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PREPARATION AND CYCLOADDITION REACTION OF 1-AMINO-2-AZABUTADIENE

Yujiro NOMURA, Yoshito TAKEUCHI, Shuji TOMODA, and Masato M. ITO
Department of Chemistry, College of General Education,
The University of Tokyo, Komaba, Meguro-ku, Tokyo 153

2-Methyl-N-(1-phenylvinyl)-1-(1-pyrrolidinyl)-1-propanimine (1), a new type of 2-azabutadiene, was readily prepared by thermolysis of 5,5-dimethyl-3-(1-phenylvinyl)-4-(1-pyrrolidinyl)-Δ^1-1,2,3-triazoline. Regioselective [4+2] cycloaddition reaction of 1 with some dienophiles afforded 2-isopropyl-6-phenylpyridine derivatives in decent yields.

Although a number of 2-azabutadienes have been isolated or generated in situ,[1] studies on their reaction as a heterodiene are very few. The only report dealing with the cycloaddition reaction of a 2-azabutadiene has been published by Aue and Thomas, who have investigated the reaction of 1-methoxy-N-(1-methylvinyl)ethanimine with dimethyl acetylenedicarboxylate (DMAD).[1d] In this paper we wish to report the preparation of a new 2-azabutadiene, 2-methyl-N-(1-phenylvinyl)-1-(1-pyrrolidinyl)-1-propanimine (1), by thermolysis of 5,5-dimethyl-3-(1-phenylvinyl)-4-(1-pyrrolidinyl)-Δ^1-1,2,3-triazoline (2), and its cycloaddition reaction with some dienophiles leading to pyridine derivatives.

The preparation of 1 was most simply achieved by heating a dimethyl-d_6 sulfoxide (DMSO-d_6) solution of 2, obtained from the cycloaddition reaction between α-azidostyrene and 1-(2-methyl-1-propenyl)pyrrolidine,[2] in an evacuated (10^{-6} Torr) NMR tube for 24 hours at 80 °C. Direct observation of the ^{1}H- and ^{13}C-NMR spectra unequivocally demonstrated the exclusive formation of 1. Table 1 collects the data pertinent to the structural confirmation of 1. In addition to a phenyl group and a 1-pyrrolidinyl moiety, the newly formed isopropyl group was indicated in ^{1}H-NMR spectrum both by the doublet at δ 1.04 (6H, J= 7 Hz) and by the septet at δ 3.01 (1H, J= 7 Hz). The two low-field protons, each of which appears as a singlet, were assigned to the terminal olefinic protons at C-5 (H^a and H^b). The structure was further supported by the study of the ^{13}C-NMR spectrum. The presence of three quaternary sp^2 carbons, one of which corresponds to the ipso

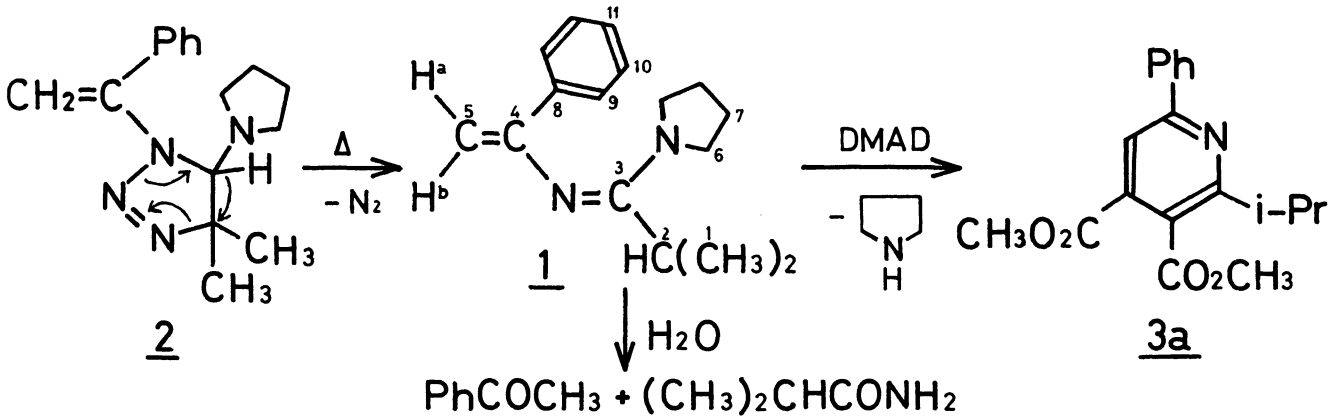


Table 1. NMR spectral data of 2-methyl-N-(1-phenylvinyl)-1-(1-pyrrolidinyl)-1-propanimine (1)

^{1}H-NMR			Assignment*	^{13}C-NMR	
δ**	Appearance (J, in Hz)	Area		δ**	Appearance***
1.04	d(J= 7)	6H	1	19.7	q
1.6-2.0	m	4H	7	24.8	t
3.01	sep(J= 7)	1H	2	29.9	d
3.2-3.7	m	4H	6	47.4	t
4.34	s	1H	H^b	93.0	t
4.94	s	1H	H^a 5		
7.2-7.7	m	5H	9	125.2	d
			11	127.2	d
			10	127.8	d
			8	139.8	s
			3	152.7	s
			4	159.4	s

* Numbers refer to the hydrogen or carbon atom (see previous page).

** Measured in DMSO-d_6 with TMS as an internal standard.

*** Splitting pattern determined by off-resonance decoupling.

carbon of the phenyl group, and one relatively high-field sp^2 carbon (δ 93.0) clearly suggested a tri-substituted azabutadiene skeleton. The location of three substituents was appropriately explained by the hydrolysis products, acetophenone and isobutyramide, as well as by the simplest decomposition mechanism involving 1,2-hydrogen shift in 2[3] as shown in the previous page.

The structure of 1 was further demonstrated by the reaction of 1 with DMAD. Thus, when 1 was treated with two molar amount of DMAD for 1 day at ambient temperature, dimethyl 2-isopropyl-6-phenylpyridine-3,4-dicarboxylate (3a)[4] was obtained in 37 % yield.

Table 2. Cycloaddition reactions of 1 with some dienophiles

Dienophile	Mol Ratio (Dienophile/1)	Time	Products	Yield (%)*
DMAD	2.1	1 day	3a	37
4a	2.0	2 days	3a	11
4b	2.0	2 days	3b	25
			5b	37
4c	1.1	5 days	3c**	44

* Yields are not optimized.

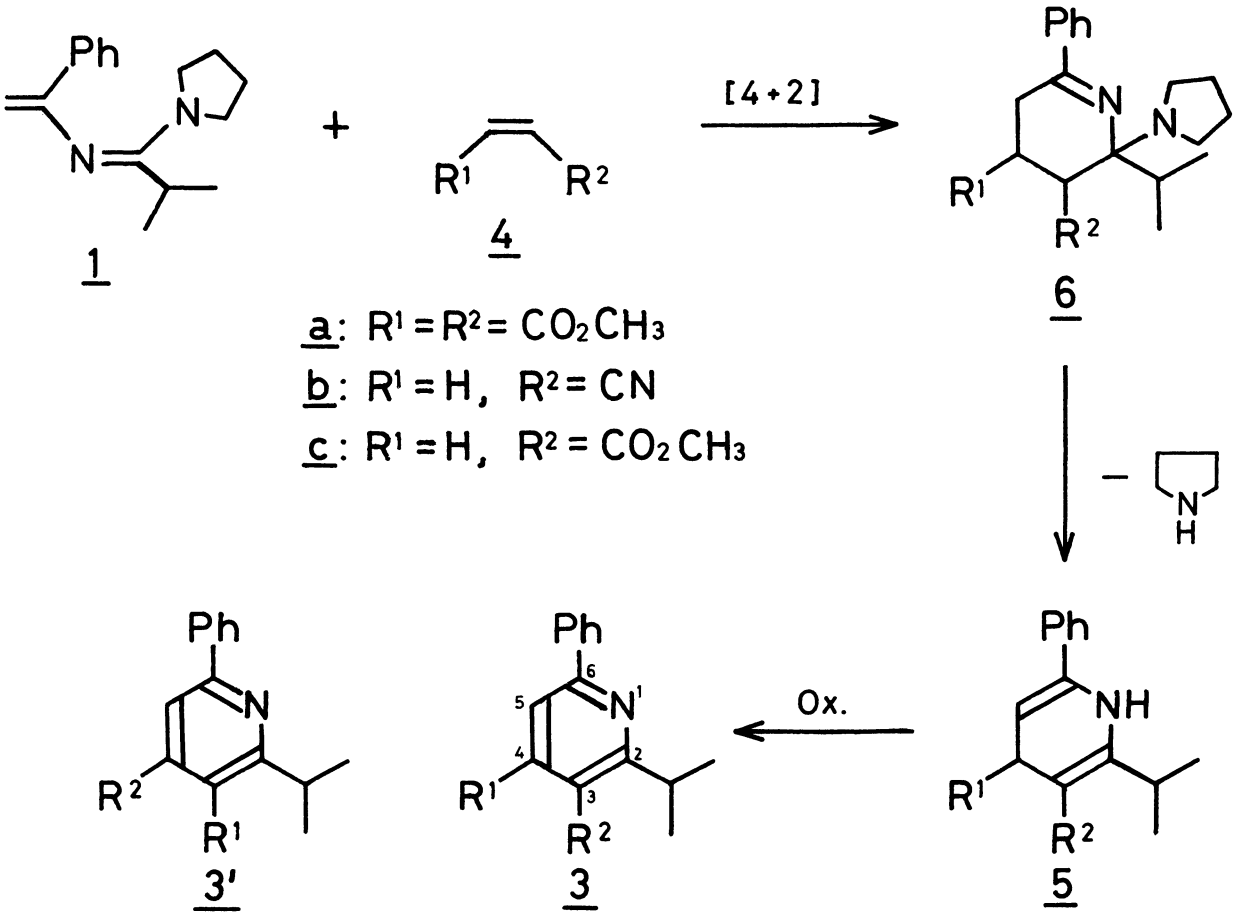
** In this case p-benzoquinone was used to oxidize the initial product.

The property of 1 as a heterodiene was further substanciated by [4+2] cycloaddition reaction with some olefinic dienophiles. The general procedure was as follows. A DMSO solution (30 ml) of 2 (1.0 g, 0.037 mol) was stirred at 80 °C for 24 hours. An appropriate dienophile (4a-c) was added to the mixture and stirred at room temperature. The usual aqueous workup followed by chromatographic separation using silica gel provided the pyridine derivatives (3a-c)[4,5] and the dihydropyridine derivative (5b).[6]

An intriguing aspect of these cycloaddition reactions involving 4b and 4c is the formation of only one of the possible regioisomers. Two regioisomeric structures (3 and 3') were expected, but only 3 was actually formed in both cases. In the case of 3b, for example, the two doublets at δ 7.68 and 7.92 in ^{1}H-NMR spectrum can be assigned to the two adjacent pyridine ring protons at C-5 and C-4. The large coupling constant between these protons (8 Hz) precluded the possibility of isomer 3'b in which only a small meta coupling constant should be observed.[7] This assignment was further supported by the general observation that the coupling constant between 4-H and 5(or 3)-H is the largest (about 8 Hz) in ordinary pyridine derivatives.

The formation of these pyridine derivatives (3a-c) can be rationalized by the mechanistic sequence shown in Scheme 1. The thermally allowed [4+2] cycloaddition reaction of 1 with an olefin would give an intermediate imine (6), which is deaminated to a dihydropyridine (5). Indeed, 3-cyano-1,4-dihydro-2-isopropyl-6-phenylpyridine (5b) was isolated from the reaction of 1 with acrylonitrile. This was smoothly oxidized into 3b upon exposure to air.

Scheme 1. A plausible mechanism for the formation of pyridines (3)



References and Notes

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2) Y. Nomura, Y. Takeuchi, S. Tomoda, and M. M. Ito, unpublished results.
3) Similar 1,2-hydrogen migration has been observed for the thermolysis of 3-aryl-4-morpholino-Δ^1-1,2,3-triazolines; R. Fusco, G. Bianchetti, and D. Pocar, Gazz. Chim. Ital., 91, 932(1961).
4) Mp 75.5-76.5 °C, M^+= 313 ($C_{18}H_{19}NO_4$), Anal. found(calcd.): C 69.16(69.00), H 6.11(6.11), N 4.52(4.47). IR(KBr): 1730, 1580, 1275, 1252, and 1085 cm^{-1}. ^{1}H-NMR($CDCl_3$): δ_{TMS} 1.40(d, J= 7 Hz, 6H), 3,09(sep, J= 7 Hz, 1H), 3.92(s, 3H), 3.95(s, 3H), 7.3-7.5(m, 3H), 7.9-8.1(m, 3H).
5) 3-Cyano-2-isopropyl-6-phenylpyridine (3b). Mp. 75.5-76.5 °C, M^+= 222 ($C_{15}H_{14}N_2$), Anal. found (calcd.): C 80.96(81.05), H 6.59(6.35), N 12.69(12.60). IR(KBr): 2205 and 1580 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ_{TMS} 1.47(d, J= 7 Hz, 6H), 3.64(sep, J= 7 Hz, 1H), 7.4-7.6(m, 3H), 7.68(d, J= 8 Hz, 1H), 7.92(d, J= 8 Hz, 1H), 8.0-8.2(m, 2H).
Methyl 2-isopropyl-6-phenylpyridine-3-carboxylate (3c). Mp 88.5-89.5 °C, M^+= 255 ($C_{16}H_{17}NO_2$), Anal. found(calcd.): C 75.45(75.27), H 6.81(6.71), N 5.71(5.49). IR(KBr): 1725, 1580, 1270, and 1080 cm^{-1}. ^{1}H-NMR($CDCl_3$): δ_{TMS} 1.42(d, J= 7 Hz, 6H), 3.90(s, 3H), 4.02(sep, J= 7 Hz, 1H), 7.3-7.5(m, 3H), 7.52(d, J= 8 Hz, 1H), 8.0-8.2(m, 3H).
6) 3-Cyano-1,4-dihydro-2-isopropyl-6-phenylpyridine (5b). Mp 107-108 °C, M^+= 224 ($C_{16}H_{17}N_2$), Anal. found(calcd.): C 80.19(80.32), H 7.16(7.19), N 12.20(12.49). IR(KBr): 3330, 2170, 1665, 1615, 1500, 1290, and 1110 cm^{-1}. ^{1}H-NMR($CDCl_3$): δ_{TMS} 1.21(d, J= 7 Hz, 6H), 3.10(sep, J= 7 Hz, 1H), 3.26(d, J= 3.5 Hz, 2H), 4.9(td, J= 3.5 and 1.7 Hz, 1H), 5.4(br, 1H), 7.32(s, 5H).
7) For example, in the case of pyridine[a] and 3-cyanopyridine,[b] the coupling constants between 4-H and 5(or 3)-H are 7.65 and 8.2 Hz respectively. Other ortho coupling constants are both about 4.8 Hz and the meta coupling constants do not exceed 2 Hz.
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