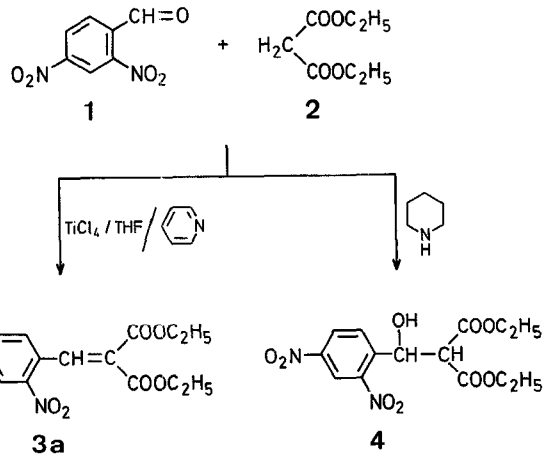
A Convenient One-Step Synthesis of Ethyl 2-[*N*-(Diethoxycarbonyl)(ethoxy)-methyl]amino-4-nitrobenzoate and Analogues by Rearrangement of 2,4-Dinitrobenzylidenemalonates

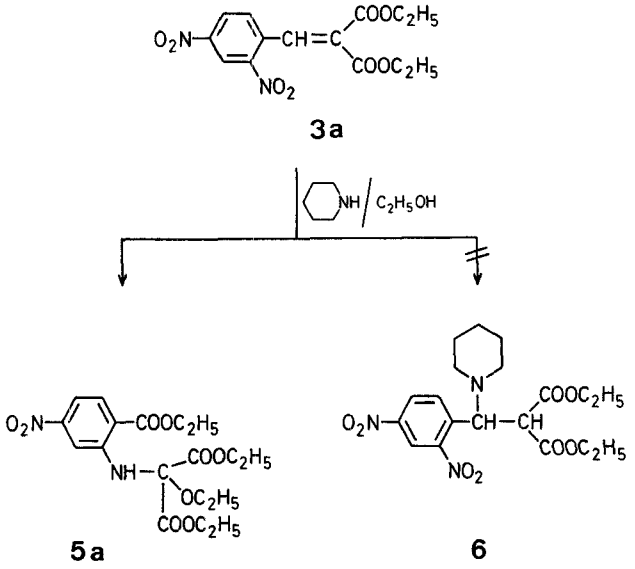
Stefan KINASTOWSKI*, Stanisław WNUK

Chemistry Department, Academy of Agriculture, ul. Wojska Polskiego 75, 60-625 Poznań, Poland

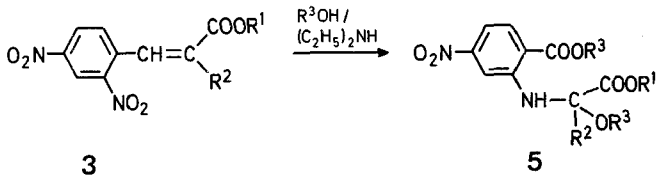
It has been proved that the product of Knoevenagel condensation of 2,4-dinitrobenzaldehyde (**1**) with diethyl malonate (**2**) catalyzed by piperidine is not diethyl 2,4-dinitrobenzylidenemalonate (**3a**) as previously assumed[1] but 1-(2,4-dinitrophenyl)-2,2-diethoxycarbonylethan-1-ol (**4**)[2]. Compound **3a** was obtained in a modified Knoevenagel synthesis catalyzed by titanium(IV) chloride according to Ref.[3].



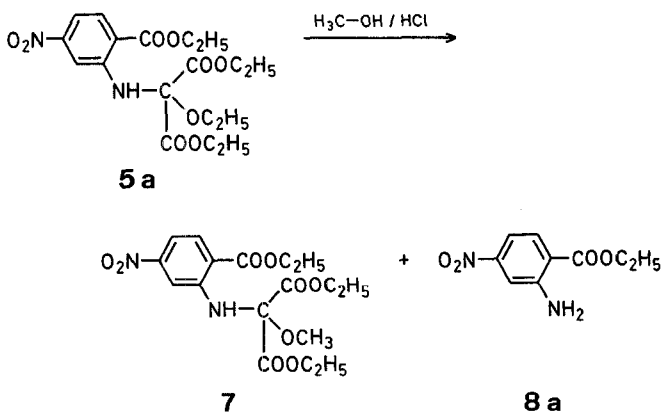
It was noted that **3a** behaves abnormally under Michael reaction conditions. On reaction with piperidine in ethanol instead of addition of piperidine to the polarized double bond, a compound with a completely changed carbon skeleton, not containing a piperidine fragment, i.e. ethyl 2-[*N*-(diethoxycarbonyl)(ethoxy)-methyl]amino-4-nitrobenzoate (**5a**) is formed. Use of pyrrolidine, diethylamine, or diisobutylamine also gave rise to **5a**.



When different alcohols were used as solvents analogous compounds **5** were obtained with corresponding groups R^3. Presumably, the reaction involves compound **3** and alcohol, while the amine serves only to generate alkoxide ions necessary to catalyze the reaction. This reaction is also catalyzed by tertiary amines and by traces of sodium alkoxides.



The structures of compounds **5** (Table) were confirmed by microanalytical, spectral, and chemical data. For example, alkaline or acidic hydrolysis of **3a, 3b, 3f** gave 2-amino-4-nitrobenzoic acid, while on heating with acetic anhydride, the *N*-acetyl derivatives of respective esters of 2-amino-4-nitrobenzoic acid are formed.

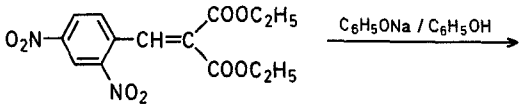


Under the above reaction conditions, no trans-esterification of ester groups was observed with respect to the malonic ester fragment. In compounds **5**, however, the group R^3 can be selectively substituted for another group by reaction with a suitable alcohol in the presence of catalytic amounts of concentrated hydrochloric acid. This reaction allows the production of selectively esterified and selectively etherified compounds of type **5** (different groups R^3); e.g. **7**.

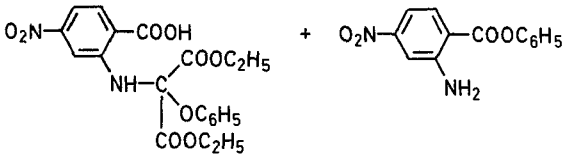
This simple, one-step preparation of compounds **5** has some limitations:

(a) For the active solvents, primary and secondary alcohols can be used while the reaction in *t*-butyl alcohol proceeds with the formation of different products which, however, when submitted to hydrolysis are transformed into 2-amino-4-nitrobenzoic acid; allowing the assumption that the same reaction type also occurs in this case.

(b) In the presence of sodium phenoxide, the compound **3a** does not form the analogues of rearrangement product **5** and, depending on reaction conditions, phenyl 2-amino-4-nitrobenzoate **(8b)** or 2-[*N*-(diethoxycarbonyl)(phenoxy)-methyl] amino-4-nitrobenzoic acid **(9)** are formed. This reaction course is probably caused by steric hindrance of phenoxy group preventing simultaneous addition of two phenoxy groups.

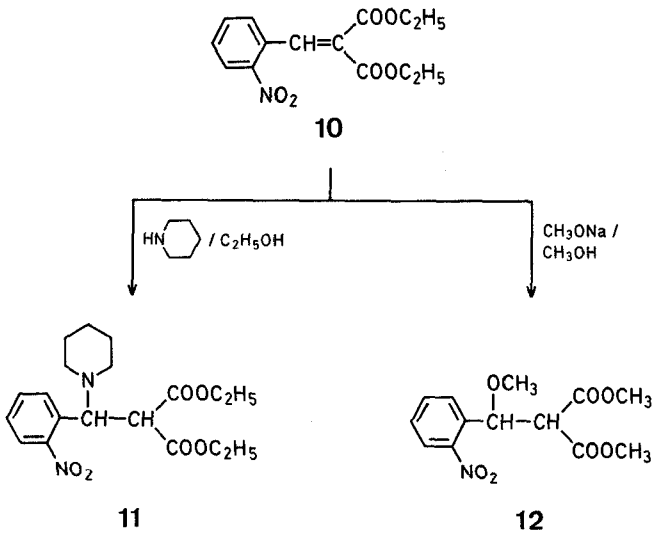


3a



9 **8b**

(c) The presence of a second nitro group in the aromatic ring is necessary since diethyl 2-nitrobenzylidenemalonate[4] and ethyl α-cyano-2-nitrocinnamate[5] undergo a normal Michael reaction with amines. Diethyl 2-nitrobenzylidenemalonate **(10)** on reaction with piperidine in ethanol yields 1-(2-nitrophenyl)-1-(1-piperidyl)-2,2-diethoxycarbonylethane **(11)**, while with sodium methoxide it forms 1-(2-nitrophenyl)-1-methoxy-2,2-dimethoxycarbonylethane **(12)**.

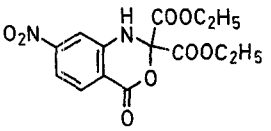


10

11 **12**

(d) The group R^2 in compound **3** should have strong electron-acceptor properties (COOR, CN) as it has been found that ethyl 2,4-dinitrocinnamate[1] and 2,4-ω-trinitrostyrene[6] do not react in this way.

Attempts to prepare compounds **5** by other methods failed; e.g. mesoxalic acid and 2-amino-4-nitrobenzoic or diethyl malonate and potassium 2-nitroso-4-nitrobenzoate reacted to give the lactone **13.**



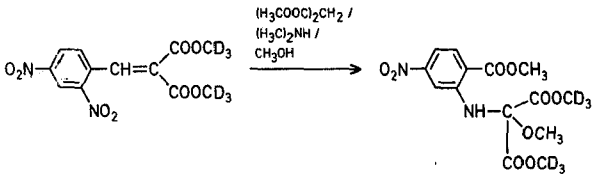
13

On reaction of ethyl 2-amino-4-nitrobenzoate with mesoxalic ester with and without an alcohol and an amine, the initial ethyl 2-amino-4-nitrobenzoate was recovered. It must be pointed out that condensation of methyl 2-nitroso-4-nitrobenzoate with diethyl malonate catalyzed by diethylamine in methanol produced **5b** in 48% yield. This condensation requires, however, harsher conditions (60 °C, 1 h), than the rearrangement, and therefore the primarily obtained compound contained the bonds formed both by condensation and by trans-esterification of the malonic ester fragment.

These results suggest, that the rearrangement is intramolecular; this assumption being additionally supported by the following experiments:

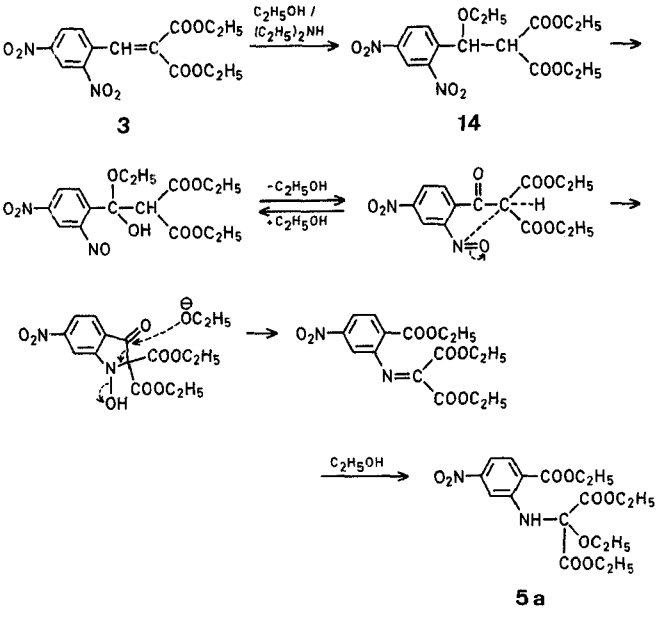
(a) Excess diethyl malonate added to a solution of **3a** in ethanol with a catalytic amount of diethylamine does not influence the rearrangement rate or yield. A similar result was obtained when excess mesoxalic ester was added.

(b) The rearrangement of dimethyl-d_6 2,4-dinitrobenzylidenemalonate **(3c)** in methanol with excess dimethyl malonate does not produce products containing an undeuterated malonic ester fragment.



3c **5i**

Considering the above, we propose the following mechanism for the rearrangement.



3 **14**

5a

Compound **14** was not isolated, however its formation was evidenced by the fact that addition of catalytic amount of diethylamine to an ethanol solution **3a** resulted in immediate disappearance of the band at 1638 cm^{-1} (C=C bond) in the Raman spectrum.

In recent years, a number of synthetic methods involving neighboring group interaction in *ortho*-substituted nitrobenzene derivatives have been reported[7,8,9]. The method described here is characterized by (a) the type of intramolecular condensation; (b) the fission of the carbon to carbon bond; and (c) the formation of the ester group in position 1.

2,4-Dinitrobenzylidenemalonates 3a–c; General Procedure:
Titanium(IV) chloride (2.2 ml, 20 mmol) in carbon tetrachloride (5 ml) is added dropwise to tetrahydrofuran (80 ml) and the mixture is cooled to 5 °C. 2,4-Dinitrobenzaldehyde (**1**; 1.96 g, 10 mmol) in tetrahydrofuran (5 ml) and the dialkyl malonate **2** (10 mmol) are added dropwise with stirring. Pyridine (3.2 ml, 40 mmol) in tetrahydrofuran (10 ml) is added dropwise over 20 min. After 24 h, water (15 ml) and ether (15 ml) are added, the organic layer is separated and the aqueous layer extracted with ether (2 × 30 ml). The combined ether solution is washed with saturated aqueous sodium chloride solution (1 × 50 ml), saturated aqueous sodium carbonate solution (2 × 50 ml), and saturated aqueous sodium chloride solution (1 × 50 ml), dried with magnesium sulfate, and concentrated. The precipitate formed on cooling is filtered and recrystallized (Table).

Compound **3d** is prepared similarly using ethyl cyanoacetate (1.13 g, 10 mmol) in benzene (5 ml) and piperidine (0.05 ml, 0.5 mmol).

1-(2,4-Dinitrophenyl)-2,2-diethoxycarbonyl-ethanol (4):
2,4-Dinitrobenzaldehyde (**1**; 1.96 g, 10 mmol) and diethyl malonate (**2**; 1.6 g, 10 mmol) are placed in benzene (5 ml) and piperidine (0.1 ml, 1 mmol) is added at room temperature. After 1 h, the precipitate is filtered and recrystallized to give **4**; yield: 3.1 g (Table).

Rearrangement of Compounds 3; General Procedure:
The 2,4-dinitrobenzylidene compound **3** (1 mmol) is dissolved in the respective alcohol (R^3OH; 4 ml) and diethylamine (0.2 ml, 2 mmol) is added dropwise at room temperature. After 24 h, the yellow crystals are separated and recrystallized from the same alcohol (Table).

Ethyl 2-[*N*-(Diethoxycarbonyl)(methoxy)-methyl]amino-4-nitrobenzoate (7):
Compound **5a** (0.21 g, 0.5 mmol) is dissolved in methanol (30 ml) and concentrated hydrochloric acid (0.3 ml) is added. The mixture is heated under reflux for 4 h, the solvent is removed under reduced pressure, and the solid residue is washed with water. Chromatography on silica gel (Merck 60 HF_{254}) eluting with 90:5:1 carbon tetrachloride/chloroform/acetone gives **8a**; yield: 0.04 g; R_f: 0.58; Ref.[11], m.p. 89 °C and **7**; yield: 0.11 g; R_f: 0.46 (Table).

2-[*N*-(Diethoxycarbonyl)(phenoxy)-methyl]amino-4-nitrobenzoic Acid (9) and Phenyl 2-Amino-4-nitrobenzoate (8b):
Compound **3a** (0.338 g, 1 mmol) is placed in a flask with warm phenol (3 ml). Sodium phenoxide [10 mg from sodium (0.43 mmol) in phenol (1 ml)] is added and the mixture is heated at 45 °C for 36 h. The resultant dark, dense oil is poured into acidified water (40 ml) and excess phenol is removed by washing with water (5 × 15 ml). The solid residue is dissolved in chloroform (10 ml) and the solution extracted with 5% sodium hydrogen carbonate solution (4 × 4 ml), followed by neutralization with dilute hydrochloric acid, and extraction with dichloromethane (3 × 3 ml) to give **9**; yield: 0.118 g (Table).

The organic chloroform layer is column chromatographed on silica gel eluting with 30:5:1 carbon tetrachloride/chloroform/acetone to give **8b**; yield: 0.062 g (Table).

1-(2-Nitrophenyl)-1-(1-piperidyl)-2,2-diethoxycarbonylethane (11):
Diethyl 2-nitrobenzylidenemalonate (**10**) is prepared from 2-nitrobenzaldehyde and diethyl malonate according to Ref.[4]; m.p. 52 °C (Ref.[4], m.p. 53 °C).

Piperidine (0.6 ml, 6 mmol) is added to a solution of **10** (0.88 g, 3 mmol) in ethanol (5 ml) and the mixture is stirred at room temperature for 15 min. After 24 h the solvent is evaporated and the residue recrystallized to give **11**; yield: 0.74 g (Table).

Table. Compounds **3**, **4**, **5**, **7**, **8**, **9**, **11**, **12**, and **13** prepared

Product No.	R^1	R^2	R^3	Yield [%][a]	m.p. [°C][b]	Molecular Formula[c]	I.R. ($CHCl_3$) ν [cm^{-1}][d]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm][e]	^{13}C-N.M.R. ($CDCl_3$) δ [ppm][f]	M.S. (75 eV) *m/e* (rel. intens. %)[g]
3a	C_2H_5	$COOC_2H_5$	—	77	54° (C_2H_5OH)	$C_{14}H_{14}N_2O_8$ (338.3)	1730 (CO)[h]	1.15 (t, 3H); 1.42 (t, 3H); 4.25 (q, 2H); 4.48 (q, 2H); 8.32 (s, 1H); 7.8–9.2 (m, 3H)	13.8, 14.1, 61.8, 62.2, 162.6, 163.7, 130.9, 136.4, 120.3, 127.6, 131.6, 138.8, 147.2, 148.1	338 (M^+, 4); 293 (31); 265 (24); 220 (57); 219 (100); 218 (89); 193 (37); 179 (70); 165 (91)
3b	CH_3	$COOCH_3$	—	81	99° (CH_3OH)	$C_{12}H_{10}N_2O_8$ (310.2)	1730 (CO)	3.67 (s, 3H); 3.93 (s, 3H); 8.25 (s, 1H); 7.7–9.2 (m, 3H)	—	—
3c	CD_3	$COOCD_3$	—	83	98° (CD_3OD)	—	1730 (CO); 2260, 1280, 2080 (CD)	8.25 (s, 1H); 7.7–9.2 (m, 3H)	—	—
3d	C_2H_5	—CN	—	80	117° (C_2H_5OH)	$C_{12}H_9N_3O_6$ (291.2)	2230 (CN); 1725 (CO)	1.45 (t, 3H); 4.45 (q, 2H); 8.60 (s, 1H); 8.1–9.2 (m, 3H)	—	—
4	—	—	—	80	97° (C_6H_6)	$C_{14}H_{16}N_2O_9$ (356.3)	3500 (OH); 1733, 1720 (CO)	1.30 (t, 6H); 4.05 (d, 1H); 4.25 (q, 4H); 4.45 (d, 1H); 6.20 (d, 1H); 8.2–9.1 (m, 3H)	13.9, 62.2, 62.5, 57.2, 67.9, 167.1, 168.1, 120.3, 127.4, 131.4, 142.8, 147.5, 148.1	356 (M^+, 0.2); 339 (1); 310 (4); 208 (12); 159 (21); 133 (58); 120 (50); 115 (100)

Table. (Continued)

Product No.	R^1	R^2	R^3	Yield [%][a]	m.p. [°C][b]	Molecular Formula[c]	I.R. ($CHCl_3$) ν [cm^{-1}][d]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm][e]	^{13}C-N.M.R. ($CDCl_3$) δ [ppm][f]	M.S. (75 eV) *m/e* (rel. intens. %)[g]
5a	C_2H_5	$COOC_2H_5$	C_2H_5	84	94° (C_2H_5OH)	$C_{18}H_{24}N_2O_9$ (412.4)	3300 (NH); 1740 (CO); 1695 (CO)	1.2–1.5 (m, 12H); 3.62 (q, 2H); 4.2–4.9 (m, 6H); 7.5–8.2 (m, 3H); 9.72 (s, 1H)[i]	13.9, 14.2, 14.9, 59.7, 61.7, 63.1, 87.7, 109.5, 111.7, 117.5, 132.8, 147.1, 151.1, 166.3, 166.7	412 (M^+, 1); 367 (8); 339 (100); 265 (89); 237 (38)
5b	C_2H_5	$COOC_2H_5$	CH_3	82	116° (CH_3OH)	$C_{16}H_{20}N_2O_9$ (384.3)	3300 (NH); 1740, 1695 (CO)	1.33 (t, 6H); 3.38 (s, 3H); 4.05 (s, 3H); 4.42 (q, 4H); 7.4–8.3 (m, 3H); 9.7 (s, 1H)	13.9, 51.2, 52.6, 63.9, 88.1, 109.3, 112.1, 117.2, 132.9, 146.9, 151.6, 166.1, 167.1	384 (M^+, 2); 311 (100); 297 (48); 207 (78)
5c	C_2H_5	$COOC_2H_5$	*n*-C_3H_7	78	47° (*n*-C_3H_7OH)	$C_{20}H_{28}N_2O_9$ (440.4)	3300 (NH); 1740, 1695 (CO)	0.9–2.0 (m, 16H); 3.30 (t, 2H); 4.38 (q t, 6H); 7.6–8.3 (m, 3H); 9.70 (s, 1H)	—	440 (M^+, 1); 381 (7); 367 (55); 325 (47); 265 (100); 193 (18); 191 (24)
5d	C_2H_5	$COOC_2H_5$	*n*-C_4H_9	61	9° (*n*-C_4H_9OH)	$C_{22}H_{32}N_2O_9$ (468.5)	3300 (NH); 1740, 1695 (CO)	0.8–2.0 (m, 20H); 3.34 (t, 2H); 4.41 (q, t, 6H); 7.6–8.3 (m, 3H); 9.70 (s, 1H)	—	468 (M^+, 0.3); 395 (29); 339 (54); 265 (100); 237 (25); 193 (19); 191 (23)
5e	C_2H_5	$COOC_2H_5$	*i*-C_3H_7	81	84° (*i*-C_3H_7OH)	$C_{20}H_{28}N_2O_9$ (440.4)	3300 (NH); 1745, 1735, 1695 (CO)[j]	1.1–1.4 (m, 18H); 4.40 (q, 4H); 5.5 (m, 2H); 7.6–8.4 (m, 3H); 9.90 (s, 1H)	—	440 (M^+, 1); 381 (3); 367 (28); 325 (79); 293 (85); 265 (100)
5f	CH_3	$COOCH_3$	CH_3	93	172° (CH_3OH)	$C_{14}H_{16}N_2O_9$ (356.3)	3300 (NH); 1740, 1695 (CO)	3.33 (s, 3H); 3.92 (s, 6H); 4.05 (s, 3H); 7.5–8.3 (m, 3H); 9.75 (s, 1H)	—	356 (M^+, 2); 325 (3); 297 (100); 265 (46); 221 (22)
5g	CH_3	$COOCH_3$	C_2H_5	85	141° (C_2H_5OH)	$C_{16}H_{20}N_2O_9$ (384.3)	3300 (NH); 1740, 1695 (CO)	1.1, 1.5 (2t, 6H); 3.40 (q, 2H); 3.85 (s, 6H); 4.40 (q, 2H); 7.5–8.3 (m, 3H); 9.75 (s, 1H)	—	384 (M^+, 2); 325 (70); 297 (16); 251 (100); 191 (33)
5h	CH_3	$COOCH_3$	*i*-C_3H_7	71	107° (*i*-C_3H_7OH)	$C_{18}H_{24}N_2O_9$ (412.4)	3300 (NH); 1740, 1695 (CO)	1.25 (d, 12H); 3.88 (s, 6H); 5.5 (m, 2H); 7.6–8.4 (m, 3H); 9.8 (s, 1H)	—	412 (M^+, 1); 353 (25); 311 (68); 269 (70); 251 (100); 191 (45)
5i	CD_3	$COOCD_3$	CH_3	92	171° (CD_3OD)	$C_{14}H_{10}D_6N_2O_9$ (362.3)	3300 (NH); 1740, 1690 (CO)	3.35 (s, 3H); 4.05 (s, 3H); 7.5–8.4 (m, 3H); 9.75 (s, 1H)	—	362 (M^+, 2); 300 (100); 268 (55); 193 (22); 191 (24)
5j	C_2H_5	CN	C_2H_5	68	124° (C_2H_5OH)	$C_{16}H_{19}N_3O_7$ (365.3)	3290 (NH); 2280 (CN); 1735, 1690 (CO)	1.2–1.6 (m, 9H); 3.50 (q, 2H); 4.40 (q, 4H); 7.6–8.4 (m, 3H); 9.7 (s, 1H)[i]	13.8, 14.2, 13.9, 60.5, 62.1, 64.8, 82.7, 109.9, 113.1, 118.5, 124.5, 132.9, 149.9, 151.5, 166.8, 167.8	365 (M^+, 3); 338 (6); 392 (68); 246 (18); 237 (28); 218 (100)
5k	CH_3	CN	CH_3	59	193° (CH_3OH)	$C_{13}H_{13}N_3O_7$ (323.3)	3290 (NH); 2280 (CN); 1735, 1690 (CO)	3.32 (s, 3H); 4.00 (s, 3H); 4.10 (s, 3H); 7.6–8.4 (m, 3H); 9.70 (s, 1H)	—	323 (M^+, 2); 296 (7); 264 (66); 232 (100)

Table. (Continued)

Product No.	R^1	R^2	R^3	Yield [%][a]	m.p. [°C][b]	Molecular Formula[c]	I.R. ($CHCl_3$) ν [cm^{-1}][d]	^{1}H-N.M.R. ($CDCl_3$) δ [ppm][e]	^{13}C-N.M.R. ($CDCl_3$) δ [ppm][f]	M.S. (75 eV) *m/e* (rel. intens. %)[g]
7	—	—	—	55	86° (hexane)	$C_{17}H_{22}N_2O_9$ (398.4)	3300 (NH); 1730, 1690 (CO)	1.30 (t, 6H); 1.45 (t, 3H); 3.35 (s, 3H); 4.40 (q, 6H); 7.6–8.4 (m, 3H); 9.80 (s, 1H)	—	398 (M^+, 6); 367 (7); 325 (100); 293 (6); 235 (16); 221 (18); 207 (58); 193 (14); 191 (11)
8a	—	—	—	38	88°	—	3510, 3390 (NH_2); 1695 (CO)	1.41 (t, 3H); 4.40 (q, 2H); 6.10 (s, 2H); 7.2–8.1 (m, 3H)	—	—
8b	—	—	—	24	132°	$C_{13}H_{10}N_2O_4$ (258.2)	3500, 3390 (NH_2); 1705 (CO)	6.20 (s, 2H); 6.8–8.4 (m, 8H)	—	258 (M^+, 20); 165 (100); 119 (35); 91 (16)
9	—	—	—	27	192° (C_6H_6/ hexane)	$C_{20}H_{20}N_2O_9$ (432.4)	3310 (NH); 3200–2800 (OH); 1730, 1675 (CO)	1.25 (t, 6H); 4.30 (q, 4H); 6.8–8.4 (m, 8H); 9.10 (s, 1H); 10.10 (s, 1H)	—	432 (M^+, 0.2); 359 (5); 313 (8); 250 (40); 205 (44); 177 (100); 164 (80)
11	—	—	—	65	93–94° (C_2H_5OH/ hexane)	$C_{19}H_{26}N_2O_6$ (378.4)	2930 (CH); 1725 (CO)	1.10 (t, 6H); 1.35 (m, 6H); 2.4 (m, 4H); 4.10 (d, 1H); 4.35 (q, 4H); 5.35 (d, 1H); 7.4–8.3 (m, 4H)	—	378 (M^+, 1); 219 (60); 84 (100)
12	—	—	—	55	76–77° (CH_3OH)	$C_{13}H_{15}NO_7$ (297.3)	1738, 1734 (CO)	3.40 (s, 3H); 3.80 (s, 3H); 3.92 (s, 3H); 4.10 (d, 1H); 5.70 (d, 1H); 7.8–8.3 (m, 4H)	—	297 (M^+, 0.1); 166 (100); 134 (43)
13	—	—	—	A: 76 B: 78	186–187° (C_6H_6 or C_2H_5OH)	$C_{14}H_{14}N_2O_8$ (338.3)	3405 (NH); 1745 (CO)	1.31 (t, 6H); 4.36 (q, 4H); 6.25 (s, 1H); 7.8–8.2 (m, 3H)	13.8, 64.2, 86.2, 111.3, 115.5, 117.1, 132.1, 143.7, 152.3, 164.2, 171.2	338 (M^+, 2); 265 (100); 237 (48); 193 (37); 191 (56); 147 (22); 145 (20)
5l	C_2H_5	$COOCH_3$	CH_3	9	155°	$C_{15}H_{18}N_2O_9$ (370.3)	3300 (NH); 1740, 1695 (CO)	1.28 (t, 3H); 3.35 (s, 3H); 3.94 (s, 3H); 4.02 (s, 3H); 4.40 (q, 2H); 7.5–8.3 (m, 3H); 9.70 (s, 1H)	—	370 (M^+, 2); 297 (100); 265 (52); 221 (15); 191 (28)

[a] Yield of recrystallized product.
[b] Not corrected.
[c] Satisfactory microanalyses obtained: C ±0.39, H ±0.23, N ±0.28; microanalyses were performed on a Perkin-Elmer 240 Elemental-Analyzer.
[d] I.R. spectra were measured with a Specord 75 IR spectrometer.
[e] ^{1}H-N.M.R. spectra were measured at 60 MHz with a Varian EM 360 A spectrometer.
[f] ^{13}C-N.M.R. spectra were measured with a Jeol FX 90 Q spectrometer used the NBD technique.
[g] Mass spectra were measured with a Jeol JMS-D-100 spectrometer.
[h] Raman ($CHCl_3$): $\nu = 1637$ cm^{-1} (C=C); (C_2H_5OH): $\nu = 1683$ cm^{-1} (C=C); Raman spectra were measured with a Raman Laser Spectrophotometer.
[i] Spectrum measured at 90 MHz with a Jeol FX 90 Q spectrometer.
[j] In KBr.

1-(2-Nitrophenyl)-1-methoxy-2,2-dimethoxycarbonylethane (12):
To a stirred solution of **10** (0.73 g, 2.5 mmol) in methanol (5 ml) a solution of sodium methoxide in methanol [sodium (34.5 mg, 1.5 mmol) in methanol (2 ml)] is added dropwise. The mixture is heated at 40 °C for 1 h and allowed to cool. The precipitate is filtered and recrystallized to give **12**; yield: 0.41 g (Table).

2,2-Diethoxycarbonyl-7-nitro-4-oxo-1,2-dihydro-4*H*-3,1-benzoxazine (13):
Method A: A solution of diethyl mesoxalate (0.348 g, 2 mmol) in benzene (5 ml) is added dropwise to a stirred suspension of 2-amino-4-nitrobenzoic acid (0.364 g, 2 mmol) in benzene (15 ml) at room temperature during 15 min. The mixture is heated under reflux for 1 h, diethyl mesoxalate (0.174 g, 1 mmol) in benzene (2 ml) and acetic acid (0.08 ml) are added, the mixture is heated under reflux for 30 min, and allowed to cool. The solvents are evaporated to leave the crude product which is recrystallized; yield: 0.515 g.

Method B: A suspension of potassium 2-nitroso-4-nitrobenzoate (0.117 g, 0.5 mmol) and diethyl malonate (0.16 g, 1 mmol) in ethanol (1 ml) and water (0.3 ml) is stirred for 1 h. About every 10 min, dilute acetic acid is added to maintain a pH value of 7. The precipitate formed is filtered and recrystallized; yield: 0.132 g (Table).

Reaction of 3a with Diethylamine/*t*-Butyl Alcohol:
Diethylamine (0.1 ml, 1 mmol) is added to a solution of **3a** (0.2 g, 0.59 mmol) in *t*-butyl alcohol (3 ml), the mixture is allowed to stand at room temperature for 48 h, and the solvent is evaporated. The crude product is dissolved in a minimum of chloroform, the solution extracted with 5% aqueous sodium hydrogen carbonate (4 × 2 ml) followed by neutralization with dilute hydrochloric acid to give *2-amino-4-nitrobenzoic acid*; yield: 81 mg (75%); m.p. 255 °C (Ref.[12], m.p. 258 °C).

Reaction of Methyl 2-Amino-4-nitrobenzoate with Diethyl Mesoxalate:
A solution of diethyl mesoxalate (0.348 g, 2 mmol) in benzene (1 ml) is added dropwise to a stirred solution of methyl 2-amino-4-nitrobenzoate (0.294 g, 1.5 mmol) in benzene (3 ml) at room temperature. The mixture is heated at 65 °C for 4 h, allowed to stand at room temperature for 20 h, and then diethyl mesoxalate (0.174 g, 1 mmol), diethylamine (0.04 ml, 0.4 mmol), and methanol (5 ml) are added. The mixture is heated under reflux for 20 min, cooled, and evaporated under reduced pressure. The residue is column chromatographed on silica gel eluting with 60:5:1 carbon tetrachloride/chloroform/acetone to give unchanged *methyl 2-amino-4-nitrobenzoate* (0.18 g) and product **5b**; yield: 57 mg (10%); m.p. 115 °C.

Reaction of Methyl 2-Nitroso-4-nitrobenzoate with Diethyl Malonate in Methanol:
Methyl 2-nitroso-4-nitrobenzoate is obtained from 2-nitroso-4-nitrobenzoic acid and dimethyl sulfate according to Ref.[10]; m.p. 137 °C (Ref.[10], m.p. 137 °C). Diethylamine (0.1 ml, 1 mmol) is added to a solution of methyl 2-nitroso-4-nitrobenzoate (0.525 g, 2.5 mmol) and diethyl malonate (0.48 g, 3 mmol) in methanol (5 ml). The mixture is heated under reflux for 1 h, allowed to cool, and the precipitate is filtered. The crude yellow crystals are purified by column chromatography on silica gel eluting with 100:5:1 carbon tetrachloride/chloroform/acetone to give **5f** (yield: 0.072 g, 8%; m.p. 172 °C), **5l** (yield: 0.08 g, Table), and **5b** (yield: 0.46 g, 48%; m.p. 115–116 °C).

Reaction of Ethyl 2,4-Dinitrocinnamate with Diethylamine in Ethanol:
Ethyl 2,4-dinitrocinnamate (0.4 g, 1.5 mol) is heated under reflux with diethylamine (0.31 ml, 3 mmol) in ethanol (5 ml) for 4 h. Alternatively, piperidine (0.15 ml, 1.5 mmol) or sodium ethoxide (from sodium (23 mg, 1 mmol) in ethanol (1 ml)) can be used. On cooling, unchanged *ethyl 2,4-dinitrocinnamate* is recovered; yield: 0.28 g (70%); m.p. 94 °C (Ref.[1], m.p. 94 °C).

Preparation of 5i from 3c and Dimethyl Malonate:
A solution of dimethyl-d_6-2,4-dinitrobenzylidenemalonate (**3c**; 0.095 g, 0.3 mmol) in methanol (2 ml) is added at room temperature to a solution of dimethyl malonate (0.21 g, 1.5 mmol) and diethylamine (0.03 ml, 0.3 mmol) in methanol (2 ml). The mixture is allowed to stand overnight and the yellow precipitate is recrystallized from hexane/benzene to give **5i**; yield: 89 mg (87%); m.p. 171–172 °C.

The research was supported by Polish Academy of Sciences, Grant No MR I 12.1.

Received: October 20, 1982
(Revised form: January 18, 1983)

[1] P. Friedländer, R. Fritsch, *Monatsh. Chem.* **23,** 534 (1902).
[2] S. Kinastowski, S. Wnuk, *Pol. J. Chem.*, in print.
[3] W. Lehnert, *Tetrahedron* **29,** 635 (1973).
[4] J. D. Loudon, J. Wellings, *J. Chem. Soc.* **1960,** 3462.
[5] K. H. Bauer, *Ber. Dtsch. Chem. Ges.* **71,** 2226 (1938).
[6] L. E. Fieser, W. H. Daudt, *J. Am. Chem. Soc.* **68,** 2248 (1946).
[7] P. N. Preston, G. Tennant, *Chem. Rev.* **72,** 627 (1972).
[8] P. N. Preston, *Chem. Rev.* **74,** 279 (1974).
[9] J. M. Bakke, *Acta Chem. Scand.* [B] **29,** 667 (1975).
[10] P. Friedländer, P. Cohn, *Monatsh. Chem.* **23,** 543 (1902).
[11] H. Seidel, J. C. Bittner, *Monatsh. Chem.* **23,** 430 (1902).
[12] E. Chapman, H. Stephen, *J. Chem. Soc.* **1925,** 1796.