On the Reaction of *N*-Vinyliminophosphoranes with 2,4,6-Cyclooctatrienone. Intermediate Formation of 8-Azabicyclo-[5.3.1]undeca-2,4,7,9-tetraene Ring System[1)]

Makoto NITTA* and Nobuhiro KANOMATA
Department of Chemistry, School of Science and Engineering, Waseda University, Shinjuku-ku, Tokyo 169
(Received November 12, 1988)

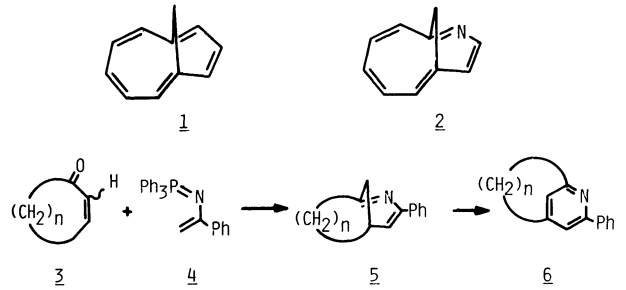
Synopsis. The reaction of *N*-(1-phenylvinyl)iminotriphenylphosphorane and of *N*-(1,3,5-cycloheptatrienyl)iminotributylphosphorane with 2,4,6-cyclooctatrienone gave an intermediacy of 8-azabicyclo[5.3.1]undeca-2,4,7,9-tetraene derivatives, which underwent an intramolecular Diels–Alder reaction to construct a tetracyclic ring system.

The 1,6-methano[10]annulenes[2,3)] and their nitrogen analogues[4,5)] have been widely investigated by Vogel et al. and have been recognized as aromatic compounds in terms of their chemical and spectroscopic properties. The synthesis of 1,5-methano[10]-annulene (**1**)[6,7)] was accomplished via two different routes, and the ^{1}H NMR clarified that the diamagnetic ring current is induced in this system, despite the expected differences in the pi-bond torsion between the two isomeric annulenes. However, no synthetic entry into 8-azabicyclo[5.3.1]undeca-1,3,5,7,9-pentaene (**2**), which is an analogue of **1**, has appeared. Thus, we attempted the synthesis of the 8-azabicyclo[5.3.1]undeca-2,4,7,9-tetraene skeleton, the dehydrogenation of which was expected to give the ring system, **2**.

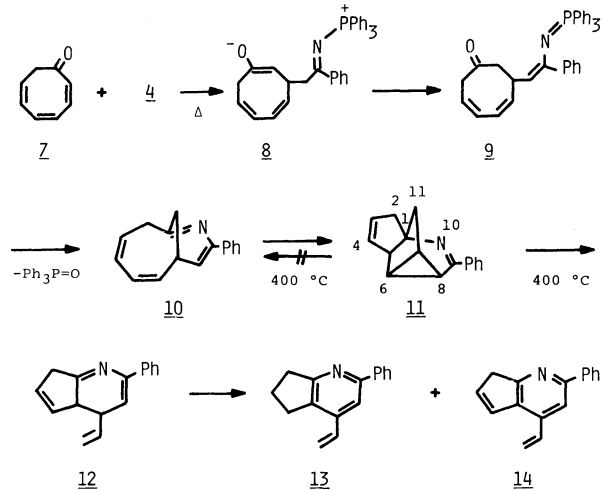
Our synthetic strategy is based upon utilizing *N*-vinyliminophosphoranes, which are very convenient synthones for constructing various heterocyclic ring systems.[8–13)] Among these synthetic reactions, *N*-(1-phenylvinyl)iminotriphenylphosphorane (**4**) reacted with a series of cyclic α,β-unsaturated ketones **3** to give [*n*](2,4)pyridinophane derivatives (**6**, n=6—9), as shown in Scheme 1.[12)] Therefore, the preparation of an 8-azabicyclo[5.3.1]undeca-2,4,7,9-tetraene ring system by using *N*-vinyliminophosphoranes, **4** and *N*-(1,3,5-cycloheptatrienyl)iminotributylphosphorane (**15**), with 2,4,6-cyclooctatrienone seemed to be promising.

The reaction of **7**[14)] and **4**[9,11)] in anhydrous 1,2-dimethylbenzene under reflux for 15 h gave 9-phenyl-10-azatetracyclo[5.3.1.0.^{1,5}0^{6,8}]undeca-3,9-diene (**11**) in 47% yield (Scheme 2). The formation of **11** can be reasonably explained as follows.[12)] The Michael addition of **4** to the β-carbon atom of **7** gives **8**, the hydrogen transfer of which gives **9**. The intramolecular aza-Wittig reaction of **9** is expected to give **10**. However, compound **10** seems to be labile under reaction conditions and underwent an intramolecular Diels–Alder reaction to give **11**. The thermal lability of **10** to give **11** is reminiscent of the thermal reactivity of bicyclo[5.3.1]undeca-2,4,7,9-tetraene, the C_2=C_3 double bond and diene system in which are located appropriate for the Diels–Alder reaction.[6a)] The assignments of ^{1}H and ^{13}C resonances of **11** are accomplished by 2D ^{1}H NMR and 2D ^{1}H–^{13}C NMR analysis. Considering the ^{1}H NMR spectrum, a pair of methylene protons (11-H_2) appears at δ 1.93 and δ 0.85, which is shielded by the C=N double bond. The remaining signals appear at δ 1.93—1.99 (5-H, 6-H, and 7-H), δ 2.56 (8-H), δ 2.66 and 2.85 (a pair of methylene protons, 2-H_2) δ 5.76 and 5.79 (a pair of vinyl protons, 3-H and 4-H), and δ 7.39 and 7.38 (phenyl group). The ^{1}H NMR and ^{13}C NMR (see Experimental) characteristics are in good accordance with the proposed structure of **11**. Since we could not succeed in isolating the intermediate **10**, we tried a retro Diels–Alder reaction of **11** to **10**. However, the flash pyrolysis of **11** at 400 °C afforded 6,7-dihydro-2-phenyl-4-vinyl-5*H*-cyclopenta[*b*]pyridine (**13**) and 2-phenyl-4-vinyl-7*H*-cyclopenta[*b*]pyridine (**14**) in 22 and 4% yield, respectively. The spectral data of **13** and **14** supported the structures (see Experimental). The formation of **13** and **14** is explained by retro Diels–Alder reaction including methylene bridge, a typical Cope rearrangement of tricyclo[3.2.1.0^{2,7}]oct-3-ene system,[15)] to result in the formation of an intermediate **12** followed by hydrogen transfer or dehydrogenation (Scheme 2).

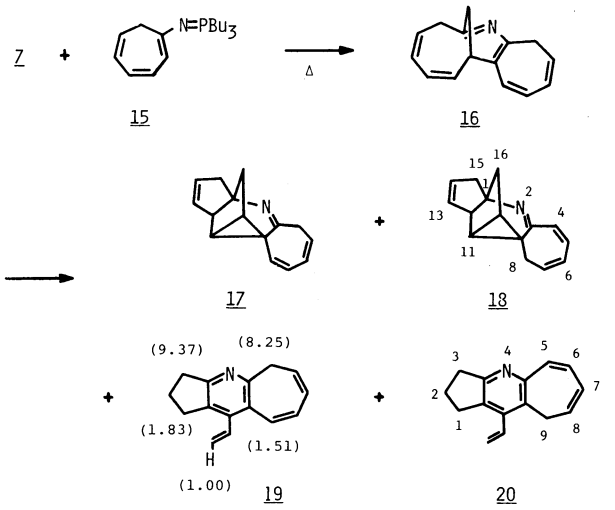
Similarly, the reaction of **9** with *N*-(1,3,5-cycloheptatrienyl)iminotributylphosphorane (**15**)[13)] in anhydrous bromobenzene under reflux afforded a mixture of 2-



Scheme 1.



Scheme 2.



Scheme 3.

azapentacyclo[8.5.1.0.^{1,12}0.^{3,9}0^{9,11}]hexadeca-2,5,7,13-tetraene (**17**) (35%), 2-azapentacyclo[8.5.1.0.^{1,12}0.^{3,9}0^{9,11}]-hexadeca-2,4,6,13-tetraene (**18**) (35%), 1,2,3,5-tetrahydro-10-vinylcyclohepta[*b*]cyclopenta[*e*]pyridine (**19**) (5%), and 1,2,3,9-tetrahydro-10-vinylcyclohepta[*b*]cyclopenta-[*e*]pyridine (**20**) (1.4%), via the possible intermediate **16** (Scheme 3). Although the isolation of both **17** and **18** was unsuccessful, compound **18** was isolated in pure form in the thermal reaction of a mixture of **17** and **18** (vide infra). The ^{1}H NMR spectrum of **18** exhibited signals of a shielded methylene proton (16-H) at δ 0.65, which is located over the C=N double bond, a pair of methylene protons (15-H$_2$) at δ 2.55 and 2.70, two vinyl protons (13-H and 14-H) at δ 5.69, and four protons (10-H, 11-H, 12-H, and 16-H) at δ 1.50—1.90. The chemical shifts and the coupling patterns of these signals are similar to the corresponding signals of **11**. The remaining signals on the cycloheptadiene moiety for **18** appear at δ 6.48 (4-H), δ 6.20 (5-H), and δ 5.99 (6-H and 7-H), in addition to the signals of a pair of methylene protons at δ 2.23 and 2.29 (8-H$_2$). The assigned ^{1}H NMR and ^{13}C NMR (see Experimental) characteristics are in good accordance with the proposed structure **18**. On the other hand, the ^{1}H NMR signals corresponding to **17** were read from the spectrum of a mixture of **17** and **18**. The signals of a shielded methylene proton (16-H) appearing at δ 0.73, three methine protons (10-H, 11-H, and 12-H) and a methylene proton (16-H) at δ 1.47—2.07, a pair of methylene protons (15-H$_2$) at δ 2.37—2.77, and a pair of vinyl protons (13-H and 14-H) appearing at around δ 5.71 are suggestive of a skeleton similar to **18**. Furthermore, two methylene protons appearing at δ 3.00—3.20 and four vinyl protons (5-H, 6-H, 7-H, and 8-H) appearing at δ 5.30—6.55 are suggestive of the cycloheptadiene moiety. A characteristic difference between **17** and **18** is the chemical shifts of methylene protons in their cycloheptadiene rings. The fact that the methylene signals (4-H$_2$) of **17** appear at lower field than those (8-H$_2$) of **18** is ascribed to a deshielding effect of the nitrogen atom which is close to 4-H$_2$ in **17**. The ^{1}H NMR and ^{13}C NMR (assigned in Experimental) spectra of **19** and **20** revealed that they have a cycloheptatriene ring fused on the pyridine ring. The methylene protons in the cycloheptatriene rings of **19** (δ 3.19) and **20** (δ 2.97), and the pseudo-contact ^{1}H NMR spectra of **19** obtained by using Eu(fod)$_3$ unequivocally supported the structures. The relative down-field shifts of the δ's of typical protons are given in parentheses in the structural formula **19**. Compound **18** could be derived from 1,5-hydrogen shift of **17**. The independent thermal reaction of a 1/1 mixture of **17** and **18** in bromobenzene under reflux gave **19** and **20**, in addition to **18**. The pathways for the formation of **19** and **20** can be expalined by a Cope rearrangement of **17** and **18**, as in the case of **11**. The thermal isomerization reaction of **19** in refluxing bromobenzene also occurred to give **20**, thus suggesting the interconversion between **19** and **20**.

The smallest cyclic α,β-unsaturated ketone which reacted with *N*-vinyliminophosphoranes is cyclononenone, giving [6](2,4)pyridinophane (Scheme 1).[12] We have clarified here that the *N*-vinyliminophosphoranes, **4** and **15**, actually react with 8-membered ketone **7** to form constrained intermediates, 8-azabicyclo[5.3.1]undeca-2,4,7,9-tetraene derivatives **10** and **16**.

Experimental

The IR spectra were recorded on a Shimadzu IR-400 spectrometer. The ^{1}H NMR spectra were recorded on a Hitachi R-24 or on a Hitachi R-90H spectrometer. The ^{13}C NMR spectra were recorded on a Hitachi R-90H or on a JEOL GSX400 spectrometer. The 2D ^{1}H NMR and 2D ^{1}H–^{13}C NMR experiments were performed on a JEOL GSX400 spectrometer. The chemical shifts are given in ppm (δ) relative to the internal SiMe$_4$ standard. The mass and high-resolution mass spectral studies were conducted using Shimadzu GCMS QP-1000 and JEOL JMS-DX300 spectrometers. The desired 2,4,6-cyclooctatrienone (**7**),[14] *N*-(1-phenylvinyl)iminotriphenylphosphorane (**4**)[9,11] and *N*-(1,3,5-cycloheptatrienyl)iminotributylphosphorane (**15**)[13] were prepared by the methods described in the literature. All the reactions were carried out under a dry nitrogen atmosphere.

Reaction of 7 with 4. A solution of **7** (60 mg, 0.50 mmol) and **4** (284 mg, 0.75 mmol) in anhydrous 1,2-dimethylbenzene (5 cm^3) was refluxed for 15 h. After the solvent was evaporated, the residue was separated by TLC on silica gel using benzene–ethyl acetate (10/1) as a developer to give **11** (52 mg, 47%), triphenylphosphine oxide (120 mg, 58%) and acetophenone (12 mg, 13%) which arise from the hydrolysis of **4**. For **11**: Mp 44—47 °C; IR (CCl_4), 3059, 2930, 2860, 1592, 1562, 1494, 1446, 1383, 1351, 1292, 1256, 1196, 1182, 1156, 1122, 1106, 1096, 1070, 1022, 992, 936, 842 cm^{-1}; ^{1}H NMR ($CDCl_3$), δ=0.85 (1H, dd, J=11.0, 1.0 Hz), 1.93 (1H, dd, J=11.0, 2.0 Hz), 1.93—1.99 (3H, m), 2.56 (1H, t, J=7.5 Hz), 2.66 (1H, ddd, J=16.0, 2.5, 1.2 Hz), 2.85 (1H, ddd, J=16.0, 2.5, 1.6 Hz), 5.76 (1H, dtd, J=6.1, 2.5, 1.6 Hz), 5.79 (1H, ddt, J=6.1, 2.5, 1.2 Hz), 7.39 (3H, m), 7.83 (2H, m); ^{13}C NMR ($CDCl_3$), δ=18.9 (d, 6-C or 7-C), 19.3 (d, 7-C or 6-C), 20.9 (d, 8-C), 31.4 (t, 11-C), 40.3 (t, 2-C), 50.9 (d, 5-C), 71.1 (s, 1-C), 126.1 (2C, d, Ph), 128.1 (2C, d, Ph), 129.2 (d, Ph), 129.8 (d, 3-C or 4-C), 131.5 (d, 4-C or 3-C), 139.2 (s, Ph), 167.0 (s, 9-C); MS, m/z (rel intensity), 221 (M^+, 68), 220 (100). Found: m/z 221.1219. Calcd for $C_{16}H_{15}N$: M, 221.1204.

Thermal Reaction of 11. A solution of **11** (100 mg, 0.45 mmol) in anhydrous benzene (20 cm^3) was passed through a Pyrex column (15 mm×120 mm) containing glass beads (ϕ=2 mm) preheated at 400 °C under a nitrogen stream (flow rate=20 cm^3 min^{-1}). After concentration of the

collected pyrolysate, the resulting residue was separated by TLC on alumina using hexane–ether (4/1) to give **13** (22 mg, 22%) and **14** (4 mg, 4%). For **13**: Yellow oil; IR (CCl_4), 3067, 2960, 2848, 1593, 1581, 1565, 1500, 1461, 1443, 1430, 1388, 1337, 1224, 1031, 990, 924, 877, 694 cm^{-1}; ^1H NMR ($CDCl_3$), δ=2.14 (2H, tt, J=8.1, 7.9 Hz), 2.99 (2H, t, J=7.9 Hz), 3.08 (2H, t, J=8.1 Hz), 5.50 (1H, dd, J=11.0, 1.1 Hz), 5.90 (1H, dd, J=17.6, 1.1 Hz), 6.76 (1H, dd, J=17.6, 11.0 Hz), 7.29—7.49 (4H, m), 7.89—8.00 (2H, m); ^{13}C NMR ($CDCl_3$), δ=22.8 (t, 6-C), 29.5 (t, 5-C), 34.4 (t, 7-C), 114.4 (d, 3-C), 118.9 (t, $=CH_2$), 126.8 (2C, d, Ph), 128.2 (d, Ph), 128.4 (2C, d, Ph), 132.6 (s, 4a-C), 133.6 (d, -CH=), 139.9 (s, Ph), 141.0 (s, 4-C), 156.2 (s, 2-C), 166.4 (s, 7a-C); MS, m/z (rel intensity), 221 (M^+, 75), 220 (100). Found: m/z 221.1199. Calcd for $C_{16}H_{15}N$: M, 221.1204. For **14**: Yellow oil; IR (CCl_4), 3071, 2930, 1593, 1502, 1461, 1433, 1378, 1226, 1027, 988, 922, 874, 693 cm^{-1}; ^1H NMR (CCl_4), δ=3.48 (2H, m), 5.50 (1H, dd, J=11.0, 1.2 Hz), 5.94 (1H, dd, J=16.8, 1.2 Hz), 6.85 (1H, dd, J=16.8, 11.0 Hz), 6.93—7.67 (6H, m), 7.85—8.08 (2H, m); MS, m/z (rel intensity), 219 (M^+, 100). Found: m/z 219.1050. Calcd for $C_{16}H_{13}N$: M, 219.1048.

Reaction of 7 with 15. A solution of **7** (600 mg, 5.00 mmol) and **15** (2.30 g, 7.50 mmol) in anhydrous bromobenzene (20 cm^3) was heated under reflux for 3 h. After the solvent was evaporated, the resulting residue was separated by column chromatography on silica gel. The fractions eluted with benzene–ethyl acetate (9/1) afforded a mixture of **19** and **20** (98 mg, 9%). The fractions eluted with benzene–ethyl acetate (8/2) afforded a mixture of **17** and **18** (741 mg, 71%) in a ratio of 1/1. The mixture of **19** and **20** was separated by TLC on alumina using hexane–ether (4/1) as developer. The first band from the TLC plates contained **19** (53 mg, 5%). The second band contained **20** (15 mg, 1.4%). For **18**: Oil; IR (CCl_4), 3035, 2931, 2855, 1600, 1551, 1442, 1427, 1345, 1294, 1180, 1114, 940, 894, 880 cm^{-1}; ^1H NMR ($CDCl_3$), δ=0.65 (1H, d, J=11.4 Hz), 1.50—1.90 (4H, m), 2.23 (1H, dd, J=14.9, 5.9 Hz), 2.29 (1H, dd, J=14.9, 5.7 Hz), 2.55 (1H, d, J=16.3 Hz), 2.70 (1H, dd, J=16.3, 3.1 Hz), 5.69 (2H, m), 5.99 (2H, m), 6.20 (1H, dd, J=11.6, 4.8 Hz); ^{13}C NMR ($CDCl_3$), δ=25.4 (d, 10-C or 11-C), 25.7 (d, 11-C or 10-C), 30.2 (t, 8-C), 31.1 (t, 16-C) 37.3 (s, 9-C), 39.9 (t, 15-C), 50.4 (d, 12-C), 72.0 (s, 1-C), 127.7 (d, 7-C), 129.6 (d, 14-C), 130.8 (d, 6-C) 131.4 (d, 13-C), 132.0 (d, 5-C), 133.5 (d, 4-C), 170.0 (s, 3-C); MS, m/z (rel intensity), 209 (M^+, 48), 208 (100). Found: m/z 209.1195. Calcd for $C_{15}H_{15}N$: M, 209.1204. The ^1H NMR signals for **17** was read from the spectrum of a mixture of **17** and **18** as follows: δ=0.73 (1H, d, J=11.0 Hz), 1.47—2.07 (4H, m), 2.37—2.77 (2H, m), 3.00—3.20 (2H, m), 5.71 (2H, m), 5.30—6.55 (4H, m). For **19**: Oil; IR (CCl_4), 3083, 3031, 2882, 2856, 2847, 1622, 1584, 1559, 1542, 1427, 1402, 1384, 1366, 1242, 1212, 1162, 998, 933, 850 cm^{-1}; ^1H NMR ($CDCl_3$), δ=2.06 (2H, tt, J=7.9, 7.7 Hz), 2.90 (2H, t, J=7.7 Hz), 3.00 (2H, t, J=7.9 Hz), 3.19 (2H, d, J=6.6 Hz), 5.52 (1H, dd, J=17.6, 1.7 Hz), 5.64 (1H, dd, J=11.6, 1.7 Hz), 5.84 (1H, dt, J=9.7, 6.6 Hz), 6.11 (1H, dd, J=9.7, 4.8 Hz), 6.53 (1H, dd, J=11.7, 4.8 Hz), 6.80 (1H, dd, J=17.6, 11.6 Hz), 7.11 (1H, d, J=11.7 Hz); ^{13}C NMR ($CDCl_3$), δ=23.2 (t, 2-C), 30.5 (t, 1-C), 34.4 (t, 3-C), 37.5 (t, 5-C), 121.9 (t, $=CH_2$), 125.0 (s, 9a-C), 125.7 (d, 6-C), 126.9 (d, 7-C), 128.4 (d, 8-C), 128.7 (d, 9-C), 131.8 (s, 10a-C), 132.7 (d, -CH=), 139.8 (s, 10-C), 153.8 (s, 4a-C), 165.7 (s, 3a-C); MS, m/z (rel intensity), 209 (M^+, 100). Found: m/z 209.1211. Calcd for $C_{15}H_{15}N$: M, 209.1204. For **20**: Oil; IR (CCl_4), 3083, 3031, 2891, 2858, 2846, 1622, 1581, 1542, 1432, 1381, 1182, 992, 930 cm^{-1}; ^1H NMR ($CDCl_3$), δ=2.08 (2H, quint, J=7.3 Hz), 2.95 (2H, t, J=7.3 Hz), 2.97 (2H, d, J=6.7 Hz), 3.01 (2H, t, J=7.3 Hz), 5.51 (1H, dd, J=17.6, 1.5 Hz), 5.65 (1H, dd, J=11.6, 1.5 Hz), 5.81 (1H, dt, J=9.7, 6.7 Hz), 6.16 (1H, dd, J=9.7, 5.3 Hz), 6.65 (1H, dd, J=11.6, 5.3 Hz), 6.88 (1H, dd, J=17.6, 11.6 Hz), 7.30 (1H, d, J=11.6 Hz); ^{13}C NMR ($CDCl_3$), δ=23.4 (2-C), 27.8 (9-C), 30.9 (1-C), 34.2 (3-C), 121.3 ($=CH_2$), 124.5 (9a-C), 126.4 (8-C), 126.8 (7-C), 129.9 (6-C), 132.7 (-CH=), 134.5 (5-C), 134.8 (10a-C), 139.4 (10-C), 153.0 (4a-C), 162.4 (3a-C); MS, m/z (rel intensity), 209 (M^+, 100). Found: m/z 209.1189. Calcd for $C_{15}H_{15}N$: M, 209.1204.

Thermal Reaction of 17 and 18. A 1/1 mixture of **17** and **18** (209 mg, 1.00 mmol) in anhydrous bromobenzene (10 cm^3) was heated under reflux for 3 h. The reaction mixture was then concentrated and separated by column chromatography on silica gel using benzene–ethyl acetate (10/1) as eluent to give a mixture of **19** and **20** (8 mg, 4%), in addition to **18** (39 mg, 19%).

Thermal Reaction of 19. A solution of **19** (35 mg, 0.167 mmol) in anhydrous bromobenzene (3 cm^3) was heated under reflux for 3 h. After solvent removal in vacuo, the resulting residue was separated by TLC on alumina using hexane–ether (8/1) as a developer to give **19** (21 mg, 60%) and **20** (7 mg, 20%).

References

1) On the reaction of *N*-vinyliminophosphoranes. Part 10. Part 9: Ref. 13.

2) E. Vogel and H. D. Roth, *Angew. Chem.*, **76**, 145 (1964).

3) D. Cremer and B. Dick, *Angew. Chem., Int. Ed. Engl.*, **21**, 865 (1982).

4) M. Schäfer-Ridder, A. Wagner, M. Schwamborn, H. Schreiner, E. Devrout, and E. Vogel, *Angew. Chem., Int. Ed. Engl.*, **17**, 853 (1978); R. J. Hunadi and G. K. Helmkamp, *J. Org. Chem.*, **46**, 2880 (1981); G. Hiken, T. Kinkel, M. Schwamborn, J. Lex, H. Schmickler, and E. Vogel, *Angew. Chem., Int. Ed. Engl.*, **21**, 784 (1982).

5) H. J. Gölz, J. M. Muchowski, and M. L. Maddox, *Angew. Chem., Int. Ed. Engl.*, **17**, 855 (1978); W. J. Lipa, H. T. Crawford, P. C. Radlick, and G. K. Helmkamp, *J. Org. Chem.*, **43**, 3813 (1978); M. L. Maddox, J. C. Martin, and J. M. Muchowski, *Tetrahedron Lett.*, **21**, 7 (1980); J. C. Martin and J. M. Muchowski, *J. Org. Chem.*, **49**, 1040 (1984); W. Tückmantel, G. Andree, A. Seidel, H. Schmickler, J. Lex, E. Kraka, M. Haug, D. Cremer, and E. Vogel, *Angew. Chem., Int. Ed. Engl.*, **24**, 592 (1985).

6) a) S. Masamune, D. W. Brooks, K. Morio, and R. L. Sobczak, *J. Am. Chem. Soc.*, **98**, 8277 (1976). b) S. Masamune and D. W. Brooks, *Tetrahedron Lett.*, **1977**, 3239.

7) L. T. Scott, W. R. Brunsvold, M. A. Kirms, and I. Erden, *J. Am. Chem. Soc.*, **103**, 5216 (1981).

8) T. Kobayashi and M. Nitta, *Chem. Lett.*, **1985**, 1459.

9) T. Kobayashi, Y. Iino, and M. Nitta, *Nippon Kagaku Kaishi*, **1987**, 1237; Y. Iino, T. Kobayashi, and M. Nitta, *Heterocycles*, **24**, 2437 (1986); T. Kobayashi and M. Nitta, *Chem. Lett.*, **1986**, 1549.

10) Y. Iino and M. Nitta, *Bull. Chem. Soc. Jpn.*, **61**, 2235 (1988).

11) M. Nitta, Y. Iino, E. Hara, and T. Kobayashi, *J. Chem. Soc., Perkin Trans. 1*, **1989**, 51; M. Nitta and T. Kobayashi, *Chem. Lett.*, **1986**, 463.

12) N. Kanomata and M. Nitta, *Tetrahedron Lett.*, **29**, 5957 (1988).

13) Y. Iino, E. Hara, and M. Nitta, *Bull. Chem. Soc. Jpn.*, **62**, 1913 (1989).

14) A. C. Cope and B. D. Teffany, *J. Am. Chem. Soc.*, **73**, 4158 (1951).

15) P. Gilgenm, J. Zsindely, and H. Schmid, *Helv. Chim. Acta*, **56**, 681 (1973); J. P-Katalinic, J. Zsindely, and H. Schmid, *Helv. Chim. Acta*, **56**, 2796 (1973); M. Nitta, A. Sekiguchi, and H. Koba, *Chem. Lett.*, **1981**, 933.