

## Reference Data

## Carbon-13 Chemical Shift Assignments of Derivatives of Benzoic Acid

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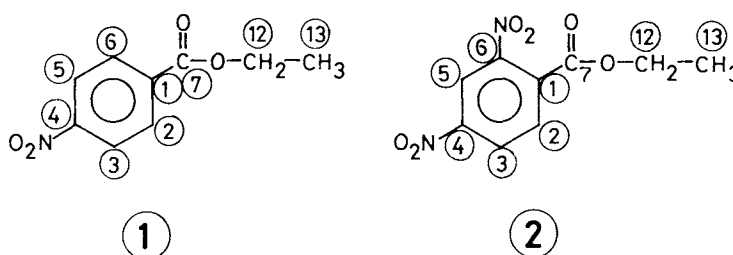
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[(alkoxy- or alkylamino) (dialkoxy-carbonyl) methylamino]-4,6-dinitro-substituted alkyl esters of benzoic acid (8-15), 2-[(alkylthio) (dialkoxy-carbonyl) methylamino]-4,6-dinitro-substituted *S*-alkyl thioesters of benzoic acid (16-21), 2-[(dialkoxy-carbonyl)(alkylamino) methylamino]-4,6-dinitro-substituted *N*-alkylamides of benzoic acid (22, 23), the 2-[(propylthio) (diethoxycarbonyl) methylamino]-4-nitro-substituted *S*-*n*-propyl

thioester of benzoic acid (24) and 2-[(diethoxycarbonyl) (1-piperidyl) methylamino]-4-nitro-substituted piperidinamide of benzoic acid (25). The ethyl esters of 4-nitrobenzoic acid (1) and 2,4-dinitrobenzoic acid (2) were included for comparative purposes. The information derived from the <sup>13</sup>C NMR spectra of 8-15 and 16-23 can be used to differentiate between 2,4,6-trisubstituted esters, thioesters and amides of benzoic acids.

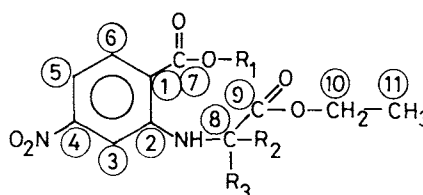


The <sup>13</sup>C NMR spectra of 23 di- and tri-substituted derivatives of esters, thioesters and amides of benzoic acids have been calculated and fully assigned. The *A*, empirical parameters of the (alkoxy)(dialkoxy-carbonyl) methylamino, (alkoxy)(alkoxy-carbonyl)(cyano)methylamino, (alkylamino) (dialkoxy-carbonyl) methylamino and (alkylthio)(dialkoxy-carbonyl) methylamino groups have been calculated for use in the prediction of the chemical shifts of substituted benzenes.

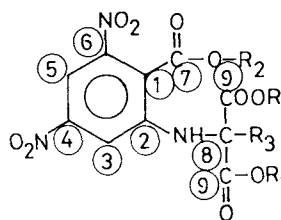
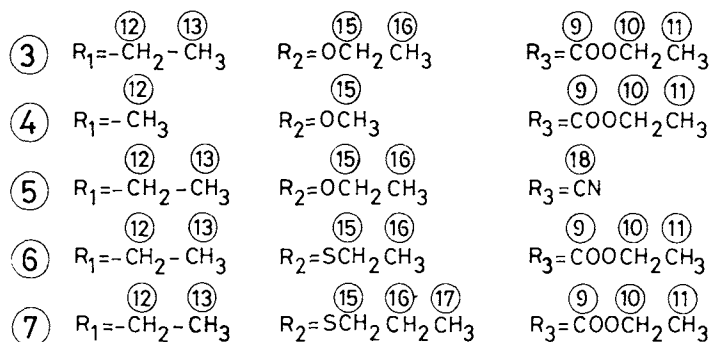
KEY WORDS Esters Thioesters Amides  
Benzoic acid <sup>13</sup>C NMR chemical shifts  
*A*, empirical parameters

## INTRODUCTION

The <sup>13</sup>C NMR spectra of many derivatives of benzoic acid, which are of great interest in connection with their reactivity and biological activity, have already been examined thoroughly.<sup>1-4</sup> However, no work has been published on the <sup>13</sup>C NMR spectra of potentially analgesic di- and tri-substituted derivatives of esters, thioesters or amides of benzoic acid with a (dialkoxy-carbonyl) (alkoxy, thioalkyl, cyano or alkylamino) methylamino substituent in the *ortho* position to the ester, thioester or amide group. We have previously reported the synthesis of these compounds.<sup>5-7</sup> We now report the <sup>13</sup>C NMR spectra of 2-[(dialkoxy-carbonyl)(alkoxy or alkylthio)methylamino]-4-nitro-substituted alkyl esters of benzoic acid (3, 4, 6, 7), 2-[(ethoxy)(ethoxycarbonyl)(cyano)methylamino]-4-nitrobenzoic acid ethyl ester (5), 2-



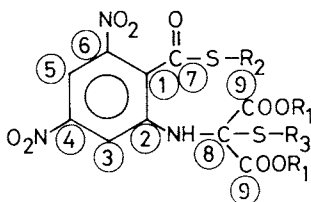
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## Reference Data

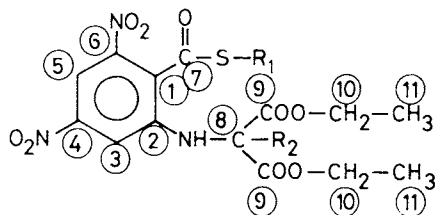
⑧ — ⑮

⑧	$R_1 = \overset{10}{\text{CH}_2\text{CH}_3}$	$R_2 = \overset{12}{\text{CH}_2\text{CH}_3}$	$R_3 = \overset{15}{\text{OCH}_2\text{CH}_3}$
⑨	$R_1 = \overset{10}{\text{CH}_2\text{CH}_3}$	$R_2 = \overset{12}{\text{CH}_3}$	$R_3 = \overset{15}{\text{OCH}_3}$
⑩	$R_1 = \overset{10}{\text{CH}_2\text{CH}_3}$	$R_2 = \overset{12}{\text{CH}_2\text{CH}(\text{CH}_3)_2}$	$R_3 = \overset{15}{\text{OCH}_2\text{CH}(\text{CH}_3)_2}$
⑪	$R_1 = \overset{10}{\text{CH}_3}$	$R_2 = \overset{12}{\text{CH}_2\text{CH}_3}$	$R_3 = \overset{15}{\text{NHCH}_2\text{CH}_3}$
⑫	$R_1 = \overset{10}{\text{CH}_3}$	$R_2 = \overset{12}{\text{CH}_3}$	$R_3 = \overset{15}{\text{NHCH}_2\text{CH}_3}$
⑬	$R_1 = \overset{10}{\text{CH}_2\text{CH}_3}$	$R_2 = \overset{12}{\text{CH}_3}$	$R_3 = \overset{15}{\text{NHCH}_2\text{CH}_3}$
⑭	$R_1 = \overset{10}{\text{CH}_2\text{CH}_3}$	$R_2 = \overset{12}{\text{CH}_2\text{CH}_3}$	$R_3 = \overset{15}{\text{NHCH}_2\text{CH}_3}$
⑮	$R_1 = \overset{10}{\text{CH}_2\text{CH}_3}$	$R_2 = \overset{12}{\text{CH}_2\text{CH}_3}$	$R_3 = \overset{15}{\text{NHCH}_2\text{CH}_2\text{CH}_3}$



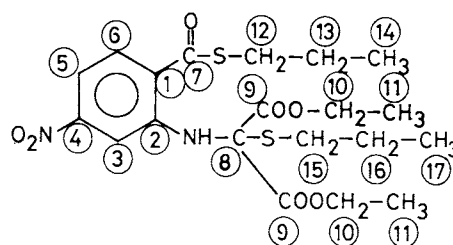
⑯ — ⑳

⑯	$R_1 = \overset{10}{\text{CH}_3}$	$R_2 = \overset{12}{\text{CH}_2\text{CH}_3}$	$R_3 = \overset{15}{\text{CH}_2\text{CH}_3}$
⑰	$R_1 = \overset{10}{\text{CH}_3}$	$R_2 = \overset{12}{\text{C}(\text{CH}_3)_3}$	$R_3 = \overset{15}{\text{C}(\text{CH}_3)_3}$
⑱	$R_1 = \overset{10}{\text{CH}_2\text{CH}_3}$	$R_2 = \overset{12}{\text{CH}_2\text{CH}_3}$	$R_3 = \overset{15}{\text{CH}_2\text{CH}_3}$
⑲	$R_1 = \overset{10}{\text{CH}_2\text{CH}_3}$	$R_2 = \overset{12}{\text{CH}_2\text{CH}_2\text{CH}_3}$	$R_3 = \overset{15}{\text{CH}_2\text{CH}_2\text{CH}_3}$
⑳	$R_1 = \overset{10}{\text{CH}_2\text{CH}_3}$	$R_2 = \overset{12}{\text{CH}(\text{CH}_3)_2}$	$R_3 = \overset{15}{\text{CH}(\text{CH}_3)_2}$
㉑	$R_1 = \overset{10}{\text{CH}_2\text{CH}_3}$	$R_2 = \overset{12}{\text{C}(\text{CH}_3)_3}$	$R_3 = \overset{15}{\text{C}(\text{CH}_3)_3}$

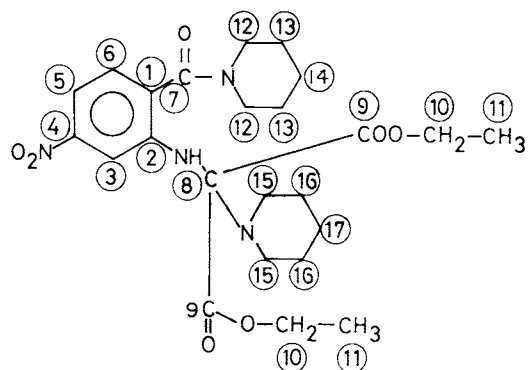


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㉒	$R_1 = \overset{12}{\text{NHCH}_2\text{CH}_3}$	$R_2 = \overset{15}{\text{NHCH}_2\text{CH}_3}$
㉓	$R_1 = \overset{12}{\text{N}(\text{CH}_2\text{CH}_3)_2}$	$R_2 = \overset{15}{\text{N}(\text{CH}_2\text{CH}_3)_2}$



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## EXPERIMENTAL

Compounds 3–25 were prepared by the rearrangement of 2,4-dinitro(or 2,4,6-trinitro) benzylidene malonate derivatives in the presence of an alcohol, thiol or amine according to the methods described previously.<sup>5–7</sup> Ethyl 4-nitrobenzoate (1) and ethyl 2,4-dinitrobenzoate (2) were prepared by esterification of the corresponding acids; their physical data were consistent with the literature values.<sup>8,9</sup>

## Spectra

The <sup>13</sup>C NMR coupled and proton decoupled spectra were recorded at 20.50 MHz on a Jeol FX-90 spectrometer. CDCl<sub>3</sub> was used as the solvent and lock with TMS as the internal standard. The number of data points in the frequency domain was 8K and the spectral width was 4000 Hz. The reproducibilities of the chemical shifts were ±0.1 ppm.

## Reference Data

### RESULTS AND DISCUSSION

Tables 1–6 give the  $^{13}\text{C}$  NMR data for 1–25. The assignments were made on the basis of the signal multiplicities and the current

understanding of the total electron density and the chemical shifts in benzene. The assignment of the chemical shifts of 3–25 was also aided by comparing the measured and calculated chemical shifts, and use was made

of substituent-induced shift increments (Tables 7–9). The  $A_i$  parameters of the nitro, ethoxycarbonyl and *N,N*-dimethylamino groups were taken from the literature.<sup>1</sup> The  $A_i$  parameters of the (alkoxy)

**Table 1.**  $^{13}\text{C}$  NMR chemical shifts (ppm) of 3–7

Carbon	3	4	5	6	7	Average
C-1	117.5	117.2	118.5	117.7	117.7	117.7
C-2	147.0	146.9	149.9	146.2	146.2	147.2
C-3	109.5	109.3	109.9	109.3	109.5	109.5
C-4	151.5	151.6	151.5	151.2	151.2	151.4
C-5	111.7	112.1	113.1	111.2	111.2	111.8
C-6	132.8	132.9	132.9	133.0	133.0	132.9

**Table 2.**  $^{13}\text{C}$  NMR chemical shifts (ppm) of 8–15<sup>a</sup>

Carbon	8	9	10	11	12	13	14	15	Average
C-1	115.1	114.9	114.8	114.3	114.3	114.4	114.4	114.5	114.5
C-2	145.4	145.1	145.4	146.2	146.2	146.3	146.3	146.3	145.7
C-3	113.2	113.1	113.3	113.2	113.3	113.6	113.4	113.4	113.3
C-4	151.3	151.3	151.3	151.2	151.2	151.2	151.2	151.1	151.2
C-5	108.4	108.7	108.2	107.4	107.4	107.3	107.3	107.2	107.8
C-6	149.5	149.7	149.4	149.2	149.3	149.3	149.2	149.1	149.3

<sup>a</sup> The constant term,  $c_k$ , of 2 (Table 5) and the  $A_i$  values of (dialkoxycarbonyl) (alkoxy or alkylthio) methylamino and (alkoxy) (alkoxycarbonyl) (cyano) methylamino groups (Table 7) reproduce these shifts with an accuracy of 0–2.2 ppm. The constant term,  $c_k$ , of  $\text{C}_6\text{H}_6$  (128.5 ppm) and the  $A_i$  values of  $\text{NO}_2$ ,  $\text{COOCH}_3$  and (dialkoxycarbonyl) (alkoxy or alkylthio) methylamino groups (Table 9) reproduce these shifts with an accuracy of 0.1–4.2 ppm.

**Table 3.**  $^{13}\text{C}$  NMR chemical shifts (ppm) of 16–21<sup>a</sup>

Carbon	16	17	18	19	20	21	Average
C-1	125.6	125.4	125.6	125.6	125.5	125.3	125.5
C-2	141.2	141.8	141.4	141.3	141.6	142.0	141.6
C-3	113.3	113.1	113.5	113.5	113.5	113.3	113.3
C-4	148.7	148.5	148.8	148.6	148.6	148.5	148.6
C-5	109.0	108.4	108.7	108.8	108.7	108.2	108.8
C-6	147.7	147.5	147.7	147.7	147.6	147.5	147.6

<sup>a</sup> The constant term,  $c_k$  of 24 (Table 5) and the  $A_i$  value of  $\text{NO}_2$  (Table 9) reproduce these shifts with an accuracy of 2.5–5.9 ppm.

**Table 4.**  $^{13}\text{C}$  NMR chemical shifts (ppm) of 22 and 23<sup>a</sup>

Carbon	22	23	Average
C-1	123.3	122.7	123.0
C-2	144.4	145.2	144.8
C-3	113.7	114.9	114.3
C-4	148.3	151.5	149.9
C-5	108.2	106.4	107.3
C-6	147.4	147.0	147.2

<sup>a</sup> The constant term,  $c_k$ , of 25 (Table 5) and the  $A_i$  value of  $\text{NO}_2$  (Table 9) reproduce these shifts with an accuracy of 0–3.6 ppm.

**Table 5.**  $^{13}\text{C}$  NMR chemical shifts (ppm) of 1, 2, 24 and 25

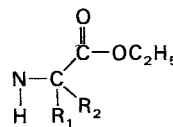
Carbon	1	2	24	25
C-1	136.1	133.0	124.4	127.5
C-2	130.7	131.4	144.0	145.0
C-3	123.5	127.6	110.0	112.1
C-4	150.7	149.1	150.9	148.8
C-5	123.5	119.5	111.4	112.6
C-6	130.7	148.3	131.8	128.1

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**Table 6. Measured chemical shifts (ppm) of 1–25**

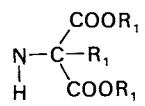
Compound	Carbon												
	7	8	9	10	11	12	13	14	15	16	17	18	
1	164.6	—	—	—	—	62.1	14.3	—	—	—	—	—	
2	163.7	—	—	—	—	63.4	13.8	—	—	—	—	—	
3	166.7	87.7	166.4	63.1	13.9	51.7	14.9	—	59.7	14.2	—	—	
4	167.1	88.1	166.1	63.3	13.9	52.6	—	—	51.2	—	—	—	
5	166.8	81.0	163.7	62.1	14.0	64.8	14.2	—	60.5	13.9	—	124.5	
6	166.8	72.0	166.8	63.6	13.9	61.8	14.3	—	23.0	13.5	—	—	
7	166.8	71.9	166.8	63.7	13.9	61.8	14.3	—	30.9	21.9	13.5	—	
8	163.9	87.5	165.7	63.5	13.9	63.5	14.9	—	60.2	13.4	—	—	
9	164.4	88.0	165.5	63.7	14.0	53.8	—	—	51.5	—	—	—	
10	164.1	87.4	165.7	63.5	14.0	73.5	28.1	19.3	70.8	27.5	19.0	—	
11	164.1	77.7	168.4	54.0	—	63.3	13.4	—	36.6	15.1	—	—	
12	164.7	77.7	168.4	54.1	—	53.6	—	—	36.5	15.1	—	—	
13	164.6	77.8	167.8	63.4	14.0	53.6	—	—	36.5	15.2	—	—	
14	164.1	77.8	167.8	63.3	14.0	63.2	13.4	—	36.5	15.2	—	—	
15	164.2	77.7	167.8	63.3	13.9	63.1	13.4	—	43.7	23.1	11.1	—	
16	190.5	71.4	166.7	54.6	—	25.0	14.2	—	23.0	13.3	—	—	
17	190.7	71.9	167.4	54.6	—	51.6	31.1	—	47.5	29.6	—	—	
18	190.5	71.7	166.3	64.1	13.9	25.1	14.2	—	22.9	13.4	—	—	
19	190.6	71.5	166.3	64.0	13.9	32.4	22.5	13.5	30.7	21.8	13.3	—	
20	190.4	71.6	166.6	64.0	13.9	37.1	24.3	—	34.3	22.5	—	—	
21	190.7	72.1	167.0	64.0	13.9	51.5	31.3	—	47.3	29.6	—	—	
22	163.3	78.0	167.9	63.4	14.0	36.5	15.2	—	35.4	14.2	—	—	
23	168.3	82.8	168.4	62.1	14.1	43.9	14.7	—	42.7	11.4	—	—	
24	193.7	71.9	166.8	63.7	13.9	31.6	22.8	13.8	30.9	21.9	13.5	—	
25	167.3	81.6	167.0	62.2	14.2	47.7	26.4	25.2	45.6	26.1	24.5	—	

**Table 7. Empirical parameters for the calculation of the chemical shifts in the *p*-nitro-substituted esters, thioesters or amides of benzoic acid<sup>a</sup>**

$R_i$ ( $i=2$ )	$A_{21}$	$A_{22}$	$A_{23}$	$A_{24}$	$A_{25}$	$A_{26}$
 $R_1 = \text{COOC}_2\text{H}_5, \text{CN}$ $R_2 = \text{OCH}_3, \text{OC}_2\text{H}_5,$ $\text{SC}_2\text{H}_5, \text{S-}n\text{-C}_3\text{H}_7,$ $\text{N-C}_5\text{H}_{10}$	-18.4	+16.5	-14.0	+0.7	-11.7	+2.5

<sup>a</sup> Constant terms,  $c_k$ , of 3–7, 24 and 25 (Table 1 and 5).

**Table 8. Empirical parameters for the calculation of the chemical shifts in 4,6-dinitro-substituted esters, thioesters and amides of benzoic acid<sup>a</sup>**

$R_i$ ( $i=2$ )	$A_{21}$	$A_{22}$	$A_{23}$	$A_{24}$	$A_{25}$	$A_{26}$
 $R_1 = \text{CH}_3, \text{C}_2\text{H}_5$ $R_2 = \text{OCH}_3, \text{OC}_2\text{H}_5, \text{NHC}_2\text{H}_5$ $\text{OCH}_2\text{CH}(\text{CH}_3)_2, \text{NH-}n\text{-C}_3\text{H}_7$ $\text{SC}_2\text{H}_5, \text{S-}n\text{-C}_3\text{H}_7, \text{S-}i\text{-C}_3\text{H}_7$ $\text{N}(\text{C}_2\text{H}_5)_2, \text{S-}t\text{-C}_4\text{H}_9$	-18.5	+14.3	-14.3	+0.7	-11.7	+2.1

<sup>a</sup> Constant terms,  $c_k$ , of 8–15, 16–21, 22 and 23 (Tables 2, 3 and 4).

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Table 9. Empirical parameters for the calculation of the chemical shifts in substituted benzenes

R	$A_i$			
	C-1	ortho	meta	para
$\begin{array}{c} \text{COOR}_1 \\   \\ -\text{N}-\text{C}-\text{R}_2 \\   \quad   \\ \text{H} \quad \text{R}_3 \end{array}$				
$R_1 = \text{CH}_3, \text{C}_2\text{H}_5$ $R_2 = \text{OCH}_3, \text{OC}_2\text{H}_5, \text{S-}t\text{-C}_4\text{H}_9,$ $\text{SC}_2\text{H}_5, \text{S-}n\text{-C}_3\text{H}_7, \text{S-}i\text{-C}_3\text{H}_7,$ $\text{N}(\text{C}_5\text{H}_{10}), \text{OCH}_2\text{CH}(\text{CH}_3)_2,$ $\text{NH-}n\text{-C}_3\text{H}_7, \text{N}(\text{C}_2\text{H}_5)_2$ $R_3 = \text{COOC}_2\text{H}_5, \text{CN}$	+15.4	-16.2	+1.5	-11.7
$\text{NO}_2$	+20	-4.8	+0.9	+5.8
$\text{COOCH}_3$	+2.1	+1.1	+0.1	+4.5
$\text{N}(\text{CH}_3)_2$	+23	-16	+1	-12

(dialkoxycarbonyl) methylamino, (alkylthio) (dialkoxycarbonyl)methylamino and (alkoxy) (alkoxycarbonyl)(cyano)methylamino groups (Table 6) were obtained from the pairs 1/3, 1/4, 1/5 and 1/7. It was possible to use the  $A_i$  parameters of the  $N,N$ -dimethylamino group for the calculation of the chemical shifts in the benzene ring of 3–7, where there is good agreement between the calculated and measured chemical shift values; of a total of 30 positions none differs by more than 3.9 ppm, and 25 differ by less than 2.0 ppm. Good agreement was also obtained between the calculated and measured values for 8–23.

A comparison of the number and positions of the carbon signals in the range 120–130 ppm in the spectra of 1–15 and 16–25 allows the differentiation of esters (1–15), thioesters (16–21, 24) and  $N$ -alkylamides (22, 23, 25) of

di- or tri-substituted derivatives of benzoic acid. For 1–15, no signals are present in the range 120–130 ppm. For 16–25, the signals of the following carbon atoms are seen at 120–130 ppm: C-1, 125.5 (16–21); C-1, 123.0 (22–23); C-1, 124.4 (24); and C-2, 127.5 ppm (25).

## Acknowledgement

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## References

1. F. W. Wehrli and T. Wirthlin, *Interpretation of Carbon-13 NMR Spectra*.

Heyden, London, New York, Rheine (1976).

2. E. Breitmaier and W. Voelter,  *$^{13}\text{C}$  NMR Spectroscopy*. Verlag Chemie, Weinheim, New York (1978).
3. D. F. Ewing, *Org. Magn. Reson.* **12**, 499 (1979).
4. K. S. Dhama and J. B. Stothers, *Can. J. Chem.* **45**, 233 (1967).
5. S. Kinastowski and S. Wnuk, *Synthesis* 654 (1983).
6. S. Kinastowski, S. Wnuk and E. Kaczmarek, *Synthesis* 111 (1988).
7. S. Kinastowski, E. Kaczmarek and S. Wnuk, *Pol. J. Chem.* in press.
8. *Beilstein*, Vol. **9**, p. 390. (1926).
9. *Beilstein*, Vol. **9**, p. 412. (1926).

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### $\alpha$ -Nitroketones. Part 10.<sup>1</sup> $^{13}\text{C}$ NMR Spectra of Alkylated 2-Nitrocyclohexanones

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The  $^{13}\text{C}$  NMR spectra of 22  $\alpha$ -nitrocyclohexanones were recorded and fully assigned. The one-bond C–H coup-

ling constants for the nitromethine resonances of these compounds were also obtained and tabulated.

KEY WORDS  $^{13}\text{C}$  NMR  $^1\text{J}(\text{CH})$  2-Nitrocyclohexanones

## INTRODUCTION

Because  $\alpha$ -nitroketones are useful intermediates in natural product synthesis, we have developed syntheses for this class of compounds.<sup>2</sup> We have also determined the conformation of 2-nitrocyclohexanones by  $^1\text{H}$  NMR.<sup>3,4</sup> However, few  $^{13}\text{C}$  NMR data have been reported for this class of compounds. Having the alkylated-2-nitrocyclohexanones

available, we obtained and analyzed their  $^{13}\text{C}$  NMR spectra and report the results in this paper.

## EXPERIMENTAL

All of the  $\alpha$ -nitrocyclohexanones were prepared from the corresponding enol acetates using ammonium nitrate and trifluoroacetic anhydride.<sup>2</sup>

The  $^{13}\text{C}$  NMR spectra were obtained on a Varian XL-200 NMR spectrometer. Fully coupled, broad band decoupled and off-resonance decoupled  $^{13}\text{C}$  NMR spectra were obtained at 50.31 MHz in  $\text{CDCl}_3$  with TMS as an internal standard. Usually, a 0.4-s