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Thermal Rearrangements of Cyclic Amine Ylides. V.[1] Thermolysis of 6-Ethynyl-1-methyl-1,2,5,6-tetrahydropyridine *N*-Imides and *N*-Ylides

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The thermolysis of the *N*-imides (**14**, **15**) of 6-ethynyl-1-methyl-1,2,5,6-tetrahydropyridines (**11**) resulted in [2,3]-sigmatropic rearrangement with either the triple bond or the double bond in the ring to give the dihydro-1,2-diazonines (**16**) presumably *via* the allenic intermediates (**19**) and the tetrahydropyrazoles (**17**, **18**). On the other hand, the *N*-ylides (**26**) of **11** gave the allenic compounds (**27**) and the Hofmann elimination products (**28**). Heating the *N*-oxides of **11** resulted in decomposition to give no characterizable products. The mechanisms, including stereochemistry, of these thermal reactions are discussed.

Keywords——thermolysis; sigmatropic rearrangement; ring-expansion; 6-ethynyl-1,2,5,6-tetrahydropyridine *N*-imide; 6-ethynyl-1,2,5,6-tetrahydropyridine *N*-ylide; cyclic allene; 1,2-diazonine; tetrahydropyrazole

Thermal sigmatropic rearrangements of open-chain allylamine *N*-ylides,[2] *N*-imides,[3] and *N*-oxides[4] have been widely investigated, as have those of allylsulfonium *S*-ylides.[5] In the case of cyclic allylamine ylides, the [2,3]-sigmatropic rearrangement takes place with either the vinyl group or the double bond in the ring in the thermolysis of the *N*-ylides (**1a**—**3a**)[6] and the *N*-imides (**1b**—**3b**),[7] whereas the *N*-oxides (**1c**—**3c**)[1] undergo only Meisenheimer [1,2] rearrangement, with no [2,3] rearrangement. On the other hand, the open-chain propargylic *S*-ylides (**4a**),[8] *N*-oxides (**4b**),[9] and *N*-ylides (**4c**)[10] are known to undergo [2,3]-sigmatropic rearrangement to give the corresponding allenic compounds (**5**). Therefore, we were interested in examining the thermal behavior of cyclic amine ylides having an ethynyl group, and we have already reported that the thermolysis of the 2-ethynylpyridine *N*-imides (**6**) afforded the 3-azaindolizines (**8**) *via* the intermediates **7**.[11] We report here the results of the thermolysis of the title *N*-imides and *N*-ylides.[12]

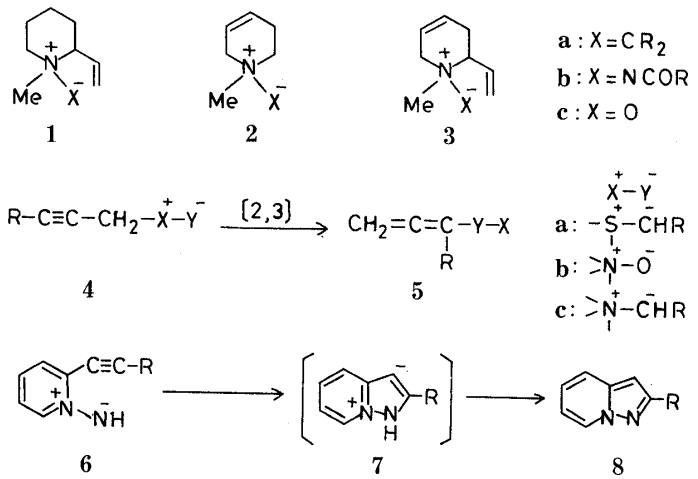


Chart 1

The synthetic routes to the 6-ethynyl-1-methyl-1,2,5,6-tetrahydropyridine *N*-imides (**14**, **15**) used in the present thermolysis are shown in Chart 2. The 2-ethynylpyridines (**9a—c**), prepared by the reaction of 2-bromopyridine with acetylenes according to the reported method,[13] were methylated with methyl iodide to give the 1-methylpyridinium iodides (**10**) in high yields. Treatment of the salts (**10**) with sodium borohydride gave the 1-methyl-1,2,5,6-tetrahydropyridines (**11**) in 40—50% yields, and these were aminated with *O*-mesitylenesulfonylhydroxylamine (H_2NOMes)[14] to afford mixtures of the *N*-amino salts **12** and **13**. These salts were too hygroscopic to be purified and thus the mixtures were successively treated with acetic anhydride and sodium hydroxide to give 4 : 1 mixtures of the desired *N*-imides **14** and **15** in moderate yields. The mixtures could be separated by chromatography on alumina.

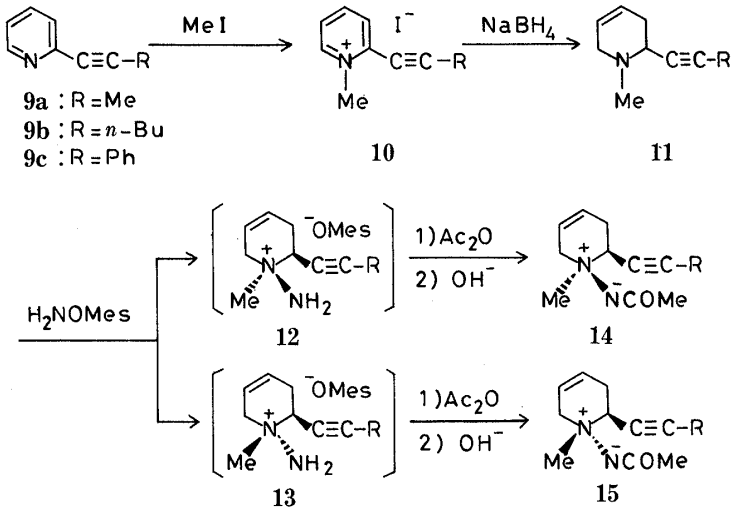


Chart 2

The major products, with the proton nuclear magnetic resonance (^{1}H-NMR) *N*-methyl signals at lower field, were assigned the structures **14**, in which the methyl group is equatorial. It is known that the equatorial *N*-methyl signal is observed at lower field than the axial one in the ^{1}H-NMR spectra of *N*-methylpiperidines.[15] The *N*-amination[16] of cyclic amines with *O*-mesitylenesulfonylhydroxylamine is known to proceed predominantly at the axial position, as is the *N*-alkylation.[17] Therefore, the axial approach of the reagent on the diequatorial conformer of the 1,2-disubstituted compounds (**11**) may predominate to give the isomers **14** as the major products, in which the ethynyl and *N*-imide groups are *cis*. Thus, the minor products are the isomers **15** in which the methyl group is axial and the other two substituents are *trans*.

Heating the *cis*-*N*-imides (**14a—c**) in xylene at 140 °C for 4 h gave the dihydro-1,2-diazonines (**16**) and the tetrahydropyrazoles (**17**) in yields of 15—20% and *ca.* 10%, respectively. On the other hand, the *trans*-*N*-imides (**15a—c**), upon heating in toluene at 110 °C for 1 h, afforded the diazonines (**16**) and the pyrazoles (**18**) in yields of 50—70 and 6—7%, respectively.

The formation of the ring-expansion products (**16**) may involve initial formation of the allenic intermediates (**19**) by a [2,3]-sigmatropic rearrangement with the triple bond, by analogy with the cases of the open-chain prop-2-ynylamine ylides (**4**),[8-10] although the key intermediates (**19**) could not be isolated. The allenic intermediates (**19**) may then undergo a 1,3-hydrogen shift to give the dihydrodiazonines (**16**). The yields of **16** from the *trans*-imides (**15**) are 3—4 times higher than those from the *cis*-imides (**14**). Furthermore, the thermolysis

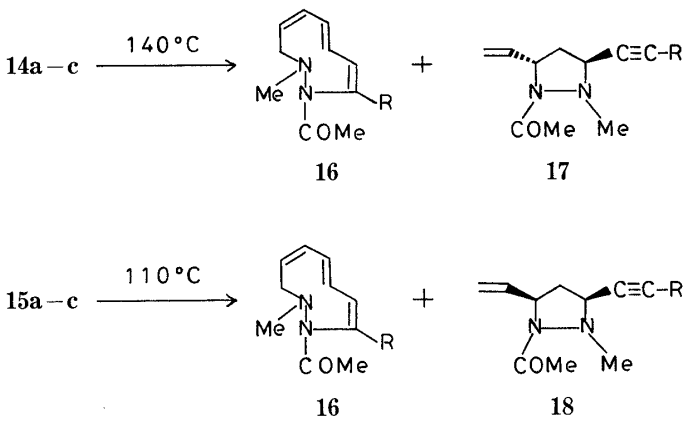


Chart 3

of **14** required somewhat higher temperatures and longer times than those for **15**. This lower susceptibility of the *cis*-imides (**14**) to the reaction is probably due to the transition state of the concerted rearrangement requiring the unfavorable half-boat form of the ring, in contrast, the *trans*-isomers (**15**) may be able to form the favored half-chair form transition state, as shown in the structures **20** and **21**, respectively.

The ^{1}H-NMR spectra of the diazonines (**16**) showed that the diazonines are mixtures of conformational isomers at room temperature. The triene function in **16** was proved to take the 6,7-*trans*-structure shown in Chart 3 by the coupling constants in the 400 MHz ^{1}H-NMR spectrum of **16c**.

Treatment of the *trans*-diazonines (**16**) with sodium ethoxide in refluxing toluene resulted in isomerization to give the *cis*-isomers (**22**) in *ca.* 50% yields as the sole conformational isomers, whose ^{1}H-NMR spectra showed no signals with the coupling constant due to the *trans*-olefin, although unambiguous assignments of the olefinic protons are difficult. These results of the present thermolysis provide a method for preparing novel nine-membered

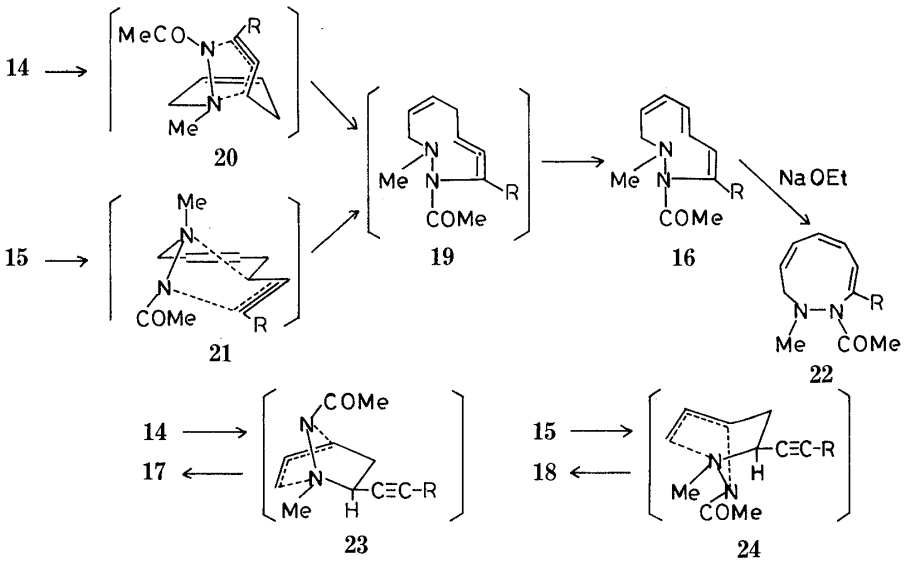
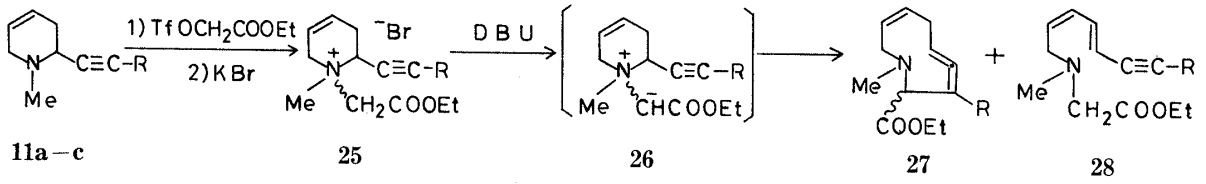


Chart 4

The tetrahydropyrazoles (**17**, **18**) may be formed directly from the *N*-imides (**14**, **15**) by another [2,3]-sigmatropic rearrangement with the double bond in the ring, analogous to that observed for the *N*-imides (**2**).[7] The ^{1}H-NMR spectra of the pyrazoles (**17**) formed from the

cis-imides (**14**) are somewhat different from those of **18** obtained from the *trans*-imides (**15**). Although the stereostructures of the pyrazoles could not be confirmed from these spectral data, we assumed that they have the structures **17** and **18** shown in Chart 3, respectively, on the basis of the following considerations. The rearrangement of the *cis*-imides (**14**) may proceed *via* the transition states **23** to give **17**, in which the ethynyl and vinyl groups are *trans*, whereas the *trans*-imides (**15**) give the *cis*-compounds (**18**) *via* the transition states **24**.

Next, the thermal behavior of the *N*-ylides (**25**) was examined. The 1-methyltetrahydropyridines (**11a—c**) were successively treated with ethoxycarbonylmethyl trifluoromethanesulfonate and potassium bromide to afford the bromides (**25**) quantitatively, as 1 : 2 (*cis* : *trans*) mixtures of their stereoisomers. It was difficult to isolate these isomers and thus the mixtures were used in the following reaction without separation.



11a—c 25 26 27 28

Chart 5

The salts (**25a—c**) were treated with 1,5-diazabicyclo[5.4.0]undecene-5 (DBU) in tetrahydrofuran at room temperature to yield the allenic compounds (**27**) and the ring-opened products (**28**) in yields of 30—40 and 15—30%, respectively. The yields of **27** were estimated from the NMR spectra of the reaction mixture, but the allenic compounds (**27**) were not very stable and were isolated in only 5—10% yields by chromatography on silica gel. This result shows that the ylides (**26**) undergo either the [2,3]-sigmatropic rearrangement with the triple bond or the Hofmann-type elimination, but do not undergo [2,3] rearrangement with the double bond in the ring. Further heating the allenic compounds (**27a, b**) resulted in decomposition, and did not give any dihydrodiazonines with conjugated trienes.

In addition, heating 6-ethynyl-1-methyl-1,2,5,6-tetrahydropyridine *N*-oxides resulted in decomposition and gave no rearrangement products.

Experimental

Melting points were measured on a Yamato MP-21 apparatus and are uncorrected. Infrared (IR) spectra were determined with a JASCO IRA-2 spectrometer and mass spectra (MS) were recorded on a JEOL DX-300 instrument. ^{1}H-NMR spectra were recorded on a JEOL JNM-MH100 spectrometer in $CDCl_3$ using tetramethylsilane as an internal standard unless otherwise stated; spectral assignments were confirmed by spin-decoupling experiments. Carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectra were recorded on a JEOL FX-100 spectrometer. Microanalyses were performed in the Microanalytical Laboratory of this school by Mrs. R. Igarashi.

Starting Materials——The 2-ethynylpyridines (**9a—c**) were prepared from 2-bromopyridine by the reported method.[13]

1-Methyl-2-ethynylpyridinium Iodides (10a—c)——General procedure: A mixture of an ethynylpyridine (**9**: 0.2 mol), methyl iodide (85 g, 0.6 mol), and ethanol (100 ml) was refluxed for 2 h. After cooling, the reaction mixture was evaporated to dryness *in vacuo*. The resulting crystalline residue was washed with ether and then recrystallized from methanol–ether to give the corresponding salts (**10**) as yellow prisms, which show IR absorption at 2250 cm^{-1} (C≡C).

10a: 97% yield, mp 136—137 °C (dec.). *Anal.* Calcd for $C_9H_{10}IN$: C, 41.70; H, 3.86; N, 5.41. Found: C, 41.39; H, 3.71; N, 5.24.

10b: 96% yield, mp 99—101 °C (dec.). *Anal.* Calcd for $C_{12}H_{16}IN$: C, 47.84; H, 5.32; N, 4.65. Found: C, 47.60; H, 5.19; N, 4.55.

10c: 88% yield, mp 186—188 °C (dec.) *Anal.* Calcd for $C_{14}H_{21}IN$: C, 52.33; H, 3.74; N, 4.36. Found: C, 52.50; H, 3.75; N, 4.30.

1-Methyl-6-ethynyl-1,2,5,6-tetrahydropyridines (11a—c)——General Procedure: Solid $NaBH_4$ (6.3 g, 1 mol eq) was added in small portions to a suspension of a salt (**10**: 0.15 mol) in ethanol (300 ml) with stirring in an ice bath. The reaction mixture was stirred for an additional 1 h at room temperature and then concentrated *in vacuo*. After addition of water (50 ml), the residue was extracted with *n*-hexane. The extract was evaporated *in vacuo* and the residue was distilled under reduced pressure to give **11** as yellow oil.

11a: 42% yield, bp 60—65 °C (10 mmHg). MS *m/z*: 135 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2250 (C≡C). ^{1}H-NMR δ: 1.80 (3H, d, J=2 Hz, C≡C–Me), 2.05—2.50 (2H, m, 5-H_2), 2.29 (3H, s, N–Me), 2.90 (2H, m, 2-H_2), 3.55 (1H, m, 6-H), 5.64 (2H, m, 3- and 4-H). *Anal.* Calcd for $C_9H_{13}N$: C, 80.00; H, 9.63; N, 10.37. Found: C, 79.72; H, 9.48; N, 10.21.

11b: 40% yield, bp 70—75 °C (6 mmHg). MS *m/z*: 177 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2250 (C≡C). ^{1}H-NMR δ: 0.90 (3H, t, J=7 Hz, *n*-Bu–Me), 1.35—1.60 (4H, m, –C<u>H</u>$_2$C<u>H</u>$_2$CH$_3$), 2.20 (2H, m, C≡C–C<u>H</u>$_2$–), 2.02—2.45 (2H, m, 5-H_2), 2.29 (3H, s, N–Me), 2.90 (2H, m, 2-H_2), 3.42 (1H, m, 6-H), 5.55 (2H, m, 3- and 4-H). *Anal.* Calcd for $C_{12}H_{19}N$: C, 81.36; H, 10.91; N, 7.91. Found: C, 81.13; H, 10.59; N, 7.92.

11c: 51% yield, bp 108—113 °C (5 mmHg). MS *m/z*: 197 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2250 (C≡C). ^{1}H-NMR δ: 2.35—2.53 (2H, m, 5-H_2), 2.40 (3H, s, N–Me), 3.05 (2H, m, 2-H_2), 3.72 (1H, m, 6-H), 5.60 (2H, m, 3- and 4-H), 7.10—7.45 (5H, m, Ph–H). *Anal.* Calcd for $C_{14}H_{15}N$: C, 85.28; H, 7.61; N, 7.11. Found: C, 85.41; H, 7.39; N, 7.02.

6-Ethynyl-1-methyl-1,2,5,6-tetrahydropyridine *N*-Acetylimides (14a—c and 15a—c)——General Procedure: A solution of *O*-mesitylenesulfonylhydroxylamine (1.1 mol eq) in CH_2Cl_2 (20 ml) was added dropwise to a solution of **11** (10—15 mmol) in CH_2Cl_2 (10—20 ml) with stirring in an ice bath. The reaction mixture was stirred for an additional 30 min and then evaporated to dryness *in vacuo* to afford a mixture of the 1-amino-6-ethynyl-1-methyl-1,2,5,6-tetrahydropyridinium mesitylenesulfonates **12** and **13**, which were too hygroscopic to be isolated and thus used in the following acetylation without separation. A mixture of the salts and acetic anhydride (50 ml) was heated at 120 °C for 4 h and then evaporated *in vacuo*. After addition of water (10 ml), the residue was titrated with 5% NaOH using phenolphthalein as an indicator and then concentrated *in vacuo* below 50 °C. The residue was chromatographed on alumina using CH_2Cl_2–MeOH (100 : 1) as an eluent to give the *cis*-imide (**14**) and the *trans*-imide (**15**), successively.

14a: 41% yield, mp 64—65 °C, colorless prisms (from acetone–*n*-hexane). MS *m/z*: 192 (M^+), IR ν_{max}^{KBr} cm^{-1}: 1580 (C=O), 2250 (C≡C). ^{1}H-NMR δ: 1.75 (3H, s, NCOMe), 1.89 (3H, d, J=2 Hz, C≡C–Me), 2.21—2.83 (2H, m, 5-H_2), 3.48 (3H, s, NMe), 3.87—4.32 (2H, m, 2-H_2), 5.52—5.92 (3H, m, 3-, 4-, and 6-H). *Anal.* Calcd for $C_{11}H_{16}N_2O$: C, 68.75; H, 8.33; N, 14.58. Found: C, 68.43; H, 8.46; N, 14.57.

15a: 10% yield, colorless oil. MS *m/z*: 192 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1580 (C=O), 2250 (C≡C). ^{1}H-NMR δ: 1.79 (3H, s, NCOMe), 1.87 (3H, d, J=2 Hz, C≡C–Me), 2.75 (2H, m, 5-H_2), 3.46 (3H, s, NMe), 3.92—4.58 (2H, m, 2-H_2), 5.40—5.45 (1H, m, 6-H), 5.61—6.00 (2H, m, 3- and 4-H). *Anal.* Calcd for $C_{11}H_{16}N_2O$: C, 68.75; H, 8.33; N, 14.58. Found: C, 68.68; H, 8.52; N, 14.37.

14b: 60% yield, colorless oil. MS *m/z*: 234 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1580 (C=O), 2250 (C≡C). ^{1}H-NMR δ: 0.92 (3H, br t, J=7 Hz, *n*-Bu–Me), 1.22—1.58 (4H, m, –CH$_2$(C<u>H</u>$_2$)$_2$–), 2.10—2.35 (2H, m, C≡C–C<u>H</u>$_2$–), 1.78 (3H, s, NCOMe), 2.33—2.80 (2H, m, 5-H_2), 3.47 (3H, s, NMe), 3.71—4.28 (2H, m, 2-H_2), 5.41—6.02 (2H, m, 3-, 4-, and 6-H). *Anal.* Calcd for $C_{14}H_{22}N_2O$: C, 71.79; H, 9.40; H, 11.97. Found: C, 71.92; H, 9.51; N, 11.82.

15b: 14% yield, colorless oil. MS *m/z*: 234 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1580 (C=O), 2250 (C≡C). ^{1}H-NMR δ: 0.88 (3H, br t, J=7 Hz, *n*-Bu–Me), 1.23—1.60 (4H, m, –CH$_2$(C<u>H</u>$_2$)$_2$–), 2.18—2.25 (2H, m, C≡C–C<u>H</u>$_2$–), 1.80 (3H, s, NCOMe), 2.61—2.65 (2H, m, 5-H_2), 3.40 (3H, s, NMe), 3.80—4.35 (2H, m, 2-H_2), 5.42—5.91 (3H, m, 3-, 4-, and 6-H). *Anal.* Calcd for $C_{14}H_{22}N_2O$: C, 71.79; H, 9.40; N, 11.97. Found: C, 71.73; H, 9.36; N, 11.78.

14c: 56% yield, mp 126—128 °C, colorless prisms (from acetone–*n*-hexane). MS *m/z*: 254 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1580 (C=O), 2250 (C≡C). ^{1}H-NMR δ: 1.81 (3H, s, NCOMe), 2.33—2.91 (2H, m, 5-H_2), 3.51 (3H, s, NMe), 3.84—4.28 (2H, m, 2-H_2), 5.39—5.90 (2H, m, 3- and 4-H), 6.11 (1H, m, 6-H), 7.21—7.28 (5H, m, Ph–H). *Anal.* Calcd for $C_{16}H_{18}N_2O$: C, 75.59; H, 7.09; N, 11.02. Found: C, 75.38; H, 6.91; N, 11.00.

15c: 14% yield, colorless oil. MS *m/z*: 254 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1580 (C=O), 2250 (C≡C). ^{1}H-NMR δ: 1.84 (3H, s, NCOMe), 2.65—2.73 (2H, m, 5-H_2), 3.44 (3H, s, NMe), 3.81—4.44 (2H, m, 2-H_2), 5.49—5.91 (3H, m, 3-, 4-, and 6-H), 7.21—7.27 (5H, m, Ph–H). *Anal.* Calcd for $C_{16}H_{18}N_2O$: C, 75.59; H, 7.09; N, 11.02. Found: C, 75.34; H, 6.89; N, 10.82.

Thermolysis of the *N*-Imides (14a—c)——General Procedure: A solution of **14** (3 mmol) in xylene (10 ml) was refluxed at 140 °C for 4 h. After cooling, the reaction solution was chromatographed on silica gel using *n*-hexane–ether (1 : 1) as an eluent to give the 1-acetyl-2-methyl-2,3-dihydro-1,2-diazonines (**16a—c**) and the 1-acetyl-3-ethynyl-2-methyl-5-vinyltetrahydropyrazoles (**17a, b**), successively.

16a: 15% yield, yellow oil. MS *m/z*: 192 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1660 (C=O), 980 (*trans* C=C). ^{1}H-NMR ($CDCl_3$, room temp.) δ: 2.04 and 2.20 (3H, each s, intensity ratio 1 : 2, NCOMe), 2.51—3.00 (3H, m, 9-Me), 2.58 and 2.97 (3H, each s, intensity ratio 2 : 1, NMe), 3.51—4.28 (2H, m, 3-H_2), 5.12—6.38 (5H, m, olefinic H); δ (toluene-d_8, 110 °C): 2.01 (3H, s, 9-Me), 2.01 (3H, s, NCOMe), 2.64 (3H, s, NMe), 3.52 (2H, m, 3-H_2), 5.00—6.15 (5H, m, olefinic H). *Anal.* Calcd for $C_{11}H_{16}N_2O$: C, 68.75; H, 8.33; N, 14.58. Found: C, 68.56; H, 8.34; N, 14.63.

16b: 18% yield, yellow oil. MS *m/z*: 234 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1660 (C=O), 980 (*trans* C=C). ^{1}H-NMR δ ($CDCl_3$, room temp.): 0.95—1.03 (3H, m, *n*-Bu–Me), 1.32—1.69 (4H, m, –CH$_2$(C<u>H</u>$_2$)$_2$–), 2.83—2.88 (2H, m, C=C–C<u>H</u>$_2$–), 1.97 and 2.16 (3H, each s, intensity ratio 1 : 2, NCOMe), 2.57 and 2.93 (3H, each s, intensity ratio 2 : 1, NMe),

3.51—4.30 (2H, m, 3-H_2), 5.42—6.49 (5H, m, olefinic H); δ (toluene-d_8, 110 °C): 0.89 (3H, t, J=7 Hz, *n*-Bu–Me), 1.20—1.62 (4H, m, $-CH_2(C\underline{H}_2)_2-$), 2.05 (2H, m, C≡C–C$\underline{H}_2$–), 1.98 (3H, s, NCOMe), 2.61 (3H, s, NMe), 3.50 (2H, m, 3-H_2), 5.35—6.30 (5H, m, olefinic H). *Anal.* Calcd for $C_{14}H_{22}N_2O$: C, 71.79; H, 9.40; N, 11.97. Found: C, 71.69; H, 9.58; N, 11.97.

16c: 16% yield, yellow oil. MS *m/z*: 254 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1670 (C=O), 990 (*trans* C=C). ^{1}H-NMR δ ($CDCl_3$, room temp. at 400 MHz): 1.88 and 2.10 (3H, each s, intensity ratio 1 : 2, NCOMe), 2.55 and 2.66 (3H, each s, intensity ratio 2 : 1, NMe), 3.44 and 3.59 (2H, each d, J=7 Hz, intensity ratio 2 : 1, 3-H_2), 5.56 and 5.68 (1H, each dt, J=11 and 7 Hz, intensity ratio, 2 : 1, 4-H), 5.85 and 5.88 (1H, each dd, J=16 and 12 Hz, intensity ratio 2 : 1, 7-H), 6.24 (1H, dd, J=12 and 11 Hz, 5-H), 6.92 (1H, dd, J=16 and 12 Hz, 6-H), 7.13 and 7.15 (1H, each d, J=12 Hz, 8-H), 7.25—7.45 (5H, m, Ph–H); δ (toluene-d_8, 110 °C): 1.89 (3H, s, NCOMe), 2.50 (3H, s, NMe), 3.52 (2H, m, 3-H_2), 5.45—7.00 (5H, m, olefinic H), 7.35—7.52 (5H, m, Ph–H). *Anal.* Calcd for $C_{16}H_{18}N_2O$: C, 75.59; H, 7.09; N, 11.02. Found: C, 75.57; H, 6.88; N, 10.92.

17a: 7% yield, colorless oil. MS *m/z*: 192 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1660 (C=O), 2100 (C≡C). ^{1}H-NMR δ: 1.83 (3H, s, C≡C–Me), 2.19 (3H, s, NCOMe), 2.62 (3H, s, NMe), 2.79—3.17 (4H, m, 3-, 4-, and 5-H), 5.24 (1H, dd, J=17 and 2 Hz, *trans*-2′-H), 5.26 (1H, dd, J=12 and 2 Hz, *cis*-2′-H), 6.01—6.06 (1H, m, 1′-H). *Anal.* Calcd for $C_{11}H_{16}N_2O$: C, 68.75; H, 8.33; N, 14.58. Found: C, 68.81; H, 8.01; N, 14.38.

17b: 8% yield, colorless oil. MS *m/z*: 234 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1660 (C=O), 2100 (C≡C). ^{1}H-NMR δ: 0.90—0.97 (3H, m, *n*-Bu–Me), 1.22—1.61 (4H, m, $-CH_2(C\underline{H}_2)_2-$), 2.03—2.12 (2H, m, C≡C–C$\underline{H}_2$–), 2.18 (3H, s, NCOMe), 2.21—2.42 (2H, m, 4-H_2), 2.62 (3H, s, NMe), 2.82—3.33 (2H, m, 3- and 5-H), 5.23 (1H, dd, J=17 and 2 Hz, *trans*-2′-H), 5.24 (1H, dd, J=12 and 2 Hz, *cis*-2′-H), 6.00—6.05 (1H, m, 1′-H). *Anal.* Calcd for $C_{14}H_{22}N_2O$: C, 71.79; H, 9.40; N, 11.97. Found: C, 71.96; H, 9.36; N, 12.02.

Thermolysis of the *N*-Imides (15a—c)——General Procedure: A solution of **15** (1 mmol) in toluene (5 ml) was refluxed at 110 °C for 1 h. After cooling, the reaction solution was chromatographed on silica gel using *n*-hexane–ether (1 : 1) as an eluent to give the diazonines (**16a—c**) and the pyrazoles (**18a, b**) successively.

16a: 55% yield.

16b: 48% yield.

16c: 70% yield.

18a: 6% yield, colorless oil, MS *m/z*: 192 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1660 (C=O), 2100 (C≡C). ^{1}H-NMR δ: 1.78 (3H, s, C≡C–Me), 2.15 (3H, s, NCOMe), 2.58 (3H, s, NMe), 2.77—3.20 (4H, m, 3-, 4-, and 5-H), 5.15 (1H, dd, J=17 and 2 Hz, *trans*-2′-H), 5.19 (1H, dd, J=12 and 2 Hz, *cis*-2′-H), 5.92 (1H, m, 1′-H). *Anal.* Calcd for $C_{11}H_{16}N_2O$: C, 68.75; H, 8.33; N, 14.58. Found: C, 68.76; H, 8.01; N, 14.49.

18b: 7% yield, colorless oil. MS *m/z*: 234 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1660 (C=O), 2100 (C≡C). ^{1}H-NMR δ: 0.92—0.95 (3H, m, *n*-Bu-Me), 1.22—1.50 (4H, m, $-CH_2(C\underline{H}_2)_2-$), 2.12 (2H, m, C≡C–$CH_2$–), 2.12 (3H, s, NCOMe), 2.25—2.40 (2H, m, 4-H_2), 2.56 (3H, s, NMe), 2.82—3.15 (2H, m, 3- and 5-H), 4.90—5.15 (2H, m, 2′-H_2), 5.52 (1H, m, 1′-H). *Anal.* Calcd for $C_{14}H_{22}N_2O$: C, 71.79; H, 9.40; N, 11.97. Found: C, 71.82; H, 9.38; N, 11.89.

Treatment of 16 with Sodium Ethoxide——General Procedure: A mixture of **16** (0.5 mmol), sodium ethoxide (200 mg), and toluene (10 ml) was refluxed for 4 h. After cooling, the reaction mixrure was washed with satd. NaCl, dried, and concentrated *in vacuo*. The residue was chromatographed on silica gel using *n*-hexane–ether (1 : 1) as an eluent to give the *cis*-diazonines (**22a, b**) as yellow oils.

22a: 48% yield. MS *m/z*: 192 (M^+). ^{1}H-NMR δ: 1.76 (3H, s, 9-Me), 2.12 (3H, s, NCOMe), 2.55 (3H, s, NMe), 2.82—3.13 (2H, m, 3-H_2), 5.40—6.02 (5H, m, olefinic H). *Anal.* Calcd for $C_{11}H_{16}N_2O$: C, 68.75; H, 8.33; N, 14.58. Found: C, 68.66; H, 8.34; N, 14.31.

22b: 52% yield. MS *m/z*: 234 (M^+). ^{1}H-NMR: 0.92—1.00 (3H, m, *n*-Bu–Me), 1.35—1.42 (4H, m, $-CH_2(C\underline{H}_2)_2-$), 2.10 (2H, m, C≡C–$CH_2$–), 2.16 (3H, s, NCOMe), 2.55 (3H, s, NMe), 2.81—3.33 (2H, m, 3-H_2), 5.21—6.03 (5H, m, olefinic H). *Anal.* Calcd for $C_{14}H_{22}N_2O$: C, 71.79; H, 9.40; N, 11.97. Found: C, 71.92; H, 9.38; N, 11.71.

1-Ethoxycarbonylmethyl-6-ethynyl-1-methyl-1,2,5,6-tetrahydropyridinium Bromides (25a—c)——General Procedure: A solution of ethoxycarbonylmethyl trifluoromethanesulfonate (3.07 g, 1.3 mol eq) in acetonitrile (10 ml) was added dropwise to a solution of an ethynyltetrahydropyridine (**11**: 10 mmol) in acetonitrile (10 ml) with stirring in an ice bath. The reaction mixture was stirred for an additional 1 h at room temperature and then evaporated *in vacuo*. The residue was washed with *n*-hexane and dissolved in ethanol (20 ml). After addition of potassium bromide (6 g), the solution was stirred for 2 h at room temperature. The resulting precipitates were filtered off and the filtrate was evaporated to dryness *in vacuo* to give the solid salt (**25**) quantitatively as a mixture of two stereoisomers (*cis* : *trans* = *ca.* 1 : 2). It was difficult to separate the isomers and thus each mixture was used in the following reaction without separation. Spectral data for the mixtures are as follows:

25a: IR ν_{max}^{KBr} cm^{-1}: 1740 (C=O), 2250 (C≡C). ^{1}H-NMR δ: 1.34 (3H, t, J=7 Hz, $CO_2CH_2C\underline{H}_3$), 1.98 (3H, d, J=2 Hz, C≡C–Me), 2.71—2.75 (2H, m, 5-H_2), 3.31 (3H×2/3, s, NMe of the isomer with axial methyl group), 3.34 (3H×1/3, s, NMe of the isomer with equatorial methyl group), 4.25—4.70 (4H, m, 2-H_2 and NCH_2–), 4.30 (2H, q, J=7 Hz, $CO_2C\underline{H}_2CH_3$), 5.03—5.08 (1H, m, 6-H), 5.62—6.11 (2H, m, 3- and 4-H).

25b: IR ν_{max}^{KBr} cm^{-1}: 1740 (C=O), 2250 (C≡C). ^{1}H-NMR δ: 0.85—0.92 (3H, m, *n*-Bu–Me), 1.50—1.58 (4H, m, $-CH_2(C\underline{H}_2)_2-$), 2.25—2.34 (2H, m, C≡C–CH_2–), 1.30 (3H, t, J=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.71—2.77 (2H, m, 5-H_2), 3.23

(3H × 2/3, s, NMe of the isomer with axial methyl group), 3.35 (3H × 1/3, s, NMe of the isomer with equatorial methyl group), 4.22 (2H, q, J=7 Hz, $CO_2C\underline{H}_2$–), 4.21—4.52 (4H, m, 2-H_2 and NCH_2–), 4.91—4.95 (1H, m, 6-H), 5.51—5.90 (2H, m, 3- and 4-H).

25c: IR ν_{max}^{KBr} cm^{-1}: 1735 (C=O), 2250 (C≡C). ^{1}H-NMR δ: 1.28 (3H, t, J=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.78—2.83 (2H, m, 5-H_2), 3.31 (3H × 2/3, s, NMe of the isomer with axial methyl group), 3.43 (3H × 1/3, s, NMe of the isomer with equatorial methyl group), 4.23 (2H, q, J=7 Hz, CO_2CH_2–), 4.31—4.70 (4H, m, 2-H_2 and NCH_2–), 5.20—5.25 (1H, m, 6-H), 5.51—5.60 (2H, m, 3- and 4-H), 7.21—7.35 (5H, m, Ph–H).

Treatment of the Salts (25a—c) with DBU——General Procedure: DBU (1 ml) was added dropwise to a solution of **25** (5 mmol) in tetrahydrofuran (30 ml) with stirring in an ice bath. The reaction mixture was stirred for an additional 1 h at room temperature and then diluted with CH_2Cl_2 (30 ml). The mixture was washed with satd. NaCl, dried, and then evaporated *in vacuo*. The residue was chromatographed on silica gel using *n*-hexane–ether (3 : 1) as an eluent to give the 1-methyl-9-ethoxycarbonylazacyclononan-3,6,7-trienes (**27**) and the 7-(*N*-ethoxycarbonylmethyl-*N*-methylamino)-3,5-heptadien-1-ynes (**28**), successively.

27a: 8% yield, colorless oil. MS m/z: 221 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1960 (C=C=C), 1730 (C=O). ^{1}H-NMR δ: 1.26 (3H, t, J=7 Hz, $CO_2CH_2C\underline{H}_3$), 1.87 (3H, d, J=2 Hz, 8-Me), 2.60 (3H, s, NMe), 2.61—2.91 (4H, m, 2- and 5-H_2), 3.68 (1H, br s, 9-H), 4.17 (2H, q, J=7 Hz, $CO_2C\underline{H}_2$–), 5.35—5.80 (3H, m, 3-, 4-, and 6-H). ^{13}C-NMR δ: 14.4 (q, $CO_2CH_2\underline{C}H_3$), 20.2 (q, 8-Me), 26.3 (t, C_5), 44.5 (q, NMe), 49.0 (t, C_2), 60.1 (t, $CO_2\underline{C}H_2$–), 69.9 (d, C_9), 91.8 (d, C_6), 103.5 (s, C_8), 122.5 (d, C_4), 134.7 (d, C_3), 171.4 (s, C=O), 204.7 (s, C_7: C=$\underline{C}$=C). *Anal.* Calcd for $C_{13}H_{19}NO_2$: C, 70.59; H, 8.60; N, 6.33. Found: C, 70.50; H, 8.79; N, 6.22.

27b: 12% yield, colorless oil. MS m/z: 263 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1960 (C=C=C), 1735 (C=O). ^{1}H-NMR δ: 0.90—0.95 (3H, m, *n*-Bu–Me), 1.21—1.43 (4H, m, $-CH_2C\underline{H}_2C\underline{H}_2CH_3$), 2.10—2.20 (2H, m, $-C\underline{H}_2CH_2CH_2CH_3$), 1.22 (3H, t, J=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.53 (3H, s, NMe), 2.41—2.93 (4H, m, 2- and 5-H_2), 3.58 (1H, br s, 9-H), 4.07 (2H, q, J=7 Hz, CO_2CH_2–), 5.25—5.57 (3H, m, 3-, 4-, and 6-H). *Anal.* Calcd for $C_{16}H_{25}NO_2$: C, 73.00; H, 9.51; N, 5.32. Found: C, 72.87; H, 9.36; N, 5.30.

27c: 11% yield, colorless oil. MS m/z: 283 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1950 (C=C=C), 1720 (C=O), ^{1}H-NMR δ: 1.26 (3H, t, J=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.63 (3H, s, NMe), 2.52—3.18 (4H, m, 2- and 5-H_2), 4.21 (2H, q, J=7 Hz, CO_2CH_2–), 4.25 (1H, br s, 9-H), 5.33—5.70 (3H, m, 3-, 4-, and 6-H), 7.40—7.45 (5H, m, Ph–H). *Anal.* Calcd for $C_{18}H_{21}NO_2$: C, 76.32; H, 7.42; N, 4.95. Found: C, 76.51; H, 7.44; N, 4.91.

28a: 30% yield, yellow oil. MS m/z: 221 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2225 (C≡C), 1730 (C=O). ^{1}H-NMR δ: 1.28 (3H, t, 7 Hz, $CO_2CH_2C\underline{H}_3$), 1.98 (3H, d, J=2 Hz, C≡C–Me), 2.38 (3H, s, NMe), 3.22 (2H, s, NCH_2–), 3.23 (2H, d, J=8 Hz, 7-H_2), 4.20 (2H, q, J=7 Hz, CO_2CH_2–), 5.49 (1H, dd, J=8 and 10 Hz, 6-H), 5.56 (1H, dd, J=2 and 16 Hz, 3-H), 6.17 (1H, dd, J=10 and 12 Hz, 5-H), 6.87 (1H, dd, J=12 and 16 Hz, 4-H). *Anal.* Calcd for $C_{13}H_{19}NO_2$: C, 70.59; H, 8.60; N, 6.33. Found: C, 70.73; H, 8.59; N, 6.07.

28b: 15% yield, yellow oil. MS m/z: 263 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2225 (C≡C), 1735 (C=O). ^{1}H-NMR δ: 0.91 (3H, t, J=7 Hz, *n*-Bu–Me), 1.40—1.62 (4H, m, $-CH_2C\underline{H}_2C\underline{H}_2CH_3$), 2.31—2.35 (2H, m, C≡C–CH_2–), 1.25 (3H, t, J=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.33 (3H, s, NMe), 3.16 (2H, s, NCH_2–), 3.25 (2H, d, J=7 Hz, 7-H_2), 4.11 (2H, q, J=7 Hz, CO_2CH_2–), 5.39 (1H, dd, J=7 and 12 Hz, 6-H), 5.50 (1H, dd, J=2 and 16 Hz, 3-H), 6.05 (1H, dd, J=10 and 12 Hz, 5-H), 6.66 (1H, dd, J=12 and 16 Hz, 4-H). *Anal.* Calcd for $C_{16}H_{25}NO_2$: C, 73.00; H, 9.51; N, 5.32. Found: C, 73.26; H, 9.66; N, 5.19.

28c: 13% yield, yellow oil. MS m/z: 283 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2225 (C≡C), 1730 (C=O), ^{1}H-NMR δ: 1.24 (3H, t, J=7 Hz, $CO_2CH_2C\underline{H}_3$), 2.34 (3H, s, NMe), 3.17 (2H, s, N–CH_2–), 3.28 (2H, d, J=7 Hz, 7-H_2), 4.09 (2H, q, J=7 Hz, CO_2CH_2–), 5.40—5.92 (4H, m, 3-, 4-, 5-, and 6-H), 7.20—7.25 (5H, m, Ph–H). *Anal.* Calcd for $C_{18}H_{21}NO_2$: C, 76.32; H, 7.42; N, 4.95. Found: C, 76.29; H, 7.58; N, 5.00.

References and Notes

1) Part IV: H. Sashida and T. Tsuchiya, *Chem. Pharm. Bull.*, **32**, 4117 (1984).
2) A. R. Lepley and A. G. Giumani, "Mechanisms of Molecular Migrations," Vol. 3, ed. by B. S. Thyagrajan, Wiley-Interscience, New York, 1971, p. 207; K. Chantrapromma, W. D. Ollis, and I. O. Sutherland, *J. Chem. Soc., Chem. Commun.*, **1978**, 670, 672, 673.
3) W. J. McKillip, E. A. Sedor, B. M. Culbertson, and S. Wawzonek, *Chem. Rev.*, **73**, 255 (1973); J. E. Baldwin, J. E. Brown, and R. W. Cordell, *J. Chem. Soc., Chem. Commun.*, **1970**, 31; K. Chantrapromma, W. D. Ollis, and I. O. Sutherland, *ibid.*, **1977**, 97; I. D. Brindle and M. S. Gibson, *J. Chem. Soc., Perkin Trans. 1*, **1979**, 517; R. W. Jemsen, T. Laird, W. D. Ollis, and I. O. Sutherland, *ibid.*, **1980**, 1450.
4) A. H. Wragg, T. S. Stevens, and D. M. Ostle, *J. Chem. Soc.*, **1958**, 4057; J. I. Brauman and W. A. Sanderson, *Tetrahedron*, **23**, 37 (1967); Y. Yamamoto, J. Oda, and Y. Inouye, *J. Chem. Soc., Chem. Commun.*, **1973**, 848; P. T. Lansbury and J. E. Rhodes, *ibid.*, **1974**, 21; S. Ranganathan, D. Ranganathan, R. S. Sidhu, and A. K. Mehrotra, *Tetrahedron Lett.*, **1973**, 3577.
5) P. A. Grieco, D. Boxler, and K. Hiroi, *J. Org. Chem.*, **38**, 2572 (1973); W. Ando, *Acc. Chem. Res.*, **10**, 179 (1977); T. L. Gilchrist and C. J. Moody, *Chem. Rev.*, **77**, 409 (1977).

6) E. Vedjes, M. J. Arco, D. W. Powell, J. M. Renga, and S. P. Singer, *J. Org. Chem.*, **43**, 4831 (1978).
7) T. Tsuchiya, H. Sashida, and H. Sawanishi, *Chem. Pharm. Bull.*, **26**, 2880 (1978); T. Tsuchiya and H. Sashida, *ibid.*, **29**, 1887 (1981).
8) J. E. Baldwin, R. E. Hackler, and D. P. Kelly, *Chem. Commun.*, **1968**, 1083; A. Terada and Y. Kishida, *Chem. Pharm. Bull.*, **17**, 966 (1969).
9) A. H. Khuthier and M. A. Al-Iraqi, *J. Chem. Soc., Chem. Commun.*, **1979**, 9; J. C. Craig, N. N. Ekwuribe, and L. D. Gruenke, *Tetrahedron Lett.*, **1979**, 4025; G. Hallström, B. Lindke, A. H. Khutier, and M. A. Al-Iraqi, *ibid.*, **1980**, 677.
10) W. D. Ollis, I. O. Sutherland, and Y. Thebtaranonth, *J. Chem. Soc., Chem. Commun.*, **1973**, 657; S. Mageswaran, W. D. Ollis, D. A. Southan, I. O. Sutherland, and Y. Thebtaranonth, *J. Chem. Soc., Perkin Trans. 1*, **1981**, 1969.
11) T. Tsuchiya and H. Sashida, *J. Chem. Soc., Chem. Commun.*, **1980**, 1109; T. Tsuchiya, H. Sashida, and A. Konoshita, *Chem. Pharm. Bull.*, **31**, 4568 (1983).
12) A part of this work has been published in a preliminary communication: H. Sashida and T. Tsuchiya, *Heterocycles*, **19**, 281 (1982).
13) K. Sonogashira, Y. Tohda, and N. Hagihara, *Tetrahedron Lett.*, **1975**, 4467.
14) Y. Tamura, J. Minamikawa, and M. Ikeda, *Synthesis*, **1977**, 1; and references cited therein.
15) J. K. Becconsall, R. A. Y. Jones, and J. McKenna, *J. Chem. Soc.*, **1965**, 1762; H. O. House, B. A. Tefertiller, and C. G. Pitt, *J. Org. Chem.*, **31**, 1073 (1966).
16) Y. Tamura, J. Minamikawa, Y. Kita, J. H. Kin, and M. Ikeda, *Tetrahedron*, **29**, 1063 (1973).
17) T. M. Bere, N. D. Hershey, H. O. House, and C. G. Swain, *J. Org. Chem.*, **37**, 997 (1972).