H), 1.39–2.03 (m, 6H), 2.82 (t, 1H, J = 6), 3.15 (q, 2H, J = 7), 3.44 (d, 2H, J = 7), 3.78–3.98 (m, 3H), 4.22 (d, 1H, J = 11), 4.81 (br t, 1H)
2'aa	oil	$C_{14}H_{27}NO_4$ (273.4)	3447, 1717	0.89 (t, 3H, J = 6), 1.28 (br s, 8H), 1.4–2.04 (m, 6H), 2.80 (t, 1H, J = 7.5), 3.17 (q, 2H, J = 7.5), 3.45 (d, 2H, J = 8), 3.81–3.99 (m, 3H), 4.26 (d, 1H, J = 11), 4.80 (br t, 1H)
2'ac	oil	$C_{17}H_{33}NO_4$ (315.5)	3447, 1715	0.89 (t, 3H, J = 7), 1.28 (br s, 14H), 1.4–2.06 (m, 6H), 2.82 (t, 1H, J = 7.5), 3.18 (q, 2H, J = 6), 3.45 (d, 2H, J = 7), 3.82–3.99 (m, 3H), 4.26 (d, 1H, J = 11), 4.82 (br t, 1H)
2'ad	oil	$C_{14}H_{27}NO_4$ (273.4)	3341, 1700	0.88 (t, 3H, J = 6), 1.14 (d, 3H, J = 7), 1.18–1.5 (m + br s, 8H), 1.6–2.05 (m, 4H), 2.91 (br, 1H), 3.45 (s, 2H), 3.55–3.75 (m, 1H), 3.8–3.99 (m, 3H), 4.23 (d, 1H, J = 11), 4.7 (br t, 1H)
3'af	72–73	$C_{23}H_{47}NO_4$ (401.6)	3325, 1685	0.88 (t, 3H, J = 6), 1.24 (br s, 30H), 1.39–1.58 (m, 2H), 2.0 (br, 1H), 3.14 (q, 2H, J = 6), 3.52–3.77 (m, 6H), 4.22 (t, 2H, J = 5), 4.77 (br t, 1H)
4'af	56–58	55–56[2]	3351, 1689	0.89 (t, 3H, J = 6.7), 1.28 (s, 32H), 2.55 (t, 1H, J = 7), 3.17 (q, 2H), 3.4–3.75 (m, 3H), 3.46 (s, 3H), 4.22 (dd, 2H), 4.82 (br, 1H)
5'af	75–76	$C_{27}H_{51}NO_4$ (453.7)	3363, 1690	0.89 (t, 3H, J = 7), 1.25 (br s, 32H), 1.39–1.89 (m, 8H), 2.1 (br s, 1H), 3.15 (q, 2H, J = 5), 3.81 (s, 2H), 4.32 (s, 2H), 4.85 (br t, 1H)
6'bf	60–61	$C_{27}H_{53}NO_4$ (455.7)	3462, 3369, 1695	0.89 (t, 3H, J = 7.5), 1.2 (s, 3H), 1.26 (s, 33H), 1.39–1.57 (m, 2H), 1.62–1.83 (m, 2H), 1.86–2.21 (m, 2H), 3.1–3.25 (m, 2H), 3.41 (q, 2H, J = 10), 4.0 (dd, 2H, J = 10), 4.73 (br t, 1H)
7'af	63–65	$C_{24}H_{49}NO_3$ (399.7)	3340, 1674	0.8–1.07 (m, 6H), 1.26 (s, 32H), 1.38–1.56 (m, 4H), 2.45 (d, 1H), 3.17 (q, 2H, J = 7), 3.81–4.25 (m, 3H), 4.8 (br t, 1H)
8'af	79–80	$C_{24}H_{49}NO_3$ (399.7)	3351, 1684	0.89 (t, 3H, J = 6), 1.26 (s, 32H), 1.4–1.76 (m, 6H), 3.17 (q, 2H, J = 7), 3.67 (q, 2H, J = 5), 4.09 (t, 2H, J = 6), 4.61 (br m, 1H)
8'bf	82–83	$C_{27}H_{55}NO_3$ (441.7)	3333, 1685	0.89 (t, 3H, J = 6), 1.12–1.69 (m, 44H), 3.15 (q, 2H, J = 5), 3.64 (q, 2H, J = 6), 4.05 (t, 2H, J = 6), 4.6 (br t, 1H)
8'cf	88–89	$C_{35}H_{71}NO_3$ (554.0)	3335, 1685	0.89 (t, 3H, J = 6), 1.07–1.7 (m, 60H), 2.9 (br, 1H), 3.12 (q, 2H, J = 6), 3.58 (t, 2H, J = 5), 4.03 (t, 2H, J = 5), 5.25 (br t, 1H)

[a] Satisfactory microanalyses obtained: C ±0.36, H ±0.21, N +0.31.

Table 4. Carbamoylation of Monoalcohols with Octadecyl Bromide (**12f**) and Potassium Cyanate in the Presence of Tetrabutylammonium Bromide (0.2 Molar Equiv)

Substrate	Reaction Time (h)	Product	Yield (%)	mp (°C)	Molecular Formula	IR (KBr) ν(cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)
9a	18	**9'af**	60[b]	64–65	$C_{26}H_{53}NO_2$ (411.7)	3336, 1686	0.89 (t, 6H, J = 6.7), 1.28 (s, 40H), 1.41–1.59 (m, 2H), 3.16 (q, 2H, J = 6.7), 4.06 (t, 2H, J = 6.7), 4.6 (br, 1H)
10a	16	**10'af**	61	68–70	$C_{24}H_{47}NO_3$ (397.6)	3348, 1685	0.89 (t, 3H, J = 5), 1.25 (br s, 32H), 1.39–1.59 (m, 2H), 1.83–2.03 (m, 2H), 3.17 (q, 2H, J = 5), 3.72–4.24 (m, 5H), 4.76 (br, 1H)
11a	24	**11'af**	45	59–60	$C_{24}H_{49}NO_2$ (383.7)	3336, 1690	0.78–1.02 (m, 6H), 1.15–1.53 (m + s, 39H), 3.14 (q, 2H, J = 6.7), 4.40–4.67 (m, 1H), 4.67–4.93 (m, 1H)
11b	24	**11'bf**	44	49–50	$C_{26}H_{53}NO_2$ (411.7)	3346, 1689	0.9 (t, 6H, J = 5), 1.18–1.62 (m + s, 43H), 3.15 (q, 2H, J = 5), 4.55 (br, 1H), 4.7–4.9 (m, 1H)

[a] Satisfactory microanalyses obtained: C ±0.27, H ±0.14, N ±0.24.
[b] The product **9'af** was formed only in 10% in the absence of Bu_4NBr (reaction time = 20 h).

Table 5. Competitive Carbamoylation of Diols and Monoalcohols with Octadecyl Bromide (**12f**) and Potassium Cyanate in the Presence of Tetrabutylammonium Bromide

Diol + Mono-alcohol (1:1 mole equiv)	Time (h)	Products	Yield[a] (%)
1b + **9a**	22	**1'bf**	61
		9'af	7
2a + **10a**	22	**2'af**	75
		10'af	10
1b + **10a**	18	**1'bf**	81
		10'af	10

[a] Isolated yield.

equimolar amounts of diol and monoalcohol were treated with octadecyl bromide potassium cyanate and tetrabutylammonium bromide in acetonitrile at 100 °C.

The findings listed in Table 5 show that monoalcohols react more slowly than diols.

Thus, the reaction of diols with alkyl halides and potassium cyanate using phase-transfer catalysis provides a convenient method for their selective monocarbamoylation. The use of a wide variety of alkyl halides in this reaction not only solved the problem of limited availability of commercial alkyl isocyanates but also made the process safer.

Diols **1a** and **2a** were prepared according to the known procedures.[8,9] Diols **1b–d** were prepared by a reported method[10] from the corresponding 2,5-disubstituted 1,5-hexadienes.[11] Diol **5a** was available in several steps[11] from the Diels–Alder adduct of 2,5-bis(hydroxymethyl)furan and nitroethylene.[12] Diol **6b** was prepared in several steps[11] from 5-methyl-5-hexene-2-one. All the melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. IR spectra were measured using an Analect FTIR FX 6260 Spectrophotometer or a Perkin-Elmer 457 Spectrophotometer. ^{1}H-NMR were measured on a JEOL FX-90Q or JEOL FX-200 NMR Spectrometer. Kiesegel 60 (230–400 mesh) from E. Merck was used for silica gel chromatography.

Selective Monocarbamoylation of Diols 1–8 and Monoalcohols 9–11; General Procedure:

To a 0.2 M solution of the appropriate diol **1–8** or the monoalcohol **9–11** (1–60 mmol) in anhydrous CH_3CN is added an appropriate alkyl halide (**12a–f**, 1.2 equiv), KCNO (1.5 equiv) and a phase-transfer catalyst (0.1–0.2 equiv). The mixture is refluxed at 100 °C with stirring under an atmosphere of N_2 for the time recorded in Tables 1,2 and 4. The reaction mixture is treated with hot CH_2Cl_2 and filtered. The filtrate was concentrated *in vacuo* and the crude product is purified by flash chromatography on silica gel using petroleumether/EtOAc as eluent.

We thank Dr. J.R. Wareing for helpful suggestions and IR, NMR and elemental analysis laboratories for spectral and analytical data.

Received: 22 September 1989

(1) Handley, D.A.; Van Valen, R.G.; Saunders, R.N. *Immunopharmacology* **1986**, *11*, 175.
Handley, D.A.; Tomesch, J.C.; Saunders, R.N. *Thrombosis and Haemostasis* **1986**, *56*, 40.
Handley, D.A.; Van Valen, R.G.; Winslow, C.M.; Tomesch, J.C.; Saunders, R.N. *Thrombosis and Haemostasis* **1987**, *57*, 187.
Jaeggi, C.; Lee, M.L.; Tomesch, J.C. *C.A.* **1986**, *105*, 79165.
(2) Tarashita, Z.; Tsushima, S.; Yoshioka, Y.; Nomura, H.; Inada, Y.; Nishikawa, K. *Life Sciences* **1983**, *32*, 1975.
(3) D'Silva, T.D.J.; Lopes, A.; Jones, R.L.; Singhawangcha, S.; Chan, J.K. *J. Org. Chem.* **1986**, *51*, 3781.
(4) Fukui, K.; Tanimoto, F.; Kitano, H. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 1586.
Argabright, P.A.; Phillips, B.L.; Sinkey, V.J. *J. Org. Chem.* **1967**, *32*, 3261.
(5) Zenner, K.F.; Appel, H.G. *C.A.* **1973**, *78*, 58473.
Nadachi, Y.; Kokura, M. *C.A.* **1976**, *84*, 164852.
(6) Olah, G.A.; Nishimura, J.; Kreienbuehl, P. *J. Am. Chem. Soc.* **1973**, *95*, 7672.
(7) Lammiman, L.A.; Satchell, R.S. *J. Chem. Soc., Perkin Trans 2* **1972**, 2300.
(8) Timko, J.M.; Moore, S.S.; Walba, D.M.; Hiberty, P.C.; Cram, D.J. *J. Am. Chem. Soc.* **1977**, *99*, 4207.
(9) Houlihan, W.J.; Lee, M.L.; Munder, P.G.; Nemecek, G.M.; Handley, D.A.; Winslow, C.M.; Happy, J.; Jaeggi, C. *Lipids* **1987**, *22*, 884.
(10) Klein, E.; Rojahn, W. *Tetrahedron* **1965**, *21*, 2353.
(11) Prashad, M.; Tomesch, J.C.; Houlihan, W.J. unpublished results.
(12) Ranganthan, D.; Rao, C.B.; Ranganathan, S.; Mehrotra, A.K.; Ayengar, R. *J. Org. Chem.* **1980**, *45*, 1185.