Double 1,3-Dipolar Cycloaddition Reaction of 3-Phenylsydnone with 1,3-Dienes

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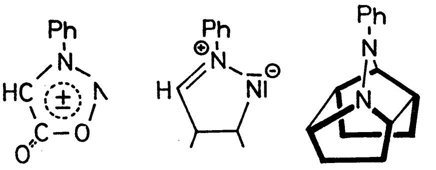
Thermal reaction of 3-phenylsydnone with isoprene or 2,3-dimethylbutadiene gave 2-methyl- or 2,6-dimethyl-7-phenyl-1,7-diazatricyclo [2.2.1.0^{2,6}]heptane, together with 3-isopropenyl-1-phenylpyrazole. The former is the product of the double 1,3-dipolar cycloaddition. A similar reaction with 1,3-butadiene gave only 3-vinyl-1-phenylpyrazole.

3-Phenylsydnone (**1**) and other sydnone derivatives have been found by Huisgen and his co-workers$^{1)}$ to undergo 1,3-dipolar cycloaddition with both electron-deficient and -abundant olefins and acetylenes.

Of the many reactions reported by Huisgen, there is only one case in which one molecule of **1** adds to two molecules of dipolarophile, *i.e.*, acenaphthylene. The intermediate of this reaction is thought to be the azomethine-imine (**2**), which has been known to behave as a 1,3-dipole.

Recently, the intramolecular case of this double 1,3-dipolar cycloaddition reaction has been reported by Weintraub$^{2)}$; he used 1,5-cyclooctadiene as the dipolarophile. The tetracyclic product (**3**) is composed of four rings, two of which are formed by the two 1,3-dipolar cycloadditions; the other two, indicated by the bold lines, may be considered to be due to the concomitant cyclization reactions.



(**1**) (**2**) (**3**)

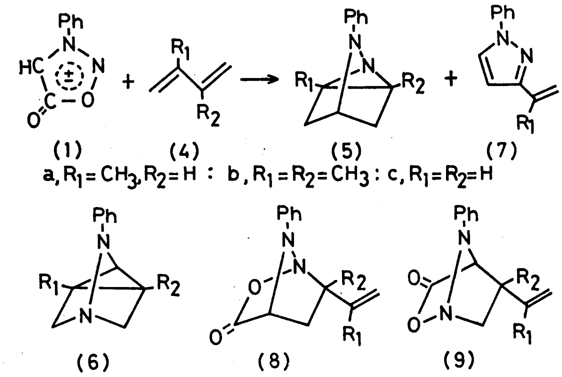
Formulas.

The formation of alicyclic rings has been discussed in terms of two kinetic factors: energy (strain) and entropy (probability) factors.$^{3)}$ The above-mentioned cyclization forming the five-membered rings is governed mainly by energy factor.$^{4)}$ The other factor contributes to the case of cyclopropane-ring formation. Therefore, if we utilize 1,3-dienes as the diene component, the intramolecular capture of the reactive intermediate can be expected to be easily done by the concomitant cyclopropane-ring formation. This prediction$^{5)}$ was substantiated in the case of the Diels-Alder reactions of 2-pyrone derivatives with 1,3-dienes.$^{6)}$

The aim of the present study is to apply this principle to the 1,3-dipolar cycloaddition reaction and to obtain the diazanortricyclenes.

Heating of a solution of **1** and isoprene (**4a**) in ethyl acetate at 150 °C for 24 hr, followed by flash distillation, gave an oily mixture which was shown by GLC analysis to consist of two components present in the ratio of about 1: 1. Preparative GLC separation allowed their isolation.

The faster-moving fraction (**5a**) gave the correct analysis for $C_{12}H_{14}N_2$. In the NMR spectrum, the absence of any signal of olefinic protons except those of aromatic protons indicates the tricyclic structure, while the absence of any prominent coupling pattern indicates the diazanortricyclyl system, since the reported coupling constants in the nortricyclyl system$^{7)}$ are small (1.5 Hz at most). The two methine protons adjacent to nitrogen atom clearly exclude the alternative structure, **6a**.



Scheme.

The slower-moving fraction (**7a**) showed the NMR signals of only aromatic and olefinic protons, except for the methyl protons. The magnitude of the coupling constants and the chemical shifts of the pyrazole ring protons revealed the 3-substituted 1-phenylpyrazole structure.$^{8)}$ The isopropenyl substituent could be derived from the olefinic proton signals, exhibiting patterns characteristic of *exo*-methylene signals.$^{9)}$

A similar reaction of **1** and 2,3-dimethylbutadiene (**4b**) at 150 °C for 6.5 hr gave, after distillation, an oily mixture consisting of two components in the ratio of 4: 1.

The isolation of the major component by preparative GLC revealed the major component to be identical with the pyrazole, **7a**, obtained in the reaction with **4a**. The formation of **10a** in the present reaction is explained by the elimination of a methane molecule after the first decarboxylation. This apparently unusual reaction is not without precedent in the 1,3-dipolar cycloaddition reaction.$^{10)}$

The minor product was proved to have a tricyclic structure (**5b**).

In the reaction of **1** with butadiene (**4c**), prepared *in situ* from sulfolene, at 150 °C for 47 hr, we could not obtain the tricyclic product (**5c**); only 1-phenyl-3-vinylpyrazole (**7c**) could be isolated.

From these structures of the products, it was concluded that the first 1,3-dipolar addition step gave, regioselectively, the adduct (**8**) and that no product originating from an alternative intermediate (**9**) was found. This regioselectivity is in the same line as the 1,3-dipolar cycloaddition reaction of **1** with stilbene[1)] and is not in conflict with the prediction made by the perturbation molecular orbital methods of Bastide[11)] and of Houk.[12)]

Our initial attempt has been successful, although the yield is far from satisfactory. In these reactions it was not possible to by-pass the formation of tarry material, and no optimization of the yield of the tricyclic products was undertaken.

Experimental

The NMR spectra were measured in CCl_4 solution, using TMS as the internal standard. The mass spectra (MS) were obtained at 70 eV. GLC was performed at the column temperature of 130 °C with a Shimadzu GC-4AIT apparatus with a 3 mm × 1 m column packed with 10% High Vacuum Silicone Grease on Chromosorb W (80—100 mesh).

Reaction of 1 with Isoprene (4a). A solution of 1.00 g (6.18 mmol) of **1** and 0.48 g (12.4 mmol) of isoprene (**4a**) in ethyl acetate (10 ml) was heated in a pressure bottle at 150 °C for 24 hr. After evaporation of the solvent, bulb-to-bulb distillation (oven temperature 150—180 °C, 3 mm) gave an oily mixture (1.15 g) which consisted of two components in the ratio of about 1 : 1. These substances were separated by preparative GLC.

The first eluate (**5a**); IR: 1601, 1500, 752, and 690 cm^{-1}. NMR: δ 7.0 (m, 5H, Ph), 1.48 (s, 3H, CH_3), 1.4 (m, 4H, 2 × CH_2). 2.24 (s, 1H, CH–N), and 3.83 (broad s, 1H, CH–N); MS: *m/e* 186 (M^+, 31), 105 (57), 81 (67), 79 (36), 77 (100%). Found: C, 77.34; H, 7.56; N, 14.84%. Calcd for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58; N, 15.04%.

The second eluate (**7a**): IR; 1516, 1500, 1341, 1280, 1146, 942, 891, 750, 692 cm^{-1}; UV: λ_{max}^{MeOH} 276 nm (ε 18000); MS: *m/e* 185 ($M^+ + 1$, 21), 184 (M^+, 100), 183 (43), 169 (23), 81 (20), 77 (38); NMR: δ 7.77 (d, 2.5 Hz, 1H), 6.47 (d, 1H, 2.5 Hz) (pyrazole), 7.0—7.9 (m, 5H, Ph–), 5.47 (m, 1H), 5.05 (m, 1H) (CH_2=), and 2.20 (s, 3H, CH_3) ppm. Found: C, 78.15; H, 6.72; N, 15.14%. Calcd for $C_{12}H_{12}N_2$: C, 78.23; H, 6.57; N, 15.21%.

Reaction of 1 with 2,3-Dimethylbutadiene (4b). A solution of 1.00 g of **1** (6.18 mmol) and 1.01 g (12.4 mmol) of **4b** in ethyl acetate (10 ml) was heated in a pressure bottle at 150 °C for 6.5 hr. Distillation gave an oily mixture (441 mg) which consisted of two components in the ratio of 4 : 1. These substances were separated by preparative GLC.

The major substance was identified as **7a**, by comparison of its IR, NMR, MS, and the retention time of GLC with those of the afore-mentioned product.

The minor substance, **5b**: MS: *m/e* 200 (M^+, 33), 105 (35), 95 (100), 77 (83), 67 (40%); NMR: δ 7.0 (m, 5H, Ph–), 3.80 (m, 1H), 1.4 (m, 4H, 2 × CH_2), 1.42 (s, 6H, 2 × CH_3) ppm. Found: C, 77.67; H, 7.91; N, 13.71%. Calcd for $C_{13}H_{16}N_2$: C, 77.96; H, 8.05; N, 13.99%.

Reaction of 1 with Butadiene (4c). A solution of 231 mg (1.42 mmol) of **1**, 252 mg (2.14 mmol) of 3-sulfolene and a trace of hydroquinone in ethyl acetate was heated in a pressure bottle at 150 °C for 47 hr. Distillation gave an oily mixture (102 mg; 1 : 1). One components was **7c**. The other was an unidentified hydrocarbon, probably originating from **4c**.

7c; MS: *m/e* 170 (M^+, 100), 169 (78), 152 (27), 149 (45), 77 (36%); NMR: δ 7.1—7.7 (m, 5H, Ph–), 7.80 (d, 3.1 Hz, 1H) and 6.48 (d, 3.1 Hz, 1H) (pyrazole), 6.76 (q, 11.0 and 17.8 Hz, 1H), 5.70 (q, 17.8 and 1.6 Hz, 1H), 5.30 (q, 11.0 and 1.6 Hz, 1H). Found: C, 77.66; H, 5.78; N, 16.70%. Calcd for $C_{11}H_{10}N_2$; C, 77.62; H, 5.92; N, 16.46%.

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4) The genuine energy factor should be considered only in the case of 1,5-hexadiene, since 1,5-cyclooctadiene is considered to be controlled by both energy and entropy factors due to the ethylene bridging of 1,5-hexadiene.

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