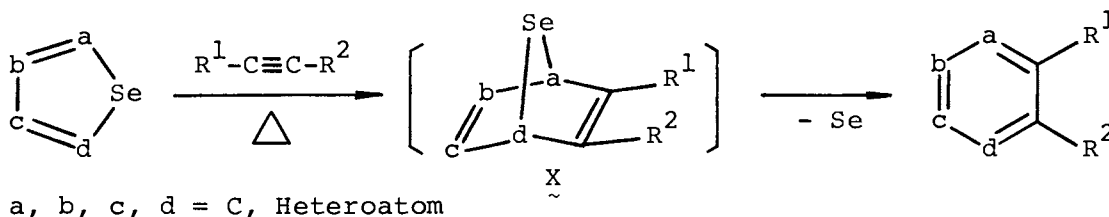


Novel Conversion of Selenium-containing Five-membered Aromatics
to Nitrogen-containing Six-membered Aromatics via Hetero
Diels-Alder Reaction with Acetylenic Dienophiles

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Treatment of selenium-containing five-membered hetero-
aromatics with acetylenic dienophiles afforded several
nitrogen heterocycles in good to moderate yields by using
thermal reaction conditions. These reactions were thought
to proceed through sequential [4+2] cycloaddition-selenium
extrusion pathway.

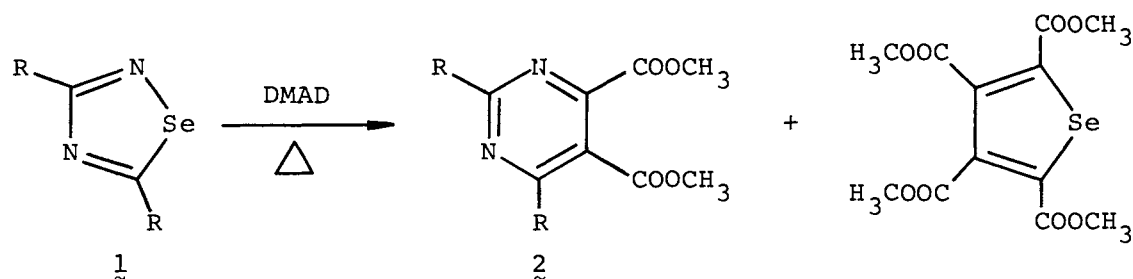
Recently Diels-Alder reactions of cyclic heterodienes have become one
of the most effective methods for the syntheses of various
heterocycles.^{1,2)} In all cases heteroatoms such as N, O, and S atoms in the
starting aromatic compounds behave as removable bridges of heterodienes
fixed in cisoid form.^{3,4)} However, synthetic applications of these
sequences to construct complicated compounds have been extremely limited
owing to their drastic reaction conditions. On the other hand, it was
assumed that selenium analogues of these substrates would behave as more
reactive cyclic heterodienes because of the weak C-Se or N-Se bond and
enhanced ring strain of the heterocycles,^{5,6)} and that the subsequent
heteroatom extrusion would be also improved.^{7,8)} From such a standpoint,
we have reported a novel preparation of primary selenoamides,⁹⁾ from which
several selenium-containing heterocycles such as 3,5-disubstituted
1,2,4-selenadiazoles were easily available by the reported



methods.¹⁰⁻¹²⁾ In this paper we would like to describe a novel conversion of selenium-containing heteroaromatics to the corresponding nitrogen heterocycles by treating with acetylenic dienophiles in thermal conditions.

A typical procedure in the reaction of 3,5-disubstituted 1,2,4-selenadiazoles 1 with dimethyl acetylenedicarboxylate (DMAD) is as follows. A 143 mg (0.5 mmol) of 3,5-diphenyl-1,2,4-selenadiazole (1a) and 710 mg (5.0 mmol) of DMAD was heated in autoclave to 150 °C for 12 h. The reaction mixture was then poured into CHCl₃, and the precipitated elemental selenium was separated by filtration. After removal of the solvent, the residue was separated by SiO₂ column chromatography to give dimethyl 3,5-diphenyl-5,6-pyrimidinedicarboxylate (2a) in 54% yield together with selenophene derivative¹³⁾ (38%) and the substrate 1a (14%). In contrast with their sulfur analogues,¹⁴⁾ this procedure was successfully applied to various 3,5-disubstituted 1,2,4-selenadiazoles 1 possessing not only aromatic but also aliphatic and heteroatomic substituents. The structures of all products were confirmed by ¹H NMR, IR, MS, and elemental analysis, and by the comparison of their physical properties with those reported by Cherkasov et al.¹⁵⁾ All results of the reactions of 1,2,4-selenadiazoles 1 with DMAD or methyl propiolate are shown in Table 1.

Table 1. Conversion of 3,5-disubstituted 1,2,4-selenadiazoles to pyrimidine derivatives



| Run | R | | Solvent | Temp/°C | Time/h | Yield/% of <u>2</u> |
|-----|--|-----------|-----------------------|---------|--------|---------------------|
| 1 | C ₆ H ₅ | <u>1a</u> | neat | 150 | 12 | 54 |
| 2 | 4-CH ₃ C ₆ H ₄ | <u>1b</u> | neat | 150 | 10 | 46 |
| 3 | 4-CH ₃ OC ₆ H ₄ | <u>1c</u> | CHCl ₃ | reflux | 110 | 31 |
| 4 | 4-CH ₃ OC ₆ H ₄ | <u>1c</u> | neat | 150 | 10 | 73 |
| 5 | 4-ClC ₆ H ₄ | <u>1d</u> | neat | 150 | 12 | 17 |
| 6 | n-C ₃ H ₇ | <u>1e</u> | benzene ^{a)} | 150 | 15 | 24 |
| 7 | n-C ₅ H ₁₁ | <u>1f</u> | xylene | reflux | 11 | 74 |
| 8 | n-C ₇ H ₁₅ | <u>1g</u> | xylene | reflux | 43 | 87 |
| 9 | PhCH ₂ S | <u>1h</u> | toluene | reflux | 14 | 19 |
| 10 | (CH ₃) ₂ N | <u>1i</u> | benzene | r. t. | 2 | 99 |

a) The reaction was carried out in autoclave.

The reaction of $\underline{1i}$ ($R=(CH_3)_2N$) with DMAD proceeded at room temperature to afford the product $\underline{2i}$ in almost quantitative yield, and even a less reactive dienophile such as methyl propiolate reacted with $\underline{1i}$ at 120 °C for 12 h (in benzene in autoclave) to afford $\underline{3}^{16}$ in quantitative yield in a highly regioselective manner as was expected from FMO theory. In contrast, phenylacetylene, methyl 3-phenylpropiolate, maleic anhydride, or TCNE, did not react at all below 200 °C, and prolonged reaction time in the elevated temperature caused decomposition of the starting material $\underline{1a}$ to benzonitrile and 2,4,6-triphenyl-1,3,5-triazine. From these results, it was easily assumed that a combination of heterodienes with higher HOMO energy levels and dienophiles with lower LUMO levels was actually needed for the conversion of 1,2,4-selenadiazoles $\underline{1}$ to the corresponding pyrimidines $\underline{2}$. Thus, the primary stage of the reaction was regarded as a typical [4+2] cycloaddition reaction with an ordinary electron-demand, and the resulting selenium-containing bicyclic intermediate \underline{X} was thought to cause facile selenium-extrusion to afford pyrimidine $\underline{2}$ and elemental selenium.

Similar reactions were also carried out by treatment of 3,4-diphenyl-1,2,5-selenadiazole ($\underline{4}$) or 2-substituted 4-phenyl-1,3-selenazoles $\underline{6}$ with DMAD, and in all cases the corresponding pyrazine $\underline{5}$ or pyridine derivatives $\underline{7}$, were obtained in moderate yields. These results are also shown in Scheme 1 and Table 2.

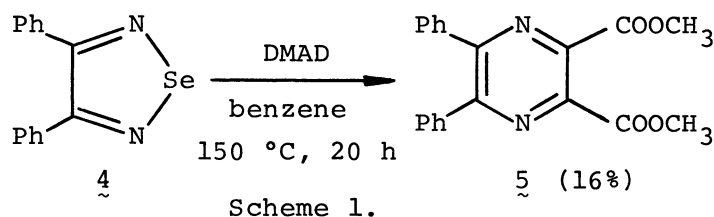
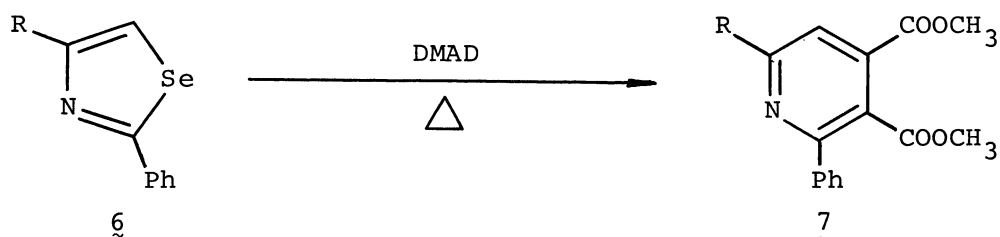


Table 2. Conversion of 2-Substituted 4-Phenyl-1,3-Selenazoles to Pyridine Derivatives^{a)}



| Run | R | | Solvent | Temp/°C | Time/h | Yield/% of $\underline{7}$ |
|-----|--|------------------|---------|---------|--------|----------------------------|
| 1 | C ₆ H ₅ | $\underline{6a}$ | neat | 100 | 78 | 47 |
| 2 | C ₆ H ₅ | $\underline{6a}$ | benzene | 150 | 82 | 53 |
| 3 | 4-CH ₃ C ₆ H ₄ | $\underline{6b}$ | benzene | 150 | 24 | 55 |
| 4 | 4-CH ₃ OC ₆ H ₄ | $\underline{6c}$ | benzene | 150 | 24 | 55 |
| 5 | 4-ClC ₆ H ₄ | $\underline{6d}$ | benzene | 150 | 24 | 41 |

a) The reaction was carried out in autoclave.

