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Studies on Reactions of Isoprenoids. V.[1] 1,3-Dipolar Cycloaddition Adducts of Myrcene with Benzonitrile Oxide

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In continuing our previous study on the diene reactivity of myrcene,[1] this paper deals with the reactivity of each double bond in myrcene with benzonitrile oxide. Although several 1,3-dipolar cycloaddition reactions with butadiene and its derivatives have been reported,[2,3] there seems no report concerning the 1,3-dipolar cycloaddition reactions with myrcene, 7-methyl-3-methylene-1,6-octadiene.

Results and Discussion

The 1,3-dipolarophilicity of myrcene toward several 1,3-dipoles such as diazomethane, diphenylnitrilimine, phenyl azide, tosyl azide, and benzonitrile oxide was examined, among which, however, only benzonitrile oxide showed enough reactivity to give the corresponding adducts. Myrcene was treated with benzonitrile oxide in refluxing ether and the reaction products were purified on a silica-gel column to give four products, I—IV as shown in Table 1.

As seen from this table, all of these products had the composition corresponding to 1 : 2-adducts. It is interesting that neither 1 : 1-adduct nor 1 : 3-adduct was obtained in the reaction using a 1 : 1-molar ratio[4] of myrcene to benzonitrile oxide, though some of the butadiene derivatives are known to give a 1 : 1-adduct with benzonitrile oxide.[3] This fact might suggest that the reactivity of the three double bonds in myrcene with benzonitrile oxide discriminates an isolated double bond from conjugated ones in the examined conditions as will be supported by the following structural

TABLE 1. 1,3-DIPOLAR CYCLOADDUCTS OF MYRCENE WITH BENZONITRILE OXIDE

Compd.	Mp(°C)	Yield[a] (%)	Formula	Anal. (%) Calcd C	Calcd H	Calcd N	Found C	Found H	Found N
I	113—114	2.0	$C_{24}H_{26}O_2N_2$	76.97	7.00	7.48	77.24	7.05	7.42
II	120—122	0.08	$C_{24}H_{26}O_2N_2$	76.97	7.00	7.48	77.12	7.02	6.79
III	139—141	1.2	$C_{24}H_{26}O_2N_2$	76.97	7.00	7.48	77.24	7.23	7.48
IV	149—151	11.5	$C_{24}H_{26}O_2N_2$	76.97	7.00	7.48	77.36	7.23	7.13

a) The molar ratio of myrcene to benzonitrile oxide was 1 : 1 and the yield was based on benzhydroxamoyl chloride from which benzonitrile oxide was generated.

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1) Part IV of this series: T. Sasaki, S. Eguchi and T. Ishii, submitted to *J. Org. Chem.*

2) For a recent review on 1,3-dipolar cycloadditions, see R. Huisgen, R. Grashey and J. Sauer, "Cycloaddition Reactions of Alkenes" in "The Chemistry of Alkenes," ed. by S. Patai, Interscience Publisher, New York, N. Y,. (1964), pp. 806—978.

3) About benzonitrile oxide, see a) A. Quilico, P. Grunanger and R. Mazzini, *Gazz. Chim. Ital.*, **82**, 349 (1952); *Chem. Abstr.*, **48**, 2039d (1954); b) V. N. Chistokletov and A. T. Troshchenko, *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk*, **1963**, 147; *Chem. Abstr.*, **59**, 13960h (1963).

4) No 1 : 3-adduct was obtained even in the reaction using a 1 : 2-molar ratio of myrcene to benzonitrile oxide.

elucidation of the four adducts.

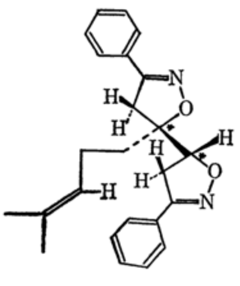
The structure of I was assigned as A or B on the basis of its NMR spectrum which had the signals at τ 2.10—2.80 (10 H, m, two phenyl protons), 4.80 (1 H, broad s, C=CH), 5.02 (1 H, unsymmetrical t, J=8.0 Hz, O–C$\underline{H}$CH$_2$– in an isoxazoline ring), 6.54 (2 H, d, J=8.0 Hz, O–CHC$\underline{H}_2$– in an isoxazoline ring), 6.58 (2 H, d, J=3.0 Hz, –CH$_2$– in an isoxazoline ring),[5] 7.60—8.03 (4 H, complex m, –CH$_2$CH$_2$–), 8.28 and 8.35 (6 H, s, C=C(CH$_3$)$_2$).

The structure of II was assumed to be similar to that of I, since its infrared spectrum was superimposable with that of II and the R_f values of I and II on TLC[6] examinations were exactly the same value of 0.43.

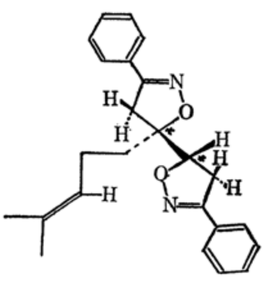
The structure of III and IV were also assignable as A or B from their NMR data; III had the signals at τ 2.20—2.78 (10 H, m, two phenyl protons), 4.81 (1 H, broad s, C=CH), 5.04 (1 H, t, J=8.0 Hz, OC$\underline{H}$CH$_2$– in an isoxazoline ring), 6.56 (2 H, d, J=8.0 Hz, OCHC$\underline{H}_2$– in an isoxazoline ring), 6.64 (2 H, d, J=3.0 Hz, –CH$_2$– in an isoxazoline ring), 7.65—8.10 (4 H, complex m, –CH$_2$CH$_2$–), 8.30 and 8.37 (6 H, s, C=C(CH$_3$)$_2$); IV had the signals at τ 2.10—2.70 (10 H, m, two phenyl protons), 4.85 (1 H, broad s, C=CH), 5.04 (1 H, unsymmetrical t, J=7.5 Hz, OC$\underline{H}$CH$_2$– in an isoxazoline ring), 6.57 (2 H, unsymmetrical d, J=7.5 Hz, OCHC$\underline{H}_2$– in an isoxazoline ring), 6.60 (2 H, s, –CH$_2$– in an isoxazoline ring), 7.54—8.10 (4 H, complex m, –CH$_2$CH$_2$–), 8.27 and 8.35 (6 H, s, C=C(CH$_3$)$_2$).

The infrared spectra of I—IV were very similar one another, I and II exhibiting absorption bands at 1600, 1570, 1500, 920, 860, 763, and 691 cm^{-1}, and III and IV, at 1600, 1570, 1500, 940, 920, 900, 860, 764, and 693 cm^{-1}. From these data, I and II could be distinguishable from III and IV, since the former group had only one band at 920 cm^{-1} and the latter, three bands at 940, 920, and 900 cm^{-1} in fingerprint regions. On the other hand, the results of TLC[6] examinations of I—IV indicated also the same discrimination[7] in I—IV.

The two possible structure A and B for the isolated four 1 : 2-adducts could now be possibly correlated with the presence of two groups, I and II, and III and IV, in these adducts. However, the observed subtle differences in their infrared and NMR spectra (Fig. 1), and R_f values on TLC were unsatisfactory to distinguish them.[8]



A



B

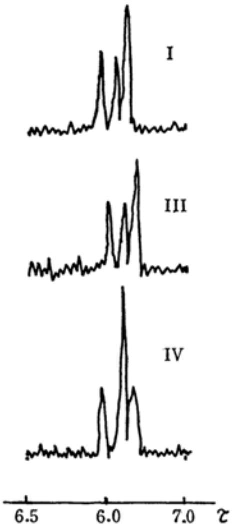


Fig. 1. NMR spectra of I, III, and IV in CDCl$_3$ at 60 Mc. Methylene protons signals of isoxazoline rings.

The isolation of the four 1 : 2-adducts could be explained by the presence of the two asymmetric

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[5] In a strict sense, this signal should be analyzed as an AB q, although both outer signals of an AB q of I at this region were very weak and they were almost hidden in noises as shown in Fig. 1. Only in the spectrum of I, the value of $J_{\mathrm{AB}/\Delta\tau}=0.86$ for this q could be obtained.

[6] TLC (Thin Layer Chromatography) was carried out by using silica-gel (Wakogel, B-5) plate, benzene as a developing solvent, and iodine as a developing reagent.

[7] The R_f values of III and IV on TLC were same each other and 0.32 which was slightly smaller than those (0.43) of I and II.

[8] A conjecture that I and II may correspond to an A structure and III and IV, to a B structure, will be favored by the facts that the combined yield of I and II was much lower than that of III and IV, and melting points of I and II were lower than those of III and IV, since A is assumed to be less stable than B because of the electrostatic repulsions of two oxygen atoms.

[9] All melting points were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. Microanalyses were carried out on a Yanagimoto C. H. N. Corder Model MT-1. The infrared spectra (KBr) were recorded on a JASCO Model IR-S infrared spectrophotometer and NMR spectra were obtained in CDCl$_3$ with a Hitachi high-resolution NMR spectrometer Model H-6013 at 60 Mc. All NMR data are reported in τ values relative to TMS as an internal standard, and singlet peaks are designated as s, doublet as d, triplet as t, and so on.

carbons in both A and B, which are responsible for diastereoisomers.

Experimental[9]

Reaction of Myrcene with Benzonitrile Oxide. A mixture of 1.50 g (0.011 mol) of myrcene and benzonitrile oxide prepared from 2.0 g (0.013 mol) of benzhydroxamoyl chloride[10] and 1.6 g (0.016 mol) of triethylamine, in 50 m*l* of ether was refluxed for 16 hrs and the crude products were obtained as a sticky residue after removal of the solvent. Purification of the crude products on a silica-gel (Wakogel, C-100-200) column eluted with benzene afforded three main fractions. From the first fraction, crude myrcene was recovered and the second fraction was a mixture of I, II, III, and IV. From the third fraction, a mixture of III and IV was obtained (*ca.* 0.30 g). Further purifications of the second fraction on a silica-gel column afforded *ca.* 0.2 g of a mixture of I and II, and 0.20 g of a mixture of III and IV. Fractional recrystallizations of the mixture of I and II, and the combined mixture of III and IV (0.5 g) from benzene - *n*-hexane afforded finally analytically pure samples of I (0.050 g) as needles, II (0.002 g) as needles, III (0.030 g) as needles, and IV (0.300 g) as needles. Their yields, melting points, and analyses are summarized in Table 1.

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[10] M. H. Benn, *Can. J. Chem.*, **42**, 2313 (1964) and references cited therein.