References and Notes

1) For a review, see "N-Nitrosamines," ed. by J.P. Anselme, ACS Symposium series 101, American Chemical Society, Washington D.C., 1979.
2) Acetonitrile obtained commercially was distilled first from calcium hydride and then from phosphorus pentoxide after the treatment by the method reported [J.F. O'Donnell, J.T. Ayres, and C.K. Mann, *Anal. Chem.*, **37**, 1161 (1965)]. The acetonitrile thus purified seems to contain oxygen enough for the electrolysis of at least 50 mM of a particular N-nitrosamine to give the products in the yields described in the text.
3) In the present study, 0.5—5 mmol of the nitrosamines were subjected to electrolysis in 10, 50, or 100 ml of anolyte. No fundamental difference in the results was observed with the changes in the substrate concentration and in the volume of the electrolysis solution. The yields of the products were determined by GLC.
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A Ring Transformation of Uracil into the Pyrazole Ring System. Reinvestigation of the Reaction of 5-Formyluracils with Hydrazines

Cheng *et al.* reported that the reaction of 5-formyluracil (**1a**) with hydrazine hydrate in the presence of acetic acid gave 4-ureidomethylene-1*H*-5-pyrazolone (**3**). However, results of our reinvestigation revealed that the Cheng's compound (**3**) should be 4-ureidocarbonylpyrazole (**4a**). Application of this ring transformation to preparation of several 4-ureidocarbonylpyrazoles (**4b**—**f**) was also described.

Keywords——ring transformation; 5-formyluracil; 4-ureidocarbonylpyrazoles; ambident nucleophile; hydrazinolysis

Although hydrazinolysis of uracil derivatives into pyrazolones has been already known,[1] further studies on its application in synthesis have been little done and the reaction has been investigated only in particular areas such as the chemical modification of nucleic acids.[2]

Recently, we found a novel ring transformation of uracil into a benzene ring system.[3] Thus, treatment of 5-formyl-1,3-dimethyluracil (**1b**) with α-substituted acetone derivatives (C–C–C type of ambident nucleophile; X=$COCH_3$, $CONH_2$, C_6H_5, $CO_2C_2H_5$) in ethanolic sodium ethoxide afforded the corresponding ethyl 4-hydroxybenzoates (**2**). In this reaction, an intermediate A was first produced by a condensation of C_5-formyl group with acetone derivatives and then it gave **2** by an intramolecular nucleophilic attack at the 6-carbon. On the other hand, Cheng *et al.* reported[4] that the reaction of 5-formyluracil (**1a**) with hydrazine hydrate (N–N type of ambident nucleophile) gave 4-ureidomethylene-1*H*-5-pyrazolone (**3**)

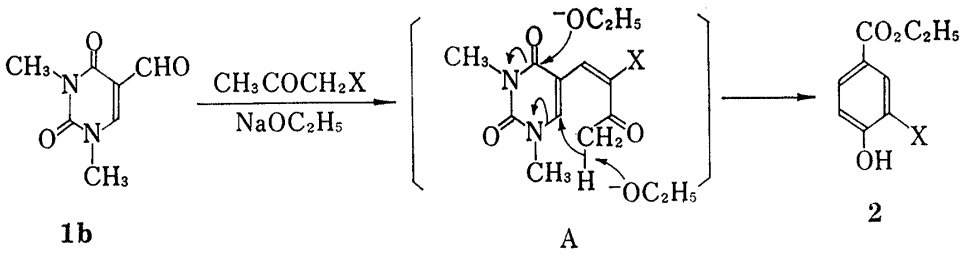
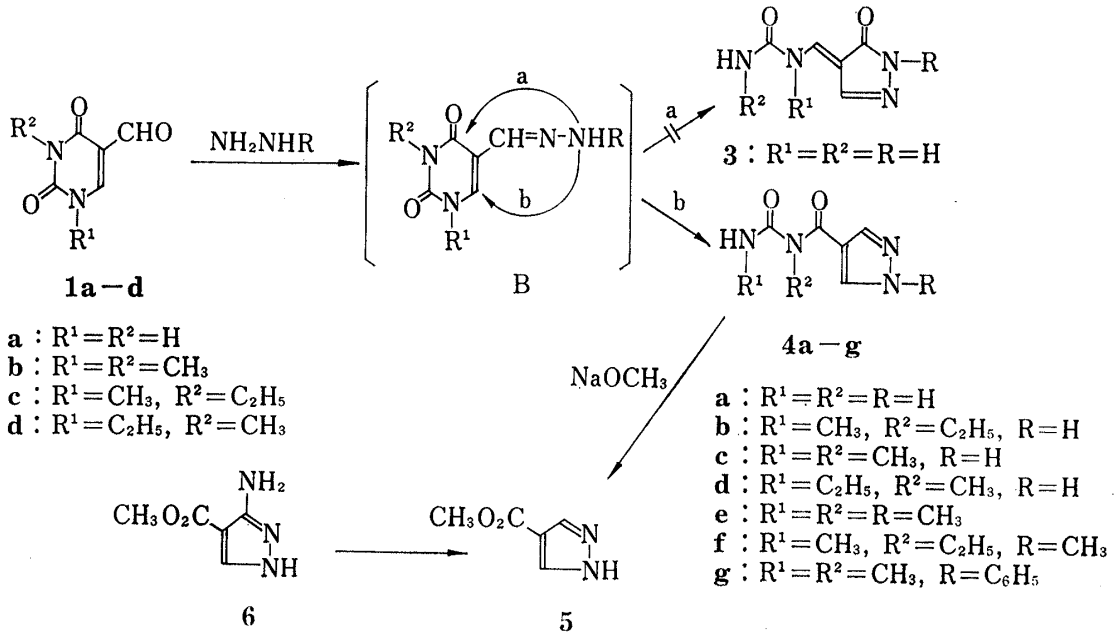


Chart 1

and they described that a hydrazone intermediate B was first produced which was transformed to **3** by an intramolecular nucleophilic attack at the 4-carbonyl carbon (Chart 2 path a). Now, the difference in attacking sites in the above two intermediates A and B led us to reinvestigate the reaction of 5-formyluracil derivatives (**1**) with hydrazines.

Thus, the reaction of **1a** with hydrazine hydrate under Cheng's conditions (in the presence of acetic acid in boiling water) gave the ring transformation product. Its spectral data satisfied both the Cheng's structure (**3**) and 4-ureidocarbonylpyrazole (**4a**) formed *via* a nucleophilic attack at the 6-carbon (path b). In order to elucidate the structure precisely, treatment of the ring transformation product with methanolic sodium methoxide was carried out and methyl 1*H*-pyrazole-4-carboxylate (**5**) was obtained in 89% yield. This compound (**5**) was identical with an authentic sample[5] prepared from methyl 3-amino-1*H*-pyrazole-4-carboxylate (**6**). This fact clearly showed that the Cheng's compound should be **4a**.



a : $R^1=R^2=H$
b : $R^1=R^2=CH_3$
c : $R^1=CH_3$, $R^2=C_2H_5$
d : $R^1=C_2H_5$, $R^2=CH_3$

a : $R^1=R^2=R=H$
b : $R^1=CH_3$, $R^2=C_2H_5$, $R=H$
c : $R^1=R^2=CH_3$, $R=H$
d : $R^1=C_2H_5$, $R^2=CH_3$, $R=H$
e : $R^1=R^2=R=CH_3$
f : $R^1=CH_3$, $R^2=C_2H_5$, $R=CH_3$
g : $R^1=R^2=CH_3$, $R=C_6H_5$

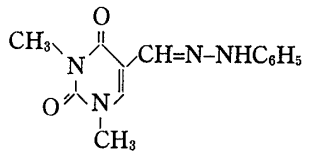
Chart 2

Further evidence for assigning a pyrazole structure to **4** was obtained by treatment of 3-ethyl-5-formyl-1-methyluracil (**1c**) with hydrazine hydrate giving the pyrazole (**4b**). Nuclear magnetic resonance (NMR) spectrum of **4b** reveals a doublet at 2.68 ppm due to NH-methyl protons which became a singlet after a deuterium oxide treatment. Treatment of the compound (**4b**) with sodium methoxide gave **5** in 83% yield.

The reaction sequence for the present ring transformation is also accounted for by involvement of the formation of the hydrazone intermediates B[6] followed by an intramolecular nucleophilic attack at position 6 of the uracil ring as discussed previously.[3]

Similar treatment of **1b** and 1-ethyl-5-formyl-3-methyluracil (**1d**) with hydrazine hydrate gave the corresponding 4-ureidocarbonylpyrazole derivatives (**4c** and **4d**). The use of methylhydrazine instead of hydrazine hydrate resulted in the formation of the 1-methylpyrazoles, *i.e.* **4e** and **4f** (see Table I). However, the treatment of **1b** with phenylhydrazine did not give the 1-phenylpyrazole (**4g**) but the corresponding phenylhydrazone (**7**) in 97% yield. Further treatment of **7** with sodium methoxide gave the expected methyl 1-phenylpyrazole-4-carboxylate (**8**) in 81% yield.

Out of those results, it is anticipated that the reaction of **1** with hydrazines provides a convenient method for preparing 4-ureidocarbonylpyrazoles and pyrazole-4-carboxylates.



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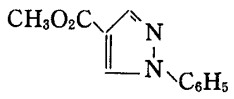

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Fig. 1

TABLE I. Reaction of 5-Formyluracils (**1**) with Hydrazines

Starting material	Hydrazine	Product	mp °C	Yield (%)
1a	NH_2NH_2	**4a**	274—277	69
1c	NH_2NH_2	**4b**	192—194	57
1b	NH_2NH_2	**4c**	224	48
1d	NH_2NH_2	**4d**	97—98	25
1b	NH_2NHCH_3	**4e**	97—98	73
1c	NH_2NHCH_3	**4f**	88—92	68
1b	$NH_2NHC_6H_5$	**7**	215—216	97

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6) The methylhydrazone of **1a** was isolated as an intermediate.[4]

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