

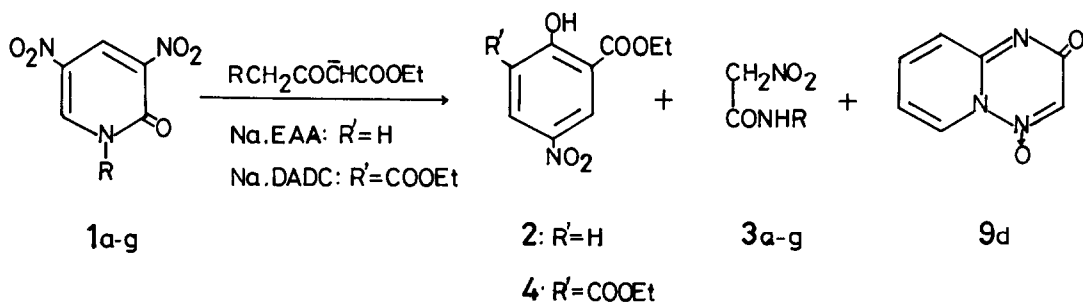
A RING TRANSFORMATION OF  
 1-SUBSTITUTED 3,5-DINITRO-2-PYRIDONES

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Summary: Reaction of 1-substituted 3,5-dinitro-2-pyridones with sodium salts of  $\beta$ -keto esters gave the ring transformation products, phenol derivatives and N-substituted nitroacetamides. Nonionic bicyclic intermediates could be isolated.

In the course of the investigation of the nucleophilic reactions on pyridine rings,<sup>1)</sup> a novel ring transformation was found in a series of the reactions of 1-substituted 3,5-dinitro-2-pyridones, electron deficient substrates, with mono sodium salt of  $\beta$ -keto esters and  $\beta$ -diketones.

The reaction of 3,5-dinitro-1-methyl-2-pyridone (1a) with three equimolar amounts of ethyl sodioacetoacetate (Na.EAA) at 70°C in pyridine gave 2-ethoxycarbonyl-4-nitrophenol (2),<sup>2)</sup> mp. 97.5-98.5°C, and N-methylnitroacetamide (3a),<sup>3)</sup> mp. 75.0-76.0°C, in 61.0% and 16.9% yields, respectively. 1a also reacted with 1.5 equimolar amounts of diethyl sodioacetonedicarboxylate (Na.DADC) at 50°C to give 2,6-bis(ethoxycarbonyl)-4-nitrophenol (4),<sup>4)</sup> mp. 58.0-59.0°C, in 90.4% and 3a in 28.3%.



a: R=methyl, b: R=m-nitrobenzyl, c: R=(2-pyridyl)methyl, d: R=2-pyridyl,  
 e: R=2,4-dinitrophenyl, f: R=methoxy, g: R=p-nitrobenzyloxy.

The results of the reactions of several 1-substituted 3,5-dinitro-2-pyridones (1a-g) and  $\beta$ -keto esters are summarized in Table 1.

Table 1. Reactions of  $1a-g$  with Na.EAA and Na.DADC.

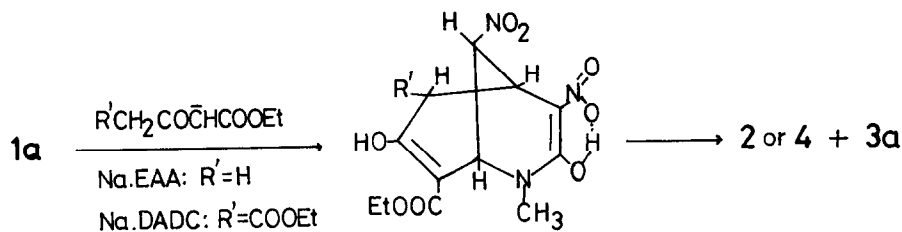
Substrate	Reaction with Na.EAA at 70°C Products (Yield %)	Reaction with Na.DADC at 50°C Products (Yield %) and mp. °C
$1a$	$2$ (61.0) $3a$ (16.9)	$4$ (90.4) $3a$ (28.3)
$1b$	$2$ (60.8) $3b$ (53.4)	$4$ (95.9) $3b$ (77.4) mp. 152.0-153.0
$1c$	$2$ (51.2) $3c$ (23.2)	$4$ (45.0) $3c$ (42.0) mp. 83.0-84.0
$1d$	$2$ (63.5) $3d$ (52.0) $9d$ (3.5)	$4$ (92.8) $3d$ (84.2) decomp. 120 $9d$ (3.8)
$1e$	$2$ (50.6) $3e$ (38.7)	$4$ (57.8) $3e$ (43.0) mp. 120.4-121.1
$1f$	$2$ (86.5) $3f$ (10.9)	$4$ (98.1) $3f$ (11.1) mp. 86.0-87.0
$1g$	$2$ (88.1) $3g$ (35.2)	$4$ (98.0) $3g$ (38.5) mp. 115.0-116.0

In the case of  $1d$ , an additional product 2-oxo-2,5-dihydropyrido[1,2-b]-1,2,4-triazine 4-oxide ( $9d$ ), decomp. 230°C, was obtained in a low yield. The formation of  $9d$  was assumed to arise from cyclodehydration of the initial product,  $3d$ , and it was proved by an experiment that a suspension of isolated  $3d$  in water was heated to give  $9d$  in a quantitative yield.

These reactions provide a new synthetic route for the preparation of  $N$ -substituted nitroacetamides which have hardly been obtainable.

On the other hand, when  $1a$  was treated with Na.EAA at room temperature, the colorless crystalline product ( $7a$ ), mp. 190.0-191.0°C was obtained together with  $2$  and  $3a$ . The empirical formula of  $7a$ ,  $C_{12}H_{15}N_3O_8$ , suggests the product to be an adduct of  $1a$  and the reagent. IR of  $7a$  showed the presence of nitro group (1530, 1340  $cm^{-1}$ ) and carbonyl group (1730  $cm^{-1}$ ). The aromatic proton signals of the parent pyridone and the singlet methyl and methylene protons of the ester disappeared, and five aliphatic proton signals coupled with each other were observed in a range between 2.8 and 5.3 ppm; 2.84 (1H, d,  $J=4Hz$ , H-6), 2.99 (1H, d,  $J=2Hz$ , H-6), 4.3 (1H, ddt,  $J=3, 4,$  and  $2Hz$ , H-5), 4.71 (1H, dd,  $J=2$  and  $3Hz$ , H-1), and 5.30 (1H, t,  $J=3Hz$ , H-9), and two singlets due to the enol 7-hydroxy and the strongly hydrogen-bonded 3-hydroxy groups were observed at 12.56 and 18.8 ppm, respectively.<sup>5)</sup> The product,  $7a$ , was easily converted to  $2$  and  $3a$  when heated with sodium ethoxide in ethanol or ethyl sodioacetoacetate in pyridine. On the basis of the physical and the chemical behaviors,  $7a$  was assigned to 3,7-dihydroxy-4,9-dinitro-8-ethoxycarbonyl-2-methyl-2-azabicyclo[3.3.1]nona-3,7-diene. Similarly, from  $1a$  and Na.DADC at room temperature, 6,8-bis(ethoxycarbonyl)3,7-dihydroxy-4,9-dinitro-2-methyl-2-azabicyclo[3.3.1]nona-3,7-diene ( $8a$ ), mp. 155.0-156.0°C, was obtained. The compounds,  $7a$  and  $8a$ , are to our knowledge, the first examples of nonionic bicyclic intermediate isolated from

the reaction of electron deficient aromatics with sodium salts of active methylene compounds.<sup>6)</sup>

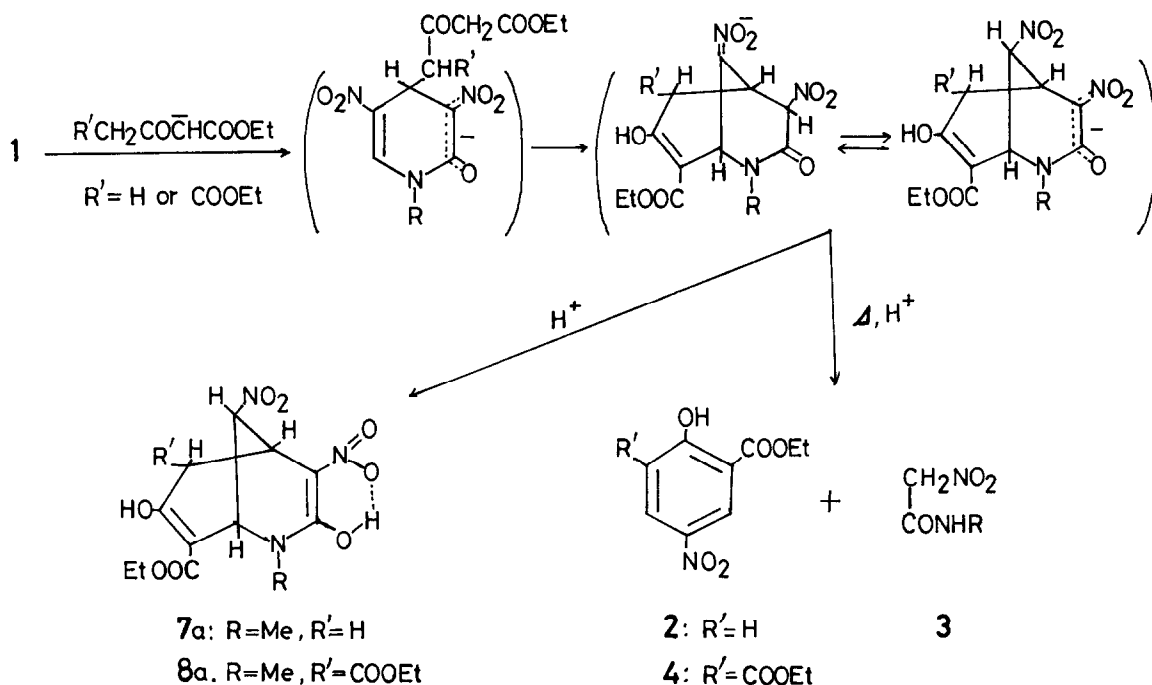


7a:  $R'=H$  (Y. 57.5%)

8a:  $R'=COOEt$  (Y. 79.8%)

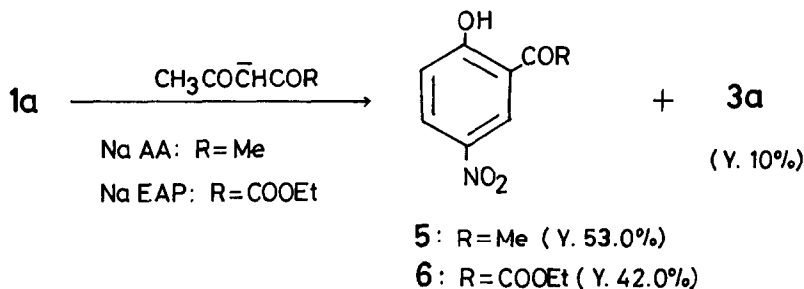
These results suggest that the phenol derivatives (2 and 4) may be made up of the reagent and the C<sub>4</sub>-C<sub>5</sub>-C<sub>6</sub> moiety of the parent pyridone, and N-substituted nitroacetamides, 3, may result from the other fragment, N-C<sub>2</sub>-C<sub>3</sub>, of the pyridone.

The mechanistic course of the reaction leading to the products via the bicyclic intermediate is proposed as follows.



The substrate, 1a, was also allowed to react with sodioacetylacetone (Na.AA) and ethyl sodioacetylpyruvate (Na.EAP) to give 2-acetyl-4-nitrophenol (5),<sup>7)</sup>

mp. 101.0-102.0°C, and 2-ethoxalyl-4-nitrophenol (**6**), mp 57.5-58.0°C, respectively, besides **3a**. The reaction of **1a** with Na.EAP, however, required a higher temperature (110°C) than that of the other cases.



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#### References and Notes

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- 2) The authentic sample was prepared by the usual esterification from commercial 4-nitrosalicylic acid.
- 3) The authentic methylammonium salt of N-methylnitroacetamide was obtained by the method of F. Ratz, *Monatsh. Chem.*, **26**, 1487 (1905).
- 4) The authentic sample was prepared by the usual method from 2-hydroxy-5-nitroisophthalic acid; W. S. Benica and O. Gisvold, *J. Am. Pharm. Assoc.*, **34**, 42 (1945).
- 5) The NMR spectra were recorded on JEOL FX-100 in CDCl<sub>3</sub> with TMS as an internal standard.
- 6) The reports on the ionic form of meta-bridging intermediates in the reaction of 1,3,5-trinitrobenzene etc were as follows: M. I. Foreman, R. Foster, and M. J. Strauss, *J. Chem. Soc., C*, 2112 (1969); M. J. Strauss, T. C. Jensen, H. Schran, and K. O'Conner, *J. Org. Chem.*, **35**, 383 (1970); M. J. Strauss, *Acc. Chem. Res.*, **7**, 181 (1974); K. Kohashi, Y. Ohkura, and T. Momose, *Chem. Pharm. Bull. (Tokyo)*, **18**, 2157 (1970); *ibid.*, **19**, 213, 2065 (1971); *ibid.*, **21**, 118 (1973).
- 7) C. T. Chang, F. C. Chen, T. S. Chen, K. K. Hsu, T. Ueng, and M. Hung, *J. Chem. Soc.*, 3414 (1961).

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