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N-SUBSTITUENT EFFECT OF 4-AMINO-3-PENTEN-2-ONE IN THE REACTION WITH PHENYLHYDRAZINE

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Abstract The reaction rates of p-substituted 4-amino-3-penten-2-ones with phenylhydrazine were not comparable to the value of superdelocalizability for a nucleophile, but for an electrophile. From this result, the rate determing step was speculated to be the protonation on a substrate. The electron-donating group on nitrogen atom accelerated the reaction of 3-amino-2-en-1-ones with nucleophiles, especially in the presence of acid.

It has been reviewed1) that 3-amino-2-en-1-ones have very interesting chemical properties. In the reaction with some nucleophiles, such as amines,2) hydroxylamines,3) ureas,4) Grignard reagents5) and sodium borohydride,6) the reaction sites of 3-amino-2-en-1-ones depend on the substituent group on nitrogen atom. That is, nucleophilic attack occurred predominantly on C-3 carbon in the case of 3-amino-2-en-1-one having an electron-donating group on nitrogen, while nucleophilic attack on C-1 carbon occurred in the case of an electron-withdrawing group. Although the reaction of 3-amino-2-en-1-ones having various substituents on nitrogen with nucleophiles are much applicable to the synthesis of various compounds, there is no quantitative work about its reactivity. Therefore, we wish to clarify the reactivity of 3-amino-2-en-1-ones having various substituents group on nitrogen atom.

Benary reported7) that some 3-amino-2-en-1-ones gave 1-phenylpyrazole derivatives by the treatment with phenylhydrazine. In the similar way, N-substituted 4-amino-3-penten-2-ones (1) gave 3,5-dimethyl-1-phenylpyrazole (3) without any by-product. Since the starting materials and the product were fairly stable and easily analyzable by vpc, we chose (1 and 2) and phenylhydrazine as

Table 1

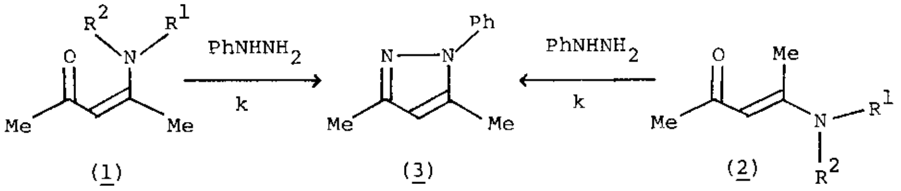
The Reaction Rates of (1) and (2)

Compound			Temperature	Rate constant
	R^1	R^2	(°C)	(s^{-1})
1-b	Me	H	50	3.6×10^{-4}
1-c	Bu	H	50	2.6×10^{-4}
2-a	Me	Me	70	3.5×10^{-4}
2-b	$(CH_2)_4$		50	1.6×10^{-4}
			70	4.5×10^{-4}
2-c	$(CH_2)_5$		70	3.1×10^{-4}

Table 2

The Values of Sr and the Reaction Rates at 70°C

Compound			Rate constant	Sr^{Nu}		Sr^E		
	R^1	R^2	(s^{-1})	C-2	C-4	O	C-3	N
1-e	p-MeO-C_6H_4	H	2.8×10^{-4}	1.2621	1.3383	0.9230	1.7959	3.9437
1-f	p-Me-C_6H_4	H	2.7×10^{-4}	1.2623	1.3386	0.9125	1.7634	3.7799
1-g	Ph	H	2.4×10^{-4}	1.2684	1.3490	0.9005	1.7233	3.5649
1-h	p-Br-C_6H_4	H	1.8×10^{-4}	1.2662	1.3451	0.9064	1.7426	3.6669
1-i	p-Cl-C_6H_4	H	1.8×10^{-4}	1.2665	1.3457	0.9054	1.7394	3.6498
1-j	p-EtO_2C-C_6H_4	H	1.5×10^{-4}	1.2854	1.3746	0.8889	1.6803	3.3365
1-k	p-O_2N-C_6H_4	H	1.1×10^{-4}	1.3055	1.4000	0.8824	1.6553	3.2094



(1) (3) (2)

a) $R^1=R^2=H$
b) $R^1=Me,\ R^2=H$
c) $R^1=Bu,\ R^2=H$
d) $R^1=Ac,\ R^2=H$
e) $R^1=MeOC_6H_4,\ R^2=H$
f) $R^1=MeC_6H_4,\ R^2=H$
g) $R^1=Ph,\ R^2=H$
h) $R^1=BrC_6H_4,\ R^2=H$
i) $R^1=ClC_6H_4,\ R^2=H$
j) $R^1=EtO_2CC_6H_4,\ R^2=H$
k) $R^1=O_2NC_6H_4,\ R^2=H$

a) $R^1=R^2=Me$
b) $R^1,R^2=(CH_2)_4$
c) $R^1,R^2=(CH_2)_5$

3-amino-2-en-1-one and a nucleophile, respectively. The results in benzene are summarized in Table 1 and Table 2. The reaction of 4-amino-3-penten-2-one (1-a) was too fast to measure the reaction rate, while N-acetyl derivative (1-d) reacted too slowly. N-Disubstituted 4-amino-3-penten-2-ones (2-a, 2-b, and 2-c) were generally less reactive than monoalkyl substituted derivatives (1-b and 1-c). However, the configuration of mono-substituted derivatives was found to be cis8) and that of disubstituted ones trans by nmr spectra.2) From this reason, it seemed to be difficult to appreciate the difference of substituent on nitrogen atom, either electronically or sterically. Therefore, the reaction rates of p-substituted-4-amino-3-penten-2-ones were compared with the values of super-delocalizability (Sr) by HMO calculation.9) As a result, these reaction rates were not comparable to the values of Sr for a nucleophile, but for an electrophile (Table 2). Furthermore, the reaction was accelerated more than 6.5 times in the presence of acetic acid.

From these results, the rate determining step of this reaction was speculated to be the protonation on 3-amino-2-en-1-one moiety, and the attack of nucleophile and the cyclization may be very fast steps.

After all, it was conculuded that the electron-donating groups on nitrogen atom accelerated the reaction of 3-amino-2-en-1-ones with nucleophiles, especially in the presence of acid.

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8) These compounds show the nmr peak at over 10 ppm, which is assigned to be the NH proton having the hydrogen bond in cis-configuration.*)

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9) The parameters in HMO calculation were quoted from "Ryoshi Kagaku Nyumon", p 56, by T. Yonezawa, T. Nagata, H. Kato, A. Imamura, and K. Morokuma, Kagaku Dojin, Kyoto, Japan (1968).

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