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NOVEL UTILIZATION OF ORGANOSELENIUM COMPOUNDS.I. A FACILE TRANSFORMATION OF FUSED ISOSELENAZOLES TO FUSED PYRIDINES

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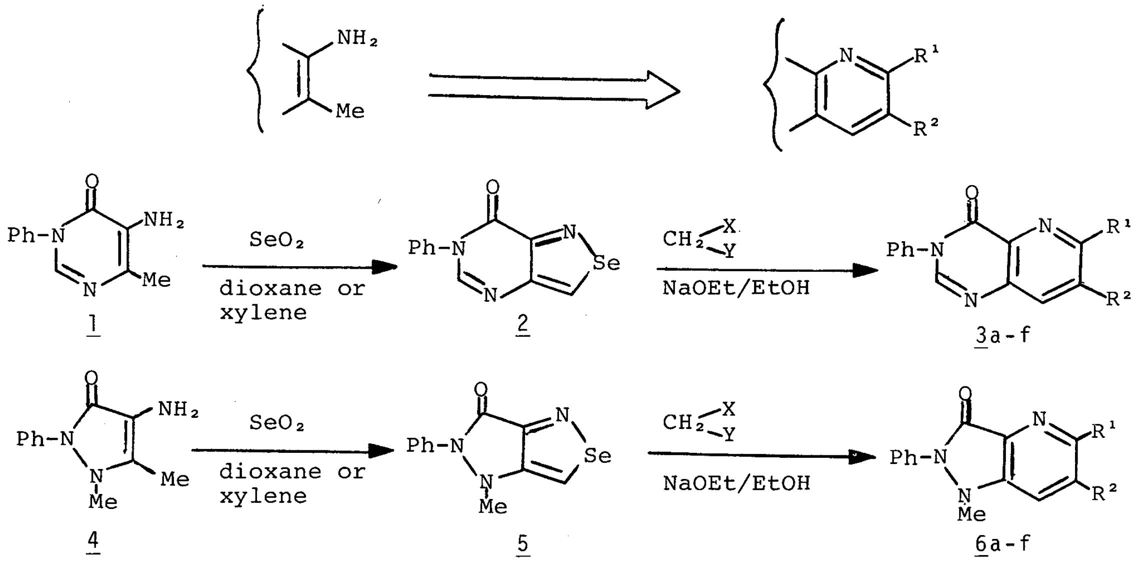
A facile transformation of 7-oxo-6-phenyl-6H-isoselenazolo[4,3-d]-pyrimidine (2) or 4,5-dihydro-4-methyl-6-oxo-5-phenyl-6H-pyrazolo[4,3-c]-isoselenazole (5) into pyrido[3,2-d]pyrimidines (3a-f) or pyrazolo[4,3-b]pyridines (6a-f) was carried out by reactions using active methylene compounds such as malononitrile, ethyl cyanoacetate, ethyl acetoacetate, ethyl malonate, and cyanoacetamide in the presence of a catalytic amount of sodium ethoxide in ethanol.

KEYWORDS——organoselenium compound; isoselenazole; deselenation; ring transformation; isoselenazolo[4,3-d]pyrimidine; pyrazolo[4,3-c]isoselenazole; pyrido[3,2-d]pyrimidine; pyrazolo[4,3-b]pyridine

Recently,functional group manipulation using inorgano- or organoselenium reagents has progressed greatly.[1,2,3,4] However, there have been no reports on the utilization of selenium-containing heterocycles to synthesize other useful heterocycles. We have studied the reaction of some fused isoselenazoles with active methylene compounds and found a facile transformation of fused isoselenazoles into fused pyridines which we report in this communication.

Previously we synthesized 7-oxo-6-phenyl-6H-isoselenazolo[4,3-d]pyrimidine[5](2) or 4,5-dihydro-4-methyl-6-oxo-5-phenyl-6H-pyrazolo[4,3-c]isoselenazole[6](5) from 5-amino-6-methyl-3-phenyl-4(3H)-pyrimidinone[7](1) or 4-aminoantipyrine[8](4) by reaction with selenium dioxide. It is said that organoselenium compounds are subject to a nucleophilic attack on selenium and selenium forms a weak σ bond which involves cleavage of C-Se.[1] Thus we examined the reactivity of the above fused isoselenazoles (2,5). The reaction of 2 or 5 with carbanions, which were generated from malononitrile, ethyl cyanoacetate, ethyl acetoacetate, ethyl malonate, and cyanoacetamide in the presence of catalytic amount of sodium ethoxide in ethanol, was carried out to give 3a-f or 6a-f as depicted in Chart 1. The results are summarized in Table I and Table II. The reaction of 2 with ethyl cyanoacetate or ethyl acetoacetate gave 3b and 3c or 3e and 3f in the ratio of 43:8 or 31:7 respectively. Similarly the reaction of 5 with ethyl cyanoacetate gave two compounds, 6b and 6c, in a ratio of 58:31.

A typical experimental procedure is as follows: a mixture of 2 (1 mmol) and malononitrile (1 mmol) was refluxed for 3 h in 30 ml of absolute ethanol in the presence of a catalytic amount of sodium ethoxide. The resulting black insoluble substance (Se) was removed by filtration. The filtrate was concentrated in vacuo, and the residue was recrystallized from ethanol.



3a: R^1=NH_2, R^2=CN; 3b: R^1=NH_2, R^2=COOEt; 3c: R^1=OH, R^2=CN; 3d: R^1=NH_2, R^2=$CONH_2$; 3e: R^1=Me, R^2=COOEt; 3f: R^1=OH, R^2=Ac; 6a: R^1=NH_2, R^2=CN; 6b: R^1=NH_2, R^2=COOEt; 6c: R^1=OH, R^2=CN; 6d: R^1=NH_2, R^2=$CONH_2$; 6e: R^1=Me, R^2=COOEt; 6f: R^1=OH, R^2=COOEt

Chart 1

Table I. 6,7-Disubstituted 3-phenyl-3H-pyrido[3,2-d]pyrimidine-4-ones (3a-f)

Run	X-CH_2-Y	Compd. (Yield, mp[a)])	MS[m/z=M^+][b)]
1	NC-CH_2-CN	3a (45%, >300°C)	263
2	NC-CH_2-COOEt	3b (43%, >300°C), 3c (8%, >300°C)	310, 264
3	NC-CH_2-$CONH_2$	3d (42%, 297-298°C)	281
4	Ac-CH_2-COOEt	3e (31%, 147-148°C), 3f (7%, >300°C)	309, 281

Table II. 5,6-Disubstituted 1,2-Dihydro-1-methyl-2-phenyl-3H-pyrazolo[4,3-c]pyridine-3-ones (6a-f)

Run	X-CH_2-Y	Compd. (Yield, mp[a)])	MS[m/z=M^+][b)]
1	NC-CH_2-CN	6a (94%, 293-295°C)	265
2	NC-CH_2-COOEt	6b (58%, 208-210°C), 6c (31%, >300°C)	312, 266
3	NC-CH_2-$CONH_2$	6d (86%, >300°C)	283
4	Ac-CH_2-COOEt	6e (93%, 109-110°C)	311
5	EtOOC-CH_2-COOEt	6f (95%, 240-241°C)	313

a) Melting points are uncorrected. The products were recrystallized from ethanol.
b) Mass spectra were recorded on a JEOL JMS-DX 300.

The reaction mechanism in the formation of 3 or 6 from 2 or 5 seems to proceed as follows: The resonanced forms of fused isoselenazoles can be depicted as in Chart 2. The nucleophilic substitution reaction seems to take place initially at the carbon atom adjacent to selenium which has exceptionally low electron density. Rupture of the isoselenazole ring followed by deselenation and recyclization to the pyridine ring gives pyrido[3,2-d]pyrimidines (3) or pyrazolo[4,3-b]pyridines (6).

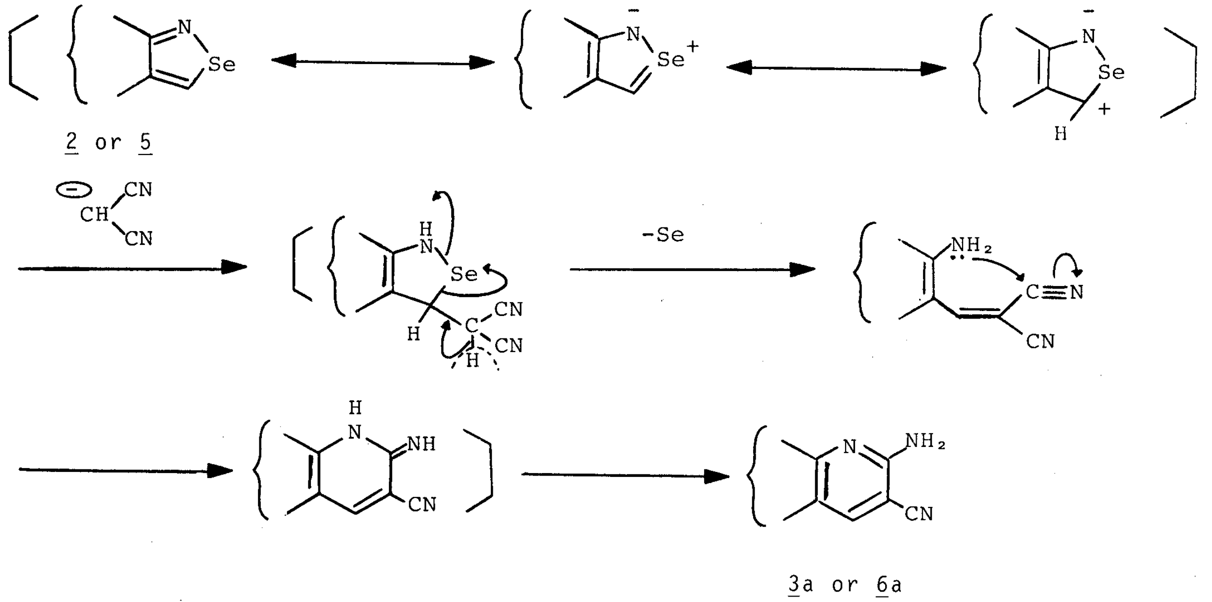


Chart 2

The above reaction is a useful method for the synthesis of fused pyridines if an amino group and a methyl group is in the vicinal position. We are now studing the application of this method to other heterocycles.

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