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Studies on Nitro Carboxylic Acids. II. Synthesis of α,β-Unsaturated β-Nitro Carboxylic Esters[1]

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Synthetic studies on ethyl α,β-unsaturated β-nitrocarboxylates (IV) through two routes are described. Ethyl α-hydroxy-β-nitrocarboxylates (II) obtained by the reactions of ethyl α,β-unsaturated carboxylates with fuming nitric acid or by those of nitroparafins with ethyl glyoxylate, were treated with acetic anhydride to afford ethyl α-acetoxy-β-nitrocarboxylates (III), which were subsequently converted into IV by treatment with bases used as catalysts. On the other hand, IV was also obtained from ethyl α-chloro-β-nitrocarboxylates derived from the reactions of ethyl α,β-unsaturated carboxylates with nitryl or nitrosyl chloride. The structural assignments of IV were made on the basis of elementary analysis, infrared spectra and its conversion into the corresponding α-methoxy derivatives.

General methods for the syntheses of ethyl α,β-unsaturated α-nitrocarboxylates (I) are found in literature. They can be classified into two methods; (a) by elimination of the corresponding β-hydroxy-carboxylates obtained from appropriate aldehydes and ethyl nitroacetate, *via* the acetoxy derivatives,[2-5] and (b) by nitration of ethyl α,β-unsaturated carboxylates with nitric acid or dinitrogen trioxide.[6-9]

However, there are no reports on the general synthesis ethyl α,β-unsaturated β-nitrocarboxylates (IV) except for that of β-nitroacrylic acids by the elimination of α-halo-β-nitropropionic acids.[10-12]

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[1] Part I of this series: C. Shin, M. Masaki, and M. Ohta, This Bulletin, **43**, 3219 (1970). A part of the present work was presented at the 24th Annual Meeting of the Chemical Society of Japan, Osaka, April, 1971.

[2] A. Dornow and H. Menzel, *Ann. Chem.*, **588**, 40 (1958).

[3] K. M. Rodionov and V. M. Belikov, *Dokl. Akad. Nauk. SSSR.*, **93**, 829 (1953); *Chem. Abstr.*, **49**, 1550 (1955).

[4] I. S. Ivanova, Yu. V. Konnova, and S. S. Novikov, *Izv. Akad. Nauk, SSSR., Otd. Khim, Nauk*, **1962**, 1677; *Chem. Abstr.*, **58**, 4419 (1962).

[5] S. Umezawa and S. Zen, This Bulletin, **36**, 1143 (1963).

[6] L. Bouveault and A. Wahl, *C. R. Acad. Sci. Paris*, **131**, 687, 1212 (1900).

[7] L. Bouveault and A. Wahl, *Bull. Soc. Chim. Fr.*, **25**, 801, 913 (1901).

[8] S. Tatsuoka, M. Murakami, and T. Tamura, *Yakugaku Zasshi*, **70**, 230 (1950).

[9] K. Yamagishi and Y. Ishibiki, *Nippon Kagaku Zasshi*, **81**, 971 (1960).

[10] a) H. Shechter, F. Conrad, A. L. Daulton, and R. B. Kaplan, *J. Amer. Chem. Soc.*, **74**, 3052 (1952); b) S. S. Novikov, G. A. Shvekhgeheimer, and N. F. Pyatakov, *Izv. Akad. Nauk, SSSR., Otd. Khim. Nauk*, **1961**, 914; *Chem. Abstr.*, **55**, 22121 (1961).

[11] K. A. Ogloblin and V. P. Semenov, *Zh, Org. Khim.*, **1** (**8**), 1361 (1965); *Chem. Abstr.*, **64**, 588 (1966).

[12] A. Hassner, *J. Org. Chem.*, **34**, 2628 (1969).

In a previous paper,[1] one of the authors (C. S.) reported on the direct synthesis of I and ethyl α-hydroxy-β-nitrocarboxylates (II) by treatment of ethyl α,β-unsaturated carboxylates with fuming nitric acid.

In this paper, we report detailed studies on the preparation of IV through two synthetic routes.

Results

Synthesis of IV from Nitroparaffins and Ethyl Glyoxylate. Condensation of appropriate nitroparaffins and ethyl glyoxylate[13] obtained by lead tetraacetate oxidation of ethyl tartrate in benzene gave II in about 50% yield (Table 1). The absorption patterns and boiling points of these nitro alcohols (II) are identical with those II prepared from the olefinic esters and fuming nitric acid.[1]

Acetylation of II with acetic anhydride under reflux for 1.5 hr afforded ethyl α-acetoxy-β-nitrocarboxylates (III) in good yields (Table 2). When III was treated with a small amount of inorganic or organic bases as catalysts in the absence of solvent by shaking for 15 minutes at 80—120°C, the expected ethyl α,β-unsaturated β-nitrocarboxylates (IV) were obtained (Table 3).

Table 1. Ethyl α-hydroxy-β-nitrocarboxylates (II)

Compound	R	Yield (%)	Bp. °C/mmHg (Mp. °C)
IIa	CH_3	52.1	108—112/3[a]
IIb	C_2H_5	51.5	122—125/4
IIc	n-C_3H_7	53.8	127—129/4.5
IId	i-C_3H_7	28.2	125—127/4
IIe	C_6H_5	65.0	(81—82)[b]

a) Found: C, 40.29; H, 6.29; N, 7.88%. Calcd for $C_6H_{11}NO_5$: C, 40.68; H, 6.26; N, 7.91%. b) Found: C, 54.98; H, 5.61; N, 5.89%. Calcd for $C_{11}H_{13}NO_5$: C, 55.23; H, 5.48; N, 5.86%. Colorless needles from benzene-petroleum ether.

Formation of ethyl α-nitroolefin carboxylates (I) by elimination of β-acetoxy group from ethyl β-acetoxy-α-nitrocarboxylates was carried out by using sodium carbonate as a catalyst in benzene.[5] However, in the case of elimination of α-acetoxy group from III, it was found that sodium hydrogen carbonate without solvent was superior to sodium carbonate in benzene.

Synthesis of IV from Ethyl α,β-Unsaturated Carboxylates. When olefinic esters were treated with nitryl chloride in ether below 0°C for 5 hr, ethyl α-chloro-β-nitrocarboxylates (V) were obtained as the main products, together with ethyl α,β-dichlorocarboxylates (VI), a small amount of higher-boiling product and polymerized reddish residue. The higher-boiling product was identified as ethyl α-nitrito-β-nitrocarboxylates (VII) from the fact that it showed an infrared absorption band of an intense nitrito group in the 1620—1630 cm^{-1} region and that it was converted into II by boiling in water.[9] Nitration by nitrosyl chloride under similar conditions also gave the same products (V and VI), but the formation of VII and the residue was found to be less than in the case of nitryl chloride. Other products such as ethyl α,β-dinitrito- and β-nitrito-α-nitrocarboxylates could not be detected. The elimination reaction of V with triethylamine afforded IV in about 50% yield.

In order to confirm its structure, compound IV was converted into the corresponding α-methoxy deriva-

Table 2. Ethyl α-acetoxy-β-nitrocarboxylates (III)

Compound	Yield (%)	Bp °C/mmHg	Formula	Found, % C	Found, % H	Found, % N	Calcd, % C	Calcd, % H	Calcd, % N	IR Spectrum cm^{-1}, in KBr disk
IIIa	80.2	99—102/2	$C_8H_{13}NO_6$	43.71	6.07	6.37	43.83	5.98	6.39	1750, 1555, 1370
IIIb	88.4	110—115/2	$C_9H_{15}NO_6$	46.62	6.19	5.93	46.35	6.48	6.01	1760, 1560, 1375
IIIc	95.0	120—123/4	$C_{10}H_{17}NO_6$	48.69	6.83	6.38	48.81	6.93	5.67	1760, 1560, 1370
IIId	72.0	100—104/3	$C_{10}H_{17}NO_6$	48.58	6.75	6.05	48.81	6.93	5.67	1755, 1570, 1370

Table 3. Elimination of α-acetoxy-4-methyl-3-nitrovalerate (IIId)

Catalyst (7×10^{-4} mol)[a]	Reaction conditions Temp (°C)	Reaction conditions Time (min)	Yield of IVd (%)
—	110—120	15	0
Na_2CO_3	110—120	15	49
Na_2CO_3	60[b]	20	5
$NaHCO_3$	110—120	15	82
CH_3COONa	110—120	15	71
$(C_2H_5)_3N$	80—90	15	71
Pyridine	110—120	15	50
Piperidine	110—120	15	26
$C_6H_5NHCH_3$	110—120	15	8
$C_6H_5N(CH_3)_2$	110—120	15	28

a) 10^{-1} mol of IIId was used. b) In dry benzene (20 *ml*).

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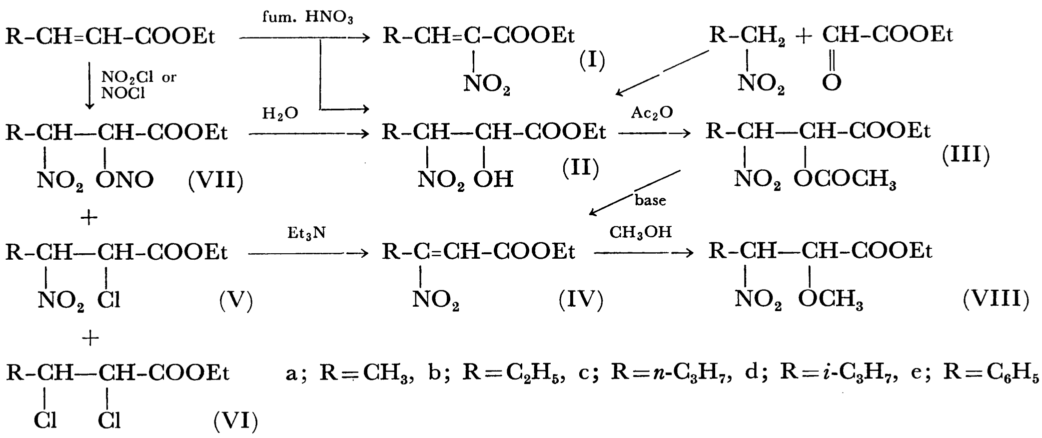
[13] Y. Hamamura, M. Otsuka, and M. Suzumoto, *Nippon Nogei Kagaku Kaishi*, **22**, 24 (1948).



Scheme 1.

tives. When IV was treated with methanol in the presence of sodium methoxide below −10°C, the expected ethyl α-methoxy-β-nitrocarboxylates (VIII) were obtained. The disappearance of carbon-carbon double bond absorption in the 1640—1680 cm^{-1} region of the infrared spectrum of IV indicates the formation of VIII.

Experimental

All boiling and melting points are uncorrected. The IR spectra were recorded with a Hitachi EPI-G2 Spectrometer.

Reaction of Nitroparaffin with Ethyl Glyoxylate Derived from Ethyl Tartrate and Lead Tetraacetate. Lead tetraacetate (0.048 mol) was added portionwise with stirring to a cooled solution of ethyl tartrate (0.048 mol) in dry benzene (50 m*l*). After stirring for 1.5 hr at room temperature, separated crystals were filtered off and washed well with dry benzene. The filtrate and the washings were combined (about 100 m*l*). Appropriate nitroparaffin (0.098 mol) and 6% ethanolic solution of sodium ethoxide (from 2.4 g of sodium in ethanol (40 m*l*)) were added to the combined solution, with vigorous stirring. The weak alkaline solution was allowed to stand overnight with stirring at room temperature. After concentration of the solution, the residual oil was added to a mixture of benzene (100 m*l*) and water (50 m*l*). The solution was then acidified with 3 N hydrochloric acid. After removal of the precipitated crystals, the solution was washed with water twice (each 30 m*l*), and then dried over anhydrous magnesium sulfate and evaporated. Distillation of the residual oil afforded ethyl β-hydroxy-α-nitrocarboxylates (II), which were confirmed to be the same as the specimens prepared from ethyl α,β-unsaturated carboxylates and fuming nitric acid from their boiling points and IR spectra. The results are summarized in Table 1.

Acetylation of Ethyl α-Hydroxy-β-nitrocarboxylates (II) with Acetic Anhydride. A mixture of II (0.05 mol) in acetic anhydride (0.1 mol) was refluxed for 1.5 hr. Subsequent distillation of the reaction product under reduced pressure afforded an almost colorless oil, which was identified as ethyl α-acetoxy-β-nitrocarboxylates (III). However, ethyl 2-acetoxy-3-nitro-3-phenylpropionate (IIIe) could not be isolated in pure state and directly converted into ethyl 3-nitro-3-phenyl-2-propenoate (IVe) during the course of distillation. The results are summarized in Table 3.

Reaction of α,β-Unsaturated Carboxylic Esters with Nitryl Chloride (Procedure A). Nitryl chloride (0.48 mol) was added drop by drop, with vigorous stirring, to a solution of ethyl α,β-unsaturated carboxylates (0.32 mol) in dry benzene (60 m*l*) cooled below 0°C with an ice-salt bath. After being stirred for 5 hr at 0°C, the reaction mixture was

TABLE 4. ETHYL α-CHLORO-β-NITROCARBOXYLATES (V)

Compound	Yield (%)		Bp °C/mmHg	Formula	Found, %			Calcd, %			IR Spectrum cm^{-1}, in KBr disk
	A[a)]	B[b)]			C	H	N	C	H	N	
Va	42.0	27.0	77—85/3	$C_6H_{10}NO_4Cl$	37.21	5.22	6.98	36.83	5.12	7.16	1750, 1560, 1385
Vb	38.6	30.0	103—112/10	$C_7H_{12}NO_4Cl$	40.71	5.82	6.55	40.09	5.73	6.68	1740, 1550, 1365
Vc	34.5	24.5	116—125/7	$C_8H_{14}NO_4Cl$	42.98	6.08	5.92	42.95	6.26	6.26	1740, 1550, 1360
Vd	28.4	23.5	91—104/2	$C_8H_{14}NO_4Cl$	43.46	6.09	5.82	42.95	6.26	6.26	1740, 1555, 1370

a) Procedure A. b) Procedure B.

TABLE 5. ETHYL α-β-DICHLOROCARBOXYLATES (VI)

Compound	Yield (%)		Bp °C/mmHg	Formula	Found, %		Calcd, %		IR Spectrum cm^{-1}, in KBr disk
	A[a)]	B[b)]			C	H	C	H	
VIa	18.7	25.1	35—37/3	$C_6H_{10}O_2Cl_2$	39.21	5.31	39.91	5.40	1750
VIb	26.1	24.8	57—60/7	$C_7H_{12}O_2Cl_2$	42.02	6.21	42.21	6.03	1750
VIc	24.2	19.9	55—60/2	$C_8H_{14}O_2Cl_2$	45.38	6.44	45.07	6.57	1750
VId	17.3	20.2	85—88/10	$C_8H_{14}O_2Cl_2$	44.80	6.82	45.07	6.57	1750

a) Procedure A. b) Procedure B.

allowed to attain room temperature and to stand for 3 days. The benzene solution was washed successively with ice water (60 m*l*), 5% aqueous solution of sodium carbonate and finally twice with water. The solution was dried over anhydrous sodium sulfate and then evaporated. Distillation of the residual oil afforded three fractions, two of which were identified as ethyl α-chloro-β-nitrocarboxylates (V) and ethyl α,β-dichlorocarboxylates (VI). The highest boiling fraction was identified as ethyl α-nitrito-β-nitrocarboxylates (VII), though it could not be obtained in a pure state. The results are summarized in Tables 4 and 5.

Reaction of α,β-Unsaturated Carboxylic Esters with Nitrosyl Chloride (Procedure B). Nitrosyl chloride (0.5 mol) was added in a stream to a solution of ethyl α,β-unsaturated carboxylates (0.3 mol) in dry benzene (100 m*l*) cooled below 0°C with an ice-salt bath. After being stirred for 3 hr at 0°C, the reaction mixture was allowed to attain room temperature and to stand for 5 days. The benzene solution was washed with 5% aqueous solution of sodium carbonate and with water, and then dried over anhydrous sodium sulfate and evaporated. Distillation of the residual oil afforded V and VI. The results are summarized in Tables 4 and 5.

Conversion of Ethyl 4-Methyl-2-nitrito-3-nitrovalerate (VIIId) into Ethyl 2-Hydroxy-4-methyl-3-nitrovalerate (IId). A mixture of the crude VIId (5 g, bp 128—160°C/2 mmHg) in water (20 m*l*) was refluxed for 5.5 hr, and the resulting yellow solution was extracted three times with ether. The ethereal solution was washed with water, and dried over magnesium sulfate. After the evaporation of ether, the residue was distilled to give an almost colorless oil (IId; 1.5 g, 34.0%), bp 125—127°C/4 mmHg.

Analogous treatment of ethyl 2-nitrito-3-nitrobutyrate (VIIa; 7 g, bp 130—160°C/3 mmHg) with boiling water afforded the corresponding hydroxy compound (IIa; 2.6 g, 60.1%), bp 108—112°C/5 mmHg.

Elimination Reaction of Ethyl α-Chloro-β-nitrocarboxylates (V) with Triethylamine (Procedure C). Dry triethylamine (0.05 mol) was added drop by drop, with shaking, to a solution of V (0.05 mol) in dry benzene (30 m*l*) at room temperature. After stirring for 1 hr, water (30 m*l*) was added to the reaction solution and then the mixture was extracted three times with benzene. The combined benzene extracts were washed with water and then dried over anhydrous sodium sulfate. After concentrating the benzene extract, distillation of the residual oil afforded a yellow oil which was identified as ethyl α,β-unsaturated β-nitrocarboxylates (IV). The results are summarized in Table 6.

Elimination Reaction of Ethyl α-Acetoxy-β-nitrocarboxylates (III) with Sodium Acetate in the Absence of Solvent (Procedure D). Compound III (0.043 mol) was heated in the presence of sodium acetate (0.06 g) with shaking for 15 min at 110—120°C and subsequent distillation of the reaction product under reduced pressure afforded IV together with a small quantity of acetic acid. The results are summarized in Table 6.

Elimination Reaction of Ethyl 2-Acetoxy-4-methyl-3-nitrovalerate (IIId) with Several Bases. Compound IIId (0.1 mol) was heated in the presence of various bases (7×10^{-4} mol) with shaking for 5—15 min at 80—120°C. Subsequent distillation of the reaction product under reduced pressure afforded ethyl 4-methyl-2-nitro-2-valerate (IVd) together with a small quantity of acetic acid. The results are summarized in Table 3.

Methoxylation of Ethyl α,β-Unsaturated β-Nitrocarboxylates (IV) with Methanol. A solution of IV (0.07 mol) in methanol (80 m*l*) was added, with vigorous stirring, to a 5% methanolic solution of sodium methoxide (from 3.5 g of sodium in methanol (70 m*l*)) cooled below −10°C. The temperature of the reaction mixture rose up to about 15°C, at which stirring was continued for 1 hr. A small amount of of crushed dry ice was then added portionwise. The cooled mixture was poured into water (500 m*l*), and the resulting solution was acidified with glacial acetic acid, whereby an oily product separated out. The product was extracted several times with ether. The combined ethereal extracts were washed with water, dried over anhydrous magnesium sulfate and evaporated. Distillation of the residual oil afforded ethyl α-methoxy-β-nitrocarboxylates (X) as an almost colorless oil. The results are summarized in Table 7.

TABLE 6. ETHYL α,β-UNSATURATED β-NITROCARBOXYLATES (IV)

Compound	Yield (%) C[a]	Yield (%) D[b]	Bp. °C/mmHg	Formula	Found, % C	Found, % H	Found, % N	Calcd, % C	Calcd, % H	Calcd, % N	IR Spectrum cm^{-1}, in KBr disk
IVa	50.2	78.9	65—70/3	$C_6H_9NO_4$	45.37	5.43	7.50	45.28	5.70	8.80	1730, 1680, 1540, 1335
IVb	52.1	80.3	65—69/2.5	$C_7H_{11}NO_4$	48.56	6.17	7.96	48.55	6.40	8.09	1730, 1670, 1540, 1340
IVc	52.8	78.7	69—72/1.5	$C_8H_{13}NO_4$	51.38	6.95	7.26	51.33	7.00	7.48	1740, 1670, 1540, 1340
IVd	54.8	71.5	79—81/2	$C_8H_{13}NO_4$	51.31	7.17	7.62	51.33	7.00	7.48	1730, 1660, 1530, 1360
IVe		61.5[c]	120—123/0.4[d]	$C_{11}H_{11}NO_4$	59.96	4.98	6.63	59.72	5.01	6.33	1725, 1640, 1540, 1360

a) Procedure C. b) Procedure D. c) Evaluated from IIe. d) Mp 69—70°C; recrystallized from petroleum ether-benzene to give colorless needles.

TABLE 7. ETHYL α-METHOXY-β-NITROCARBOXYLATES (VIII)

Compound	Yield (%)	Bp °C/mmHg	Formula	Found, % C	Found, % H	Found, % N	Calcd, % C	Calcd, % H	Calcd, % N	IR Spectrum cm^{-1}, in KBr disk
VIIIa	65.6	72—75/1	$C_7H_{13}NO_5$	43.66	7.02	7.43	43.97	6.85	7.33	1745, 1550, 1365, 1120
VIIIb	55.7	80—83/3	$C_8H_{15}NO_5$	47.11	7.25	6.59	46.82	7.37	6.83	1750, 1555, 1375, 1120
VIIIc	60.5	95—98/3	$C_9H_{17}NO_5$	49.27	7.68	6.61	49.30	7.82	6.39	1760, 1560, 1370, 1120
VIIId	63.9	94—99/3	$C_9H_{17}NO_5$	48.97	7.72	6.18	49.30	7.82	6.39	1760, 1560, 1375, 1120