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# 5-Amino-1-vinyl-4,5-dihydro-1*H*-1,2,3-triazoles as a Source of 1-Amino-2-aza-1,3-butadiene[1]

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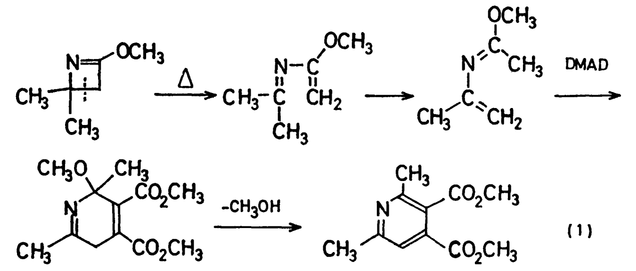
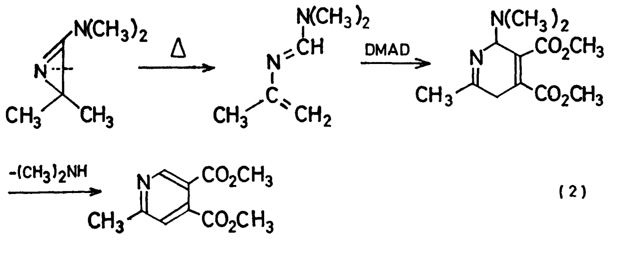
Thermolysis of 4,4-dimethyl-1-(1-phenylvinyl)-5-(1-pyrrolidinyl)-4,5-dihydro-1*H*-1,2,3-triazole gave 2-methyl-*N*-(1-phenylvinyl)-1-(1-pyrrolidinyl)-1-propanimine, which reacted as a 2-azabutadiene with electron-deficient dienophiles to afford the corresponding [4+2] cycloadducts. Reactivity and regioselectivity of the cycloaddition reactions were rationalized with the frontier molecular orbital treatment.

In the numerous examples cummulated previously for the Diels-Alder type [4+2] cycloaddition reaction of heterodienes[2] the cases of 2-aza-1,3-butadienes are few, and in most of the few cases the azadiene system is a part of the ring system.[3] To the best of our knowledge, three examples have been reported concerning the [4+2] cycloaddition reaction of *acyclic* 2-azabutadienes. Aue and Thomas have trapped methyl *N*-isopropenylacetimidate formed by thermolysis of 2-methoxy-4,4-dimethyl-1-azetine with dimethyl acetylenedicarboxylate (DMAD) (Eq. 1).[4] Ghosez and coworkers have reported the [4+2] cycloaddition reaction of $N^2$-isopropenyl-$N^1$,$N^1$-dimethylformamidine formed by thermolysis of 3-dimethylamino-2,2-dimethyl-2*H*-azirine with electron-deficient dienophiles (Eq. 2).[5] On the other hand, Taylor and coworkers have reported that the reaction of $N^1$,$N^1$-diethyl-$N^2$-(1-propenyl)benzamidine with DMAD gave $N^1$,$N^1$-diethyl-$N^2$-[2,3-bis(methoxycarbonyl)-1,3-pentadienyl]benzamidine *via* [2+2] cycloaddition reaction and that no [4+2] adduct was formed (Eq. 3).[6]



(1)



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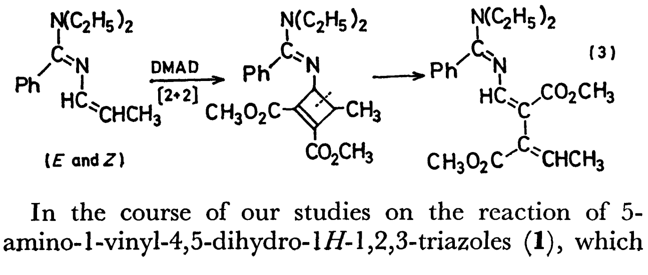
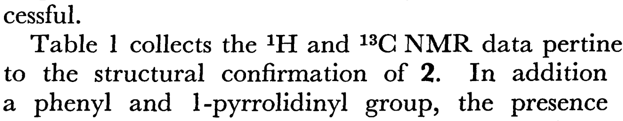


(3)

In the course of our studies on the reaction of 5-amino-1-vinyl-4,5-dihydro-1*H*-1,2,3-triazoles (**1**), which were prepared by the 1,3-dipolar cycloaddition reaction of vinyl azides with enamines,[7] we noticed that the $N^2$-vinylamidine (**2**) formed by thermolysis of **1a** acted as a 2-aza-1,3-butadiene to form the [4+2] cycloadduct with some dienophiles.

## Results and Discussion

*Thermolysis of 4,4-Dimethyl-1-(1-phenylvinyl)-5-(1-pyrrolidinyl)-4,5-dihydro-1*H*-1,2,3-triazole (**1a**).* 4,4-Dimethyl-1-(1-phenylvinyl)-5-(1-pyrrolidinyl)-4,5-dihydro-1*H*-1,2,3-triazole (**1a**) was thermolyzed at 80 °C in DMSO-$d_6$ for 22 h in a sealed NMR tube. The NMR spectra of the solution showed that 2-methyl-*N*-(1-phenylvinyl)-1-(1-pyrrolidinyl)-1-propanimine (**2**) was formed in quantitative yield (Eq. 4).



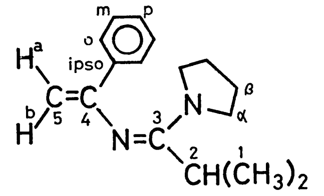
(4)

Since **2** was rapidly hydrolyzed into acetophenone and isobutyramide upon exposure to air, the isolation in pure form or combustion analysis of **2** was unsuccessful.

Table 1 collects the $^1$H and $^{13}$C NMR data pertinent to the structural confirmation of **2**. In addition to a phenyl and 1-pyrrolidinyl group, the presence of newly formed isopropyl group was indicated in its characteristic $^1$H NMR peak pattern (a doublet at $\delta$ 1.04 and a septet at $\delta$ 3.01). The two low field singlets were assigned to the terminal olefinic protons at C-5. The structure was further supported by the $^{13}$C NMR spectra. The presence of three singlets at low field, one of which corresponds to the *ipso* carbon of the phenyl group, and a triplet at $\delta$ 93.0 suggested a trisubstituted 2-aza-1,3-butadiene skeleton. The location of the three substituents was appropriately explained by the hydrolysis products, acetophenone and isobutyramide.

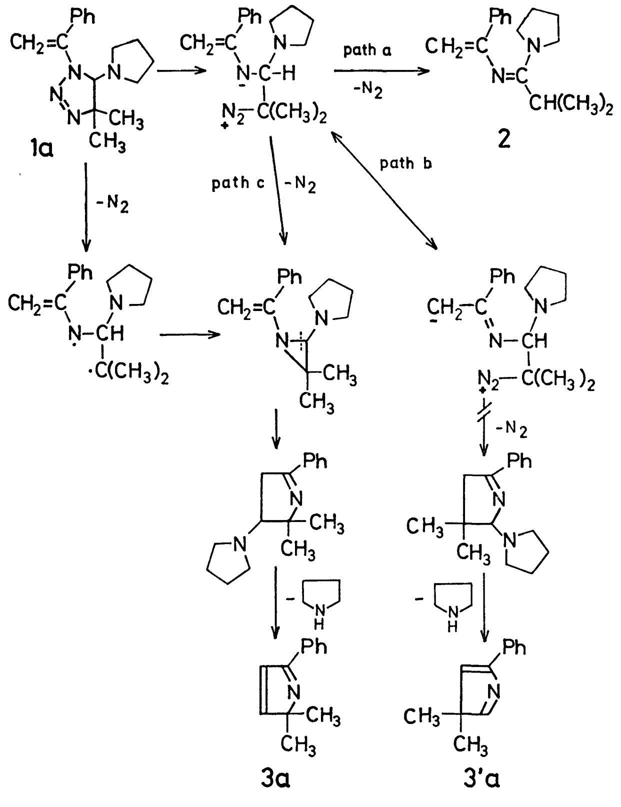
In other solvents (cyclohexane, benzene, diglyme, *etc.*) the amidine **2** was formed in much lower yields accompanied by 2,2-dimethyl-5-phenyl-2*H*-pyrrole (**3a**) (Scheme 1). The compound **3a** was separated with alumina column chromatography, and its structure was determined by spectral and analytical results.

TABLE 1. NMR SPECTRAL DATA OF 2-METHYL-*N*-(1-PHENYLVINYL)-1-(1-PYRROLIDINYL)-1-PROPANIMINE (**2**) (in DMSO-$d_6$)



| ¹H NMR | | | Assignment | ¹³C NMR | |
|---|---|---|---|---|---|
| δ | Appearance (*J*/Hz) | Area | | δ | Appearance^a)^ |
| 1.04 | d (*J*=7) | 6H | 1 | 19.7 | q |
| 1.6—2.0 | m | 4H | β | 24.8 | t |
| 3.01 | sep (*J*=7) | 1H | 2 | 29.9 | d |
| 3.2—3.7 | m | 4H | α | 47.4 | t |
| 4.34<br>4.94 | s<br>s | 1H<br>1H | $H^b$<br>$H^a$ } 5 | 93.0 | t |
| 7.2—7.7 | m | 5H | *o*<br>*p*<br>*m* | 125.2<br>127.2<br>127.8 | d<br>d<br>d |
| | | | *ipso* | 139.8 | s |
| | | | 3[b)] | 152.7 | s |
| | | | 4[b)] | 159.4 | s |

a) Splitting pattern determined by off-resonance decoupling. b) May be reversed.



Scheme 1. Formation of the $N^2$-vinylamidine (**2**) and the 2*H*-pyrrole (**3a**) by thermolysis of the vinyltriazoline (**1a**).

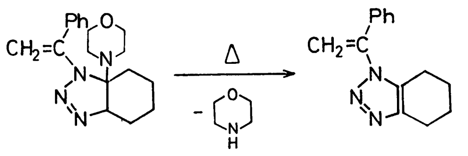
In ¹H NMR the singlet at δ 1.45 corresponds to the two methyl groups and the doublet at δ 6.73 (*J*=4.5 Hz) corresponds to the proton at C-4. In ¹³C NMR the two doublets at δ 162.6 and 123.1 correspond to the C-3 and C-4 of the 2*H*-pyrrole ring, and the singlets at δ 169.6 and 79.5 correspond to the C-5 and C-2 of the pyrrole ring, respectively.[8a)] The alternative structure of the 3*H*-pyrrole (**3'a**) is eliminated because the signal at δ 79.5 should be assigned to the quaternary $sp^3$ carbon adjacent to one nitrogen atom.[8b)]

The formation of the $N^2$-vinylamidine (**2**) and the 2*H*-pyrrole (**3a**) was most simply explained by the tentative routes shown in Scheme 1. In the thermolysis of 5-amino-4,5-dihydro-1*H*-1,2,3-triazoles, it is generally accepted that the heterolytic cleavage of the bond between N-1 and N-2 occurs first,[9–11)] and that the loss of nitrogen followed by 1,2-hydride (or carbanion) shift gives amidines.[10–12)] In the present case the $N^2$-vinylamidine (**2**) would be formed *via* the similar path (path a). Since the ring closure *via* path b would lead to the 3*H*-pyrrole (**3'a**), which was not actually formed, the 2*H*-pyrrole (**3a**) should be formed *via* another path. A plausible path involves the formation of aziridine, followed by the subsequent ring conversion to the pyrroline and elimination of pyrrolidine to the 2*H*-pyrrole (**3a**) (path c).[12)] The homolytic extrusion of nitrogen from **1a** can also lead to the aziridine as was the case of thermolysis and photolysis of other 4,5-dihydro-1*H*-1,2,3-triazoles.[13)] The fact that **3a** was not formed by thermolysis in DMSO but was formed in the less polar solvents may be suggestive of the homolytic mechanism for the aziridine formation (and the heterolytic one for the amidine), although no example of homolytic extrusion of nitrogen by thermolysis of 5-amino-4,5-dihydro-1*H*-1,2,3-triazoles has been reported.

*Thermolysis of Other Vinyltriazolines.* In contrast with the quantitative formation of the $N^2$-vinylamidine (**2**) from **1a** in DMSO, 4-ethyl-1-(1-phenylvinyl)-5-

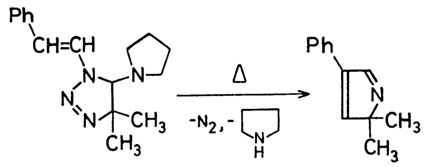
(1-pyrrolidinyl)-4,5-dihydro-1*H*-1,2,3-triazole (**1b**) was stable at 80 °C. Thermolysis at 100 °C in DMSO-$d_6$, diglyme-$d_{14}$, or pyridine-$d_5$ caused decomposition with evolution of nitrogen, but the NMR spectra of the resulting solution showed that neither amidine nor pyrrole was formed.

Thermolysis of 7a-morpholino-1-(1-phenylvinyl)-3a,4,5,6,7,7a-hexahydro-1*H*-1,2,3-benzotriazole (**1c**) also gave neither amidine nor pyrrole. Chromatographic separation of the reaction mixture gave faint yellow oil, whose spectral data were identical with those of previously reported 1-(1-phenylvinyl)-4,5,6,7-tetrahydro-1*H*-1,2,3-benzotriazole (**4**; 36% yield) (Eq. 5).[7)]



1c 4

(5)



1d 3d

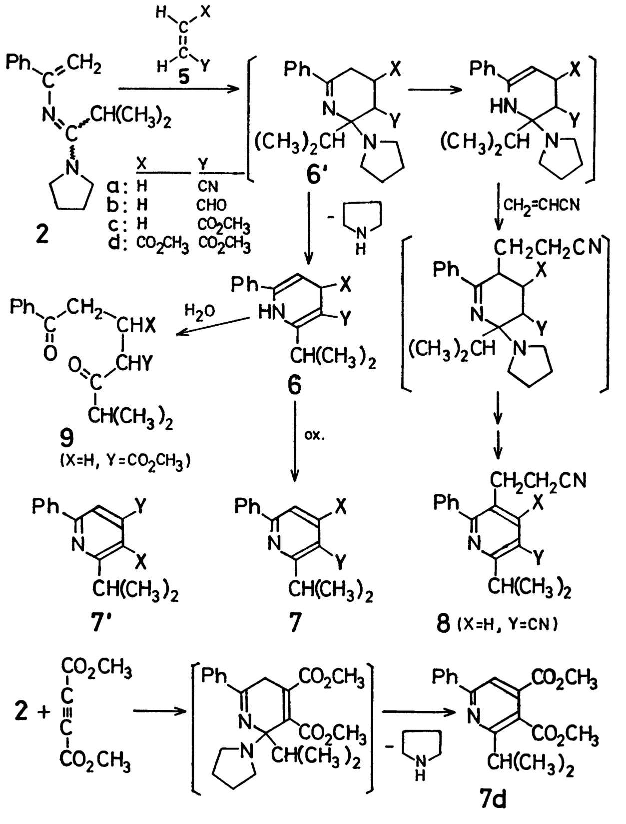
(6)

Thermolysis of 4,4-dimethyl-5-(1-pyrrolidinyl)-1-styryl-4,5-dihydro-1*H*-1,2,3-triazole (**1d**) was carried out at 80 °C in DMSO and in benzene to give the corresponding 2,2-dimethyl-4-phenyl-2*H*-pyrrole (**3d**) in 38 and 80% yields, respectively (Eq. 6). No amidine was detected in the crude solution. The 2*H*-pyrrole (**3d**) seems to be formed *via* aziridine as in the case of **3a**.

These results were in sharp contrast with the Fusco's results of thermolysis of 1-aryl-5-amino-1,2,3-triazolines, in which the corresponding $N^2$-arylamidines were the sole products.[10—12)]

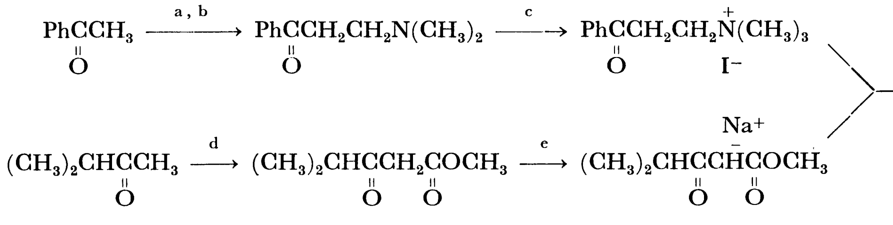
*[4+2] Cycloaddition Reaction of the 2-Aza-1,3-butadiene (2).* In order to examine the reactivity of 2-methyl-*N*-(1-phenylvinyl)-1-(1-pyrrolidinyl)-1-propanimine (**2**) as a 2-aza-1,3-butadiene, **2** prepared by heating **1a** in DMSO at 80 °C for 1 d was allowed to react with an appropriate dienophile (**5**) at room temperature.

The results were summarized in Scheme 2 and Table 2. In the case of some electron-deficient dienophiles (**5a**—**d**, and DMAD), the corresponding dihydropyridines (**6**) and pyridines (**7**) were formed at room temperature for 1—5 d, but reaction with *p*-benzoquinone (**5e**) or *N*-phenylmaleimide (**5f**) gave only polymeric substances. With 3,4-dihydro-2*H*-pyran (**5g**), an olefin with a $\pi$-donating group, no reaction occurred even at 110 °C and **5g** remained unchanged.



Scheme 2. Cycloaddition reaction of the 2-azabutadiene (**2**) with electron-deficient dienophiles.

In the case of the reaction with acrylonitrile (**5a**) or acrylaldehyde (**5b**), the initially formed dihydropyridine (**6a,b**) was gradually oxidized to the pyridine (**7a,b**) upon exposure to air. In the case of **5a**, the reaction at 80 °C for 36 h or at room temperature for 30 d gave the 1:2 adduct **8** besides **6a** and **7a**. In the case of methyl acrylate (**5c**), dihydropyridine was not isolated but considerable amount of methyl 2-isobutyryl-5-oxo-5-phenylpentanoate (**9**) was isolated. The dioxo ester **9** was identified by spectral comparison with the authentic sample prepared according to the route shown in Eq. 7.



$$\mathrm{Ph}\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{CH_3} \xrightarrow{\mathrm{a,\,b}} \mathrm{Ph}\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{CH_2CH_2N(CH_3)_2} \xrightarrow{\mathrm{c}} \mathrm{Ph}\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{CH_2CH_2\overset{+}{N}(CH_3)_3}\ \mathrm{I^-}$$

$$\mathrm{(CH_3)_2CH}\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{CH_3} \xrightarrow{\mathrm{d}} \mathrm{(CH_3)_2CH}\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{CH_2}\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{OCH_3} \xrightarrow{\mathrm{e}} \mathrm{(CH_3)_2CH}\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\overset{\mathrm{Na^+}}{\overset{-}{\mathrm{C}}}\mathrm{H}\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{OCH_3}$$

$$\longrightarrow \mathbf{9}$$

(7)

a) $(CH_3)_2NH\cdot HCl$, HCHO b) NaOH c) $CH_3I$ d) $(CH_3O)_2CO$ e) $CH_3ONa$

Table 2. Reaction of **2** with dienophiles in DMSO[a)]

| Dienophile | X | Y | Molar ratio (**5**/**1a**) | Reaction time/d | Yield/% of products **6** | **7** | **8** | **9** |
|---|---|---|---|---|---|---|---|---|
| **5a** | H | CN | 2.0 | 2 | 37 | 25 | — | — |
| | | | 2.0 | 30 | 16 | 7 | 24 | — |
| | | | 2.0 | 1.5[b)] | — | 13 | 10 | — |
| **5b** | H | CHO | 1.3 | 3 | 24 | 22 | — | — |
| **5c** | H | $CO_2CH_3$ | 1.1 | 5 | — | 21 | — | 24 |
| | | | 1.1 | 5 | — | 44 | — | —[c)] |
| **5d** | $CO_2CH_3$ | $CO_2CH_3$ | 2.1 | 2 | — | 11 | — | — |
| | | | 2.1 | 2 | — | 23 | — | —[c)] |
| **5e** | -COCH=CHCO- | | 1.1 | 2 | — | — | — | —[d)] |
| **5f** | -CONPhCO- | | 1.0 | 2 | — | — | — | —[d)] |
| **5g** | $-O(CH_2)_3-$ | | 1.8 | 3[e)] | — | — | — | — |
| DMAD | $CO_2CH_3$ | $CO_2CH_3$ | 2.1 | 1 | — | 37 | — | — |

a) Carried out at room temperature, unless otherwise noted. b) Carried out at 80 °C. c) Initial crude products were oxidized with *p*-benzoquinone prior to work up. d) Only polymeric products were formed. e) Carried out at 80—110 °C, but dienophile remained unchanged.

A plausible mechanism for the formation of these products was depicted in Scheme 2. The [4+2] cycloaddition reaction of **2** with a dienophile would give the cyclic imine intermediate **6′**, which is deaminated to the dihydropyridine **6**. The Michael addition of acrylonitrile to the isomeric enamine form of **6′a** would lead to **8**.[14)] Formation of **9** would indicate the initial formation of dihydropyridine **6c**, which was hydrolyzed into **9** on silica gel. This was prevented by oxidation of **6c** to **7c** with *p*-benzoquinone prior to work up.

An intriguing aspect of these cycloaddition reactions involving **5a**—**c** is the formation of only one of the possible regioisomers. Two regioisomeric structures **7** and **7′** were expected, but only **7** was actually formed in all cases. In the case of **7a**, for instance, the two doublets at δ 7.68 and 7.92 in $^1$H NMR spectra 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 **7′a** in which only a small *meta* coupling should be observed. 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.[15)] These structural assignments were further confirmed by $^{13}$C NMR data (see Experimental).

Taylor and coworkers suggested that the preference of [2+2] to [4+2] cycloaddition in the case of $N^1$,$N^1$-diethyl-$N^2$-(1-propenyl)benzamidine (Eq. 3) could be caused by the inaccessibility of the *s-cis* conformation in the 2-aza-1,3-butadiene system.[6)] In the present case *s-cis* conformation is not sterically unfavorable due to the presence of phenyl group at 3-position of the 2-aza-1,3-butadiene system of **2**, so that the preference of the [4+2] cycloaddition is in accord with the Taylor's postulate. But further experimental results about the cycloaddition reactions of various 2-aza-1,3-butadienes are necessary to examine the validity of his postulate. Useful synthetic methods of 2-aza-1,3-butadienes are awaited.

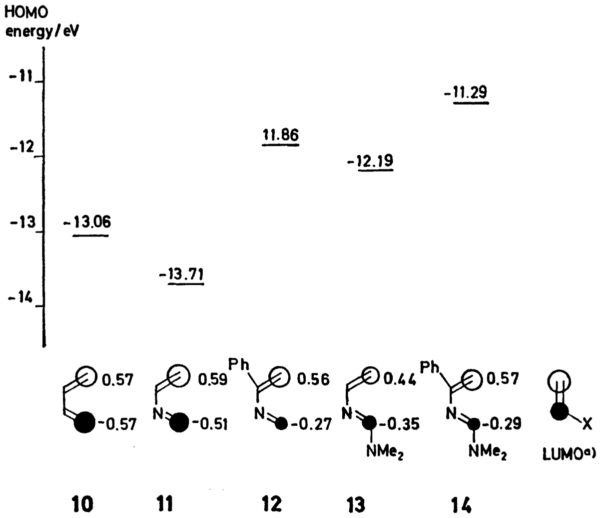


Fig. 1. Energies and coefficients of HOMO of 2-azabutadienes estimated with CNDO/2 method.
a) LUMO of a typical electron-deficient dienophile.

*Frontier Molecular Orbital Treatment.* Frontier molecular orbital treatment was successfully applied to rationalize the reactivity and regioselectivity of cycloaddition reactions such as Diels-Alder reactions and 1,3-dipolar cycloaddition reactions.[16)] We found that this treatment also rationalized the rather high reactivity and high regioselectivity in the [4+2] cycloaddition reactions of the 2-aza-1,3-butadiene (**2**).

Frontier orbital energies and coefficients of various 2-azabutadienes were estimated with CNDO/2 method (Fig. 1).

In Diels-Alder reaction with electron-deficient dienophiles, the interaction between HOMO (highest occupied molecular orbital) of the diene and LUMO (lowest unoccupied molecular orbital) of the dienophile is important.[16)] As shown in Fig. 1, the HOMO of 2-azabutadiene (**11**) is lower than that of butadiene (**10**), suggesting the lower reactivity of **11** compared with **10**. However, the HOMO of 3-phenyl-2-azabutadiene (**12**) or 1-amino-2-azabutadiene (**13**) is raised by their substituents (phenyl and amino groups), so that the HOMO of the 2-azabutadiene **14** (a model of **2**) is much higher in energy than that of **10** or **11**. The higher energy of HOMO would increase the interaction with LUMO of dienophiles, resulting the rather high reactivity in cycloaddition reaction of **2** with electron-deficient dienophiles.

On the other hand, the LUMO of enol ethers is higher in energy so that the interaction would be too small to cause the reaction with **2** in spite of the high energy of HOMO of **2**.

The magnitude of coefficients of HOMO of 2-azabutadienes were also in accord with the observed regioselectivity in the reactions of non-symmetrical dienophiles (**5a**—**c**). The coefficient of HOMO of **11** was larger at 4-position than at 1-position, and this trend was enhanced by the substitution of the phenyl and amino groups (**12**, **13**). Consequently the coefficients of HOMO of **14** was much larger at 4-position than at 1-position, so that the high regioselectivity in the [4+2] cycloaddition reaction of **2** would be induced.

## Experimental

*General.* Melting points were determined on a Mitamura Riken hot-stage melting point apparatus and were uncorrected. Infrared spectra were determined on a JASCO DS-403G grating infrared spectrophotometer. Nuclear magnetic resonance spectra were determined on a JEOL MH-100, FX-90Q, and Varian FT-80A NMR spectrometer (splitting pattern in $^{13}$C NMR data was obtained by off-resonance decoupling). Ultraviolet spectra were determined on a Hitachi EPS-3T recording spectrophotometer. Mass spectra were determined on a Hitachi RMU-6MG mass spectrometer. The vinyltriazolines (**1**) were prepared by the previously described method.[7] Solvents were distilled under anhydrous conditions before use.

*Thermolysis of 4,4-Dimethyl-1-(1-phenylvinyl)-5-(1-pyrrolidinyl)-4,5-dihydro-1*H*-1,2,3-triazole (**1a**).* *Method A*: In 0.5 ml of an appropriate solvent was dissolved 71—118 mg (0.26—0.44 mmol) of **1a** with 3.8—5.7 mg of 2,2,3,3-tetramethylbutane as an internal standard in a 5 mm diameter NMR sample tube. The tube was then sealed *in vacuo*, and was heated in an 80 °C bath until **1a** was completely consumed.

*Method B*: In 100 ml of an appropriate solvent was dissolved 1.0 g (3.7 mmol) of **1a** and the solution was heated to reflux under nitrogen until **1a** was completely consumed.

*In Dimethyl-*d$_6$ *Sulfoxide (DMSO-*d$_6$*, Method A)*: Thermolysis of **1a** was carried out in DMSO-$d_6$ at 80 °C for 22 h. NMR spectra of the resulting solution showed that 2-methyl-*N*-(1-phenylvinyl)-1-(1-pyrrolidinyl)-1-propanimine (**2**) (see Table 1) was formed in quantitative yield.

*In Toluene (Method B)*: Thermolysis of **1a** (1.0 g, 3.7 mmol) was carried out in refluxing toluene (110 °C) for 75 min. Removal of the solvent *in vacuo* gave 700 mg of the residue, whose $^1$H NMR spectra showed the existence of **2** and 2,2-dimethyl-5-phenyl-2*H*-pyrrole (**3a**) in 6:7 ratio. Chromatographic separation of 220 mg of the residue afforded 40 mg (28% yield) of acetophenone and 62 mg (37% yield) of **3a**, respectively. Analytically pure sample of **3a** was obtained by distillation with the Kugelrohr apparatus at 55 °C/3 mmHg†: mp 19—20 °C; MS *m/e* 171 (M$^+$); IR (neat) 1605, 1446, 1358, 1198, 1020, 760, and 694 cm$^{-1}$; UV$_{\max}$ (methanol) 212.5 ($\varepsilon$, 12000), 217.5 (12000), and 249 nm (10000); $^1$H NMR (CDCl$_3$) $\delta$ 1.45 (6H, s), 6.73 (1H, d, $J$=4.5 Hz), 7.3—7.5 (4H, m), and 7.8—8.0 (2H, m); $^{13}$C NMR (CDCl$_3$) $\delta$ 23.4 (q), 79.5 (s), 123.1 (d), 127.6 (d), 128.6 (d), 130.2 (d), 134.3 (s), 162.6 (d), and 169.6 (s, C=N).

Found: C, 84.04; H, 7.63; N, 8.27%. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18%.

The rest of the residue (480 mg) was left at room temperature for 3 d. Then 1 ml of diethyl ether was added, and the precipitates of isobutyramide was collected by filtration and washed three times with 1 ml of diethyl ether (yield, 30 mg, 14%).

*In Toluene-*d$_8$ *(Method A)*: Thermolysis of **1a** was carried out in toluene-$d_8$ at 80 °C for 21 h. The $^1$H NMR spectra of the resulting solution showed the formation of **2** and **3a** in 58 and 23% yields, respectively.

*In Diglyme-*d$_{14}$ *(Method A)*: Thermolysis of **1a** was carried out in diglyme-$d_{14}$ at 80 °C for 20 h. The $^1$H NMR spectra of the resulting solution showed the formation of **2** and **3a** in 31 and 8% yields, respectively.

*In Benzene (Method B)*: Thermolysis of **1a** was carried out in refluxing benzene (80 °C) for 1 d. The $^1$H NMR spectra of the residue after removal of the solvent showed the formation of **2** and **3a** in 42 and 11% yields, respectively.

*In Cyclohexane (Method B)*: Thermolysis of **1a** was carried out in refluxing cyclohexane (80 °C) for 1 d. The $^1$H NMR spectra of the residue after removal of the solvent showed the formation of **2** and **3a** in 50 and 20% yields, respectively.

*Thermolysis of 7a-Morpholino-1-(1-phenylvinyl)-3a,4,5,6,7,7a-hexahydro-1*H*-1,2,3-benzotriazole (**1c**).* Toluene (20 ml) solution of **1c** (92 mg, 0.29 mmol) was heated to reflux for 16 h under nitrogen until **1c** was completely consumed. The toluene was removed *in vacuo* at room temperature. The $^1$H NMR spectra of the residue showed that no $N^2$-vinylamidine was formed. Chromatographic separation of the residue through silica-gel column eluting with diethyl ether gave 1-(1-phenylvinyl)-4,5,6,7-tetrahydro-1*H*-1,2,3-benzotriazole (**4**)[7] in 36% yield.

*Thermolysis of 4,4-Dimethyl-5-(1-pyrrolidinyl)-1-styryl-4,5-dihydro-1*H*-1,2,3-triazole (**1d**).* *In DMSO-*d$_6$: The DMSO-$d_6$ (0.5 ml) solution of **1d** (0.16 g, 0.60 mmol) was heated at 80 °C according to Method A for 2 d. The $^1$H NMR spectra of the resulting solution showed that $N^2$-vinylamidine was not formed. Diethyl ether (50 ml) was added to the solution, and the ether solution was washed four times with water (50 ml) and once with saturated aqueous solution of sodium chloride (50 ml) and dried over anhydrous magnesium sulfate. The ether was removed *in vacuo* and the residue was purified with silica gel preparative thin layer chromatography (Merck Art. 7747) developing with dichloromethane to give 38 mg (38% yield) of 2,2-dimethyl-4-phenyl-2*H*-pyrrole (**3d**). Analytically pure sample was obtained by distillation with the Kugelrohr apparatus at 65 °C/4 mmHg): mp 16.5—17.5 °C; MS *m/e* 171 (M$^+$); IR (neat) 1620, 1600, 1530, 1490, 1450, 925, 765, and 695 cm$^{-1}$; UV$_{\max}$ (methanol) 224 ($\varepsilon$, 15000), 268 (5000), 287 (sh), and 296 nm (sh); $^1$H NMR (CDCl$_3$) $\delta$ 1.43 (6H, s), 7.4—7.8 (6H, m), and 8.55 (1H, s); $^{13}$C NMR (CDCl$_3$) $\delta$ 23.2 (q), 80.3 (s), 126.3 (d), 128.1 (d), 128.8 (d), 132.4 (s), 138.1 (s), 153.6 (d), and 161.3 (d, C=N).

Found: C, 84.04; H, 7.65; N, 8.10%. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18%.

*In Benzene*: The benzene (40 ml) solution of **1d** (0.68 g, 2.5 mmol) was heated to reflux for 42 h under nitrogen

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† 1 mmHg≈133.322 Pa.

until **1d** was completely consumed. After removal of the benzene *in vacuo*, the residue was purified with alumina dry column chromatography (Woelm 04511) eluting with dichloromethane to give 0.35 g (80% yield) of **3d**.

*Cycloaddition Reaction of* **2** *with Dienophiles.* *Method A*: The $N^2$-vinylamidine (**2**) was prepared by heating the DMSO solution of the vinyltriazoline (**1a**, 1.0 g, 3.7 mmol) at 80 °C for 24 h under nitrogen atmosphere. After it was cooled to room temperature, an appropriate dienophile (molar ratio described in Table 2) was added to the solution with a micro syringe, and the solution was stirred at room temperature for 1—5 d. Then diethyl ether (50 ml) was added, and the ether layer was washed four times with water (50 ml) and once with saturated aqueous solution of sodium chloride (50 ml) successively, and dried over anhydrous magnesium sulfate. After removal of the ether *in vacuo*, the residue was purified with silica gel dry column chromatography (Woelm 04526, eluting with hexane–dichloromethane (1:1)) and/or with silica gel preparative thin layer chromatography (developing with dichloromethane).

*Method B*: The reaction procedure and the method of purification were similar to Method A, but *p*-benzoquinone (0.40 g, 3.7 mmol) was added to the DMSO solution in order to oxidize the initial products after the cycloaddition was completed.

*Reaction with Acrylonitrile (**5a**)*: (*i*) Reaction of **2** with 2.0 molar amount of **5a** according to Method A for 2 d gave 3-cyano-1,4-dihydro-2-isopropyl-6-phenylpyridine (**6a**) and 3-cyano-2-isopropyl-6-phenylpyridine (**7a**) in 37 and 25% yields, respectively. Analytically pure samples of **6a** and **7a** were obtained respectively by recrystallization from methanol as colorless crystals: 3-cyano-1,4-dihydro-2-isopropyl-6-phenylpyridine (**6a**): mp 107—108 °C; MS *m/e* 224 (M$^+$); IR (KBr) 3330 (N–H), 2270 (C≡N), 1665 (C=C), 1610, 1495, 1290, 1110, 760, and 705 cm$^{-1}$; UV$_{\max}$ (methanol) 243 ($\varepsilon$ 14000) and 335 nm (3000); $^1$H NMR (CDCl$_3$) $\delta$ 2.21 (6H, d, $J$=7 Hz), 3.15 (1H, septet, $J$=7 Hz), 3.26 (2H, d, $J$=3.5 Hz), 4.90 (1H, td, $J$=3.5 and 1.7 Hz), 5.4 (1H, NH), and 7.32 (5H, $C_6H_5$).

Found: C, 80.19; H, 7.16; N, 12.20%. Calcd for $C_{15}H_{16}N_2$: C, 80.32; H, 7.19; N, 12.49%.

3-Cyano-2-isopropyl-6-phenylpyridine (**7a**): mp 75.5—76.5 °C; MS *m/e* 222 (M$^+$); IR (KBr) 2305 (C≡N), 1580, 1445, 1380, 860, 840, 770, and 695 cm$^{-1}$; UV$_{\max}$ (methanol) 260 (sh), 266 ($\varepsilon$, 15000), and 297 nm (20000); $^1$H NMR (CDCl$_3$) $\delta$ 1.47 (6H, d, $J$=7 Hz), 3.64 (1H, septet, $J$=7 Hz), 7.4—7.6 (3H, m), 7.68 (1H, d, $J$=8 Hz), 7.92 (1H, d, $J$=8 Hz), and 8.0—8.2 (2H, m); $^{13}$C NMR (CDCl$_3$) $\delta$ 21.7 (q), 34.8 (d), 105.8 (s), 116.9 (d), 117.1 (s, C≡N), 127.3 (d), 128.8 (d), 130.3 (d), 137.7 (s), 140.9 (d), 158.9 (s), and 169.1 (s).

Found: C, 80.96; H, 6.59; N, 12.69%. Calcd for $C_{15}H_{14}N_2$: C. 81.05; H, 6.35; N, 12.60%.

(*ii*) Reaction of **2** with 2.0 molar amount of **5a** according to Method A for 30 d gave **6a**, **7a**, and 3-cyano-5-(2-cyanoethyl)-2-isopropyl-6-phenylpyridine (**8**) in 16, 7, and 24% yields, respectively. Analytically pure sample of **8** was obtained by recrystallization from methanol as colorless crystals: mp 111.5—112 °C; MS *m/e* 275 (M$^+$); IR (KBr) 2235 (C≡N), 2230 (C≡N), 1590, 1435, 1070, 980, 785, 750, 715, and 700 cm$^{-1}$; UV$_{\max}$ (ethanol) 254 ($\varepsilon$, 10100) and 289 nm (10300); $^1$H NMR (CDCl$_3$) $\delta$ 1.38 (6H, d, $J$=6.5 Hz), 2.24 (2H, t, $J$=7.5 Hz), 3.11 (2H, t, $J$=7.5 Hz), 3.58 (1H, septet, $J$=6.5 Hz), 7.48 (5H, $C_6H_5$), and 7.81 (1H, s). $^{13}$C NMR (CDCl$_3$) $\delta$ 17.5 (t), 21.7 (q), 27.6 (t), 34.5 (d), 106.4 (s), 116.8 (s, C≡N), 118.4 (s, C≡N), 128.6 (s), 128.8 (d), 128.9 (s), 129.1 (d), 138.8 (s), 141.5 (d), 161.6 (s), and 167.7 (s).

Found: C, 78.50; H, 6.52; N, 15.11%. Calcd for $C_{18}H_{17}N_3$: C, 78.52; H, 6.22; N, 15.26%.

(*iii*) The vinyltriazoline (**1a**, 0.87 g, 3.2 mmol) and **5a** (0.34 g, 6.4 mmol) was dissolved in DMSO (20 ml) and stirred at 80 °C for 36 h under nitrogen atmosphere. After removal of excess **5a** and DMSO *in vacuo* at about 60 °C, the residue was dissolved in dichloromethane (50 ml) and the solution was washed with water (3×50 ml) and saturated aqueous solution of sodium chloride (50 ml) successively, and was dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was purified according to Method A to give 90 mg of **7a** (13% yield) and 0.18 g of **8** (20% yield).

*Reaction with Acrylaldehyde (**5b**)*: Reaction of **2** with 1.3 molar amount of **5b** according to Method A for 3 d gave 1,4-dihydro-2-isopropyl-6-phenylnicotinaldehyde (**6b**) and 2-isopropyl-6-phenylnicotinaldehyde (**7b**) in 24 and 22% yields, respectively. Analytically pure sample of **6b** was obtained by recrystallization from benzene as faint yellow crystals: mp 105—106.5 °C; MS *m/e* 227 (M$^+$); IR (KBr) 3230 (N–H), 1680 (C=C), 1595, 1505, 1390, 1365, 1290, 1240, 1110, 765, and 700 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.28 (6H, d, $J$=7.5 Hz), 3.17 (2H, d, $J$=3 Hz), 3.60 (1H, septet, $J$=7.5 Hz), 5.11, (1H, m), 5.81 (1H, NH), 7.34 (5H, $C_6H_5$), and 9.83 (1H, s, CHO).

Found: C, 79.21; H, 7.58; N, 6.21%. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16%.

The compound **7b** was obtained as colorless oil: MS *m/e* 225 (M$^+$); IR ($CH_2Cl_2$) 1685 (C=O), 1580, and 1370 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.44 (6H, d, $J$=7 Hz), 3.97 (1H, septet, $J$=7 Hz), 7.4—7.7 (3H, m), 7.77 (1H, d, $J$=8.5 Hz), 8.1—8.4 (3H, m), and 10.50 (1H, s, CHO). *p*-Nitrophenylhydrazone of **7b**: mp 248.5—249.5 °C.

Found: C, 70.12; H, 5.33; N, 15.60%. Calcd for $C_{21}H_{20}N_4O_2$: C, 69.98; H, 5.59; N, 15.55%.

*Reaction with Methyl Acrylate (**5c**)*: (*i*) Reaction of **2** with 1.1 molar amount of **5c** according to Method A for 5 d gave methyl 2-isopropyl-6-phenylnicotinate (**7c**) and methyl 2-isobutyryl-5-oxo-5-phenylpentanoate (**9**) in 21 and 24% yields, respectively. Analytically pure sample of **7c** was obtained by recrystallization from methanol as colorless crystals: mp 88.5—89.5 °C; MS *m/e* 255 (M$^+$); IR (KBr) 1720 (C=O), 1580, 1270, 1080, 760, and 688 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.42 (6H, d, $J$=7 Hz), 3.92 (3H, s), 4.02 (1H, septet, $J$=7 Hz), 7.3—7.5 (3H, m), 7.52 (1H, d, $J$=7.5 Hz), and 8.0—8.2 (3H, m); $^{13}$C NMR (CDCl$_3$) $\delta$ 22.4 (q), 32.6 (d), 52.2 (q, OCH$_3$), 116.8 (d), 123.1 (s), 127.4 (d), 128.8 (d), 129.8 (d), 138.3 (s), 139.3 (d), 158.4 (s), and 167.3 (s).

Found: C, 75.45; H, 6.81; N, 5.70%. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.99%.

The dioxo ester **9** was obtained as faint yellow oil: IR (neat) 1740 (C=O), 1710 (C=O), 1680 (C=O), 1595, 1580, 1450, 755, and 695 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.13 (3H, d, $J$=6 Hz), 1.17 (3H, d, $J$=6 Hz), 2.28 (2H, q, $J$=7 Hz), 2.89 (1H, septet, $J$=6 Hz), 3.07 (2H, t, $J$=7 Hz), 3.74 (3H, s), 3.91 (1H, t, $J$=7 Hz), 7.3—7.6 (3H, m), and 7.8—8.1 (2H, m).

(*ii*) Reaction of **2** with 1.1 molar amount of **5c** according to Method B for 5 d gave **7c** in 44% yield.

*Reaction with Dimethyl Maleate (**5d**)*: (*i*) Reaction of **2** with 2.1 molar amount of **5d** according to Method A for 2 d gave dimethyl 2-isopropyl-6-phenylpyridine-3,4-dicarboxylate (**7d**) in 11% yield. Analytically pure sample was obtained by recrystallization from methanol as colorless crystals: mp 75.5—76.5 °C; MS *m/e* 313 (M$^+$); IR (KBr)

1730 (C=O), 1580, 1330, 1275, 1250, 1085, 990, 755, 740, and 690 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 1.40 (6H, d, $J$=7 Hz), 3.09 (1H, septet, $J$=7 Hz), 3.92 (3H, s), 3.95 (3H, s), 7.3—7.5 (3H, m), 7.9—8.1 (3H, m); $^{13}$C NMR (CDCl$_3$) $\delta$ 22.5 (q), 33.8 (d), 52.7 (q, OCH$_3$), 52.9 (q, OCH$_3$), 116.7 (d), 125.8 (s), 127.1 (d), 128.8 (d), 136.6 (s), 138.2 (s), 157.9 (s), 164.3 (s, C=O), 165.5 (s), and 168.9 (s).

Found: C, 69.16; H, 6.11; N, 4.52%. Calcd for $C_{18}H_{19}NO_4$: C, 69.00; H, 6.11; N, 4.47%.

(*ii*) Reaction of **2** with 2.1 molar amount of **5d** according to Method B for 2 d gave **7d** in 23% yield.

*Reaction with Dimethyl Acetylenedicarboxylate (DMAD)*: Reaction of **2** with 2.1 molar amount of DMAD according to Method A for 1 d gave **7d** in 37% yield.

*Synthesis of an Authentic Sample of Methyl 2-isobutyryl-5-oxo-5-phenylpentanoate (9).* Methyl 4-methyl-3-oxopentanoate was prepared from 3-methyl-2-butanone and dimethyl carbonate according to Corey's method.17) 3-Dimethylamino-1-phenyl-1-propanone was prepared from acetophenone, formaldehyde, and dimethylamine hydrochloride by Mannich reaction,18) quaternized with methyl iodide, and it was condensed with the 3-oxo ester in methanol at 0 °C by means of sodium methoxide.19) The dioxo ester **9** formed was purified with alumina (Woelm 04511) dry column chromatography eluting with hexane–dichloromethane (1:1). Its IR and $^1$H NMR spectra were identical with the dioxo ester formed in the reaction of **2** with methyl acrylate (**5c**). Analytically pure sample was obtained by distillation with the Kugelrohr apparatus at 140 °C/0.1 mmHg.

Found: C, 69.58; H, 7.51%. Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.29%.

*Method for CNDO/2 Calculation.* The CNDO/2 calculation programme used was made by Professor Nozomu Ebara and members in his laboratory of College of General Education of The University of Tokyo, based mainly on the Pople's method.20) Calculation was carried out at The Computer Center of The University of Tokyo.

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