New Synthesis of α-Nitroalkyl- and α-Nitroaralkylcarboxylic Esters from α-Nitroalkyl- and α-Nitroaralkyl-2-oxazolines

Henry Feuer*, Hanamanthsa S. Bevinakatti [1] and Xuan-Gan Luo [2]

Richard B. Wetherill Laboratory, Purdue University,
West Lafayette, Indiana 47907

2-Nitroalkyl- and 2-nitroaralkyl-2-oxazolines are readily converted, in one step, to α-nitroalkyl- and α-nitroaralkylcarboxylic esters on treatment with the appropriate alcohol and trifluoroacetic acid (TFA). The initial products of the ring cleavage are the TFA salts of the ammonioalkyl esters of α-nitroalkyl- and α-nitroaralkylcarboxylic acids. These salts undergo facile transesterification to the α-nitrocarboxylic esters on refluxing with the appropriate alcohol.

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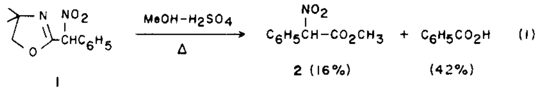
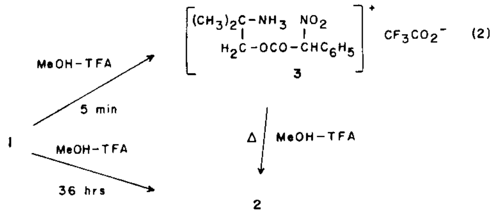
Recently, we reported on the synthesis of 2-nitroalkyl- and 2-nitroaralkyl-2-oxazolines [3]. The present paper deals with ring opening reactions of these compounds giving rise to a new and convenient synthesis of α-nitroalkyl- and α-nitroaralkylcarboxylic esters.

Published methods [4] which describe the preparation of esters from 2-substituted 2-oxazolines were found to be unsatisfactory. For example, refluxing 2-(α-nitrobenzyl)-4,4-dimethyl-2-oxazoline (**1**) with 7% methanolic sulfuric acid gave methyl nitrophenylacetate and methyl benzoate in yields of 16% and 42%, respectively (eq 1). Apparently, at these reaction conditions in sulfuric acid, the nitro group was subjected to a Nef-type reaction [5] which explains the origin of benzoic acid [6] (eq 1).

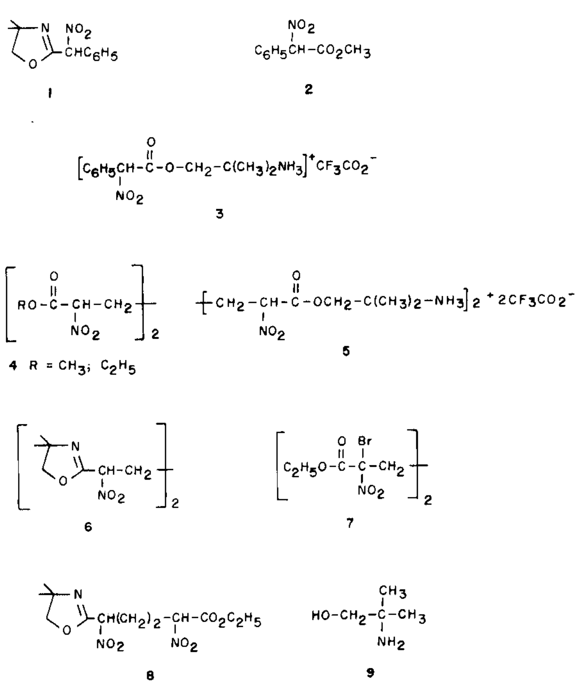


However, the nitro ester **2** was obtained in high yield (See Table I) when **1** was refluxed for about 36 hours in a mixture consisting of methanol and trifluoroacetic acid (TFA) (eq 2). The progress of ester formation was monitored by tlc. The initial product involved in the transformation of **1** to ester **2** was found to be the TFA salt of 2-ammonio-2-methylpropyl nitrophenylacetate (**3**). It was obtained in 100% yield when the reaction time was limited to about 5 minutes. Salt **3** was readily converted to **2** on refluxing in methanolic-TFA (eq 2).



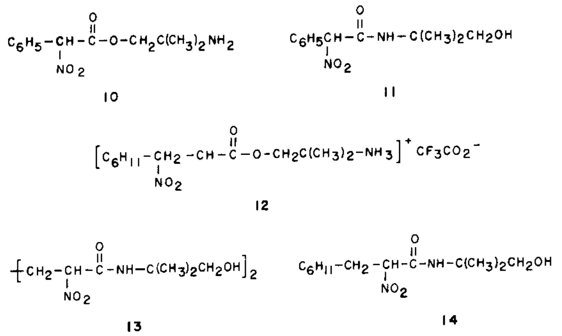
A

Formula Sheet



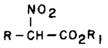
B

Formula Sheet



The ring opening of **1** requires a nucleophilic attack of water at the C-2 position of the ring. Since the reaction was carried out under anhydrous conditions, the required water was apparently formed in the esterification reaction

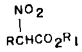
Table I

Preparation of α-Nitrocarboxylic Acid Esters, 
$R-\overset{NO_2}{\overset{|}{C}}H-CO_2R_1$

R	R_1	Yield % [a]	Yield % [b]	Bp/torr (°C)	n_{20}^{D}	Molecular Formula	Analysis % Calcd.			Analysis % Found		
							C	H	N	C	H	N
C_6H_5	CH_3	76	80	112/0.6	1.5191	[c]						
C_6H_5	C_2H_5	75	85	102-103/0.3	1.5095	[d]						
C_6H_5	C_3H_7	81	80	120-124/0.7	1.5130	$C_{11}H_{13}NO_4$	59.19	5.83	6.27	59.33	5.89	6.57
CH_3	C_2H_5		73	46-47/0.5	1.4126	[e]						
CH_3	C_4H_9	70		58-59/0.5	1.4250	[e]						
C_4H_9	C_3H_7	82	75	91-92/1	1.4272	$C_9H_{17}NO_4$	53.29	8.37	6.89	52.93	8.76	6.83
C_4H_9	C_4H_9	86	75	85-86/0.4	1.4311	$C_{10}H_{19}NO_4$	55.29	8.75	6.45	54.90	8.99	6.54
$C_6H_{11}CH_2$	C_3H_7	84		112-114/0.8	1.4607	$C_{12}H_{21}NO_4$	59.24	8.70	5.75	58.91	9.08	5.85
$C_6H_{11}CH_2$	C_4C_9	82		122-123/0.8	1.4594	$C_{13}H_{23}NO_4$	60.27	9.01	5.44	60.84	9.24	5.33
[f]	CH_3		68	[g]		$C_8H_{12}N_2O_8$	36.37	4.58	10.60	36.29	4.62	10.33

[a] Prepared from α-nitrooxazolines directly. [b] Prepared from the isolated TFA-Salts of ammonioalkyl nitrocarboxylic acid esters. [c] Reference [7]. [d] Reference [8]. [e] Reference [9]. [f] R = $(CH_2)_2$-$CHNO_2CO_2CH_3$. [g] Mp 61-62° (ethanol).

Table II

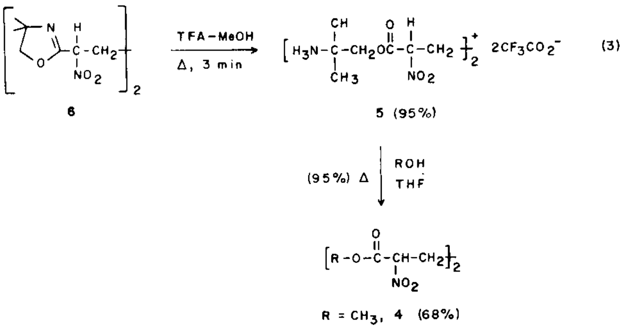
Spectroscopic Data of α-Nitrocarboxylic Acid Esters, 
$R\overset{NO_2}{\overset{|}{C}}HCO_2R_1$

R	R_1	IR (cm^{-1}) [a]			^{1}H-NMR δ (ppm) [b]
		ν CO	ν NO_2	ν C-O-C	
C_6H_5	C_3H_7	1753	1570, 1359	1201	0.78-0.94 (t, J = 7.2 Hz, 3, CH_3), 1.44-1.84 (sext, J = 7.2 Hz, 2, $C\mathit{H}_2CH_3$), 4.13-4.28, (t, J = 6.75 Hz, 2, OCH_2), 6.19 (s, 1, CH), 7.46 (s, 5, C_6H_5)
C_4H_9	C_3H_7	1751	1566, 1360	1193	0.90-0.98 (t, 6, CH_3), 1.34-1.44 (m, 4, CH_2), 1.61-1.79 (sext, J = 7.2 Hz, 2, OCH_2-$C\mathit{H}_2$), 2.07-2.39 (m, 2, $C\mathit{H}_2$-CH), 4.16-4.22 (t, J = 6 Hz, 2, OCH_2), 5.08-5.15 (dd, J = 5.73 Hz, 1, CH
C_4H_9	C_4H_9	1750	1561, 1360	1182	0.90-0.97 (t, J = 7 Hz, 6, CH_3), 1.32-143 [m, 6, $CH_3(C\mathit{H}_2)_2$ and $O(CH_2)_2C\mathit{H}_2$], 1.59-1.73 (pent, J = 7 Hz, 2, $OCH_2C\mathit{H}_2$), 2.07-2.39 (m, 2, $C\mathit{H}_2CH$), 4.20-4.26 (t, J = 6 Hz, 2, OCH_2), 5.07-5.14 (dd, J = 5.76 Hz, 1, CH)
$C_6H_{11}CH_2$	C_3H_7	1650	1565, 1365	1200	0.90-2.30 (m, 18, CH_3-CH_2 and $CH_2C_6H_{11}$), 4.21 (t, 2, CH_2O), 5.22 (t, 1, CH)
$C_6H_{11}CH_2$	C_4H_9	1650	1565, 1365	1200	0.90-2.35 (m, 20, $CH_3(CH_2)_2$ and $CH_2C_6H_{11}$), 4.25 (t, 2, CH_2O), 5.25 (t, 1, CH)
[c]	CH_3	1760	1550, 1370	1156	2.38 (m, 4, CH_2), 3.42 (s, 6, CH_3), 5.30 (m, 2, CH)

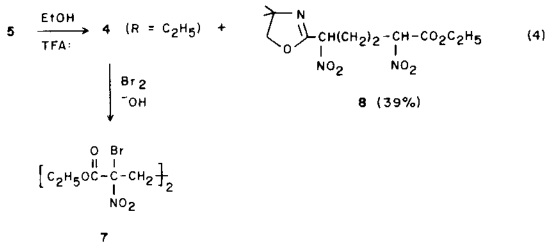
[a] Determined neat or in Nujol on Perkin Elmer spectrophotometer Model 267. [b] Recorded in deuteriochloroform on Varian XL-200 MHz Model or 90 MHz R32 Perkin Elmer spectrometers using tetramethylsilane as an internal standard. [c] R = -$(CH_2)_2$-$CHNO_2CO_2CH_3$.

between TFA and methanol. In fact, when methanol was replaced by dichloromethane or carbon tetrachloride, oxazoline **1** was recovered unchanged.

As shown in Table I, (spectroscopic data are compiled in Table 2) various nitro esters were obtained directly from the appropriate oxazolines or *via* the isolated aminonitroester salts. An exception was found in preparing dimethyl α-α′-dinitroadipate (4, R = CH_3), which was only obtained from salt **5** in 65% yield. The ring opening of oxazoline **6** to **5** was effected in high yield (95%) (eq 3).

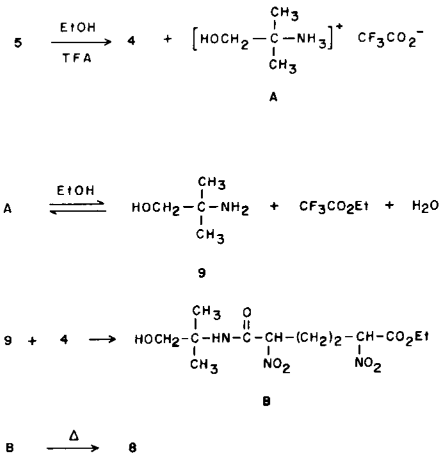


When the transesterification reaction with **5** was carried out in ethanolic-TFA, the diethyl ester **4** (R = C_2H_5) was obtained as an oil which could not be purified. It was identified by spectral data and by its conversion to diethyl α,α′-dibromo-α,α′-dinitroadipate (**7**). In addition to **4**, there was isolated in 39% yield a compound which was identified as ethyl 2,5-dinitro-5-[2-(4,4-dimethyl-2-oxazolinyl)]pentanoate (**8**) (eq 4).



The formation of the oxazoline **8** can be explained by partial amidation of diester **4** by the amino alcohol, 2-amino-2-methyl-1-propanol (**9**), which in its turn originated from the transesterification reaction of **5**. A possible reaction path is proposed in Scheme 1

Scheme I



$$5 \xrightarrow[TFA]{EtOH} 4 + \left[HOCH_2-\overset{CH_3}{\underset{CH_3}{C}}-NH_3\right]^+ CF_3CO_2^-$$

A

$$A \overset{EtOH}{\rightleftharpoons} HOCH_2-\overset{CH_3}{\underset{CH_3}{C}}-NH_2 + CF_3CO_2Et + H_2O$$

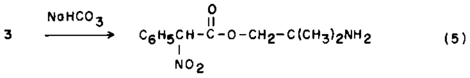
9

$$9 + 4 \longrightarrow HOCH_2-\overset{CH_3}{\underset{CH_3}{C}}-HN-\overset{O}{\overset{\|}{C}}-\underset{NO_2}{CH}-(CH_2)_2-\underset{NO_2}{CH}-CO_2Et$$

B

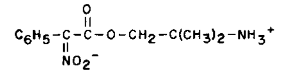
$$B \xrightarrow{\Delta} 8$$

As shown in Table III, the trifluoroacetate salts of the aminonitroesters were obtained in high yield from the various oxazolines. The structure of the salts was confirmed by spectral data (Table IV) and elemental analyses. Also, on neutralization with sodium bicarbonate they were converted into the amino-nitroesters. For example, compound **3** afforded 2-amino-2-methylpropyl phenylnitroacetate (**10**) (eq 5). The nmr and uv spectra of **10** indicated that in polar solvents the zwitterionic structure **10a** is a major contributor. In the nmr in DMSO-d_6, the signal for the ammonium ion was present at 7.83 ppm. The uv spectrum in ethanol or DMSO showed the characteristic nitronate maxima at 334 and 340 nm. They were absent in chloroform or carbon tetrachloride.



$$3 \xrightarrow{NaHCO_3} C_6H_5\underset{NO_2}{CH}-\overset{O}{\overset{\|}{C}}-O-CH_2-C(CH_3)_2NH_2 \qquad (5)$$

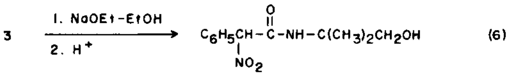
10



$$C_6H_5-\underset{\underset{NO_2^-}{\|}}{C}-\overset{O}{\overset{\|}{C}}-O-CH_2-C(CH_3)_2-NH_3^+$$

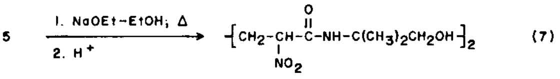
10a

It is interesting to note that Meyers [4] reported that salts of amino esters rearranged to amides on neutralization with sodium bicarbonate. Apparently, sodium bicarbonate is not a strong enough base to effect this rearrangement with salts of amino-nitroesters such as compound **3**. Indeed, when **3** was treated with sodium ethoxide, intra-amidation occurred readily to give a 73% yield of *N*-[2-(1-hydroxy-2-methyl)propyl]nitrophenylacetamide (**11**) (eq 6). Similarly TFA salts of **5** and of 2-ammonio-2-methylpropyl 2-nitro-3-cyclohexylpropionate (**12**) were readily converted into the corresponding amides **13** and **14** (eqs 7-8).



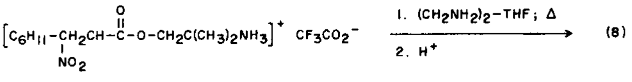
$$3 \xrightarrow[2.\ H^+]{1.\ NaOEt-EtOH} C_6H_5\underset{NO_2}{CH}-\overset{O}{\overset{\|}{C}}-NH-C(CH_3)_2CH_2OH \qquad (6)$$

11



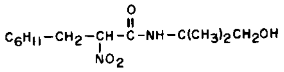
$$5 \xrightarrow[2.\ H^+]{1.\ NaOEt-EtOH;\ \Delta} \left[CH_2-\underset{NO_2}{CH}-\overset{O}{\overset{\|}{C}}-NH-C(CH_3)_2CH_2OH\right]_2 \qquad (7)$$

13



$$\left[C_6H_{11}-CH_2\underset{NO_2}{CH}-\overset{O}{\overset{\|}{C}}-O-CH_2C(CH_3)_2NH_3\right]^+ CF_3CO_2^- \xrightarrow[2.\ H^+]{1.\ (CH_2NH_2)_2-THF;\ \Delta} \qquad (8)$$

12

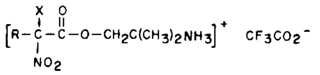


$$C_6H_{11}-CH_2-\underset{NO_2}{CH}-\overset{O}{\overset{\|}{C}}-NH-C(CH_3)_2CH_2OH$$

14

The intra-amidation of **12** was studied in various base-solvent systems. It was found that the highest yield of amide **14** was realized when **12** was refluxed in ethylenediamine-THF for about 20 hours. The results are compiled in Table V.

Table III

Preparation of 
$[R-C(X)(NO_2)-C(=O)-O-CH_2C(CH_3)_2NH_3]^+\ CF_3CO_2^-$

R	X	Yield %	MP (°C) (solvent)	Molecular Formula	Analysis % Calcd. C	H	F	N	Found C	H	F	N
C_6H_5	H	100	158-159 (MeOH-Et_2O)	$C_{14}H_{17}F_3N_2O_6$	45.90	4.64	15.56	7.65	45.63	4.79	15.44	7.49
α-Naphthyl	H	92	236-138 ($CHCl_3$-Et_2O)	$C_{18}H_{19}F_3N_2O_6$	51.93	4.60	13.69	6.73	51.89	4.65	13.51	6.56
H	H	89	90-92 dec (MeOH-Et_2O)	$C_8H_{13}F_3N_2O_6$	33.11	4.51	19.64	9.64	33.39	4.69	19.49	9.56
CH_3	H	100	105-106 ($CHCl_3$)	$C_9H_{15}F_3N_2O_6$	35.52	4.93	18.75	9.21	35.28	4.99	18.58	8.97
CH_3	CH_3	82	138-139 (MeOH-Et_2O)	$C_{10}H_{17}F_3N_2O_6$	37.74	5.39	17.91	8.80	37.80	5.14	17.86	8.90
$C_6H_{11}CH_2$	H	92	108-109	$C_{15}H_{25}F_3N_2O_6$	46.63	6.52	14.75	7.24	46.86	6.62	14.68	7.15
[a]	H	98	173-174 dec (MeOH-Et_2O)	$C_{18}H_{28}F_6N_4O_{12}$	35.65	4.65	18.80	9.24	35.79	4.66	18.72	9.02

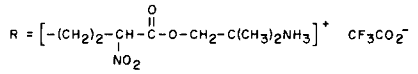
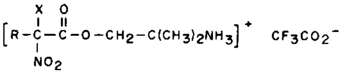
[a] R = 
$[-(CH_2)_2-CH(NO_2)-C(=O)-O-CH_2-C(CH_3)_2NH_3]^+\ CF_3CO_2^-$

Table IV

Spectroscopic Data of 
$[R-C(X)(NO_2)-C(=O)-O-CH_2-C(CH_3)_2NH_3]^+\ CF_3CO_2^-$

R	X	IR (cm^{-1}) [a] ν CO	ν CO_2^-	ν NO_2	ν C-O-C	^{1}H-NMR δ (ppm) [b]
C_6H_5	H	1754	1680	1563, 1382	1180	1.22-1.29 (s, 6, CH_3), 4.16-4.50 (dd, J = 10.8 Hz, 2, CH_2), 7.01 (s, 1, CH), 7.53 (s, 5, C_6H_5), 8.50 (br, 3, NH_3^+)
α-Naphthyl	H	1765	1678	1563, 1378	1199	1.12-1.22 (s, 6, CH_3), 3.87-4.45 (dd, J = 11.8 Hz, 2, CH_2), 7.23 (s, 1, CH), 7.5-8.0 (m, 10, aromatic + NH_3^+)
H	H	1770	1660	1540, 1389	1190	1.36 (s, 6, CH_3), 4.28 (s, 2, CH_2), 5.52 (d, 2, CH_2), 8.50 (br, 3, NH_3^+)
CH_3	CH_3	1770	1685	1560, 1380	1185	1.20 (s, 6, CH_3), 1.67 (s, 6, CH_3), 4.02 (s, 2, CH_2), 8.56 (br, s, NH_3^+)
$C_6H_{11}CH_2$	H	1755	1680	1563, 1379	1200	0.94 (m, 2, ring CH_2), 1.18 (m, 4, ring CH_2), 1.38 (s, 6, CH_3), 1.67 (m, 5, ring CH_2), 1.86-2.38 (m, 2, $CHNO_2C\mathit{H}_2$), 4.18-4.31 (dd, J = 12 Hz, 2, OCH_2), 5.31-5.43 (dd, J = 5.2 Hz, CH), 7.51 (br, 3, NH_3^+)
[c]	H	1768	1674	1560, 1380	1172	1.30 (s, 12, CH_3), 2.32 (m, 4, CH_2), 4.23 (s, 4, OCH_2), 5.78 (m, 2, CH), 8.40 (br, 6, NH_3^+)

[a] Determined in Nujol on Perkin Elmer spectrophotometer Model 267. [b] Recorded in a mixture of deuterated dimethyl sulfoxide (DMSO-d_6) and deuteriochloroform on Varian XL-200 MHz Model or 90 MHz R-32 Model Perkin Elmer spectrometers using tetramethylsilane as an internal standard. [c] R = $[-(CH_2)_2-CHNO_2-CO_2CH_2-C(CH_3)_2-NH_3]^+\ CF_3CO_2^-$

EXPERIMENTAL

Equipment.

Ultraviolet spectra were obtained on a Cary 17D recording spectrophotometer. Solvents were evaporated on a Buchler flash evaporator.

General Preparation of α-Nitroalkyl- and α-Nitroaralkylcarboxylic Acid Esters.

A. Using 2-Nitroalkyl- or 2-Nitroaralkyl-2-oxazolines.

A mixture consisting of the appropriate 2-nitrooxazoline (0.05 mole), the alcohol (1 mole) and trifluoroacetic acid (0.1 mole) was refluxed for about 36 hours. The excess alcohol was removed *in vacuo* and the residue taken up in ether. The solution was washed with water, dried with magnesium sulfate and the ether removed. The remaining ester was then distilled *in vacuo.*

B. Using TFA Salts of Ammonioalkyl Esters of α-Nitroalkyl- and α-Nitroaralkylcarboxylic Acids.

The experimental procedure was essentially the same as in method A

Table V

Influence of Base-Solvent Systems on the Conversion of Ester **12** to Amide **14**

Ratio of **12** to base, moles [a]	Base	Solvent	Amide **14**, Yield %
1:2.5	sodium ethoxide	EtOH	69
1:3.0	piperidine	THF	77
1:3.0	ethylenediamine	THF	92
1:3.0	ethylenediamine	EtOH	70
1:3.0	ethylenediamine	hexane	57
1:3.0	ethylenediamine	benzene	44

[a] Reactions were run for about 20 hours at reflux temperature.

except that 0.05 mole of the appropriate TFA salt, 1.2 moles of the alcohol and 0.1 mole of TFA were used.

The spectral data of the various nitro esters are reported in Table II.

General Preparation of TFA Salts of Ammonioalkyl Esters of α-Nitroalkyl- and α-Nitroaralkylcarboxylic Esters.

A mixture consisting of the appropriate 2-nitrooxazoline (0.05 mole), methanol (2.5 moles) and TFA (0.5 mole) was refluxed until a clear solution was obtained. Methanol was removed *in vacuo* and ether was added to the residue. The resulting solid was then recrystallized (Table III).

Diethyl 2,5-Dinitroadipate (**4**) and Ethyl 2,5-Dinitro-5-[2-(4,4-dimethyl-2-oxazolinyl)]pentanoate (**8**).

TFA-salt **5** (10 g, 0.0165 mole), ethanol (115 ml) and TFA (5 ml) were refluxed for about 36 hours. The excess ethanol was removed *in vacuo*, the light yellow oil was dissolved in ether and the solution washed with water and dried (magnesium sulfate). Cooling the solution for 24 hours gave 2.03 g (39%) of compound **8**, mp 115-116° (ethanol); ir (Nujol): 3210 (NH^+), 1707 (CO), 1605 (C=N), 1540 and 1350 cm^{-1} (NO_2); nmr (deuteriochloroform): δ 1.30 (t, 3, CH_3CH_2), 1.53 (s, 6, CH_3), 2.50 (t, 2, CH_2CHNO_2), 2.69 (t, 2, $CH_2C=NO_2^-$), 4.15-4.32 (m, 4H, ring CH_2 + CH_2CH_3), 5.10 (t, 1, $CHNO_2$), and 9.50 (s, 1H, NH^+).

Anal. Calcd. for $C_{12}H_{19}N_3O_7$: C, 45.42; H, 6.03; N, 13.24. Found: C, 45.39; H, 6.04; N, 13.25.

Evaporation of the ether filtrate gave 1.5 g (31%) of diester **4** (R = C_2H_5) as a light-yellow oil; ir (neat): 1760 (CO), 1550 and 1370 cm^{-1} (NO_2); nmr (deuteriochloroform): δ 1.30 (t, 6, CH_3), 2.32 (m, 4, CH_2), 4.36 (q, 4, CH_2CH_3), and 5.29 (t, 1, CH).

Diethyl 2,5-Dibromo-2,5-dinitroadipate (**7**).

Compound **4** (2.19 g, 0.0075 mole) was dissolved in 20 ml of water containing 1.33 g (0.024 mole) of potassium hydroxide. To the stirred solution was added dropwise at 0-5° a freshly prepared potassium hypobromite solution obtained from 85% assay potassium hydroxide (4.66 g, 0.083 mole) and bromine (4.16 g, 0.026 mole) dissolved in 20 ml of water. The reaction mixture was stirred for an additional 30 minutes, the solid filtered and recrystallized with ethanol to give 1.63 g (48%) of compound **7**, mp 65-66°; ir (Nujol): 1650 (CO), 1565 and 1365 (NO_2), 1200 cm^{-1} (C-O-C); nmr (deuteriochloroform): δ 1.49 (t, 3, CH_3), 2.70 (s, 2, CH_2), and 4.45 (q, 2, CH_2CH_3).

Anal. Calcd. for $C_{10}H_{14}Br_2N_2O_8$: C, 26.67; H, 3.14; Br, 35.49; N, 6.22. Found: C, 26.64; H, 3.09; Br, 35.35; N, 6.11.

2-Amino-2-methylpropyl α-Nitrophenylacetate (**10**).

To a stirred suspension of TFA-salt **3** (1 g, 0.0027 mole) in 10 ml of water was added dropwise a saturated aqueous solution of sodium bicarbonate until the mixture became just basic (*p*H 7.5). The mixture turned clear with effervescence and a pale yellow solid separated. Stirring was continued for 30 minutes and the solid filtered to give 0.54 g (80%) of ester **10**, mp 148-149° (water); ir (Nujol): 1695 (CO), 1257 and 1060 ($=NO_2^-$), and 1232 cm^{-1} (C-O-C); nmr (DMSO-d$_6$): 200 MHz δ 1.20 (s, 3, CH_3), 4.09 (s, 2, CH_2), 7.01-7.08 (t, J = 7.2 Hz, 1, CH), 7.18-7.25 (t, J = 7.5 Hz, 2, CH), 7.42-7.45 (d, J = 7.4 Hz, 2, CH), and 7.84 (br s, 3, NH_3^+).

Anal. Calcd. for $C_{12}H_{16}N_2O_4$: C, 57.13; H, 6.39; N, 11.10. Found: C, 57.23; H, 6.40; N, 11.19.

N-[2-(1-Hydroxy-2-methyl)propyl]nitrophenylacetamide (**11**).

To a freshly prepared solution of sodium (0.483 g, 0.021 g-atom) in ethanol (20 ml) was added compound **3** (3 g, 0.008 mole) with stirring. The reaction mixture became a clear solution in about 5 minutes. The solvent was removed *in vacuo* to give a thick yellow oil which was dissolved in 30 ml of water and acidified with glacial acetic acid. Then the solution was extracted with methylene chloride. The extract was dried with magnesium sulfate, the solvent removed to give a yellow oil which after trituration with ether solidified. Recrystallization with benzene gave 1.50 g (75%) of colorless amide **11**, mp 111-112°; ir (Nujol): 3420 (OH), 3240 and 3080 (NH), 1665 (CO), 1557 and 1372 cm^{-1} (NO_2); nmr (deuteriochloroform + DMSO-d$_6$): 200 MHz δ 1.22 (s, 6, CH_3), 3.40 (s, J = 11.3 Hz, 2, CH_2), 4.77 (br s, 1, OH), 6.55 (s, 1H, CH), 7.47 (m, 5H, aromatics) and 8.12 (s, 1, NH).

Anal. Calcd. for $C_{12}H_{16}N_2O_4$: C, 57.13; H, 6.39; N, 11.10. Found: C, 57.39; H, 6.64; N, 10.77.

N,N'-Bis[2-(2-methyl-1-hydroxy)propyl]-2,5-dinitroadipamide (**13**).

The experimental procedure was similar to that described for preparing compound **11**, except that compound **5** (3 g, 0.005 mole), sodium (0.68 g, 0.0029 g-atom) and ethanol (60 ml) were employed, and that the reaction mixture was refluxed for 20 hours. Purification by dissolving that solid in dimethylformamide and reprecipitating with ether gave 1.10 g (58%) of **13**, mp 156-157° dec; ir (Nujol): 3282 and 3103 (NH), 1665 (CO), 1550 and 1360 cm^{-1} (NO_2); nmr (deuteriochloroform + DMSO-d$_6$): δ 1.25 (s, 12, CH_3), 2.14 (d, 4, CH_2), 3.50 (s, 2, CH_2), 4.56 (s, 2, OH), 5.32 (t, 2, CH), and 7.91 (s, 2, NH).

Anal. Calcd. for $C_{14}H_{26}N_4O_8$: C, 44.44; H, 6.93; N, 14.81. Found: C, 44.46; H, 7.20; N, 14.68.

N-2-(2-Methyl-1-hydroxy)propyl-2-nitro-3-cyclohexylpropionamide (**14**).

The reaction mixture which consisted of the TFA-salt **12** (2 g, 0.0052 mole), ethylenediamine (0.94 g, 0.0016 mole) and THF (20 ml) was refluxed for over 20 hours until a clear solution resulted. Then, the solvent was removed *in vacuo* to give a yellow oil which was dissolved in 100 ml of water. Acidification of the solution with glacial acetic acid and cooling afforded a colorless solid. Recrystallization with benzene gave 1.29 g (91%) of compound **14**, mp 108-109°; ir (Nujol): 3400 (OH), 3250 and 3065 (NH), 1755 (CO), 1545 and 1368 cm^{-1} (NO_2); nmr (deuteriochloroform + DMSO-d$_6$): δ: 1.22 (m, 17, CH_3 + ring CH_2), 1.62 (d, 2, CH_2), 3.42 (s, 2, CH_2O), 4.80 (br s, 1, OH), 5.30 (t, 1, CH), and 7.87 (s, 1, NH).

Anal. Calcd. for $C_{13}H_{24}N_2O_4$: C, 57.33, H, 8.88; N, 10.29. Found: C, 57.20; H, 8.92; N, 10.05.

REFERENCES AND NOTES

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[6] The Nef reaction was minimized when the reaction temperature was lowered to 60° for 3 minutes. Compound **1** was converted to the amino ester, $C_6H_5CH(NO_2)CO_2CH_2C(CH_3)_2NH_3^+$, $CH_3SO_4^-$, which was difficult to purify. Moreover, attempts to convert it to ester **2** were unsuccessful.

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