The Nucleophilic Reaction of Electron-deficient Pyridone Derivatives. I. The Ring Transformation of 1-Substituted 3,5-Dinitro-2-pyridones with Sodio β-Keto Esters

Eizo MATSUMURA, Masahiro ARIGA,* and Yasuo TOHDA
Department of Chemistry, Osaka Kyoiku University, Tennoji-ku, Osaka 543
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A novel ring transformation is found in a series of reactions of 1-substituted 3,5-dinitro-2-pyridones, electron-deficient substrates, with monosodium salts of β-keto esters. A variety of 1-substituted 3,5-dinitro-2-pyridones are treated with diethyl sodio-3-oxopentanedioate and ethyl sodioacetoacetate to give, in addition to *N*-substituted nitroacetamides (**3**), 2,6-bis(ethoxycarbonyl)-4-nitrophenol (**2**), and 2-ethoxycarbonyl-4-nitrophenol (**4**) respectively. The bicyclic intermediates, 2-azabicyclo[3.3.1]nona-3,7-dienes, can be isolated on the reaction of 3,5-dinitro-1-methyl-2-pyridone at room temperature. The phenol derivatives (**2** and **4**) may consist of the reagent and a C_4–C_5–C_6 moiety of the parent pyridone, while *N*-substituted nitroacetamides, **3**, may result from the other fragment, N–C_2–C_3, of the pyridone. A probable course of the reaction, involving the step-by-step nucleophilic attack of the ambident nucleophiles, sodio β-keto esters, at the ambident electrophilic centers of 2-pyridones to form bicyclic intermediate, is proposed.

In our earlier studies[1] of the nucleophilic substitution reactions of pyridine derivatives, we showed that the reaction of 1-methyl-2-(pyridiniomethyl)pyridinium salt or its homologues with potassium hydroxide solution at a low temperature gave 1-methyl-2-pyridone or its homologues respectively.

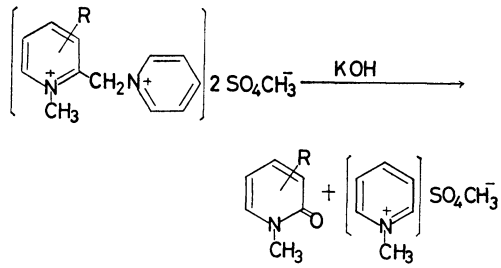


Fig. 1.

In these reactions, the bis(quaternary salts) were converted, without the heterolysis of the N–C_2 bond, to 1-methyl-2-pyridone or its homologues by the easy loss of the pyridiniomethyl group. This reaction has since offered a convenient route for the preparation of 1-methyl-2-pyridone homologues.

On the other hand, the ease of the heterolysis at the N–C_2 bond of the well-known Zincke reaction[2] of 2,4-dinitrophenylpyridinium chloride under similar basic conditions may be ascribed to the presence of a strongly electron-attractive 2,4-dinitrophenyl group on the nitrogen atom.

We have also shown[3] that the reaction of 3-bromo-4-nitropyridine *N*-oxide with one of the monosodium salts of β-keto esters (*i.e.*, ethyl sodioacetoacetate) gave the β-substituted product (*i.e.*, 3-[acetyl(ethoxycarbonyl)-methyl]-4-nitropyridine *N*-oxide), from which 2,3-disubstituted furo[3,2-*c*]pyridine *N*-oxide (*i.e.*, 3-ethoxycarbonyl-2-methylfuro[3,2-*c*]pyridine *N*-oxide) was obtained when it was warmed for a short time in an ethanol solution of sodium ethoxide.

This reaction is an example of a reaction which proceeds step-by-step between an ambident nucleophile and an ambident electrophile.

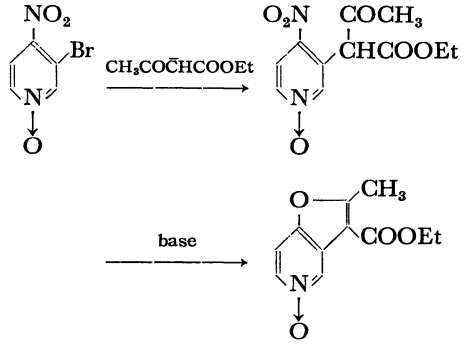
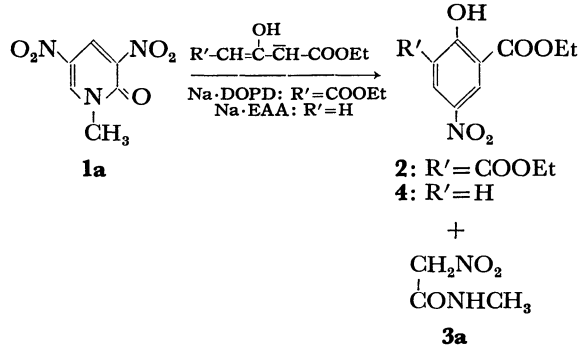


Fig. 2.

The above interesting results prompted us to expand the related reactions in this series to the nucleophilic reaction of 1,3,5-trisubstituted 2-pyridones with monosodium salts of β-keto esters and β-diketones.

Results and Discussion

The reaction of 3,5-dinitro-1-methyl-2-pyridone (**1a**) with 1.5 equimolar amounts of diethyl sodio-3-oxopentanedioate (Na·DOPD) at 50 °C in pyridine gave, after neutralization, 2,6-bis(ethoxycarbonyl)-4-nitrophenol (**2**) and *N*-methyl-α-nitroacetamide (**3a**). The same reaction of **1a** with 3 equimolar amounts of ethyl sodioacetoacetate (Na·EAA) at 70 °C gave 2-ethoxycarbonyl-4-nitrophenol (**4**) and **3a** in good yields. These



1a

2: R′=COOEt
4: R′=H
+
3a

Fig. 3.

Table 1. Reaction of 3,5-dinitro-1-methyl-2-pyridone (**1a**) with sodium salts of β-keto esters and β-diketones

Substrate	Reagent	Reaction conditions				Product (Yield/%)	
		Solvent	Mole ratio	Temp °C	Time h		
1a	Na·DOPD	Pyridine	1.5	50	5	**2** (90.4)	**3a** (28.3)
1a	Na·EAA	Pyridine	3.0	70	5	**4** (61.0)	**3a** (16.9)
1a	Na·AA	DMF	3.0	70	5	**5** (53.0)	**3a** (11.5)
1a	Na·EAP	Pyridine	3.0	110	5	**6** (42.0)	**3a** (8.3)

products were identified by their IR, NMR, and results of elemental analysis, and by a mixed-melting-point determination with authentic samples.

The reaction of **1a** with monosodium salts of β-diketones were also carried out. The reaction of **1a** with sodioacetylacetone (Na·AA) gave 2-acetyl-4-nitrophenol (**5**) and **3a**, and a similar reaction of **1a**, at a higher temperature (110 °C), with ethyl sodioacetopyruvate (Na·EAP) gave 2-ethoxyoxalyl-4-nitrophenol (**6**) and **3a**.

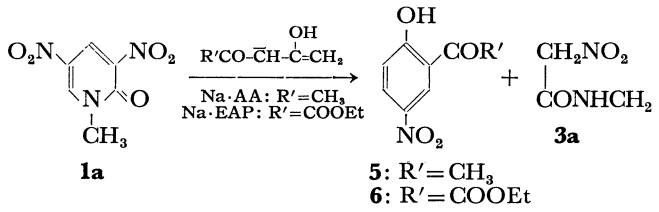


Fig. 4.

It may be considered to be characteristic of these reactions to form a phenol derivative from the active methylene compound used as the ambident nucleophile and the pyridone moiety containing C_4, C_5, and C_6. The formation of the residual moiety of the pyridone would lead to *N*-methyl-α-nitroacetamide (**3a**).

In order to prove the generality of these reactions, various kinds of 1-substituted 3,5-dinitro-2-pyridones, such as 1-(*m*-nitrobenzyl)- (**1b**), 1-(2-pyridylmethyl)- (**1c**), 1-unsubstituted- (**1d**), 1-(2,4-dinitrophenyl)- (**1e**), 1-(2-pyridyl)- (**1f**), 1-(4-methyl-2-pyridyl)- (**1g**), 1-(5-methyl-2-pyridyl)- (**1h**), 1-(6-methyl-2-pyridyl)- (**1i**), 1-hydroxy- (**1j**), 1-methoxy- (**1k**), and 1-(*p*-nitrobenzyloxy)- (**1l**), were prepared and then reacted with either Na·DOPD or Na·EAA.

The reaction of each 1-substituted 3,5-dinitro-2-pyridone with Na·DOPD gave 2,6-bis(ethoxycarbonyl)-4-nitrophenol (**2**) and the corresponding *N*-substituted nitroacetamide (**3**). With each 1-substituted 3,5-dinitro-2-pyridone and Na·EAA, on the other hand, 2-ethoxycarbonyl-4-nitrophenol (**4**) and the corresponding *N*-substituted nitroacetamide (**3**) were obtained.

The results of the above reactions and the spectral data (NMR and IR) of *N*-substituted nitroacetamides are shown in Tables 2 and 3 respectively.

In the case of the reaction of 3,5-dinitro-1-(2-pyridyl)-2-pyridone (**1f**) with Na·DOPD or Na·EAA, the same yellow compound, **7f**, was obtained, together with **3f** and either **2** or **4** respectively. The empirical formula,

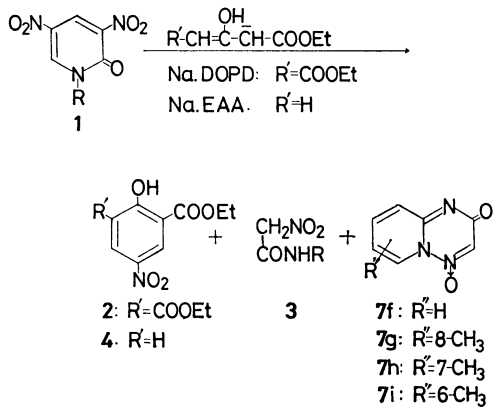


Fig. 5.

$C_7H_5N_3O_2$, of this yellow compound corresponded to the loss of one molecule of water from *N*-(2-pyridyl)-α-nitroacetamide (**3f**). The IR spectra of **7f** showed the presence of an *N*-oxide group (1205 cm^{-1}), a carbonyl group (1730 cm^{-1}), and a C=N double bond (1650 cm^{-1}), while the absorption bands due to the nitro group and the N–H bond which were confirmed in that of **3f** were absent. During the melting-point measurement, **3f** was converted to **7f** by heating it to 120 °C in a capillary. Compound **7f** was also prepared from ethyl nitroacetate and 2-aminopyridine by only heating. The catalytic reduction of **7f** on Raney Nickel in ethanol at 110 °C under 50 atm gave ethyl 2-pyridylcarbamate. From the above observations, 2-oxo-2*H*-pyrido[1,2-*b*]-[1,2,4]triazine 4-oxide was assigned to **7f**, though the C_3 proton was not observed in the NMR spectra of **7f** in trifluoroacetic acid or trifluoroacetic acid-d_1. With **1g**, **1h**, and **1i** all of which correspond to the homologues of **1f**, and Na·DOPD or Na·EAA, **7g**, **7h**, and **7i** were obtained respectively, but on the reaction of **1g**, **7g** was obtained exclusively without any isolation of *N*-(4-methyl-2-pyridyl)-α-nitroacetamide (**3g**). The ease of the cyclization of *N*-(2-pyridyl)-α-nitroacetamide to **7f** in an aqueous solution is likely to be due to the increasing acidic α-amino group which is bonded to the electron-attractive nitroacetyl and 2-pyridyl group, accordingly, the conversion of the resultant *N*-anion with a 1,6-dipole structure to the **7f** compound is favorably oriented for an intramolecular nucleophilic attack on the ω-nitronium ion with a loss of water. Under the same conditions, the fused-ring products (**7h** and **7i**) were also obtained from **3h** and **3i** respectively.

Further information was obtained under milder conditions. From the reaction of **1a** with Na·DOPD

Table 2. Reactions of **1** (**b**—**l**) with sodio β-keto esters

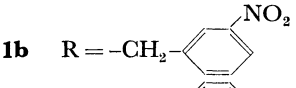
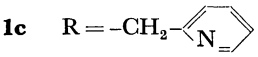
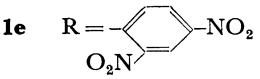
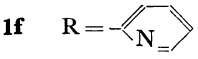
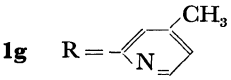
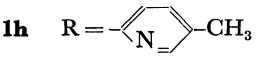
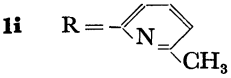
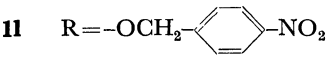
Substrate	Reaction with Na·DOPD at 50 °C Product (Yield/%)			Reaction with Na·EAA at 70 °C Product (Yield/%)		
1b R= 	**2** (95.5)	**3b** (77.9)		**4** (60.8)	**3b** (53.4)	
1c R= 	**2** (95.0)	**3c** (42.0)		**4** (51.2)	**3c** (23.2)	
1d R=-H	**2** (42.5)			**4** (21.9)		
1e R= 	**2** (57.0)	**3e** (43.0)		**4** (50.6)	**3e** (38.7)	
1f R= 	**2** (92.8)	**3f** (84.2)	**7f** (3.8)	**4** (63.5)	**3f** (52.0)	**7f** (3.5)
1g R= 	**2** (77.2)		**7g** (63.2)	**4** (52.0)		**7g** (43.2)
1h R= 	**2** (78.5)	**3h** (59.7)	**7h** (29.9)	**4** (13.4)	**3h** (18.8)	**7h** (1.4)
1i R= 	**2** (82.4)	**3i** (39.5)	**7i** (38.6)	**4** (63.4)	**3i** (17.8)	**7i** (41.5)
1j R=-OH	**2** (96.6)			**4** (83.4)		
1k R=-OCH_3	**2** (98.1)	**3k** (11.1)		**4** (86.5)	**3k** (10.5)	
1l R= 	**2** (98.0)	**3l** (38.5)		**4** (88.1)	**3l** (35.2)	

Table 3. *N*-Substituted nitroacetamides

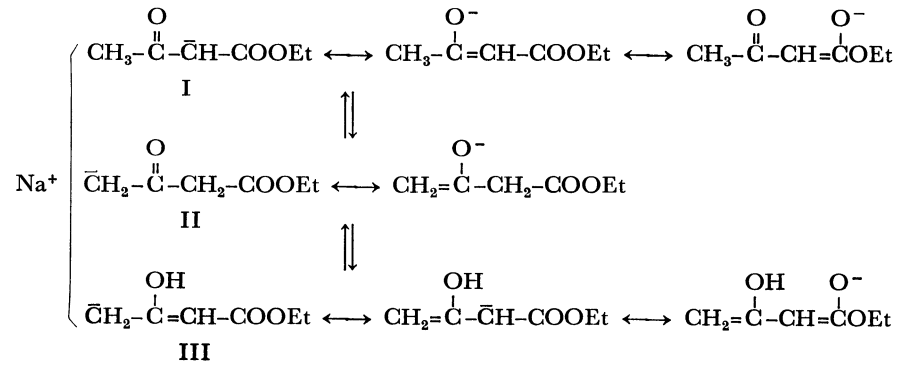
Nitroacetamide O_2NCH_2-CONHR	IR			NMR		
	N-H cm^{-1}	C=O cm^{-1}	NO_2 cm^{-1}	CH_2 δ	NH δ	Solvent
3a	3300	1670	1570, 1340	5.16	7.00	acetone-d_6
3b	3300	1660	1525, 1355	5.38	9.10	acetone-d_6
3c	3170	1690	1565, 1340	5.40	8.20	acetone-d_6
3e	3300	1690	1540, 1340	5.62	11.10	DMSO-d_6
3f	3300	1690	1540, 1340	5.62	9.85	acetone-d_6
3h	3290	1680	1545, 1340	5.52	10.98	acetone-d_6
3i	3300	1690	1530, 1350	5.62	9.95	acetone-d_6
3k	3225	1690	1550, 1330	5.15	11.70	acetone-d_6
3l	3125	1675	1575, 1345	5.18	11.80	acetone-d_6

at room temperature, a colorless crystalline product (**8a**) (mp 155.0—156.0 °C) was obtained in addition to **2** and **3a**. The empirical formula of **8a**, $C_{12}H_{15}N_3O_8$, suggests that it is an adduct of **1a** and diethyl 3-oxopentanedioate. The IR spectra of **8a** showed the presence of a nitro group (1540, 1350 cm^{-1}) and a carbonyl group (1730 cm^{-1}). The NMR spectra of **8a** showed the following: aromatic proton signals of the parent pyridone and the singlet methyl and methylene signals of the reagent disapeared, and the four aliphatic proton signals coupled with each other were observed in the range between 3.9 and 5.4 ppm. Two singlets due to the enol 7-hydroxyl group at 12.64 ppm and due to the strongly hydrogen-bonded 3-hydroxyl group at 18.82 ppm were also observed. On the treatment with only ethanolic sodium ethoxide at 70 °C or with Na·DOPD in pyridine, **8a** was easily converted to **2** and **3a**. On the basis of the above physical and chemical data, 6,8-bis(ethoxycarbonyl)-3,7-dihydroxy-2-methyl-4,9-dinitro-2-azabicyclo[3.3.1]nona-3,7-diene was assigned to **8a**. Similarly, with **1a** and Na·EAA 6-ethoxycarbonyl-3,7-dihydroxy-2-methyl-4,9-dinitro-2-azabicyclo[3.3.1]nona-3,7-diene (**9a**) was obtained.

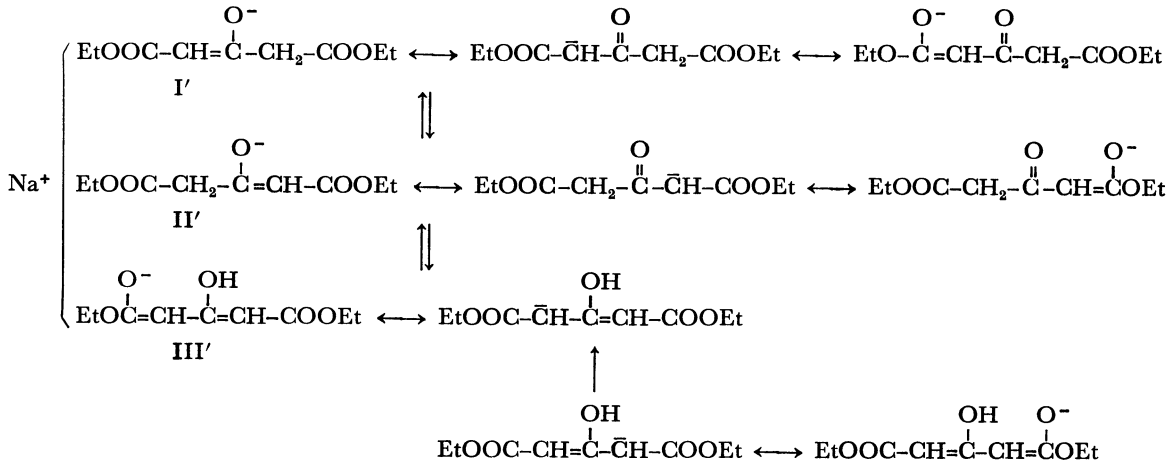
Meta-bridging bicyclic structures anoalogous to **8a** and **9a** have been described by Strauss *et al.*[4] and Momose *et al.*[5] in connection with the reaction of electron-deficient aromatics (*e.g.*, 1,3,5-trinitrobenzene or 3,5-dinitrobenzene derivatives) with active methylene compounds under basic conditions, but these addition compounds were sodium derivatives.

From the above results, the formation of the intermediate, **8a** or **9a**, may be ascribed to the reaction of an ambident electrophilic end at the 4 and 6-positions of 1,3,5-trisubstituted 2-pyridones with the ambident nucleophilic end of the enolate ion which is obtained from the sodio β-keto esters.

The treatment of ethyl acetoacetate and diethyl 3-oxopentanedioate with 1 mol of sodium ethoxide in ethanol easily gives ethyl sodioacetoacetate and diethyl 3-oxopentanedioate respectively. These ambident



Ethyl sodioacetoacetate



Diethyl sodio-3-oxopentanedioate

anions can be accounted for as shown above:

In the respective ambident tautomers, the enol types of III and III′ are softer uncleophiles than the enolate types of the others. For example, in the case of III with 3,5-dinitro-1-methyl-2-pyridone, the softer C_α-anion would be favorably attacked at the softer C_6-atom of the pyridone nucleus, and another soft C_γ-anion of the resultant adduct (**10**) at the soft C_4-atom, by the step-by-step nucleophilic and intramolecular nucleophilic mechanism leading to **8a** and **9a**.

The ring transformation of **8a** and **9a** which are obtained by the reaction at a low temperature, to **2** and **4** can be carried out by heating under basic conditions. It is proposed that the transformation of the inter-

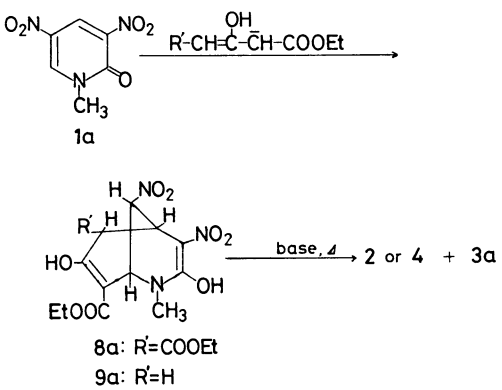
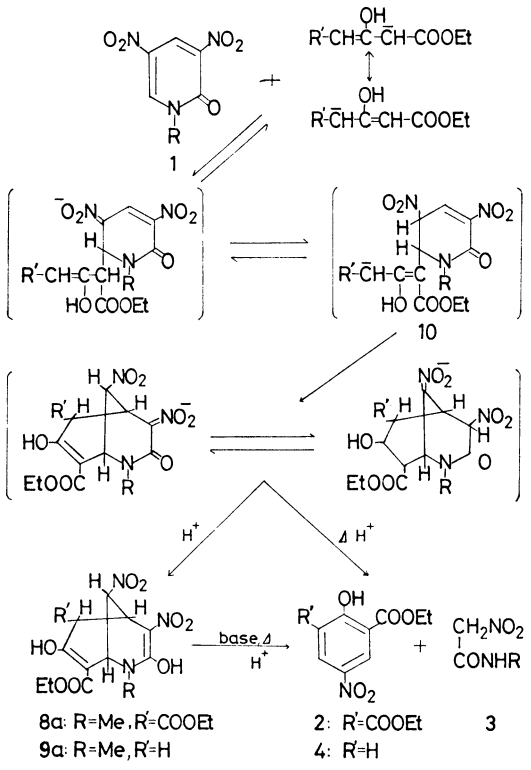


Fig. 6.



Scheme 1.

mediate **8a** or **9a** into **2** or **4** proceeds by means of the initial nucleophilic attack of the 9-carbanion on the C_5-atom, with the concomitant heterolysis of the C_4–C_5 bond, leaving the electron pair at the C_4-atom. The aromatization of the resultant homolytic moiety, which leads to **2** or **4** can occur with the heterolysis of the C_1–N bond, leaving the electron pair at the N-atom. The residual moiety of the 2-pyridone nucleus yields **3**. In the reaction at a higher temperature, the same products can be obtained without the isolation of the intermediates.

Experimental

All the melting points are uncorrected. The IR spectra were obtained on a Hitachi EPI-S2 as Nujol mulls. The NMR spectra were recorded on a Hitachi R-20B or JEOL FX-100 (unless otherwise noted the former was used), with TMS as the internal standard.

*3,5-Dinitro-1-methyl-2-pyridone (**1a**).* To 30 ml of fuming nitric acid (*d* 1.52) we added 5.0 g of 1-methyl-2-pyridone,[6] then the mixture was heated at 80 °C for 5 h. After almost all the nitric acid has been evaporated under reduced pressure, the mixture was poured onto crushed ice, and the precipitates were recrystallized from water to give 4.7 g (51.4%) of 3,5-dinitro-1-methyl-2-pyridone (**1a**); mp 178.0—179.0 °C (lit, mp 178 °C).[7] IR: 1700 cm^{-1} (C=O), 1530, 1350 (NO_2). NMR (DMSO-d_6): δ 3.65 (3H, s), 8.93 (1H, d), 9.52 (1H, d).

*3,5-Dinitro-1-(m-nitrobenzyl)-2-pyridone (**1b**).* Five grams of 1-(*m*-nitrobenzyl)-2-pyridone[8] were worked-up according to the above method to give 3.1 g (30.0%) of 3,5-dinitro-1-(*m*-nitrobenzyl)-2-pyridone (**1b**); mp 139.0—141.0 °C (recrystallized from aqueous acetic acid). IR: 1690 cm^{-1} (C=O), 1530, 1340 (NO_2). NMR (DMSO-d_6): δ 5.43 (2H, s), 7.62 (1H, d), 7.80 (1H, dt), 8.03 (1H, dt), 8.31 (1H, t), 8.96 (1H, d), 9.84 (1H, d). Found: C, 44.91; H, 2.46; N, 17.71%. Calcd for $C_{12}H_8N_4O_7$: C, 45.01; H, 2.52; N, 17.50%.

*3,5-Dinitro-1-(2-pyridylmethyl)-2-pyridone (**1c**).* Similarly, the nitration of 2-amino-1-(2-pyridylmethyl)-pyridinium chloride, which had been prepared from 2-chloromethylpyridine and 2-aminopyridine by heating, gave 3,5-dinitro-1-(2-pyridylmethyl)-2-pyridone (**1c**) in a 32.0% yield; mp 155.0 °C with dec (water). IR: 1700 cm^{-1} (C=O), 1580, 1340 (NO_2). NMR (DMSO-d_6): δ 5.52 (2H, s), 7.1—7.9 (3H, m), 8.43 (1H, dd), 8.97 (1H, d), 9.49 (1H, d). Found: C, 47.66; H, 2.61; N, 20.16%. Calcd for $C_{11}H_8N_4O_5$: C, 47.85; H, 2.92; N, 20.28%.

*3,5-Dinitro-2-pyridone (**1d**).* This pyridone was obtained by the method of Takahashi *et al.*[9]

*3,5-Dinitro-1-(2,4-dinitrophenyl)-2-pyridone (**1e**).* A mixture of a sodium salt of 2-hydroxypyridine and a 1.1 equimolar amount of 2,4-dinitrochlorobenzene in DMSO was heated at 140 °C for 5 h. The subsequent evaporation of the solvent was followed by extraction with chloroform to give 1-(2,4-dinitrophenyl)-2-pyridone (mp 163.8—164.2 °C) in a 48.0% yield. To a solution of 5.0 g of 1-(2,4-dinitrophenyl)-2-pyridone in 50 ml of fuming sulfuric acid (30% SO_3) we added 9.7 g of potassium nitrate, portion-by-portion, the mixture was then heated at 130 °C for 5 h. The reaction mixture was poured onto crushed ice, the precipitates were recrystallized from aqueous acetic acid to give 3.3 g (49.0%) of 3,5-dinitro-1-(2,4-dinitrophenyl)-2-pyridone (**1e**); mp 165.3—165.5 °C. IR: 1720 cm^{-1} (C=O), 1530, 1350 (NO_2). NMR (DMSO-d_6): δ 7.92 (1H, d), 8.07 (1H, dd), 8.11 (1H, d), 9.18 (1H, d), 9.68 (1H, d). Found: C, 37.84; H, 1.36; N, 20.04%. Calcd for $C_{11}H_5N_5O_9$: C, 37.60; H, 1.44, N, 19.95%.

*3,5-Dinitro-1-(2-pyridyl)-2-pyridone (**1f**).* Three grams of 1-(2-pyridyl)-2-pyridone[10] were treated according to the above method to give 3.05 g (66.7%) of 3,5-dinitro-1-(2-pyridyl)-2-pyridone (**1f**); mp 179.5—180.5 °C (aqueous acetic acid). IR: 1710 cm^{-1} (C=O), 1540, 1350 (NO_2). NMR (DMSO-d_6): δ 7.4—8.1 (3H, m), 8.60 (1H, dd), 9.02 (1H, d), 9.42 (1H, d). Found: C, 45.81; H, 2.31; N, 21.37%. Calcd for $C_{10}H_6N_4O_5$: C, 45.76; H, 2.16; N, 21.67%.

*3,5-Dinitro-1-(4-methyl-2-pyridyl)-2-pyridone (**1g**).* Similarly, the nitration of 1-(4-methyl-2-pyridyl)-2-pyridone[10] gave 3,5-dinitro-1-(4-methyl-2-pyridyl)-2-pyridone (**1g**) in a 63.8% yield; mp 164.0—165.0 °C (aqueous acetic acid). IR: 1720 cm^{-1} (C=O), 1530, 1355 (NO_2). NMR (DMSO-d_6): δ 2.43 (3H, s), 7.41 (1H, dd), 7.30 (1H, d), 8.44 (1H, dd), 9.03 (1H, d), 9.39 (1H, d). Found: C, 48.08; H, 2.73; N, 20.29%. Calcd for $C_{11}H_8N_4O_5$: C, 47.83; H, 2.92; N, 20.29%.

*3,5-Dinitro-1-(5-methyl-2-pyridyl)-2-pyridone (**1h**).* The similar nitration of 1-(5-methyl-2-pyridyl)-2-pyridone[10] gave 3,5-dinitro-1-(5-methyl-2-pyridyl)-2-pyridone (**1h**) in a 53.9% yield; mp 174.0—175.0 °C (aqueous acetic acid). IR: 1720 cm^{-1} (C=O), 1535, 1330 (NO_2). NMR (DMSO-d_6): δ 2.40 (3H, s), 7.8 (2H, m), 8.5 (1H, m), 9.05 (1H, d), 9.40 (1H, d). Found: C, 47.64; H, 2.69; N, 20.01%. Calcd for $C_{11}H_8N_4O_5$: C, 47.83; H, 2.93; N, 20.29%.

*3,5-Dinitro-1-(6-methyl-2-pyridyl)-2-pyridone (**1i**).* Similarly, 3,5-dinitro-1-(6-methyl-2-pyridyl)-2-pyridone (**1i**) was obtained from 1-(6-methyl-2-pyridyl)-2-pyridone[10] in a 58.8% yield; mp 175.5—176.5 °C (aqueous acetic acid). IR: 1710 cm^{-1} (C=O), 1530, 1340 (NO_2). NMR (DMSO-d_6): δ 2.67 (3H, s), 7.4 (1H, m), 7.7 (1H, m), 8.3 (1H, m), 9.02 (1H, d), 9.48 (1H, d). Found: C, 47.96; H, 2.80; N, 20.38%. Calcd for $C_{11}H_8N_4O_5$: C, 47.83; H, 2.93; N, 20.29%.

*3,5-Dinitro-1-hydroxy-2-pyridone (**1j**).* The pyridone was obtained according to the method in the literature[11] in an 80.0% yield; mp 190.0—191.0 °C.

*3,5-Dinitro-1-methoxy-2-pyridone (**1k**).* A mixture of 7.0 g of 1-methoxy-2-pyridone[12] and 70 ml of fuming nitric acid (*d* 1.52) was heated at 80 °C for 10 h. The cold reaction mixture was then poured onto crushed ice, the precipitates were collected by filtration, the filtrate was concentrated, and diluted with water, and the second crop was obtained combined with the above precipitates, and crystallized from water to give 6.5 g (54.0%) of 3,5-dinitro-1-methoxy-2-pyridone (**1k**); mp 158.0—159.0 °C. IR: 1740 cm^{-1} (C=O), 1560, 1330 (NO_2). NMR (DMSO-d_6): δ 3.25 (3H, s), 8.95 (1H, d), 9.82 (1H, d). Found: C, 33.57; H, 2.50; N, 19.50%. Calcd for $C_6H_5N_3O_6$: C, 33.50; H, 2.34; N, 19.54%.

*3,5-Dinitro-1-(p-nitrobenzyloxy)-2-pyridone (**1l**).* 1-(*p*-Nitrobenzyloxy)-2-pyridone[12] was nitrated according to the preceding method to give 3,5-dinitro-1-(*p*-nitrobenzyloxy)-2-pyridone (**11**) in a 70.0% yield; mp 192.0—193.0 °C (water). IR: 1730 cm^{-1} (C=O), 1535, 1330 (NO_2). NMR (DMSO-d_6): δ 5.45 (2H, s), 7.85 (2H, d), 8.25 (2H, d), 9.02 (1H, d), 10.00 (1H, d). Found: C, 42.92; H, 2.28; N, 16.38%. Calcd for $C_{12}H_8N_4O_8$: C, 42.86; H, 2.40; N, 16.67%.

*General Procedure of the Reaction of Pyridones (**1**) with Sodium Salts.* To a solution of pyridone (**1**) in pyridine we added a solution of sodium salt in pyridine with cooling, then the mixture was heated at the required temperature for 5—10 h. The solvent was evaporated under reduced pressure, and the residue was neutralized to pH 3—4 with dil. Hydrochloric acid and then extracted with chloroform. After the extract has been dried over anhydrous sodium sulfate, the chloroform was distilled off, and the residual syrup was column-chromatographed on silica gel (Wakogel C-300). From the benzene elute, phenol derivatives (**2**, **4**, **5**, and **6**)

were obtained, and from the diethyl ether elute, *N*-substituted nitroacetamide (**3**).

*Reaction of 3,5-Dinitro-1-methyl-2-pyridone (**1a**) with Diethyl Sodio-3-oxopentanedioate.* To a solution of 1.0 g of 3,5-dintro-1-methyl-2-pyridone (**1a**) in 100 ml of pyridine we added diethyl sodio-3-oxopentanedioate, prepared from 0.17 g of sodium and 1.7 g of diethyl 3-oxopentanedioate in absolute ethanol, in pyridine with cooling. When the mixture was heated at 50 °C for 5 h and then worked-up according to the general procedure, 1.3 g of (90.4%) of 2,6-bis(ethoxycarbonyl)-4-nitrophenol (**2**)[13] was obtained from the benzene elute and 0.17 g (28.3%) of *N*-methyl-α-nitroacetamide (**3a**),[14] from the diethyl ether elute.

2,6-Bis(ethoxycarbonyl)-4-nitrophenol (**2**); colorless needles (petroleum benzine); mp 58.0—59.0 °C. IR: 3100 cm^{-1} (O–H), 1720 (C=O), 1540, 1340 (NO_2). NMR ($CDCl_3$): δ 1.42 (6H, t), 4.45 (4H, q), 8.81 (2H, s), 12.42 (1H, s). Found: C, 50.94; H, 4.64; N, 4.81%. Calcd for $C_{12}H_{15}NO_7$: C, 50.84; H, 4.63; N, 4.95%.

N-Methyl-α-nitroacetamide (**3a**); colorless needles (diisopropyl ether); mp 75.0—76.0 °C. IR: 3300 cm^{-1} (N–H), 1670 (C=O), 1570, 1340 (NO_2). NMR (acetone-d_6): δ 2.78 (3H, d), 5.16 (2H, s), 7.00 (1H, d). Found: C, 30.32; H, 5.09; N, 23.70%. Calcd for $C_3H_6N_2O_3$: C, 30.51; H, 5.08; N, 23.73%.

*2-Ethoxycarbonyl-4-nitrophenol (**4**).* The treatment of 1.0 g of 3,5-dinitro-1-methyl-2-pyridone (**1a**) with ethyl sodioacetoacetate, prepared from 0.3 g of sodium and 2.2 g of ethyl acetoacetate, at 70 °C for 5 h gave 0.65 g (60.8%) of 2-ethoxycarbonyl-4-nitrophenol (**4**)[15] and 0.05 g (16.9%) of **3a**.

2-Ethoxycarbonyl-4-nitrophenol (**4**); colorless plates (petroleum benzine); mp 97.5—98.0 °C. IR: 3420 cm^{-1} (O–H), 1680 (C=O), 1524, 1335 (NO_2). NMR ($CDCl_3$): δ 1.45 (3H, t), 4.45 (2H, q), 7.03 (1H, d), 8.03 (1H, dd), 8.67 (1H, d), 11.35 (1H, s). Found: C, 51.46; H, 4.24; N, 6.45%. Calcd for $C_9H_9NO_5$: C, 51.19; H, 4.30; N, 6.63%.

*2-Acetyl-4-nitrophenol (**5**).* Colorless needles (petroleum benzine); mp 101.0—102.0 °C (lit, mp 101—102 °C).[16] IR: 3365 cm^{-1} (O–H), 1650 (C=O), 1520, 1350 (NO_2). NMR ($CDCl_3$): δ 2.71 (3H, s), 7.05 (1H, d), 8.26 (1H, dd), 8.62 (1H, d), 12.76 (1H, s). Found: C, 52.98; H, 3.77; N, 7.45%. Calcd for $C_8H_7NO_4$: C, 53.05; H, 3.90; N, 7.73%.

*2-Ethoxyoxalyl-4-nitrophenol (**6**).* Colorless needles (petroleum benzine); mp 57.5—58.5 °C. IR: 3360 cm^{-1} (O–H), 1730 (C=O), 1690 (C=O), 1530, 1340 (NO_2). NMR ($CDCl_3$): δ 1.45 (3H, t), 4.51 (2H, q), 7.11 (1H, d), 8.38 (1H, dd), 8.76 (1H, d), 11.73 (1H, s). Found: C, 50.35; H, 3.66; N, 5.57%. Calcd for $C_{10}H_9NO_6$: C, 50.21; H, 3.77; N, 5.86%.

N-*(m-Nitrobenzyl)-α-nitrocaetamide (**3b**).* Colorless needles (benzene); mp 152.0—153.0 °C. NMR (acetone-d_6): δ 4.47 (2H, d), 5.38 (2H, s), 7.55—8.15 (4H, m), 9.10 (1H, br). Found: C, 45.02; H, 3.53; N, 17.33%. Calcd for $C_9H_9N_3O_5$: C, 45.19; H, 3.79; N, 17.57%.

N-*(2-Pyridylmethyl)-α-nitroacetamide (**3c**).* Colorless needles (diisopropyl ether); mp 83.0—84.0 °C. NMR (acetone-d_6): δ 4.55 (2H, d), 5.40 (2H, s), 7.0—7.9 (3H, m), 8.20 (1H, br), 8.44 (1H, d). Found: C, 49.55; H, 4.29; N, 21.62%. Calcd for $C_8H_9N_3O_3$: C, 49.25; H, 4.65; N, 21.53%.

N-*(2,4-Dinitrophenyl)-α-nitroacetamide (**3e**).* Pale yellow needles (benzene); mp 120.4—121.1 °C. NMR (DMSO-d_6): δ 5.62 (2H, s), 8.5 (2H, m), 8.9 (1H, m), 11.10 (1H, br). Found: C, 35.53; H, 2.08; N, 20.54%. Calcd for $C_8H_6N_4O_7$: C, 35.56; H, 2.24; N, 20.76%.

N-*(2-Pyridyl)-α-nitroacetamide (**3f**).* Colorless needles; dec 120 °C. NMR (acetone-d_6): δ 5.62 (2H, s), 7.1—8.2 (4H, m), 9.85 (1H, br). Found: C, 46.63; H, 3.67; N, 23.26%. Calcd for $C_7H_7N_3O_3$: C, 46.41; H, 3.87; N, 23.20%.

*2-Oxo-2H-pyrido[1,2-b][1,2,4]triazine 4-Oxide (**7f**).* After *N*-(2-pyridyl)-α-nitroacetamide (**3f**) had been obtained, the column was washed with acetone and ethanol to give 0.21—0.24 g (3.5—3.8%) of 2-oxo-2*H*-pyrido[1,2-*b*][1,2,4]-triazine 4-oxide (**7f**); yellow needles (water); dec 210 °C. NMR (CF_3COOD): δ 7.5—7.9 (2H, m), 8.52 (1H, dt), 9.65 (1H, dd). Found: C, 51.35; H, 2.97; N, 25.89%. Calcd for $C_7H_5N_3O_2$: C, 51.54; H, 3.09; N, 25.76%.

*8-Methyl-2-oxo-2H-pyrido[1,2-b][1,2,4]triazine 4-Oxide (**7g**).* Yellow needles (water); dec 210 °C. IR: 1730 cm^{-1} (C=O), 1635 (C=N), 1210 (N→O). NMR (CF_3COOD): δ 3.58 (3H, s), 7.70 (1H, d), 8.35 (1H, dd), 9.38 (1H, d). Found: C, 54.10; H, 3.73; N, 23.60%. Calcd for $C_8H_7N_3O_2$: C, 54.23; H, 3.98; N, 23.72%.

N-*(5-Methyl-2-pyridyl)-α-nitroacetamide (**3h**).* Colorless needles; dec 120 °C. NMR (acetone-d_6): δ 2.43 (3H, s), 5.52 (2H, s), 7.56 (1H, dd), 7.87 (1H, d), 8.11 (1H, s), 10.98 (1H, s). Found: C, 49.38; H, 4.71; N, 21.50%. Calcd for $C_8H_9N_3O_3$: C, 49.23; H, 4.65; N, 21.53%.

*7-Methyl-2-oxo-2H-pyrido[1,2-b][1,2,4]triazine 4-Oxide (**7h**).* Yellow needles (water); dec 248 °C. IR: 1735 cm^{-1} (C=O), 1645 (C=N), 1210 (N→O). NMR (CF_3COOD): δ 2.50 (3H, s), 7.70 (1H, d), 8.37 (1H, dd), 9.37 (1H, d). Found: C, 54.36; H, 3.82; N, 23.68%. Calcd for $C_8H_7N_3O_2$: C, 54.23; H, 3.98; N, 23.72%.

N-*(6-Methyl-2-pyridyl)-α-nitroacetamide (**3i**).* Colorless needles; dec 120 °C. NMR (acetone-d_6): δ 2.36 (3H, s), 5.62 (2H, s), 6.96 (1H, dd), 7.61 (1H, dd), 7.87 (1H, dd), 9.95 (1H, s). Found: C, 49.11; H, 4.55; N, 21.73%. Calcd for $C_8H_7N_3O_3$: C, 49.23; H, 4.65; N, 21.53%.

*6-Methyl-2-oxo-2H-pyrido[1,2-b][1,2,4]triazine 4-Oxide (**7i**).* Yellow needles (water); dec 182 °C. IR: 1730 cm^{-1} (C=O), 1640 (C=N), 1210 (N→O). NMR (CF_3COOD): δ 2.54 (3H, s), 6.5—6.9 (2H, m), 7.5—7.8 (1H, m). Found: C, 54.48; H, 3.81; N, 23.61%. Calcd for $C_8H_7N_3O_2$: 54.23; H, 3.98; N, 23.72%.

*2-Oxo-2H-pyrido[1,2-b][1,2,4]triazine 4-Oxide (**7f**) from N-(2-Pyridyl)-α-nitroacetamide (**3f**).* A mixture of 0.5 g of *N*-(2-pyridyl)-α-nitroacetamide (**3f**) in 10 ml of water was refluxed for 30 min. The mixture was then cooled and the precipitates were collected by filtration to give 0.44 g (98.0%) of 2-oxo-2*H*-pyrido[1,2-*b*][1,2,4]triazine 4-oxide (**7f**). Similarly, **7h** and **7i** were obtained quantitatively from **3h** and **3i** respectively.

*2-Oxo-2H-pyrido[1,2-b][1,2,4]tiazine 4-Oxide (**7f**) (Alternative Method).* A mixture of 2.0 g of 2-aminopyridine and 2.0 g of ethyl nitroacetate[17] was heated slowly then kept at 90 °C for 1 h. When to the reaction mixture we then added a small amount of ethanol, 2.1 g (85.5%) of 2-oxo-2*H*-pyrido[1,2-*b*][1,2,4]triazine 4-oxide (**7f**) were obtained.

*Catalytic Hydrogenation of 2-Oxo-2H-pyrido[1,2-b][1,2,4]-triazine 4-Oxide (**7f**).* A mixture of 0.5 g of 2-oxo-2*H*-pyrido[1,2-*b*][1,2,4]triazine 4-oxide (**7f**), 0.1 g of Raney Nickel, and 50 ml of ethanol in a 100 ml autoclave was heated at 100 °C under 100 atm of hydrogen gas for 5 h. After filtration, the ethanol was distilled off, and the residual syrup was column-chromatographed on silica gel; 0.3 g of ethyl 2-pyridylcarbamate[18] was obtained from the benzene elute, and 0.05 g of 2-aminopyridine, from the diethyl ether elute.

*Reaction of 3,5-Dinitro-1-methyl-2-pyridone (**1a**) with Diethyl Sodio-3-oxopentanedioate at a Low Temperature.* One gram of 3,5-dinitro-1-methyl-2-pyridone (**1a**) was worked-up according to the general procedure at room temperature with diethyl sodio-3-oxopentanedioate, and then before column-

chromatography, diethyl ether was added to the residual syrup. Crystalline precipitates were collected by filtration to give 1.3 g of **8a**, and the filtrate was column-chromatographed with benzene. From the benzene elute 0.13 g of **2**, and from the chloroform elute, and additional 0.3 g of **8a** were obtained.

6,8-Bis(ethoxycarbonyl)-3,7-dihydroxy-2-methyl-4,9-dinitro-2-azabicyclo[3.3.1]nona-3,7-diene (**8a**); colorless plates; mp 155.0—156.0 °C (ethanol). IR: 1740 cm^{-1} (C=O), 1730 (C=O), 1560, 1335 (NO_2). NMR (JEOL FX-100)($CDCl_3$): δ 1.35 (3H, t), 1.42 (3H, t), 3.20 (3H, s), 3.95 (1H, d, J= 2 Hz, H-6), 4.29 (2H, q), 4.40 (2H, q), 4.42 (1H, ddd, J=2, 3, and 4 Hz, H-5), 5.15 (1H, dd, J=4 and 3 Hz, H-1), 5.42 (1H, dd, J=4 and 4 Hz, H-9), 12.64 (1H, s), 18.82 (1H, s). Found: C, 45.31; H, 4.71; N, 10.53%. Calcd for $C_{15}H_{19}N_3O_{10}$: C, 45.26; H, 4.77; N, 10.42%.

*Reaction of 3,5-Dinitro-1-methyl-2-pyridone (**1a**) with Ethyl Sodioacetoacetate at a Low Temperature.* Similarly, the reaction of 1.0 g of 3,5-dinitro-1-methyl-2-pyridone (**1a**) with 3 equimolar amounts of ethyl sodioacetoacetate gave 0.1 g of **4**, 0.05 g of **3a**, and 0.9 g of 8-ethoxycarbonyl-3,7-dihydroxy-2-methyl-4,9-dinitro-2-azabicyclo[3.3.1]nona-3,7-diene (**9a**); colorless needles (ethanol); mp 190.0—191.0 °C. IR: 1730 cm^{-1} (C=O), 1550, 1340 (NO_2). NMR (JEOL FX-100) ($CDCl_3$): δ 1.41 (3H, t), 2.84 (1H, d, J=4 Hz, H-6), 2.99 (1H, d, J=2 Hz, H-6), 3.20 (3H, s), 4.30 (1H, ddt, J=3, 4, and 2 Hz, H-5), 4.37 (2H, q), 4.71 (1H, dd, J=3 and 2 Hz, H-1), 5.30 (1H, t, J=3 Hz, H-9), 12.59 (1H, s), 18.83 (1H, s). Found: C, 43.48; H, 4.31; N, 12.76%. Calcd for $C_{12}H_{15}N_3O_8$: C, 43.79; H, 4.56; N, 12.76%.

*Treatment of 6,8-Bis(ethoxycarbonyl)-3,7-dihydroxy-2-methyl-4,9-dinitro-2-azabicyclo[3.3.1]nona-3,7-diene (**8a**) with Sodium Ethoxide.* A solution of 0.5 g of **8a** and 0.4 g of sodium ethoxide in 50 ml of ethanol was refluxed for 2 h. The solvent was then distilled off, and the residue was neutralized to pH 3.5 with dil. hydrochloric acid and extracted with chloroform. After the extract had then been dried over anhydrous sodium sulfate, the chloroform was evaporated to dryness and the residual syrup was column-chromatographed on silica gel. From the benzene elute 0.1 g of **2**, and from the diethyl ether elute, 0.06 g of **3a** were obtained.

*Treatment of 6,8-Bis(ethoxycarbonyl)-3,7-dihydroxy-2-methyl-4,9-dinitro-2-azabicyclo[3.3.1]nona-3,7-diene (**8a**) with Diethyl Sodio-3-oxopentanedioate.* A mixture of 0.5 g of **8a** and diethyl sodio-3-oxopentanedioate, prepared from 0.03 g of sodium and 0.3 g of diethyl 3-oxopentanedioate, in pyridine was heated at 70 °C for 2 h. The reaction mixture was then worked-up according to the usual procedure to give 0.20 g of **2** and 0.06 g of **3a**.

References

1) E. Matsumura, F. Ishibashi, and T. Nashima, *Bull. Chem. Soc. Jpn.*, **43**, 3540 (1970).
2) T. Zinncke, *Ann.*, **330**, 367 (1904).
3) E. Matsumura and M. Ariga, *Bull. Chem. Soc. Jpn.*, **46**, 3144 (1973); *ibid.*, **50**, 237 (1977).
4) M. I. Foreman, R. Foster, and M. J. Strauss, *J. Chem. Soc., C*, **1969**, 2112; M. J. Strauss, T. Jensen, H. Schran, and K. O'Conner, *J. Org. Chem.*, **35**, 383 (1970); M. J. Strauss, *Acc. Chem. Res.*, **7**, 181 (1974); M. J. Strauss, *Chem. Rev.*, **70**, 667 (1970).
5) K. Kohashi, Y. Ohkura, and T. Momose, *Chem. Pharm. Bull. (Tokyo)*, **18**, 2157 (1970); *ibid.*, **19**, 213, 2065 (1971); *ibid.*, **21**, 118 (1973).
6) E. A. Prill and S. M. McElvain, *Org. Synth.*, Coll. Vol. II, 419 (1951).
7) A. Raczka, A. Swirska, and H. Bojarska Dahlig, *Acta Pol. Pharm.*, **20**, 155 (1063); *cf. Chem. Abstr.*, **62**, 442 (1965).
8) A. H. Barrie, G. T. Newbold, and F. S. Spring, *J. Chem. Soc.*, **1951**, 2590.
9) T. Takahashi and F. Yoneda, *Chem. Pharm. Bull. (Tokyo)*, **6**, 442 (1958).
10) F. Ramirez and P. W. von Ostwalden, *J. Am. Chem. Soc.*, **81**, 156 (1959).
11) M. von Ammers and H. J. den Hertog, *Recl. Trav. Chim. Pays-Bas*, **75**, 1261 (1956).
12) F. T. Dinan and H. Tieckelman, *J. Org. Chem.*, **29**, 1650 (1954).
13) The authentic sample was prepared by the usual esterification from 2-hydroxy-5-nitroisophthalic acid; W. S. Benica and O. Gisvold, *J. Am. Pharm. Assoc.*, **34**, 42 (1945).
14) The authentic methylammonium salt of *N*-methyl-α-nitroacetamide was obtained by the method of F. Ratz, *Monatsh. Chem.*, **26**, 1487 (1905).
15) The authentic sample was obtained by the usual method from commercial 4-nitrosalicylic acid.
16) C. T. Chang, F. C. Chen, T. S. Chen, K. K. Hsu, T. Ueng, and M. Hung, *J. Chem. Soc.*, **1961**, 3414.
17) V. W. Rodinov, I. V. Machinskaya, and V. W. Belikov, *Zh. Obshch. Khim.*, **18**, 917 (1948); *cf. Chem. Abstr.*, **43**, 127 (1949).
18) A. R. Katritzky, *J. Chem. Soc.*, **1956**, 2063.