Nucleophilic Reaction upon Electron-deficient Pyridone Derivatives. IV. Ring Transformation of 1-Substituted 3,5-Dinitro-2-pyridones with Ketones in the Presence of Amines

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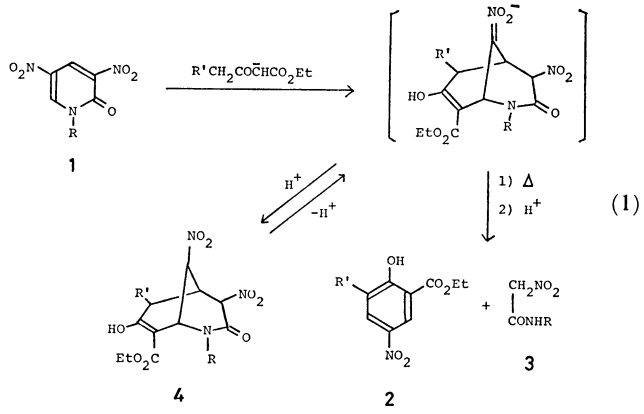
Ring transformation of 1-substituted 3,5-dinitro-2-pyridones with 1,3-disubstituted acetones in the presence of secondary or primary amines gave *p*-nitroaniline derivatives and *N*-substituted 2-nitroacetamide. Two types of enamine intermediates, 2-azabicyclo[3.3.1]nonene derivatives and *N*-substituted 2-(5-amino-2-nitro-2,4-cyclohexadienyl)-2-nitroacetamides were isolated and characterized. The course of the base-catalyzed reaction is interpreted.

Recently we reported the ring transformation of 1-substituted 3,5-dinitro-2-pyridones (**1**) into *p*-nitrophenol derivatives (**2**) and 2-nitroacetamide derivatives (**3**) by treatment with monosodium salts of β-keto esters. In the case of the reaction of 3,5-dinitro-1-(2-pyridyl)-2-pyridone (**1b**), 2-oxo-2*H*-pyrido[1,2-*b*][1,2,4]triazine 4-oxide (**3b**) was isolated as the dehydration product of *N*-(2-pyridyl)-2-nitroacetamide (**3**, R=2-pyridyl). The course of these reactions was elucidated by the isolation of bicyclo intermediates (**4**) (Eq. 1).[1] The similar ring transformations of 1,3,5-

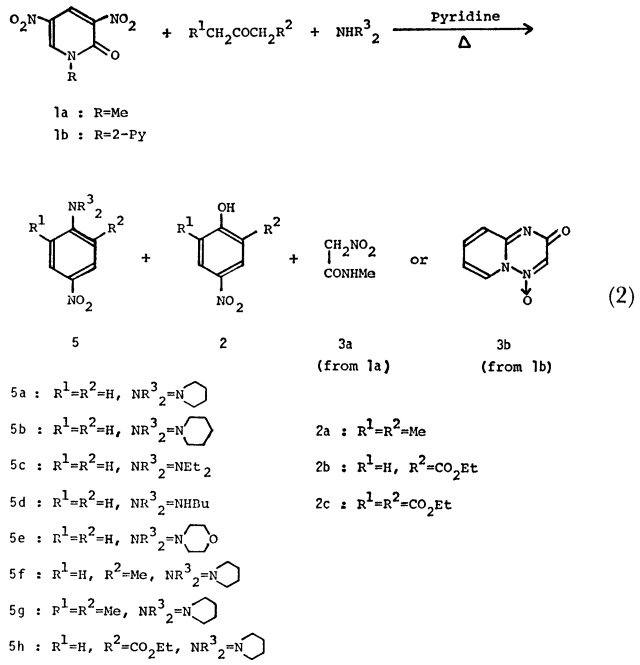


(1)

triazine[2,3] and 5-substituted uracils[4] into other six-membered aromatic systems have been studied by using sodium salts of β-keto esters or other 1,3-ambident nucleophiles. However these reactions were postulated to take place *via* open-chain intermediates rather than via such bicyclo intermediates. Another example of a similar ring transformation has been reported for 1,3,5-trinitrobenzene, which reacts with acetone and diethylamine to form *N*,*N*-diethyl-*p*-nitroaniline.[5] In this case, Strauss suggested the presence of a bicyclo[3.3.1]nonane derivative.[6] He also showed the generation of such meta-bridged compounds by the reaction of 1,3,5-trinitrobenzene with various 1,3-ambident nucleophiles.[7] In this paper, we wish to report on the reactions of 1-substituted 3,5-dinitro-2-pyridones (**1**) with 1,3-disubstituted acetones in the presence of secondary or primary amines.

Results and Discussion

Treatment of *N*-substituted 3,5-dinitro-2-pyridones (**1a**: R=Me, **1b**: R=2-pyridyl) with ketones, $R^1CH_2COCH_2R^2$ (R^1=R^2=H; R^1=H, R^2=Me; R^1=R^2=Me; R^1=H, R^2=CO_2Et; R^1=R^2=CO_2Et), in the presence of secondary or primary amines in pyridine at 80 °C for 5 h gave *p*-nitroaniline derivatives (**5a**—**h**) or *p*-nitrophenol derivatives (**2a**—**c**). The results are summarized in Eq. 2 and Table 1. Under



(2)

the reduced amount of pyrrolidine, *N*-methyl-2-nitroacetamide (**3a**) was obtained as the residual moiety of the substrate, **1a**, in poor yield (Table 1, run 6′). This fact suggests that excess of the amines in the reaction mixtures may decompose the acetamide produced (**3a**) under such conditions. In the case of the reaction of **1b**, 2-oxo-2*H*-pyrido[1,2-*b*][1,2,4]triazine 4-oxide (**3b**)[1] was isolated as the dehydration product of *N*-(2-pyridyl)-2-nitroacetamide (**3**, R=2-pyridyl).

In the presence of pyrrolidine, ketones such as acetone, 2-butanone, or 3-pentanone as well as ethyl acetoacetate (EAA) gave the corresponding *p*-nitroaniline derivatives (**5**) in good yields. The experimental data for a number of the ring transformations make it clear that the yields of **5** depend not only on the bulkiness of the ketones but also on the basicity

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Table 1. Reaction of 1-substituted 3,5-dinitro-2-pyridones (**1**) with ketones and amines

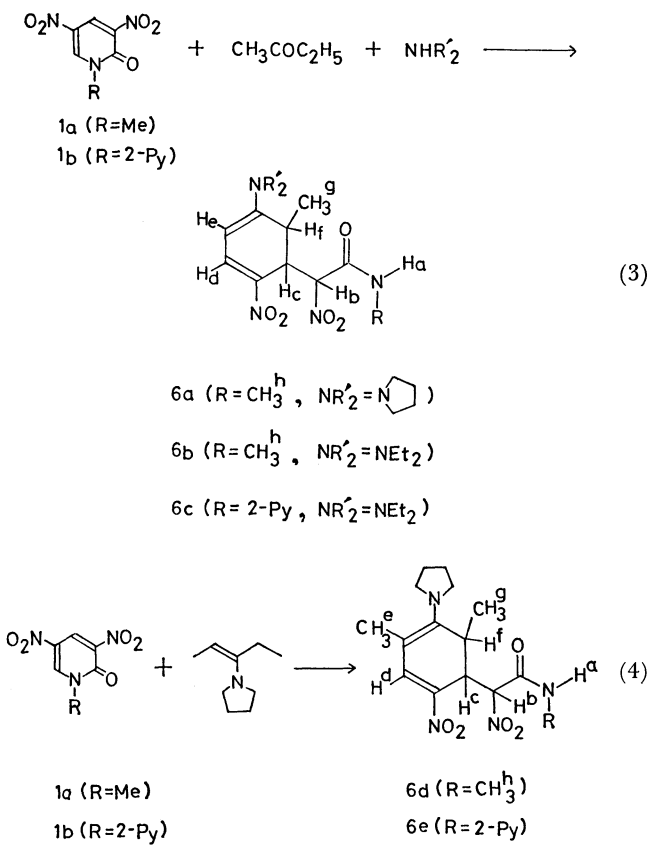
Run	Substrate (mmol)	Ketone (mmol)	Amine (mmol)	Solvent (ml)	Temp °C	Time h	Products (Yields/%) 5	2	3	
1	**1a**	Acetone	Pyrrolidine	Pyridine			**5a**			
	(1)	(10)	(3)	(10)	(80)	(5)	(95)	(0)	(0)	
1′	(1)	(1)	(1)	(10)	(80)	(5)	(69)	(0)	(0)	
2	**1a**	Acetone	Piperidine	Pyridine			**5b**			
	(1)	(10)	(3)	(10)	(80)	(5)	(97)	(0)	(0)	
3	**1a**	Acetone	Diethylamine	Pyridine			**5c**			
	(1)	(10)	(3)	(10)	(80)	(5)	(93)	(0)	(0)	
4	**1a**	Acetone	Butylamine	Pyridine			**5d**			
	(1)	(10)	(3)	(10)	(80)	(5)	(93)	(0)	(0)	
5	**1a**	Acetone	Morpholine	Pyridine			**5e**			
	(1)	(10)	(3)	(10)	(80)	(5)	(2)	(0)	(0)	
6	**1a**	2-Butanone	Pyrrolidine	Pyridine			**5f**		**3a**	**6a**
	(1)	(10)	(3)	(10)	(80)	(5)	(98)	(0)	(0)	(0)
6′	(1)	(1)	(1)	(10)	(80)	(5)	(53)	(0)	(8)	(19)
7	**1a**	2-Butanone	Diethylamine	Pyridine						
	(1)	(10)	(3)	(10)	(80)	(5)	(0)	(0)	(0)	
8	**1a**	3-Pentanone	Pyrrolidine	Pyridine			**5g**	**2a**		
	(1)	(10)	(3)	(10)	(80)	(5)	(58)	(11)	(0)	
8′	(1)	(1)	(1)	(10)	(80)	(5)	(2)	(4)	(0)	
9	**1a**	3-Pentanone	Diethylamine	Pyridine						
	(1)	(10)	(3)	(10)	(80)	(5)	(0)	(0)	(0)	
10	**1a**	EAA	Pyrrolidine	Pyridine			**5h**			
	(1)	(6)	(10)	(10)	(80)	(5)	(85)	(0)	(0)	
11	**1a**	EAA	Diethylamine	Pyridine				**2b**		
	(1)	(6)	(10)	(10)	(80)	(5)	(0)	(14)	(0)	
12	**1a**	DOPD	Pyrrolidine	Pyridine				**2c**		
	(1)	(6)	(10)	(10)	(80)	(5)	(0)	(98)	(0)	
13	**1b**	Acetone	Piperidine	Acetone			**5b**		**3b**	
	(2)	—	(6)	(20)	(60)	(5)	(85)	(0)	(25)	
14	**1b**	Acetone	Morpholine	Acetone			**5e**		**3b**	
	(2)	—	(6)	(20)	(60)	(5)	(53)	(0)	(20)	
15	**1b**	DOPD	Piperidine	Pyridine				**2c**	**3b**	
	(2)	(6)	(6)	(20)	(60)	(5)	(0)	(94)	(88)	

1a=1-Methyl-3,5-dinitro-2-pyridone, **1b**=3,5-dinitro-1-(2-pyridyl)-2-pyridone, **2a**=2,6-dimethyl-4-nitrophenol, **2b**=ethyl 5-nitrosalicylate, **2c**=diethyl 2-hydroxy-5-nitroisophthalate, **3a**=*N*-methyl-2-nitroacetamide, **3b**=2-oxo-2*H*-pyrido[1,2-*b*][1,2,4]triazine 4-oxide, **5a**=1-nitro-4-(1-pyrrolidinyl)benzene, **5b**=1-nitro-4-piperidinobenzene, **5c**=1-diethylamino-4-nitrobenzene, **5d**=1-butylamino-4-nitrobenezen, **5e**=1-morpholino-4-nitrobenzene, **5f**=2-methyl-4-nitro-1-(1-pyrrolidinyl)benzene, **5g**=1,3-dimethyl-5-nitro-2-(1-pyrrolidinyl)benzene, **5h**=ethyl 5-nitro-2-(1-pyrrolidinyl)benzoate, EAA=ethyl acetoacetate, DOPD=diethyl 3-oxopentanedioate.

of the amines. Thus easy formation of enamines can be postulated to take place in a series of reactions involving an initial nucleophilic attack of the amino group to the carbonyl carbon atom of the ketones. On the other hand, the treatment of **1a** or **1b** with highly acidic ketones such as diethyl 3-oxopentanedioate (DOPD) in the presence of the amines yields diethyl 2-hydroxy-5-nitroisophthalate (**2c**) quantitatively. The formation of the 4-nitrophenol suggests that the amines play a role of an acceptor of the proton of the acidic ketone to form the enolate ion. The reaction of the enolate ion with **1a** or **1b** follows essentially the identical course with that of diethyl 2-sodio-3-oxopentanedioate as shown in Eq. 1.[1] The reactivity of EAA was found to be intermediate between DOPD and the other dialkyl ketones. The treatment of **1a** with EAA in the presence of diethylamine only gave the phenol (**2b**) in 14% yield. The lower yield of the phenol can be attributed to the lower acidity of EAA, while the treatment of **1a** with EAA in the presence of pyrrolidine gave the *p*-nitroaniline derivative (**5h**) in 85% yield. This indicates that the basicity of the pyrrolidine is sufficient to bring about the formation of the enamine from EAA.

In order to isolate the intermediates, the reactions of **1a** or **1b** with ketones in the presence of secondary amines were carried out under somewhat milder conditions. When **1a** was treated with 2-butanone and pyrrolidine in pyridine at 70 °C for 1 h, **6a** was obtained as deep red crystals in 55% yield. The analytical data of **6a** were consistent with the formula, $C_{14}H_{20}N_4O_5$. The IR spectra had a carbonyl band at 1676 cm^{-1} and an N–H stretching band at 3270 cm^{-1}, which were attributable to a secondary amide group. The ^{1}H-NMR spectra also showed signals due to an *N*-methyl amide moiety at δ 2.44 (NCH_3, d, J=4 Hz) and 8.52 (N–H, m), and showed two doublets at δ 4.83 (J=8.5 Hz) and 7.71 (J=8.5 Hz), corresponding to two vicinal olefinic protons. The NMR spectra also showed a doublet of methyl protons at δ 1.16 (J=7 Hz). On the basis of these data, **6a** was assigned to be *N*-methyl-2-[6-methyl-2-nitro-5-

(1-pyrrolidinyl)-2,4-cyclohexadienyl]-2-nitroacetamide. The presence of a highly polarized 1-amino-4-nitro-1,3-butadiene system in the molecule was also suggested by very intense absorption at 497 nm (ε= 4.78×10^4) (Fig. 1). Similar cyclohexadiene intermediates (**6b** and **6c**) were also isolated by the reaction of **1a** or **1b** with 2-butanone and diethylamine (Eq. 3). Furthermore, reactions of **1a** or **1b** with 3-(pyrrolidinyl)-2-pentene gave similar enamine adducts, **6d** or **6e** (Eq. 4). The NMR, IR, and electronic spectra of **6** are summarized in Tables 2, 3, and Fig. 1.



The intermediate, **6a**, on heating at 80 °C for 5 h in pyridine, afforded a mixture, which was separated by column chromatography on silica gel to give the final products, **5f** and **3a** in 78 and 47% yields, respectively. The intermediate, **6d**, was also converted into **5g** in 55% yield under the same reaction conditions (Eq. 5). Only by standing for 24 h in DMSO-d_6 at 35 °C, **6e** was completely converted into **5g**. These facts reveal that the cyclohexadiene derivatives (**6**) are one of the intermediates of the ring transformation.

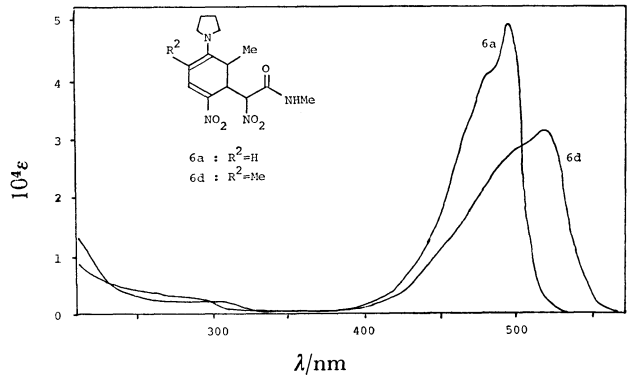


Fig. 1. Electronic spectra of the intermediate, **6a** and **6d**, in methanol.

Table 2. ^{1}H-NMR spectra of the intermediates, **6**[a,b]

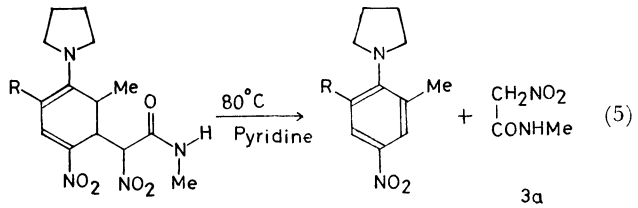
Compound	Chemical shift (δ)							Coupling constant (Hz)			
	H_a	H_b	H_c	H_d	H_e	H_g	H_h	$J(H_d-H_e)$	$J(H_f-H_g)$	$J(H_b-H_c)$	$J(H_a-H_h)$
6a	8.52 (d-m)	5.20 (d)	3.83 (d-m)	7.71 (d)	4.83 (d)	1.16 (d)	2.44 (d)	8.5	7	2	4
6b	8.5 (d-m)	5.21 (d)	3.90 (d-m)	7.70 (d)	5.00 (d)	1.13 (d)	2.50 (d)	9	8	4	5
6c		5.69 (d)	4.02 (m)	7.68 (d)	4.80 (d)	1.15 (d)	—	8	7	3	—
6d	8.5 (m)	5.23 (d)	3.76 (m)	7.61 (s)	2.00 (d)	1.10 (d)	2.50 (d)	0	7	2	4
6e		5.67 (d)	3.90 (d)	7.64 (s)	1.65 (s)	1.10 (d)	—	0	7	8	—

a) In a DMSO-d_6 solution. b) Notations of the protons are shown in Eqs. 3 and 4.

Table 3. IR and UV Spectra of the intermediates, **6**

Compound	IR spectra (ν/cm^{-1})[a]				UV spectra[b]	
	ν(N-H)	ν(C=O)	$\nu(C_{vinyl}-H)$	$\nu_{as}(NO_2)$	λ_{max}/nm(ε)	
6a	3262	1676	3090	1546, 1517	497 (4.78×10^4)	476 (sh)
6b	3270	1685	3085	1550, 1525	498 (5.00×10^4)	480 (sh)
6c	3240	1693	3110, 3070	1545, 1530	497 (2.52×10^4)	
6d	3245	1692	3070	1550, 1533	520 (2.98×10^4)	476 (sh)
6e	3210	1689	3085	1553, 1542	523 (2.97×10^4)	476 (sh)

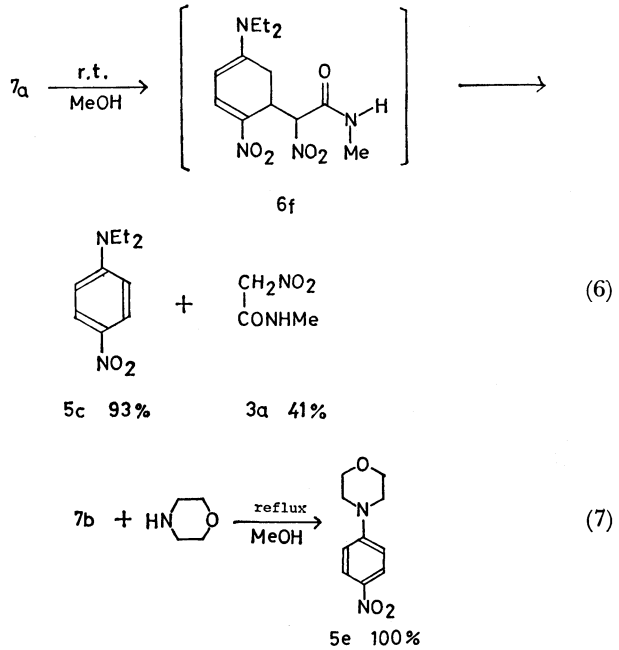
a) In Nujol. b) In methanol.



(5)

When **1a** was treated with diethylamine in acetone at room temperature, another type of intermediate, **7a**, was obtained in quantitative yield. The analytical data indicate that **7a** consists of **1a**, diethylamine, and an enamine derived from acetone and diethylamine in molar ratio 1:1:1. Similar treatment of **1a** with morpholine in acetone gave **7b** in quantitative yield. The analytical data of **7b** is composed of each one molecule of **1a**, morpholine, and an enamine derived from acetone and morpholine, and a half molecule of water. In a similar experiment using pyrrolidine as the amine component, the analogue of **7a** or **7b** was not afforded. However the final product, **5a**, was obtained from this reaction mixture.

When a methanol solution of **7a** was allowed to stand at room temperature, spontaneous decomposition occurred, **5c** and **3a** being obtained as the final products in 93 and 41% yields, respectively (Eq. 6). Under similar conditions, the contraction of **7b** did not occurred. However, on boiling with excess morpholine in methanol, **7b** afforded **5e** in quantitative yield (Eq. 7).



(6)

(7)

Figure 2 shows a change in the electronic spectrum of **7a** in methanol at room temperature. The intensity of the band at 310 nm decreases and that at 400 nm increases. It could be reasonably explained that the absorption at 300 nm corresponds to the diethylammonium salt of *N*-methyl-2-nitroacetamide (**3a**) and

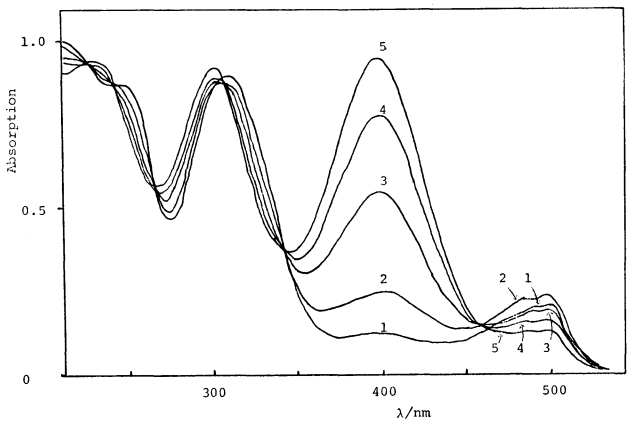
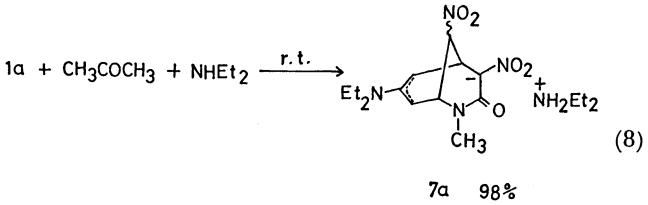


Fig. 2. Changes in electronic spectra of **7a** in methanol (8.34×10^{-5} mol/l) after (1) 3 min, (2) 18 min, (3) 52 min, (4) 82 min, and (5) 110 min at 20 °C.

that of 400 nm corresponds to 1-diethylamino-4-nitrobenzene (**5c**), because the authentic samples of **3a** and **5c** showed strong absorption maxima at 295 and 400 nm, respectively. An absorption band at about 500 nm indicates formation and subsequent decomposition of a transient species, which could be identified as the cyclohexadiene intermediate, 2-(5-diethylamino-2-nitro-2,4-cyclohexadienyl)-*N*-methyl-2-nitroacetamide (**6f**), by comparing the absorption band at 500 nm (Fig. 2) with that of the similar intermediates, **6a**—**c** (Fig. 1).

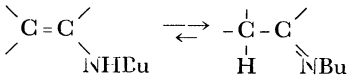
The ^{1}H-NMR spectra of **7a** showed an olefinic proton at δ 4.6 (a broad doublet, J=3 Hz). The IR spectra showed a C=C band at 1628 cm^{-1}, and the UV spectra showed an absorption at 248 nm (ε=11400). These data indicate the presence of an enamine moiety in **7a**. Broad absorptions at 2800—2300 cm^{-1} imply that **7a** is a diethylammonium salt. Since the diethylammonium salt of *N*-methyl-2-nitroacetamide absorbs UV light at 295 nm, the absorption of **7a** at 310 nm suggests the presence of a salt of the 2-nitroacetamide moiety. On the basis of these spectral data, as well as the elemental analysis and the chemical behavior shown in Eq. 6, the structure of diethylammonium 7-diethylamino-2-methyl-4,9-dinitro-3-oxo-2-azabicyclo[3.3.1]non-6(or 7)-en-4-ide was assigned to **7a** (Eq. 8).



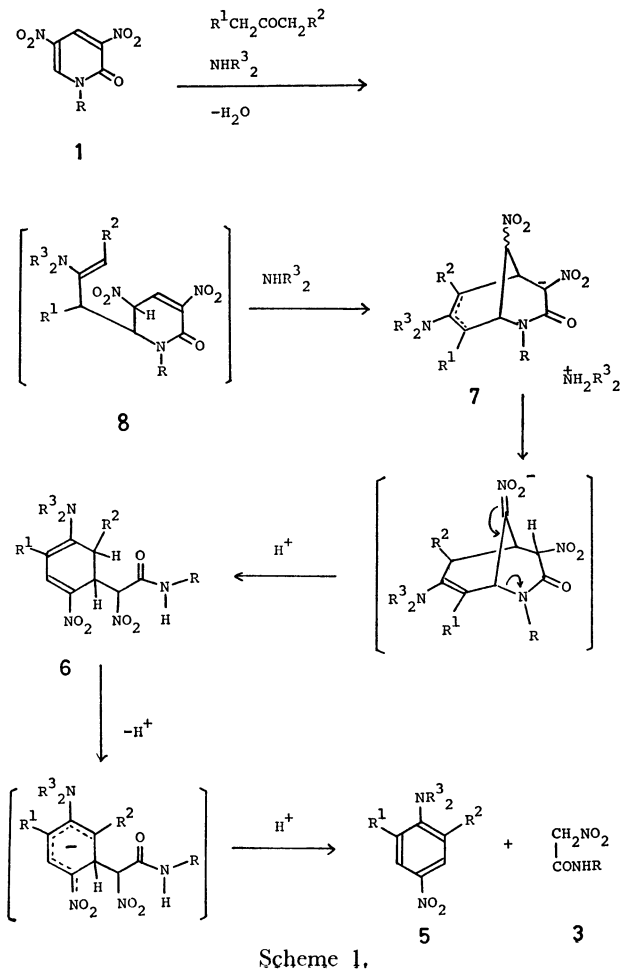
(8)

From these results, a possible process which occurs during the treatment of *N*-substituted 3,5-dinitro-2-pyridones (**1**) with the dialkyl ketones in the presence of the amines may start with the reaction of the ketones with the secondary amines to form an intermediate enamine. Usually the reaction of primary amines with aldehydes or ketones affords products which primarily contain imines (Schiff bases) rather than the enamine tautomers. Thus, in the initial reaction of

acetone and butylamine, the enamine may be a minor tautomer.



The amino olefinic component in the enamine as well as the enolate ion component in the β-keto ester anions has an electron-donating trend. Both the HOMO and the LUMO of these olefins are raised in energy relative to the HOMO and the LUMO of ethylene. The HOMO of enamine is the one which has the coefficient on the β-carbon atom larger than the α-carbon atom. On the other hand, the 1,3-dinitro-1,3-butadiene component of *N*-substituted 3,5-dinitro-2-pyridones has an electron-withdrawing trend, and the conjugation with the nitro group lowers both the energy of the HOMO and the LUMO relative to those of butadiene. The LUMO of the diene component is the one which has the largest coefficient on the C_6 atom of the 2-pyridone nucleus. By using the data given by Houk,[8] we can predict, as a favorable pathway, that the nucleophilic attack of the β-carbon of the enamine (HOMO) at the C_6 atom of the pyridone nucleus (LUMO of 1,3-dinitro-1,3-butadiene system) may lead to an adduct, **8**, as shown in Scheme 1. In this adduct, the intramolecular interaction between the β′-carbon of the enamine component and C_4 of the pyridone moiety would lead to the bicyclo adduct (**7**).



Scheme 1.

As described above, an excess amount of morpholine promotes the conversion of the intermediate, **7b**, to the final product, **5e** (Eq. 7). This suggests that the fission of the C_1–N_2 bond of the 2-azabicyclo[3.3.1]-nonene intermediate (**7**) is a base-catalyzed step. The transformation of **6** to **5** and **3** may also occur via base-catalyzed C–C bond fission. When the proton on C_6 of the intermediate, **6**, is removed by base, the heterolysis between C_6 and C_α in the deprotonated Meisenheimer-type species may lead to the final products. In the case of **6a**—**e**, the intermediates may be stabilized by the electron-donating character of the methyl group at C_6 and the deprotonation from this carbon atom may be more difficult than that in the case of **6f** which does not have any substituents at C_6.

From these results, it is concluded that the ring transformation of the 3,5-dinitro-2-pyridones to the *p*-nitroanilines is strongly promoted by the secondary or primary amines in each step.

Experimental

^{1}H-NMR spectra were measured using a Hitachi R-20 B spectrometer with TMS as an internal reference. UV spectra were recorded using a Hitachi EPS-3 spectrophotometer. Mass spectra were recorded with a JMS-D100 mass spectrophotometer. IR spectra were collected with a Hitachi 225 Grating IR spectrophotometer. All the melting points were uncorrected.

*Reaction of 1-Methyl-3,5-dinitro-2-pyridone (**1a**) with Dialkyl Ketones and Amines.* In a typical procedure, 0.21 g of pyrrolidine in 5 ml of pyridne was added slowly at 0 °C to a solution of 0.20 g of 1-methyl-3,5-dinitro-2-pyridone (**1a**) and 0.86 g of 3-pentanone in 5 ml of pyridine. Then the mixture was heated at 80 °C for 5 h. The solvent was removed under reduced pressure and the residual oil was column-chromatographed on silica gel (Wakogel C-300) and eluted with benzene. From the first elute, 0.13 g (58%) of 1,3-dimethyl-5-nitro-2-(1-pyrrolidinyl)benzene (**5g**) was obtained. The second elute gave 0.02 g (11%) of 2,6-dimethyl-4-nitrophenol (**2a**).

*1,3-Dimethyl-5-nitro-2-(1-pyrrolidinyl) benzene (**5g**)*: Yellow prisms (from hexane); mp 93—93.5 °C. NMR (CCl_4): δ 2.0 (4H, m), 2.28 (6H, s), 3.2 (4H, m), 7.73 (2H, s). Found: C, 65.83; H, 7.27; N, 12.70%. Calcd for $C_{12}H_{16}N_2O_2$: C, 65.43; 7.32; N, 12.70%.

*2,6-Dimethyl-4-nitrophenol (**2a**)*: Pale yellow needles (from hexane–benzene); mp 168—169 °C. NMR ($CDCl_3$): δ 2.28 (6H, s), 7.79 (2H, s). Found: C, 57.43; H, 5.28; N, 8.44%. Calcd for $C_8H_9NO_3$: C, 57.48; H, 5.43; N, 8.38%.

From the similar treatment of **1a** with other dialkyl ketones and amines, following compounds were obtained.

*1-Nitro-4-(1-pyrrolidinyl)benzene (**5a**)*: Yellow plates (from hexane); mp 167 °C. NMR ($CDCl_3$): δ 2.03 (4H, m), 3.34 (4H, m), 6.38 (2H, d, J=10 Hz), 8.00 (2H, d, J=10 Hz). Found: C, 62.77; H, 6.52; N, 14.58%. Calcd for $C_{10}H_{12}N_2O_2$: C, 62.48; H, 6.29; N, 14.58%.

*1-Nitro-4-piperidinobenzene (**5b**)*: Yellow plates (from hexane); mp 99.5—100 °C. NMR (CCl_4): δ 1.7 (6H, m), 3.3 (4H, m), 6.73 (2H, d, J=9.5 Hz), 8.01 (2H, d, J=9.5 Hz). Found: C, 64.36; H, 7.05; N, 13.72%. Calcd for $C_{11}H_{14}N_2O_2$: C, 64.06; H, 6.86; N, 13.58%.

*1-Diethylamino-4-nitrobenzene (**5c**)*: Yellow needles (from hexane); mp 73—74 °C. NMR (CCl_4): δ 1.19 (6H, t,

J=7 Hz), 3.41 (4H, q, J=7 Hz), 6.45 (2H, d, J=10 Hz), 7.90 (2H, d, J=10 Hz). Found: C, 61.61; H, 7.09; N, 14.20%. Calcd for $C_{10}H_{14}N_2O_2$: C, 61.83; H, 7.27; N, 14.42%.

1-Butylamino-4-nitrobenzene (5d): Yellow needles (from hexane); mp 56 °C. NMR (CCl_4): δ 1.05 (3H, t, J=6 Hz), 1.5 (4H, m), 3.15 (2H, t, J=8 Hz), 4.65 (1H, m), 6.47 (2H, d, J=9 Hz), 7.99 (2H, d, J=9 Hz). Found: C, 62.01; H, 7.48; N, 14.59%. Calcd for $C_{10}H_{14}N_2O_2$: C, 61.83; H, 7.27; N, 14.42%.

1-Morpholino-4-nitrobenzene (5e): Yellow needles (from hexane); mp 149.5—150 °C. NMR ($CDCl_3$): δ 3.33 (4H, m), 3.86 (4H, m), 6.79 (2H, d, J=10 Hz), 8.09 (2H, d, J=10 Hz). Found: C, 57.92; H, 6.06; N, 13.23%. Calcd for $C_{10}H_{12}N_2O_3$: C, 57.68; H, 5.81; N, 13.46%.

2-Methyl-4-nitro-1-(1-pyrrolidinyl) benzene (5f): Yellow plates (from hexane); mp 100—100.5 °C. NMR (CCl_4): δ 1.96 (4H, m), 2.36 (3H, s), 3.40 (4H, m), 6.49 (1H, d, J=10 Hz), 7.7 (2H, m). Found: C, 63.90; H, 6.92; N, 13.64%. Calcd for $C_{11}H_{14}N_2O_2$: C, 64.06; H, 6.84; N, 13.58%.

Reaction of 1-Methyl-3,5-dinitro-2-pyridone (1a) with Equimolar Amount of 2-Butanone and Pyrrolidine. To a solution of 0.199 g of **1a** and 0.072 g of 2-butanone in 5 ml of pyridine 0.071 g of pyrrolidine in 5 ml of pyridine was added at 0 °C. The solution was heated at 80 °C for 5 h. The solvent was distilled off and the residual oil was dissolved in a minimum amount of tetrahydrofuran; then ether was added to the solution until it turned to cloudy. After 0.062 g (19%) of red precipitate (**6a**) was filtered off, the solvent was removed and the residue was column-chromatographed on silica gel. From a benzene elute, 0.109 g (53%) of 2-methyl-4-nitro-1-(1-pyrrolidinyl)benzene (**5f**) was obtained and 0.009 g (8%) of *N*-methyl-2-nitroacetamide (**3a**) was obtained from an ether elute; mp 75—75.5 °C; colorless needles (from i-Pr_2O).

Reaction of 1-Methyl-3,5-dinitro-2-pyridone (1a) with Ethyl Acetoacetate and Diethylamine. To a solution of 0.20 g of **1a** and 0.39 g of ethyl acetoacetate in 5 ml of pyridine, 0.38 g of diethylamine in 5 ml of pyridine was added slowly at 0°C. The mixture was heated at 80 °C for 5 h and the pyridine removed *in vacuo*. The residue was neutralized to pH 3—4 with dil. hydrochloric acid and extracted with chloroform. After the extract had been dried over anhydrous sodium sulfate, the chloroform was distilled off and the residue was column-chromatographed on silica gel. From a benzene elute, 0.060 g (14%) of ethyl 5-nitrosalicylate (**2b**) was obtained; mp 57.5—58.5 °C, colorless needles (from hexane).

The similar treatment of 0.40 g of **1a** with 1.21 g of DOPD and 0.43 g of pyrrolidine gave 0.54 g (98%) of diethyl 2-hydroxy-5-nitroisophthalate (**2c**); colorless needles (from hexane); mp 58—59 °C.

Reaction of 1-Methyl-3,5-dinitro-2-pyridone (1a) with Ethyl Acetoacetate and Pyrrolidine. To a solution of 0.40 g of **1a** and 0.78 g of ethyl acetoacetate in 10 ml of pyridine was added 0.71 g of pyrrolidine in 10 ml of pyridine at 0 °C. The mixture was heated at 80 °C for 5 h and the solvent was removed *in vacuo*. To the residue was added 20 ml of 10% sodium hydroxide and the mixture was extracted with chloroform. After the extract had been dried over anhydrous sodium sulfate, the chloroform was distilled off and the residual oil was column-chromatographed on silica gel. A benzene elute gave 0.45 g (85%) of ethyl 5-nitro-2-(1-pyrrolidinyl)benzoate (**5h**): yellow needles (from diisopropyl ether–diethyl ether); mp 128.5—129 °C. NMR ($CDCl_3$): δ 1.40 (3H, t, J=6.6 Hz), 2.0 (4H, m), 3.3 (4H, m), 4.36 (2H, q, J=6.6 Hz), 6.67 (1H, d, J=9 Hz), 8.07 (1H, dd, J=9 and 3 Hz), 8.42 (1H, d, J=3 Hz). Found: C, 59.08; H, 5.94; N, 10.70%. Calcd for $C_{13}H_{16}N_2O_4$: C, 59.08; H, 6.10; N, 10.60%. The water layer was acidified with 6 M (1 M=1 mol dm^{-3}) hydrochloric acid to pH 1—2 and then extracted with chloroform but the organic layer failed to give ethyl 5-nitrosalicylate (**2b**) or *N*-methyl-2-nitroacetamide (**3a**) after the usual work up.

Reaction of 3,5-Dinitro-1-(2-pyridyl)-2-pyridone (1b) with Acetone and Piperidine. To a solution of 0.54 g of **1b** in 20 ml of acetone was added 0.51 g of piperidine at 0 °C. After the mixture had been refluxed gently for 5 h, the acetone was removed under reduced pressure. The residual oil was washed with *ca.* 20 ml of chloroform. After insoluble solids had been filtered off, the organic layer was concentrated to a few milliliters and column-chromatographed on silica gel. A benzene elute gave 0.39 g (94%) of 1-nitro-4-piperidinobenzene (**5b**). A methanol elute and the chloroform-insoluble solids were combined together and recrystallized from water to give 0.08 g (25%) of 2-oxo-2*H*-pyrido-[1,2-*b*][1,2,4]triazine 4-oxide (**3b**); yellow needles; dec 210 °C.

Reaction of 3,5-Dinitro-1-(2-pyridyl)-2-pyridone (1b) with DOPD and Piperidine. To a solution of 0.54 g of **1b** and 1.21 g of DOPD in 15 ml of pyridine was added 0.51 g of piperidine in 5 ml of pyridine at 0 °C. The mixture was heated at 60 °C for 5 h and the pyridine was removed *in vacuo*. To this mixture 50 ml of chloroform and 20 ml of 1 M hydrochloric acid was added. Insoluble solids were filtered off and the organic layer was dried over anhydrous sodium sulfate. The organic layer was concentrated to a few milliliters and column-chromatographed on silica gel. A benzene elute gave 0.51 g (94%) of diethyl 2-hydroxy-5-nitroisophthalate (**2c**). A methanol elute and the chloroform-insoluble solids were combined and recrystallized from water to give 0.36 g (88%) of **3b**.

Reaction of 1-Methyl-3,5-dinitro-2-pyridone (1a) with 3-(1-Pyrrolidinyl)-2-pentene. To a solution of 0.20 g of **1a** in 5 ml of pyridine at 0 °C was added 0.42 g of 3-(1-pyrrolidinyl)-2-pentene in 5 ml of pyridine. The deep red solution was heated at 80 °C for 5 h. After the usual work up, 0.144 g (66%) of **5g** was obtained.

Isolation of the Cyclohexadiene Intermediates (6). *N*-Methyl-2-[6-methyl-2-nitro-5-(1-pyrrolidinyl)-2,4-cyclohexadienyl]-2-nitroacetamide (**6a**): To a mixture of 0.40 g of **1a** and 5 ml of 2-butanone in 10 ml of pyridine was added 0.43 g of pyrrolidine at 0 °C. The solution was heated at 70 °C for 1 h, and then the solvent was removed *in vacuo*. The residual oil was washed with water and crystallized from tetrahydrofuran–ether to give 0.37 g (55%) of **6a**; wine-red prisms; decomp 154—155 °C. Found: C, 51.95; H, 6.34; N, 17.44%. Calcd for $C_{14}H_{20}N_4O_5$: C, 51.84; H, 6.22; N, 17.28%.

N-Methyl-2-(5-diethylamino-5-methyl-2-nitro-2,4-cyclohexadienyl)-2-nitroacetamide (6b): The treatment of 0.40 g of **1a** with 0.46 g of diethylamine and 5 ml of 2-butanone in 10 ml of pyridine at 70 °C for 2 h gave 0.30 g (43%) of **6b**; wine-red prisms (from methanol-ether); decomp 138—138.5 °C. Found: C, 51.49; H, 6.70; N, 17.18%. Calcd for $C_{14}H_{22}N_4O_5$: C, 51.52; H, 6.80; N, 17.17%.

N-(2-Pyridyl)-2-(5-diethylamino-6-methyl-2-nitro-2,4-cyclohexadienyl)-2-nitroacetamide (6c): A treatment of 0.26 g of **1b** with 1.44 g of 2-butanone and 0.22 g of diethylamine in 10 ml of pyridine at 50 °C for 5 h gave 0.06 g (15%) of **6c**; wine-red prisms (from chloroform); decomp 135—136 °C. Found: C, 55.26; H, 6.23; N, 17.61%. Calcd for $C_{18}H_{23}N_5O_5$: C, 55.52; H, 5.95; N, 17.99%.

N-Methyl-2-[4,6-dimethyl-2-nitro-5-(1-pyrrolidinyl)-2,4-cyclo-

*hexadienyl]-2-nitroacetamide (**6d**)*: To a solution of 0.40 g of **1a** in 10 ml of pyridine was added 0.42 g of 3-(1-pyrrolidinyl)-2-pentene in 10 ml of pyridine at 0 °C. The solution immediately turned purple; it was heated at 70 °C for 1 h. After the pyridine was removed *in vacuo*, the residual oil was washed with ether and crystallized from tetrahydrofuran–ether to give 0.26 g (38%) of **6d**; purple prisms; decomp 156—157 °C. Found: C, 53.02; H, 6.67; N, 16.77%. Calcd for $C_{15}H_{22}N_4O_5$: C, 53.24; H, 6.55; N, 16.56%.

*N-(2-Pyridyl)-2-[4,6-dimethyl-2-nitro-5-(1-pyrrolidinyl)-2,4-cyclohexadienyl]-2-nitroacetamide (**6e**)*: Treatment of 0.26 g of **1b** with 0.21 g of 3-(1-pyrrolidinyl)-2-pentene in 10 ml of pyridine at 45 °C for 2 h gave 0.08 g (20%) of **6e**; purple prisms (from methanol–ether); decomp 156—157 °C. Found: C, 56.68; H, 5.62; N, 17.17%. Calcd for $C_{19}H_{23}N_5O_5$: C, 56.85; H, 5.78; N, 17.45%.

*Conversion of N-Methyl-2-[6-methyl-2-nitro-5-(1-pyrrolidinyl)-2,4-cyclohexadienyl]-2-nitroacetamide (**6a**) into 2-Methyl-4-nitro-1-(1-pyrrolidinyl)benzene (**5f**) and N-Methyl-2-nitroacetamide (**3a**)*. A solution of 0.324 g of **6a** and 0.71 g of pyrrolidine in 20 ml of pyridine was heated at 80 °C for 5 h. The solvent was removed *in vacuo*. When the residual solids were washed with a small portion of chloroform, 0.04 g of **6a** was recovered. The chloroform solution was concentrated and column-chromatographed on silica gel. A benzene elute gave 0.16 g (78%) of 2-methyl-4-nitro-1-(1-pyrrolidinyl)-benzene (**5f**) and an ether elute gave 0.055 g (47%) of *N*-methyl-2-nitroacetamide (**3a**).

*Isolation of the Bicyclo Intermediates (**7**)*. To a solution of 0.20 g of **1a** in 10 ml of acetone, 0.44 g of diethylamine was added slowly at 0 °C. After standing several hours at room temperature, yellow crystals began to precipitete. The crystals were collected by filtration and washed with acetone to give 0.76 g (98%) of **7a**; yellow prisms; decomp 122.5 °C. Found: C, 52.69; H, 8.38; N, 17.89%. Calcd for $C_{17}H_{31}N_5O_5$: C, 52.96, H, 8.11, N, 18.17%. IR (Nujol): 2740 cm^{-1} (ν_{N^+-H}), 1625 cm^{-1} ($\nu_{C=C}$ and $\nu_{C=O}$), 1540 cm^{-1} (ν_{NO_2}). NMR ($CDCl_3$): δ 0.97 ($NCH_2C\underline{H}_3$, 6H, t, J=7 Hz), 1.22 ($NCH_2C\underline{H}_3$, 6H, t, J=7 Hz), 2.2—3.3 ($\approx$11H, m), 2.90 (N-CH_3, 3H, s), 4.2—4.5 (2H, m), 4.6 (a broad doublet, J=3 Hz), 8.1—9.0 (N^+H_2, 2H, m). UV (MeOH): 250 nm (ε=9620), 309 nm (ε=9620).

Similarly **7b** was obtained in 96% yield; pale yellow prisms; decomp 139—140 °C. Found: C, 48.83; H, 6.48; N, 16.56%. Calcd for $C_{17}H_{28}N_5O_{7.5}$: C, 48.34; H, 6.68; N, 16.58%. IR: 2750, 2690, and 2530 cm^{-1} (ν_{N^+-H}), 1628 cm^{-1} ($\nu_{C=C}$ and $\nu_{C=O}$), 1548 cm^{-1} (ν_{NO_2}). NMR ($CDCl_3$): δ 2.3—3.3 (10H, m), 2.94 (N-CH_3, 3H, s), 3.5—4.0 (8H, m), 4.2—4.5 (2H, m), 4.5—4.9 (2H, m), 6.4—7.0 (N^+H_2, 2H, m). UV (MeOH): 314 nm (ε=12400).

*Conversion of **7a** into 1-Diethylamino-4-nitrobenzene (**5c**) and N-Methyl-2-nitroacetamide (**3a**)*. A solution of 0.39 g of **7a** in 50 ml of methanol was allowed to stand for 24 h at room temperature. The solvent was removed *in vacuo* and the residue was dissolved in 10 ml of chloroform and chromatographed on silica gel. A benzene elute gave 0.18 g (93%) of 1-diethylamino-4-nitrobenzene (**5c**). An ether elute gave 0.048 g (41%) of *N*-methyl-2-nitroacetamide (**3a**).

*Conversion of **7b** into 1-Morpholino-4-nitrobenzene (**5e**)*. When a solution of 0.42 g of **7b** in 50 ml of methanol was refluxed for 3 h, **7b** was recovered quantitatively. To the solution was added 0.87 g of morpholine and then refluxed for 3 h to give 1-morpholino-4-nitrobenzene (**5e**) quantitatively after the usual work up.

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