

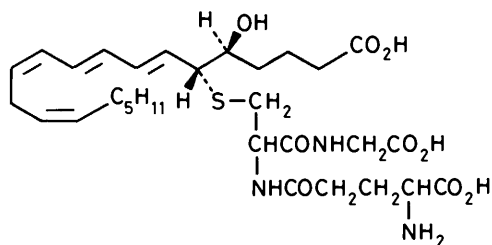
# Synthesis and Properties of Amidoalkenes involving Azidoalkenoates and 1-Phenylalkan-1-ols

Marcel S. F. Lie Ken Jie,\* Wilson L. K. Lam, and H. B. Lao

Department of Chemistry, University of Hong Kong, Pokfulam Road, Hong Kong

(*Z*)-Methyl 12-azido-octadec-9-enoate was converted into several amido derivatives (**1a–f**) when treated with short-chain alkanolic, amino, or aromatic acids in the presence of triphenylphosphine. 1-Phenylalkan-1-ols (**2a–c**) were prepared and converted into the 1-amido-1-phenylalkanes (**3a–d**) by reaction of their tricarbonylchromium complexes with acetonitrile or benzene-acetonitrile in sulphuric acid. The amide derivatives were characterized by spectroscopic and mass spectral analyses. In the <sup>1</sup>H n.m.r. analysis the amide proton (NHCO) shift appeared at δ 5.4–5.9 and 4.9–6.03 for the C<sub>18</sub> amidoalkenoates and 1-amido-1-phenylalkanes respectively. The amide carbonyl carbon atom (NHCO) <sup>13</sup>C chemical shift appeared at δ 167.01–173.14 p.p.m. The mass spectral fragmentation pattern of the C<sub>18</sub> amido fatty esters gave a characteristic base peak at *m/z* 114 [<sup>+</sup>NH<sub>2</sub>=CH(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub>], except for (**1d**) where it was found at *m/z* 105 [<sup>+</sup>O≡CPh]; and in the 1-amido-1-phenylalkanes the base peak appeared at *m/z* 106 [<sup>+</sup>NH<sub>2</sub>=CHPh] for (**3a–c**), and *m/z* 99 [<sup>+</sup>CH<sub>2</sub>Ph] for (**3d**).

Leukotrienes, such as LTC<sub>4</sub>, produced from arachidonic acid *via* the 5-lipoxygenase pathway, form an important class of natural products (known as peptido-lipids) with interesting physiological activities.<sup>1–4</sup> In an effort to study the physical and biological properties of peptido-lipids, our immediate objective was to prepare a number of long-chain alkenoic acids containing an amide group attached to a specific carbon atom.



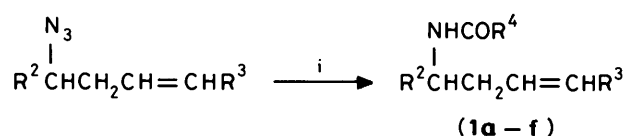
We have recently reported the synthesis of a number of azido derivatives of C<sub>18</sub> alkenoates,<sup>5</sup> which can be readily transformed into the amidoalkenoates when treated with a carboxylic acid in the presence of triphenylphosphine.<sup>6</sup> One other route to amides involves the reaction of 1-phenylalkan-1-ols with nitriles under acid conditions.<sup>7</sup> The latter approach provides a means of incorporating a phenyl and an amide group into the same derivative. However, since phenylated long-chain alkenoic acids are not readily available in Nature, a number of 1-phenylalkan-1-ols were prepared instead and used as model compounds to study their transformation to the corresponding amidophenyl derivatives. The various synthetic routes are given in the Scheme and the physical properties of the derivatives are presented in Tables 1–3.

## Results and Discussion

Treatment of (*Z*)-methyl 12-azido-octadec-9-enoate with triphenylphosphine in the presence of short-chain alkenoic or aromatic acids, gave low but consistent yields (18.0–22.7%) of the corresponding amido derivatives (**1a–f**, Table 1). I.r. spectroscopic analysis of the C<sub>18</sub> amidoalkenoates gave characteristic absorptions at 3 300 (NH str.) and 1 640 cm<sup>-1</sup> (amide C=O str.) for the amide function. The chemical shift of the proton of the methine group (CHNHCO) appeared at δ

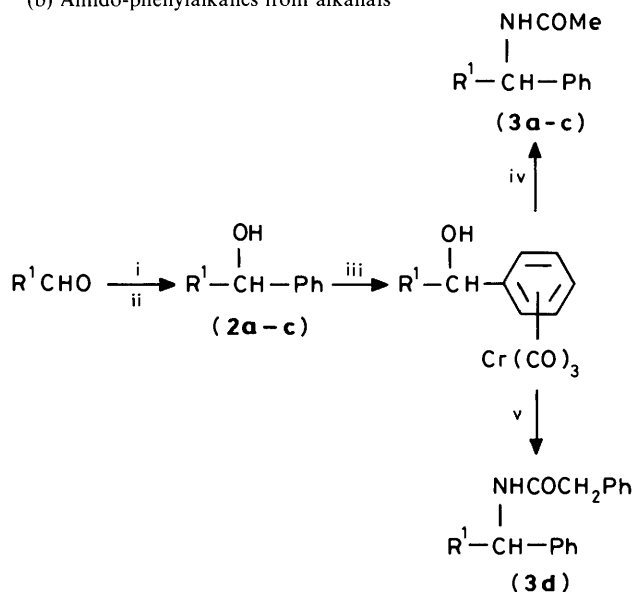
**Scheme.** Preparation of amidoalkenoates and amido(phenyl)alkanes

(a) Amidoalkenoates from azidoalkenoates



R<sup>2</sup> = Me(CH<sub>2</sub>)<sub>5</sub>; R<sup>3</sup> = (CH<sub>2</sub>)<sub>7</sub>CO<sub>2</sub>Me; R<sup>4</sup> = Me, Et, Pr, Ph, or PhCH<sub>2</sub>CO<sub>2</sub>NHCH<sub>2</sub>. Reagents and conditions: i, Ph<sub>3</sub>P, R<sup>4</sup>CO<sub>2</sub>H, C<sub>6</sub>H<sub>6</sub>, 48 h

(b) Amido-phenylalkanes from alkanals

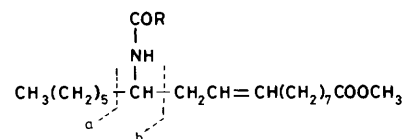


R<sup>1</sup> = Me, Me(CH<sub>2</sub>)<sub>6</sub> or Me(CH<sub>2</sub>)<sub>8</sub>. Reagents and conditions: i, PhMgBr, THF, 2 h; ii, HCl-H<sub>2</sub>O; iii, Cr(CO)<sub>6</sub>, Bu<sub>2</sub>O, THF, 12 h; iv, MeCN, CH<sub>2</sub>Cl<sub>2</sub>, conc. H<sub>2</sub>SO<sub>4</sub>, 15 min, 0–5°C; v, PhCH<sub>2</sub>CN, CH<sub>2</sub>Cl<sub>2</sub>, conc. H<sub>2</sub>SO<sub>4</sub>, 15 min, 0–5°C

3.9–4.0 as a multiplet, while the signal for the NH proton appeared as a doublet at *ca.* δ 5.4. Where the amide contains a phenyl group (**1d**), the NH proton was shifted to δ 5.9. In compound (**1e**), although the presence of a benzyl group did not

Table 1. Physical properties of amido-C<sub>18</sub> alkenoates (1a—f)

Compound	Yield (%)	T.l.c. (R <sub>F</sub> ) LP40*	G.l.c. (e.c.l.) SE-30	<sup>1</sup> H N.m.r. (δ)
(1a)	18.1	0.25	22.73	$  \begin{array}{c}  \text{COCH}_3 \\    \\  \text{NH}_i \\    \\  \text{CH}_3(\text{CH}_2)_5\text{CHCH}_2\text{CH}=\text{CH}(\text{CH}_2)_6\text{CH}_2\text{COOCH}_3 \\  \text{a} \quad \text{b} \quad \text{c} \quad \text{d} \quad \text{e} \quad \text{e} \quad \text{f} \quad \text{g} \quad \text{h}  \end{array}  $ <p>           a = 0.89 (t, <i>J</i> 7.5)      f = 1.2–1.4 (m)            b = 1.2–1.4 (m)      g = 2.3 (t, <i>J</i> 8.0)            c = 3.94 (m)      h = 3.66 (s)            b = 2.10 (m)      i = 5.41 (d, <i>J</i> 7.0)            e = 5.2–5.4 (t, <i>J</i> 7.0)      j = 1.95 (s)         </p>
(1b)	20.1	0.30	23.60	$  \begin{array}{c}  \text{COCH}_2\text{CH}_3 \\    \\  \text{NH}_i \\    \\  \text{CH}_3(\text{CH}_2)_5\text{CHCH}_2\text{CH}=\text{CH}(\text{CH}_2)_6\text{CH}_2\text{COOCH}_3 \\  \text{a} \quad \text{b} \quad \text{c} \quad \text{d} \quad \text{e} \quad \text{e} \quad \text{f} \quad \text{g} \quad \text{h}  \end{array}  $ <p>           c = 3.9 (m)            d = 2.1 (m)            i = 5.4 (d, <i>J</i> 7.0)            j = 2.1 (q, <i>J</i> 8.0)            k = 1.14 (t, <i>J</i> 8.0)         </p>
(1c)	22.7	0.25	24.80	$  \begin{array}{c}  \text{COCH}_2\text{CH}_2\text{CH}_3 \\    \\  \text{NH}_i \\    \\  \text{CH}_3(\text{CH}_2)_5\text{CHCH}_2\text{CH}=\text{CH}(\text{CH}_2)_6\text{CH}_2\text{COOCH}_3 \\  \text{a} \quad \text{b} \quad \text{c} \quad \text{d} \quad \text{e} \quad \text{e} \quad \text{f} \quad \text{g} \quad \text{h}  \end{array}  $ <p>           c = 4.0 (m)            d = 2.1 (m)            i = 5.42 (d, <i>J</i> 7.0)            j = 2.0 (m)            k = 1.6 (m)            l = 0.94 (t, <i>J</i> 8.0)         </p>

Mass spectral analysis  
*m/z* (fragment, intensity)<sup>13</sup>C N.m.r. (p.p.m.)

	20	21		
	CO-CH <sub>3</sub>			
	NH			
	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH	CH <sub>2</sub> CH=CH <sub>2</sub>	CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> COOCH <sub>3</sub>	
18		12	9	1 19
C-1 = 174.17	C-6 = 29.15	C-7 = 29.15	C-11 = 32.45	C-16 = 31.80
C-2 = 34.08	C-8 = 27.41	C-9 = 132.62	C-12 = 49.30	C-17 = 22.59
C-3 = 24.97	C-10 = 125.09	C-14 = 26.06	C-13 = 34.40	C-18 = 14.03
C-4 = 29.15		C-15 = 29.58	C-14 = 26.06	C-19 = 51.36
C-5 = 29.15			C-15 = 29.58	C-20 = 169.45
				C-21 = 23.40

R = Me

354 (*M* + 1, 0.3)  
 353 (*M*, 0.4)  
 322 (*M* - 31, 2.7)  
 157 (*b* + 1, 9.0)  
 156 (*b*, 80.8)  
 114 [ $\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{NH}_2^+$ , 100]  
 85(*a*, 26.3)

	20	21	22	
	CO-CH <sub>2</sub> CH <sub>3</sub>			
	NH			
	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH	CH <sub>2</sub> CH=CH <sub>2</sub>	CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> COOCH <sub>3</sub>	
18		12	9	1 19
C-1 = 174.22	C-6 = 29.16	C-7 = 29.63	C-11 = 32.45	C-17 = 22.64
C-2 = 34.13	C-8 = 27.11	C-9 = 132.72	C-12 = 49.03	C-18 = 14.03
C-3 = 24.97	C-10 = 124.98	C-14 = 26.06	C-13 = 34.51	C-19 = 51.41
C-4 = 29.36		C-15 = 29.63	C-14 = 26.06	C-20 = 173.14
C-5 = 29.16		C-16 = 31.80	C-15 = 29.63	C-21 = 34.51
			C-16 = 31.80	C-22 = 10.22

R = CH<sub>2</sub>CH<sub>3</sub>

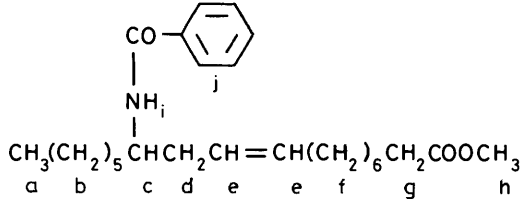
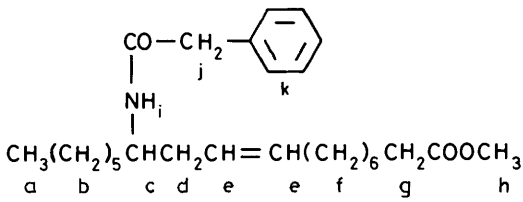
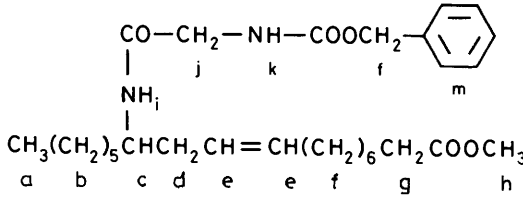
368 (*M* + 1, 0.4)  
 367 (*M*, 0.6)  
 336 (*M* - 31, 3.7)  
 171 (*b* + 1, 11.0)  
 170 (*b*, 89.8)  
 114 [ $\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{NH}_2^+$ , 100]  
 85 (*a*, 1.2)

	20	21	22	23
	CO-CH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>			
	NH			
	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH	CH <sub>2</sub> CH=CH <sub>2</sub>	CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> COOCH <sub>3</sub>	
18		12	9	1 19
C-1 = 174.06	C-7 = 29.03	C-8 = 27.30	C-13 = 34.34	C-19 = 51.20
C-2 = 33.96	C-9 = 132.29	C-10 = 125.14	C-14 = 26.00	C-20 = 172.32
C-3 = 24.86	C-11 = 31.69	C-12 = 49.84	C-15 = 29.47	C-21 = 38.79
C-4 = 29.31	C-13 = 34.34		C-16 = 31.80	C-22 = 19.23
C-5 = 29.03	C-14 = 26.00		C-17 = 22.53	C-23 = 13.65
C-6 = 29.03	C-15 = 29.47		C-18 = 13.92	

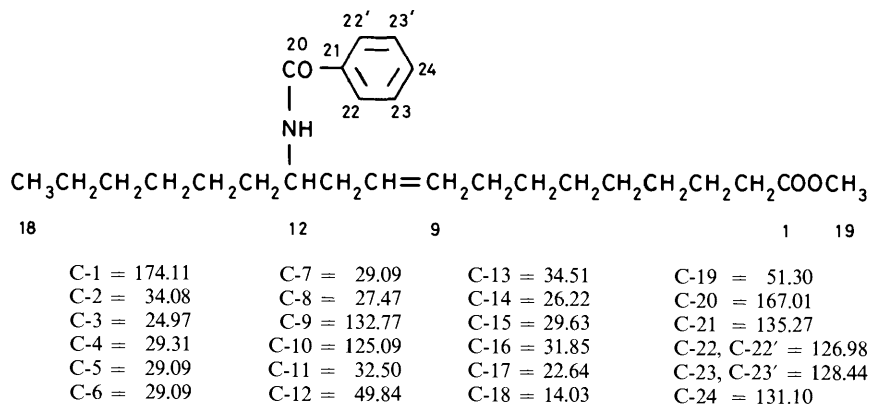
R = CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>

382 (*M* + 1, 0.6)  
 381 (*M*, 0.9)  
 350 (*M* - 31, 5.0)  
 185 (*b* + 1, 10.7)  
 184 (*b*, 78.0)  
 114 [ $\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{NH}_2^+$ , 100]  
 85 (*a*, 1.7)

Table 1 (continued)

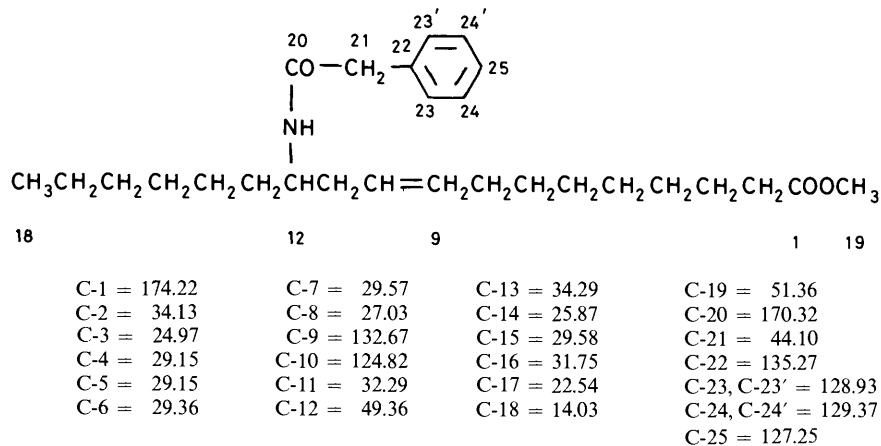
Compound	Yield (%)	T.l.c. (R <sub>F</sub> ) LP40*	G.l.c. (e.c.l.) SE-30	<sup>1</sup> H N.m.r. (δ)
(1d)	18.0	0.25	28.0	 <p> <math>\text{CH}_3(\text{CH}_2)_5\text{CHCH}_2\text{CH}=\text{CH}(\text{CH}_2)_6\text{CH}_2\text{COOCH}_3</math>            a b c d e e f g h         </p> <p>           c = 4.20 (m)            d = 2.05 (m)            i = 5.9 (m)            j = 7.2–7.8 (m)         </p>
(1e)	19.5	0.30	28.5	 <p> <math>\text{CH}_3(\text{CH}_2)_5\text{CHCH}_2\text{CH}=\text{CH}(\text{CH}_2)_6\text{CH}_2\text{COOCH}_3</math>            a b c d e e f g h         </p> <p>           c = 3.9 (m)            d = 2.1 (m)            i = 5.4 (m)            j = 3.54 (s)            k = 7.28 (m)         </p>
(1f)	18.4	0.45	N.A.	 <p> <math>\text{CH}_3(\text{CH}_2)_5\text{CHCH}_2\text{CH}=\text{CH}(\text{CH}_2)_6\text{CH}_2\text{COOCH}_3</math>            a b c d e e f g h         </p> <p>           c = 3.95 (m)            d = 2.0 (m)            i = 5.5 (m)            j = 3.95 (d, J 7.0)            k = 5.5 (m)            l = 5.13 (s)            m = 7.34 (s)         </p>

\* LP40 = Light petroleum–diethyl ether (60:40, v/v). N.A. = Not available.



R = Ph

- 416 ( $M + 1$ , 0.8)
- 415 ( $M$ , 1.2)
- 384 ( $M - 31$ , 6.7)
- 219 ( $b + 1$ , 43.0)
- 218 ( $b$ , 98)
- 122 ( $\text{NH}_3\text{COPh}$ , 26.5)
- 114 [ $\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{NH}_2^+$ , 7.0]
- 105 ( $\text{Ph}-\text{C}=\text{O}^+$ , 100)
- 85 ( $a$ , 1.2)



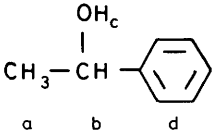
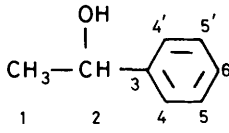
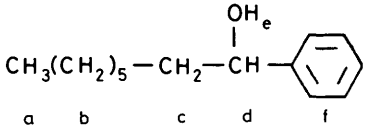
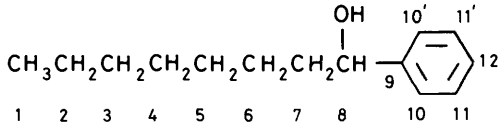
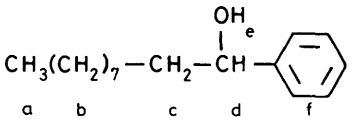
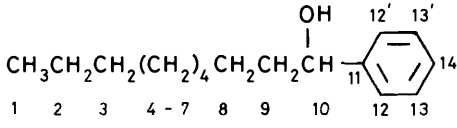
R = CH<sub>2</sub>Ph

- 430 ( $M + 1$ , 0.4)
- 429 ( $M$ , 0.9)
- 398 ( $M - 31$ , 3.1)
- 223 ( $b + 1$ , 11.0)
- 232 ( $b$ , 64.5)
- 136 ( $\text{NH}_3\text{COCH}_2\text{Ph}$ , 13.7)
- 114 [ $\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{NH}_2^+$ , 100]
- 85 ( $a$ , 1.1)

N.A.

N.A.

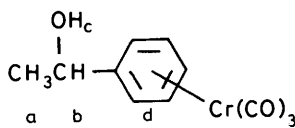
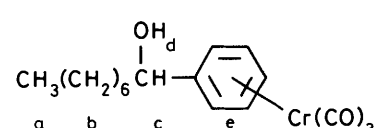
**Table 2.** Physical properties of 1-phenylalkan-1-ols and their tricarbonylchromium complexes (**2a—c**)

Compound	Yield (%)	$\delta_{\text{H}}$	$\delta_{\text{C}}$	$\nu/\text{cm}^{-1}$
<b>(2a)</b>	62.5			3 350 (s, OH str.) 3 050 (w, arom. str.) 1 480 (m, C=C, arom. str.) 1 580
		a = 1.295 (d, <i>J</i> 7.5) b = 4.75 (q, <i>J</i> 7.5) c = 2.60 (s) d = 7.29 (s)	C-1 = 25.08 C-2 = 70.26 C-3 = 145.89 C-4, C-4' = 125.41 C-5, C-5' = 128.45 C-6 = 127.36	
<b>(2b)</b>	70.6			3 300 (s, OH str.) 3 050 (w, arom. CH str.) 1 600 (m, C=C arom. str.) 1 490
		a = 0.87 (t, <i>J</i> 3.5) b = 1.2—1.4 (m) c = 1.63 (m) d = 4.53 (t, <i>J</i> 7.5) e = 2.65 (s) f = 7.3 (s)	C-1 = 14.14 C-2 = 22.81 C-3 = 32.02 C-4 = 29.42 C-5 = 29.69 C-6 = 26.02	C-7 = 39.33 C-8 = 74.33 C-9 = 145.29 C-10, C-10' = 126.06 C-11, C-11' = 128.39 C-12 = 127.42
<b>(2c)</b>	48.2			3 400 (s, OH str.) 3 060 (w, arom. CH str.) 1 620 (m, C=C arom. str.) 1 500
		a = 0.89 (t, <i>J</i> 3.5) b = 1.2—1.5 (m) c = 1.70 (m) d = 4.58 (t, <i>J</i> 7.1) e = 2.40 (s) f = 7.28 (s)	C-1 = 13.97 C-2 = 22.69 C-3 = 31.96 C-4, C-7 = 29.36—29.63 C-8 = 25.89 C-9 = 39.23 C-10 = 74.59	C-11 = 145.18 C-12, C-12' = 125.89 C-13, C-13' = 128.28 C-14 = 127.30

affect the chemical shift of the NH proton,  $\delta$  5.4, the methylene protons (NHCOCH<sub>2</sub>Ph) were shifted to  $\delta$  3.54. The protected glycine derivative (**If**) was characterized by the appearance of a doublet at  $\delta$  3.95 (*J* 7.0 Hz) for the signal of the protons of the methylene group of the glycine residue (NHCOCH<sub>2</sub>NHCO<sub>2</sub>CH<sub>2</sub>Ph), while the methylene protons of the protective group (NHCOCH<sub>2</sub>NHCO<sub>2</sub>CH<sub>2</sub>Ph) were shifted to  $\delta$  5.13 and appeared as a singlet.

In the <sup>13</sup>C n.m.r. analysis, compounds (**1a—e**) were characterized by the signal appearing at 167.01—173.14 p.p.m. for the amide carbonyl carbon atom. The carbon nuclei of the alkyl substituents of the amide group were readily assigned. In compounds (**1a—c**) the methyl carbon atom was shifted to 23.40 (C-21), 10.22 (C-22), and 13.65 p.p.m. (C-23), as a result of the  $\alpha$ -,  $\beta$ -, and  $\gamma$ -effect of the carbonyl group of the amide on

these carbon atoms respectively. In compounds (**1d**) and (**1e**), the presence of an aromatic ring resulted in the appearance of signals at 126.98—135.27 p.p.m. for the aromatic carbon nuclei. The shift of the substituted aromatic carbon atom appeared at 135.27 p.p.m., while the *para*-positioned carbon nuclei were shifted to 131.10 and 127.25 p.p.m. in compounds (**1d**) and (**1e**) respectively. These signals were recognized in the spectra, since they appeared at half the intensity when compared with the signals due to the *ortho*- and *meta*-positioned carbon atoms. In compound (**1d**) the signal at 126.98 p.p.m. was assigned to the shift of the *ortho*-positioned carbon atoms, and the signal at 128.44 p.p.m. to the *meta*-positioned carbon nuclei based on the chemical-shift increments proposed by Breitmaier and Bauer.<sup>8</sup> In compound (**1e**) the shift of the methylene carbon atom of the benzyl group appeared at 44.10 p.p.m., while the *ortho*- and *meta*-

Yield (%)	Tricarbonylchromium complexes		Microanalysis	
	<sup>1</sup> H N.m.r. (δ)	v/cm <sup>-1</sup>	Calc. (Found)	H
87.0	 <p>a = 1.42 (d, <i>J</i> 7.5) b = 2.90 (m) c = 2.0 (s) d = 5.18–5.3 (m)</p>	3 400 (s, OH str.) 1 920 (s, C=O str.) 1 620 (w, C=C arom.)	51.17 (51.3)	3.90 (4.0)
69.8	 <p>a = 0.85 (t, <i>J</i> 7.5) b = 1.2–1.6 (m) c = 2.85 (m) d = 2.20 (s) e = 5–5.3 (m)</p>	3 410 (s, OH str.) 1 910 (s, C=O str.) 1 560 (m, C=C arom.) 1 620	70.32 (70.7)	7.64 (7.75)
85.4	N.A.	3 400 (s, OH str.) 1 910 (s, C=O str.) 1 600 (m, C=C arom.) 1 560	N.A.	N.A.

positioned aromatic carbon nuclei were assigned to the signals at 128.93 and 129.37 p.p.m. respectively.

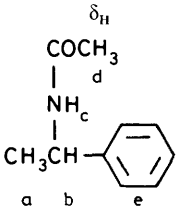
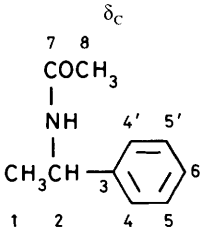
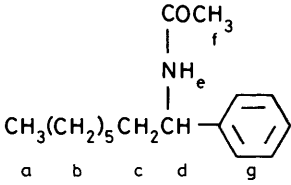
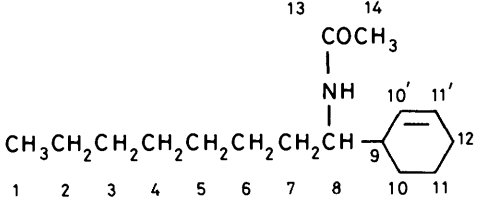
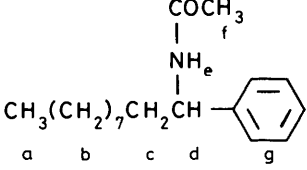
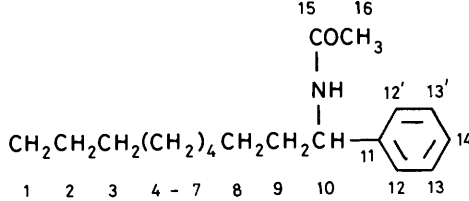
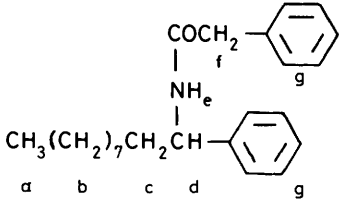
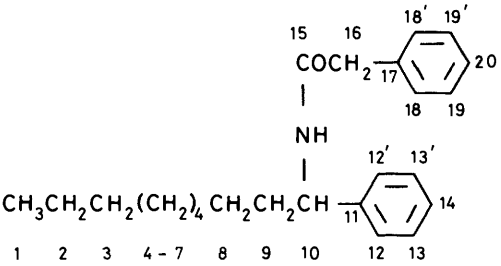
The signal for the methine carbon atom (C-12) of the alkenoic acid chain, to which the amide group is attached, appeared at 49.03–49.84 p.p.m. The  $\gamma$ -effect of the amide group on the neighbouring carbon nuclei caused an upfield shift to the ethylenic carbon atom (C-10), which appeared at 124.82–125.14 p.p.m.; while the methylene carbon at the C-14 atom was shifted upfield to 25.87–26.22 p.p.m. The  $\beta$ -effect of the C-13 amide group gave a characteristic signal at 34.69–34.51 p.p.m., and C-11 a signal at 31.69–32.50 p.p.m., the latter being additionally affected by the adjacent ethylenic system. The remaining carbon nuclei of the alkenoic acid were assigned by referring to data published previously.<sup>9,10</sup>

In the mass spectral analysis of compounds (1a–f), the  $M^+$

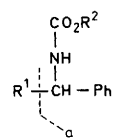
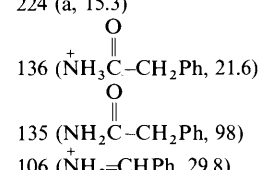
and  $(M + 1)^+$  ions were of low intensity as expected from methyl ester derivatives. Compounds (1a–d) produced a significant ion fragment from a  $\beta$ -cleavage (from the nitrogen atom) between the methine carbon and the methylene carbon adjacent to the unsaturated centre. A subsequent cleavage of this ion fragment between the N–C bond at the amide part resulted in a base peak  $m/z$  114 [ $\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{NH}_2^+$ , 100%] for compounds (1a–c,e). Compound (1d) gave a base peak at  $m/z$  105 ( $^+\text{O}=\text{CPh}$ , 100%) arising from a cleavage between the N–C bond of the amide. The ion fragment at  $m/z$  114 for this compound was unexpectedly low in intensity (7.0%).

In selecting model compounds for the reaction with nitriles, 1-phenyl-ethanol (2a), -octanol (2b), and -decanol (2c) were chosen. These compounds were prepared from acetaldehyde, octanal, and decanal respectively by reaction with phenyl-

Table 3. Physical properties of 1-amido-1-phenylalkanes (3a-d)

Compound	Yield (%)	M.p. (°C)	$\delta_H$	$\delta_C$
(3a)	39.2	72—73 (needle)	 <p>a b c d e</p>	 <p>1 2 3 4 5 6 7 8</p>
			a = 1.36 (d, $J = 9$ ) b = 5.14 (q, $J = 9$ ) c = 5.63 (m) d = 1.99 (s) e = 7.26—7.32 (m)	C-1 = 21.77 C-2 = 48.91 C-3 = 143.28 C-4, C-4' = 126.22 C-5, C-5' = 128.71 C-6 = 127.41 C-7 = 169.23 C-8 = 23.29
(3b)	74.1	58—59 (plate)	 <p>a b c d e f g</p>	 <p>1 2 3 4 5 6 7 8 9 10 11 12 13 14</p>
			a = 0.86 (t, $J 7.5$ ) b = 1.2—1.4 (m) c = 1.80 (m) d = 4.92 (q, $J 8.5$ ) e = 6.03 (d, $J 8.5$ ) f = 1.95 (s) g = 7.2—7.3 (m)	C-1 = 14.03 C-2 = 22.59 C-3 = 31.75 C-4 = 29.36 C-5 = 29.15 C-6 = 26.33 C-7 = 36.25 C-8 = 53.58 C-9 = 142.80 C-10, C-10' = 126.61 C-11, C-11' = 128.50 C-12 = 127.15 C-13 = 169.25 C-14 = 23.24
(3c)	61.5	63—64 (plate)	 <p>a b c d e f g</p>	 <p>1 2 3 4-7 8 9 10 11 12 13 14 15 16</p>
			a = 0.87 (t, $J 7.5$ ) b = 1.2—1.4 (m) c = 1.78 (m) d = 4.85 (q, $J 8.5$ ) e = 4.9 (m) f = 1.92 (s) g = 7.2—7.3 (m)	C-1 = 14.19 C-2 = 23.08 C-3 = 32.29 C-4—C-7 = 29.69—29.90 C-8 = 26.65 C-9 = 36.84 C-10 = 53.96 C-11 = 143.62 C-12, C-12' = 126.88 C-13, C-13' = 128.88 C-14 = 127.42 C-15 = 169.30 C-16 = 23.46
(3d)	96.0	88—89 (plate)	 <p>a b c d e f g</p>	 <p>1 2 3 4-7 8 9 10 11 12 13 14 15 16 17 18 19 20</p>
			a = 0.87 (t, $J 7.0$ ) b = 1.2—1.4 (m) c = 1.70 (m) d = 4.84 (q, $J 8.5$ ) e = 5.7 (m) f = 3.52 (s) g = 7.2—7.3 (m)	C-1 = 14.25 C-2 = 23.08 C-3 = 32.39 C-4—C-7 = 29.63—29.85 C-8 = 26.49 C-9 = 36.84 C-10 = 53.76 C-11 = 143.45 C-12, C-12' = 126.66 C-13, C-13' = 128.83 C-14 = 127.47 C-15 = 170.16 C-16 = 44.15 C-17 = 135.87 C-18, C-18' = 129.15 C-19, C-19' = 129.69 C-20 = 129.15



v/cm <sup>-1</sup>	Microanalysis (%)			Mass spectral analysis m/z (fragment, intensity)
	Calc. (Found)			
	C	H	N	
3 300 (m, NH, str.)	73.62	7.98	8.59	 <p>R<sup>1</sup> = Me, R<sup>2</sup> = Me</p> <p>164 (<i>M</i> + 1, 4.3) 163 (<i>M</i>, 38.4) 148 (a, 13.5) 120 (<i>M</i> - 43, 28.9) 106 (<sup>+</sup>NH<sub>2</sub>=CHPh, 100) 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>, 28.4) 43 (CH<sub>3</sub>C≡O<sup>+</sup>, 46.0)</p>
3 050 (w, arom. CH str.)	(73.85)	(7.8)	(8.5)	
1 660 (m, NH bend)				
1 550 (m, C=C arom. str.)				
3 290 (s, NH str.)	77.7	10.12	5.67	<p>R<sup>1</sup> = Me(CH<sub>2</sub>)<sub>6</sub>, R<sup>2</sup> = Me</p> <p>248 (<i>M</i> + 1, 5.5) 247 (<i>M</i>, 23.7) 204 (<i>M</i> - 43, 5.4) 148 (a, 100) 120 (? , 41.5) 106 (<sup>+</sup>NH<sub>2</sub>=CHPh, 100) 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>, 17.0) 43 (CH<sub>3</sub>C≡O<sup>+</sup> 96)</p>
3 060 (m, arom. CH str.)	(77.8)	(10.0)	(5.45)	
1 660 (s, NH bend)				
1 550 (s, C=C)				
1 600 (arom. str.)				
3 400 (s, NH str.)	78.55	10.55	5.09	<p>R<sup>1</sup> = CH<sub>3</sub>(CH<sub>2</sub>)<sub>8</sub>, R<sup>2</sup> = CH<sub>3</sub></p> <p>276 (<i>M</i> + 1, 1.8) 275 (<i>M</i>, 6.3) 232 (<i>M</i> - 43, 2.3) 148 (a, 99) 120 (? , 25.0) 106 (<sup>+</sup>NH<sub>2</sub>=CHPh, 100) 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup> 13.7) 43 (CH<sub>3</sub>C≡O<sup>+</sup>, 42.6)</p>
3 050 (w, arom. CH str.)	(78.55)	(10.6)	(4.9)	
1 660 (s, NH bend)				
1 550 (s, C=C arom. str.)				
3 300 (m, NH str.)	82.05	9.40	3.99	<p>R<sup>1</sup> = CH<sub>3</sub>(CH<sub>2</sub>)<sub>8</sub>, R<sup>2</sup> = CH<sub>2</sub>Ph</p> <p>352 (<i>M</i> + 1, 0.5), 91 (C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub><sup>+</sup>, 100) 351 (<i>M</i>, 1.8) 225 (a + 1, 10.4), 77 (+C<sub>6</sub>H<sub>5</sub><sup>+</sup>, 12.5) 224 (a, 15.3)</p> <p></p> <p>136 (<sup>+</sup>NH<sub>3</sub>C-CH<sub>2</sub>Ph, 21.6) 135 (NH<sub>2</sub>C-CH<sub>2</sub>Ph, 98) 106 (NH<sub>2</sub>=CHPh, 29.8)</p>
3 050 (w, arom. CH str.)	(81.9)	(9.2)	(3.95)	
1 660 (m, NH bend)				
1 550 (m, C=C arom. str.)				

magnesium bromide. The physical properties of (2a–c) are given in Table 2. The i.r. analysis of these compounds showed strong absorptions at *ca.* 3 400 (OH str.) and 1 550, 1 600  $\text{cm}^{-1}$  (Ar C=C str.). In the  $^1\text{H}$  n.m.r. analysis the most characteristic signals were those for the methine proton (CHOH–Ph), which appeared at  $\delta$  4.53–4.75 and for the aromatic protons at  $\delta$  7.28–7.30. In the  $^{13}\text{C}$  n.m.r. analysis the signals at 125.41, 126.06, and 125.89 p.p.m. were assigned to the *ortho*-positioned aromatic carbon nuclei of compounds (2a), (2b), and (2c) respectively, since these nuclei were influenced by the adjacent hydroxy group. The methine carbon nucleus to which the hydroxy, phenyl, and methyl groups are attached appeared at 70.26 p.p.m. for compound (2a), while the methine (RCHOHPh) carbon nucleus in (2b) and (2c) was shifted to 74.33 and 74.59 p.p.m. respectively. In compound (2a) the combined effects of the hydroxy and phenyl groups on the methyl carbon atom caused the latter to be shifted to 25.08 p.p.m.

Tricarbonylchromium complexed aromatic compounds were reported to enhance chemical reactivities.<sup>11</sup> Jaouen *et al.*<sup>7</sup> demonstrated the increase in the yield of amide derivatives from the reaction between the tricarbonylchromium complexes of 1-phenylalkan-1-ols and nitriles under acid conditions. Consequently, the substrates (2a–c) were converted into the tricarbonylchromium complex by the method described by Mahaffy and Pauson<sup>12</sup> prior to treatment with sulphuric acid in an excess of acetonitrile or benzene–acetonitrile. Good yields (average 67%) of the amido derivatives (3a–c) were obtained, when the reactions were carried out at 0 °C for 15–20 min. The fairly stable tricarbonylchromium complex intermediates absorbed strongly at 1 910–1 920  $\text{cm}^{-1}$  in the i.r. region, while in the  $^1\text{H}$  n.m.r. analysis the aromatic protons signal appeared upfield at  $\delta$  5.1–5.3.

Reaction of the tricarbonylchromium complex intermediates of (2a–c) with acetonitrile and concentrated sulphuric acid furnished (3a–c), while (2d) with benzene–acetonitrile gave (3d) (Table 3). The tricarbonylchromium ligand was readily decomplexed when the reaction mixture was poured into water as part of the isolation procedure. The amide derivatives (3a–d) were solids and gave characteristic amide absorptions at 3 300 and 1 660  $\text{cm}^{-1}$ . In the  $^1\text{H}$  n.m.r. analysis the shift of the methyl protons of the acetamide group appeared at  $\delta$  1.92–1.99, while the methine proton (RCHPhNHCO) was shifted to  $\delta$  5.63 for compound (3a) and to  $\delta$  4.84–4.92 for (3b–d). The aromatic protons appeared at  $\delta$  7.2–7.3 and the methylene protons of the benzyl group of (3d) was found at  $\delta$  3.52 as a singlet.

In the  $^{13}\text{C}$  n.m.r. analysis of (3a–c) the signal for the acetamide carbonyl carbon atom appeared at 169.23–169.30 p.p.m., while in (3d) the effect of the benzyl group shifted the amide carbonyl carbon atom to 170.16 p.p.m. The aromatic carbon nuclei were readily assigned as the shift of the *ortho*-positioned carbon atoms of the aromatic ring were affected by the amide group. The additional aromatic system in (3d) furnished signals at 135.87 p.p.m. for the substituted aromatic carbon (C-17) and the signals for the remaining aromatic nuclei appeared at 129.15–129.69 p.p.m. The effect of the amide group on the methine carbon (RCHPhNHCO) in (3b) and (3c) caused this nucleus to appear at 53.58 and 53.96 p.p.m. respectively, while the additional methyl effect on the similarly positioned methine carbon atom in (3a) caused this nucleus to shift to 48.91 p.p.m. instead. The signals for the methyl carbon atoms of (3a) were unique, where the acetamide methyl carbon nucleus appeared at 23.39 and the remaining methyl carbon at 21.77 p.p.m.

The mass spectral analysis revealed in all cases a distinct  $M^+$  and  $(M + 1)^+$  ion by ion-molecule reactions. A  $\beta$ -cleavage (from the nitrogen) between the methine carbon and the alkyl group was preferred, rather than between the methine carbon and the phenyl group. Subsequent cleavage of this ion fragment

occurred, at the N–C bond of the amide moiety, resulting in a base peak  $m/z$  106 [ $\text{NH}_2^+=\text{CHPh}$ , 100%] for (3a–c). In the case of (3d), the base peak appeared at  $m/z$  99 [ $\text{CH}_2^+\text{Ph}$ , 100%] with another high intensity fragment ion at  $m/z$  135 [ $\text{NH}_2\text{COCH}_2\text{Ph}$ , 98%].

### Experimental

Methyl (Z)-12-azido-octadec-9-enoate was synthesized as described earlier.<sup>5</sup> Hexacarbonylchromium was obtained from Strem Inc., Newburyport, MA 01950, U.S.A. T.l.c. analysis was performed on microscope glass plates coated with silica (*ca.* 0.1 mm thickness) and a mixture of light petroleum–diethyl ether used as the developer [LP30 denotes a mixture of light petroleum–diethyl ether 70:30 (v/v) where the numeral stands for the percentage of diethyl ether in the developer]. Preparative t.l.c. separations were carried out on silica (Merck, art. 7730, GF254, type G) coated glass plates (20 × 20 cm, 0.7 mm thickness) and developed with mixtures of hexane and diethyl ether. Flash column chromatographic purifications were conducted according to the method described by Still *et al.*<sup>13</sup> Gas Chromatographic analysis was conducted on a Hewlett Packard HP5890A gas chromatograph fitted with a 10 m microbore glass column (0.53 mm diam., 2.65  $\mu\text{m}$  film thickness SE-30 stationary phase) using nitrogen (20 ml/min) as the carrier gas at an isothermal column temperature of 190 °C with a flame ionization detector. External standards of methyl myristate, palmitate, and stearate were used as reference compounds and the equivalent chain length (e.c.l.) value calculated accordingly for each component.<sup>14</sup> I.r. spectra were obtained on a Perkin-Elmer model 577 spectrophotometer and n.m.r. spectra on a JEOL FX90Q (90 MHz) instrument. Mass spectral analysis was conducted by direct insertion on a VG 7070F or Hitachi RMS-4 mass spectrometer. Spectra were normally run at 70 eV with a source pressure of  $10^{-6}$  Torr and a temperature of 150–180 °C. M.p.s (uncorrected) were determined on a Reichert thermovar apparatus.

*Preparation of C<sub>18</sub> Amidoalkenoates (1a–e).*—A mixture of (Z)-methyl 12-azido-octadec-9-enoate (0.5 g, 1.48 mmol),  $\text{Ph}_3\text{P}$  (0.5 g, 1.91 mmol), carboxylic acid (10 ml of acetic, propionic, butyric, benzoic, or phenylacetic acid) and benzene (30 ml) was boiled for 48 h. The cooled mixture was washed with 1M HCl, saturated aqueous  $\text{NaHCO}_3$ , and water, then dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated to give the crude amido derivative. This was purified by t.l.c. on silica gel with hexane–ether (3:1) as developer to afford the pure methyl  $\text{C}_{18}$  amidoalkenoates (1a–e). Results and analytical data are given in Table 1.

*Reaction of (Z)-Methyl 12-Azido-octadec-9-enoate with Benzoyloxyglycine.*—To a stirred solution of glycine (7.5 g, 0.1 mol) in 2M HCl (50 ml) cooled to 0°C was added a solution of benzyl chloroformate (17 g, 0.11 mol) in toluene (100 ml) followed by 1M NaOH (25 ml). The reaction mixture was stirred vigorously for 1 h. The toluene layer was separated and the aqueous solution was cooled and acidified with concentrated HCl using Congo Red as indicator. The precipitate was filtered off, washed with cold water, and dried. Pure benzoyloxyglycine was obtained (16.5 g, 79%), m.p. 119 °C.<sup>15</sup>

A mixture of (Z)-methyl 12-azido-octadec-9-enoate (0.5 g, 1.48 mmol), benzoyloxyglycine (0.5 g, 2.4 mmol),  $\text{Ph}_3\text{P}$  (0.5 g, 1.91 mmol), and benzene (30 ml) was boiled for 48 h. The cooled mixture was washed successively with 1M HCl, saturated aqueous  $\text{NaHCO}_3$  and water, dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated to give crude (1f), which was purified by t.l.c. over silica gel with hexane–ether (1:1) as developer to afford pure (1f) (0.13 g, 18.4%). The analytical data are given in Table 1.

**1-Phenylalkan-1-ols (2a—c).**—A solution of alkanal (0.1 mol) and THF (20 ml) was added dropwise to phenylmagnesium bromide [prepared from Mg (2.4 g, bromobenzene (15.7 g), and THF (100 ml)] at room temperature and boiled for 2 h. The cooled reaction mixture was poured into water (200 ml) and acidified with concentrated HCl (20 ml). The solution was extracted with diethyl ether (3 × 100 ml), and the organic extract was washed with water, dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated to give the crude 1-phenylalkan-1-ols, which were purified by flash column chromatography on silica gel (75 g) with hexane–ether (4:1) as eluant. Fractions were analysed by t.l.c. and pooled. The results and analytical data are given in Table 2.

**Tricarbonyl-1-phenylalkan-1-olchromium Complexes.**—A mixture of 1-phenylalkan-1-ol (4.0 mmol), dibutyl ether (30 ml), THF (4 ml), and hexacarbonylchromium (1.0 g, 5.5 mmol) was boiled under nitrogen for 24 h. The reaction mixture was cooled and suction filtered under nitrogen through a 1-cm thick layer of chromatographic silica gel contained in a sinter glass funnel (2 cm diam.). The silica gel was washed with hexane (30 ml) and the filtrate evaporated under reduced pressure to give a yellow oil. The analytical results are given in Table 2.

**1-Amido-1-phenylalkanes (3a—d).**—A mixture of tricarbonyl-1-phenylalkan-1-olchromium complex (1.0 mmol) and acetonitrile or benzene–acetonitrile (20 ml) was cooled to 0 °C. Concentrated H<sub>2</sub>SO<sub>4</sub> (10 ml) was added dropwise and the mixture stirred for 15 min at 0–5 °C. The reaction mixture was poured into water (50 ml) and extracted with diethyl ether (2 × 50 ml). The organic extract was washed with water, saturated aqueous NaHCO<sub>3</sub>, and water, dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated to give the crude amidophenylalkane which was recrystallized from hexane. The results and analytical data are summarized in Table 3.

### Acknowledgements

We thank the Lipid Research Fund and the Research Grants Committee of the University of Hong Kong for financial assistance.

### References

- 1 B. Samuelsson, *Progr. Lipid Res.*, 1986, **25**, 13.
- 2 P. Borgeat, M. Hamberg, and B. Samuelsson, *J. Biol. Chem.*, 1976, **251**, 7816.
- 3 P. Borgeat and B. Samuelsson, *J. Biol. Chem.*, 1979, **254**, 2643.
- 4 C. N. Serhan, M. Hamberg, and B. Samuelsson, *Proc. Natl. Acad. Sci. U.S.A.*, 1984, **81**, 5335.
- 5 M. S. F. Lie Ken Jie, and H. B. Lao, *Chem. Phys. Lipids*, 1987, **45**, 65.
- 6 J. Garcia, F. Urpi, and J. Vilarrasa, *Tetrahedron Lett.*, 1984, **25**, 4841.
- 7 S. Top and G. Jaouen, *J. Org. Chem.*, 1981, **46**, 78.
- 8 E. Breitmaier and G. Bauer, <sup>13</sup>C NMR Spectroscopy—A Working Manual with Exercises, Harwood Academic, London, 1984, p. 62.
- 9 J. Bus, I. Sies, and M. S. F. Lie Ken Jie, *Chem. Phys. Lipids*, 1976, **17**, 501.
- 10 M. S. F. Lie Ken Jie, J. Bus, A. Groenewegen, and I. Sies, *J. Chem. Soc., Perkin Trans. 2*, 1986, 1275.
- 11 M. F. Semmelhack, G. R. Clark, J. L. Garcia, J. J. Harrison, Y. Thebtaranonth, W. Wulff, and A. Yamashita, *Tetrahedron*, 1981, **37**, 3957.
- 12 C. A. L. Mahaffy and P. A. L. Pauson, *Inorg. Synth.*, 1979, **19**, 154.
- 13 W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.
- 14 T. K. Miwa, K. L. Mikolajczak, F. R. Earle, and I. A. Wolff, *Anal. Chem.*, 1960, **32**, 1739.
- 15 H. E. Carter, R. L. Frank, and H. W. Johnston, *Org. Synth.*, Coll. Vol. III, 1955, 167.

Received 27th July 1987; Paper 7/1359