

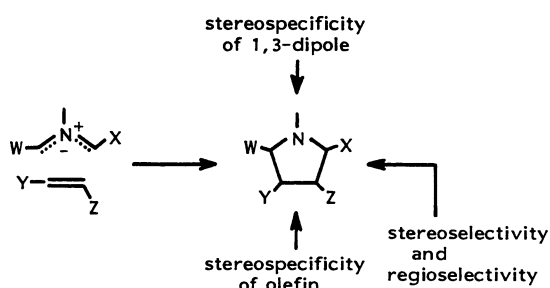
## Stereochemical Study on 1,3-Dipolar Cycloaddition Reactions of Heteroaromatic *N*-Ylides with Symmetrically Substituted *cis* and *trans* Olefins

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Stereochemistry of the cycloadditions of twenty-four heteroaromatic *N*-ylides with several symmetrically substituted *cis* and *trans* olefins has been investigated. Cyclic and acyclic *cis* olefins cycloadd to the *anti* form of the ylides in a highly *endo*-selective manner giving almost quantitative yields of stereospecific *endo* 3+2 cycloadducts. *N*-Ylides stabilized with a substituent of carbonyl type react with *trans* olefins to form mostly two stereoisomeric 3+2 cycloadducts to the *anti* form of the ylides. In most cases, they undergo the stereospecific interconversion through a retro cycloaddition process, the isomer ratios and the easiness of transformation depending upon the nature and size of substituents on the five-membered ring which has been built up in the cycloaddition step. On the other hand, *N*-ylides stabilized with a substituent of noncarbonyl type react with *trans* olefins to give stereospecific and stereoselective 3+2 cycloadducts as single isomers which are assigned as the cycloadducts to the *syn* form of the ylides.

1,3-Dipolar cycloaddition reaction is a process by which heterocyclic five-membered ring systems can be prepared. As exemplified below by the reaction between an azomethine ylide 1,3-dipole and an olefinic dipolarophile, this reaction involves several stereochemical and regiochemical aspects: the regioselectivity (the orientation between both an unsymmetrical 1,3-dipole and an olefin), the stereospecificity of a 1,3-dipole and an olefin (whether the stereochemistry of a 1,3-dipole and an olefin can be faithfully transmitted to the cycloadduct or not), and the stereoselectivity (the *endo* or *exo* approach between a 1,3-dipole and an olefin). Sixteen stereoisomers are possible for the cycloadduct of this reaction. Therefore, stereochemical and regiochemical control of this reaction is necessary for the wide applications of 1,3-dipolar cycloaddition reactions to organic synthesis as a useful process, especially the application to natural product synthesis.

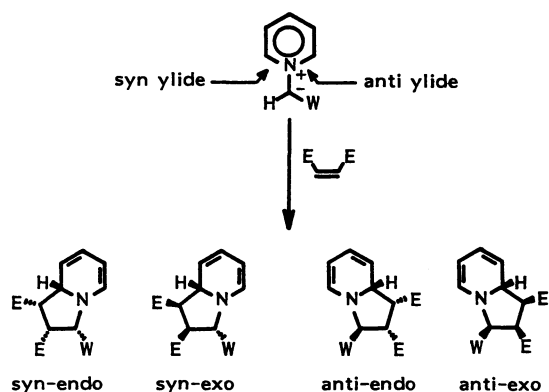


Among the above stereo- and regiochemical aspects, it has been well documented that 1,3-dipolar cycloadditions usually take place in a highly regioselective manner with the preservation of stereochemistry of olefins.<sup>1-7)</sup> Some stereospecific cycloadditions have been also demonstrated by the use of highly reactive dipolarophiles and *anti* and

*syn*, or *trans* and *cis*, azomethine ylides which can be selectively accessible by the thermal conrotatory ring opening of *cis* and *trans* aziridines, respectively.<sup>8-15)</sup> In most cases, the selectivity between the *endo* and *exo* approaches is awfully poor.<sup>8-12)</sup> Only when the azomethine ylide is substituted with an acyl group at the terminal carbon, stereoselective cycloadducts have been obtained.<sup>13,14)</sup> However, the kind of approach (*endo* or *exo*) and the origin of stereoselectivity have not been solved since two geometrical isomers are possible for each isomer of the ylide and because it was hardly able to specify the species that was actually concerned in the cycloaddition.

Heteroaromatic *N*-ylides as reactive azomethine ylide 1,3-dipoles, readily available from nitrogen-containing aromatic heterocycles by the sequence of alkylation at the nitrogen and deprotonation, have been long applied to the cycloadditions with acetylenic dipolarophiles yielding fused heterocycles with a nitrogen at the point of fusion.<sup>16-19)</sup> It is only quite recent that several reports on the stereochemical study of 1,3-dipolar cycloadditions of heteroaromatic *N*-ylides have started to appear, most of them being not inclusive but fragmentary.<sup>20-28)</sup>

As shown below, the pyridinium methylide with a ylide-stabilizing substituent, as a representative of heteroaromatic *N*-ylides, contains both *anti* and *syn* azomethine ylide 1,3-dipolar structures. Unlike the open-chained systems derived from aziridines, there is no isomeric structure possible for both the *anti* and *syn* ylide. Accordingly, the simple structural analysis of cycloadducts formed in the reaction with an olefinic dipolarophile will give us answers to the following questions: 1) Which is more reactive, *anti* or *syn* ylide? 2) How is this cycloaddition stereospecific with respect to the ylide? 3) Is this reaction *endo*-selective or *exo*-selective?



In the present paper, the 1,3-dipolar cycloaddition reactions of a variety of heteroaromatic *N*-ylides with symmetrically substituted *cis* and *trans* olefinic dipolarophiles were investigated, and it was attempted to figure out the stereochemical feature of 1,3-dipolar cycloaddition of heteroaromatic *N*-ylides on the basis of structural analysis of the cycloadducts.

### Results and Discussion

In the present research were employed twenty-four heteroaromatic *N*-ylides involving six different heterocyclic ring systems (Scheme 1): Pyridinium methylides **1a**—**g** with several ylide-stabilizing substituents, pyridinium phenacylides **1h**—**n** substituted on the pyridine nucleus, isoquinolinium methylides **2a**—**d** also substituted at the ylide carbon, isoquinolinium 1-benzoyl ethylide **3**, quinolinium phenacylide **4**, pyridazinium phenacylide **5**, thiazolium methylides **6a** and **6b**, and benzothiazolium phenacylide **7**.

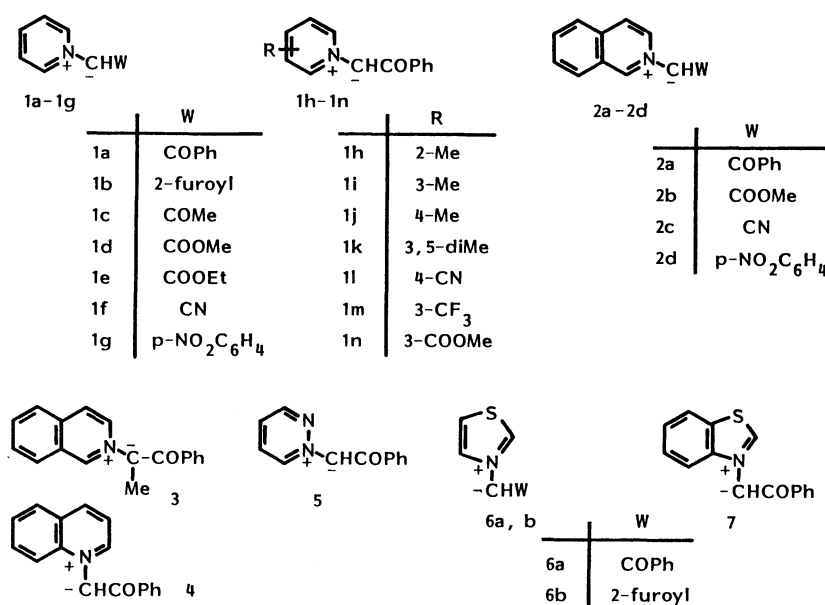
As these heteroaromatic *N*-ylides are all labile, they

were generated *in situ* from the corresponding quaternary salts and triethylamine, and used without isolation for the cycloadditions to olefinic dipolarophiles.

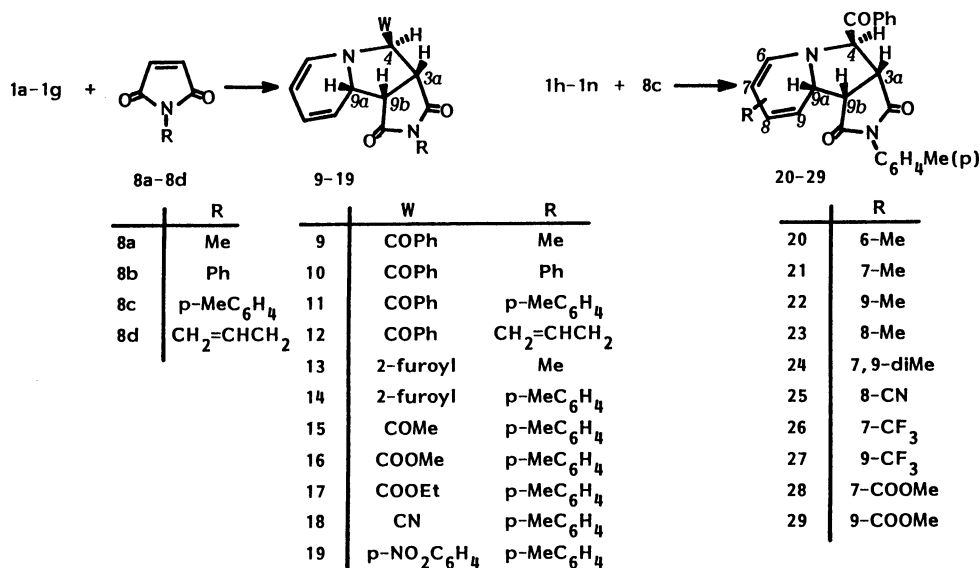
**Cycloadditions to Cyclic *cis* Olefins.** The suspension of *N*-phenacylpyridinium bromide in dry chloroform containing an equivalent of *N*-methylmaleimide **8a** was treated with triethylamine at 0°C. In a few minutes at room temperature, the suspension dissolved into a clean orange solution. After the reaction was completed (10 min), triethylamine hydrobromide was removed off by washing the reaction mixture with sufficient water. Dryness and evaporation of the chloroform under vacuum below room temperature gave a quantitative yield of the 1:1 adduct **9** as a single isomer (Scheme 2 and Table 2).

Other pyridinium methylides **1b**—**f** as well as **1a** readily reacted with several *N*-substituted maleimides **8a**—**d**, under similar conditions, to afford almost quantitative yields of the corresponding cycloadducts **10**—**18** as single isomers. Although the reaction of pyridinium *p*-nitrobenzylide **1g** with **8c** in chloroform was so sluggish that only 59% of the cycloadduct **19** was obtained after 24 h at room temperature with the recovery of *N*-(*p*-nitrobenzyl)pyridinium bromide (40%), the same reaction in dimethyl sulfoxide (12 h at room temperature) afforded a quantitative yield of **19** also as a single product.

A <sup>1</sup>H-NMR spectroscopic observation of the reaction of *N*-(2-furoylmethyl)pyridinium bromide with **8a** in the presence of triethylamine at 0°C in deuteriochloroform showed that the cycloaddition was completed in a few minutes and that the only products formed in this solution were the cyclo-



Scheme 1.



Scheme 2.

TABLE 1. CYCLOADDITIONS TO CYCLIC CIS OLEFINS

| Ylide | Olefin | Reaction conditions <sup>a)</sup> |      |          | Product | Mp<br>θ <sub>m</sub> /°C | Yield/% <sup>b)</sup> |
|-------|--------|-----------------------------------|------|----------|---------|--------------------------|-----------------------|
|       |        | Solvent <sup>c)</sup>             | Temp | Time/min |         |                          |                       |
| 1a    | 8a     | CF                                | rt   | 10       | 9       | 150—153 (d)              | 100                   |
| 1a    | 8b     | CF                                | rt   | 10       | 10      | 72—73                    | 100                   |
| 1a    | 8c     | DM                                | rt   | 10       | 11      | 59—62                    | 100                   |
| 1a    | 8d     | CF                                | rt   | 2 h      | 12      | oil                      | 100                   |
| 1b    | 8a     | DM                                | rt   | 10       | 13      | 127—130 (d)              | 100                   |
| 1b    | 8c     | CF                                | rt   | 10       | 14      | 145—146                  | 100                   |
| 1c    | 8c     | CF                                | rt   | 1 h      | 15      | 100—102                  | 93                    |
| 1d    | 8c     | CF                                | rt   | 10       | 16      | 133—136                  | 100                   |
| 1e    | 8c     | CF                                | rt   | 10       | 17      | 94—97                    | 100                   |
| 1f    | 8c     | CF                                | rt   | 20       | 18      | oil                      | 87                    |
| 1g    | 8c     | DMSO                              | rt   | 12 h     | 19      | 146—147                  | 100                   |
| 1h    | 8c     | DM                                | rt   | 10       | 20      | 110—113                  | 100                   |
| 1i    | 8c     | DM                                | rt   | 10       | 21      | d)                       | 100 (21:22 = 3:7)     |
|       |        |                                   |      |          | 22      | oil                      |                       |
| 1j    | 8c     | DM                                | rt   | 10       | 23      | 70—75                    | 98                    |
| 1k    | 8c     | DM                                | rt   | 10       | 24      | 90—92 (d)                | 100                   |
| 1l    | 8c     | DM                                | rt   | 10       | 25      | 124—127 (d)              | 100                   |
| 1m    | 8c     | DM                                | rt   | 10       | 26      | 80—85 <sup>e)</sup>      | 100 (26:27 = 1:2)     |
|       |        |                                   |      |          | 27      |                          |                       |
| 1n    | 8c     | DM                                | rt   | 10       | 28      | 92—96 <sup>e)</sup>      | 100 (28:29 = 5:3)     |
|       |        |                                   |      |          | 29      |                          |                       |
| 3     | 8c     | CF                                | rt   | 10       | 30      | 176—178 (d)              | 100                   |
| 4     | 8c     | CF                                | rt   | 10       | 31      | 218—220 (d)              | 100                   |
| 6a    | 8c     | DM                                | rt   | 10       | 32      | 87—90                    | 97                    |
| 6b    | 8a     | DMSO                              | rt   | 10       | 33      | 178—179                  | 100                   |
| 7     | 8e     | CF                                | rt   | 3 h      | 34      | 195—196                  | 97                    |
| 7     | 35     | CF                                | rt   | 3 h      | 36      | 173—174                  | 97                    |

a) All the ylides were generated *in situ* from the corresponding precursors and triethylamine. b) Isolated yields. The isomer ratios were determined by a <sup>1</sup>H-NMR spectroscopy. c) CF: chloroform; DM: dichloromethane; DMSO: dimethyl sulfoxide. d) Not separated. e) The melting points for the mixtures.

adduct **13** and triethylamine hydrobromide, no other product being formed. This indicates that **13** is the cycloadduct from a kinetically controlled reaction. The cycloadduct **13** was found too labile to be purified by crystallization. In deuteriochloroform **13** gradually decomposed even at room temperature and in 24 h at the same temperature it completely changed into a complex mixture of the secondary products. In deuteriobenzene the decomposition was suppressed, but when warmed at 50–60°C the complete decomposition of **13** was observed in a few hours.

The other cycloadducts **9–19** showed comparable instability, their purification providing authentic samples for elemental analyses being unsuccessful. However, their structures were confirmed on the basis of the spectral data as well as the molecular weight measurement.

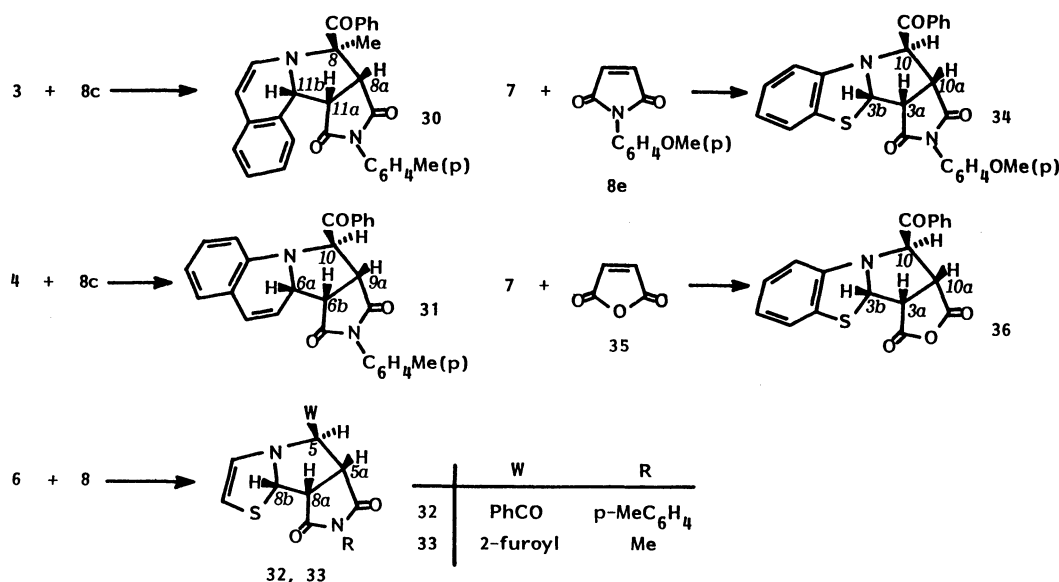
The  $^1\text{H-NMR}$  spectra were most informative to determine the stereostructures of cycloadducts **9–19** (Table 2). Very small coupling constants between 4-H and 3a-H (0–0.8 Hz) confirm a trans relationship of these hydrogens. As the only possible manner of ring fusion at the 3a- and 9b-positions is cis geometry, 3a-H and 9b-H are cis each other. A structural inspection using molecular models shows that the coupling constants of 7.7–8.0 Hz are only possible for the cis configuration between 9b-H and 9a-H. Thus, all the cycloadducts **9–19** were assigned as the endo 3+2 cycloadducts to the anti ylides of **1a–g**. An additional evidence for the assigned structures is the extraordinarily big difference of chemical shifts between 7-H and 9-H. Since the difference of the corresponding hydrogens of 1-phenyl-1,2-dihydropyridine<sup>29</sup> is only 0.27 ppm (3-H: 5.21 ppm and 5-H: 4.94 ppm), this big differences which are more than

1.3 ppm must be because of the unusual low field shifts of 9-Hs. In the endo cycloadducts, these hydrogens are so closely located to a carbonyl of fused maleimide ring that they are suffering from its anisotropy showing unusual low chemical shifts.

When a substituent is introduced at the 2- or 3-position of pyridine nucleus of **1**, two unidentical ylide forms are possible. As each of them contains two 1,3-dipolar systems, anti and syn azomethine ylides, in the same molecule, there are four stereoisomers possible to form for the endo cycloadducts to a maleimide.

The reactions of pyridinium phenacylides **1h–n** bearing a variety of substituents on the pyridine ring with **8c** under similar conditions gave, in all cases, the endo 3+2 cycloadducts **20–29** to the corresponding anti ylides (Scheme 2, Table 1, and 2). When the 2-position of ylide is substituted by a methyl group, the cycloaddition occurred only at the 6-position of **1h** to give **20**, steric hindrance around the reaction sites being the major factor which determined the periselectivity of cycloaddition. In fact, the reaction of 2,6-dimethylpyridinium phenacylide with **8c** gave no cycloadduct under various reaction conditions. On the other hand, in the reactions of 3-substituted pyridinium ylides **1i**, **1m**, and **1n**, regioisomeric mixtures of endo 3+2 cycloadducts to the anti ylides, **21+22**, **26+27**, and **28+29** were obtained. On the basis of these results, it is easily indicated that two ylide forms of the 3-substituted pyridinium phenacylides actually exist and only the anti ylides of them preferentially participate in the cycloaddition to a cyclic dipolarophile. These regioisomers could not be separated each other because of their instability which will be discussed later.

Similar reactions of other heteroaromatic *N*-ylides



Scheme 3.

TABLE 2. SPECTRAL DATA FOR THE CYCLOADDUCTS TO CYCLIC CIS OLEFINS

| IR<br>cm <sup>-1</sup>              | <sup>1</sup> H-NMR spectra measured in CDCl <sub>3</sub> (δ, ppm and Hz) |              |           |              |              |              |              |              |                   |                    | MS<br>m/z |                                                     |                                     |
|-------------------------------------|--------------------------------------------------------------------------|--------------|-----------|--------------|--------------|--------------|--------------|--------------|-------------------|--------------------|-----------|-----------------------------------------------------|-------------------------------------|
|                                     | 4-H                                                                      | 3a-H         | 9b-H      | 9a-H         | 9-H          | 8-H          | 7-H          | 6-H          | J <sub>4-3a</sub> | J <sub>3a-9b</sub> |           | J <sub>9b-9a</sub>                                  |                                     |
| <b>9</b> 1780, 1697,<br>1680        | 5.36<br>d                                                                | 3.69<br>dd   | 3.35<br>t | 4.76<br>ddd  | 5.90<br>ddd  | 5.44<br>ddt  | 4.52<br>ddd  | 6.40<br>dt   | 0.6               | 7.7                | 7.7       | 2.93 (N-Me)<br>s                                    | 308 (M <sup>+</sup> )<br>a)         |
| <b>10</b> 1776, 1720,<br>1705       | 5.48<br>d                                                                | 3.96<br>dd   | 3.51<br>t | 4.85<br>ddd  | 5.99<br>ddd  | 5.52<br>ddt  | 4.56<br>ddd  | 6.14<br>dt   | 0.8               | 8.0                | 8.0       |                                                     | 370 (M <sup>+</sup> )               |
| <b>11</b> 1780, 1710,<br>1690       | 5.48<br>d                                                                | 3.93<br>dd   | 3.48<br>t | 4.84<br>ddd  | 5.99<br>ddd  | 5.53<br>ddt  | 4.56<br>ddd  | 6.14<br>dd   | 0.6               | 8.0                | 8.0       | 2.34 (p-Me)<br>s                                    | 384 (M <sup>+</sup> )               |
| <b>12</b> 1775, 1710,<br>1690, 1600 | 5.37<br>d                                                                | 3.64<br>dd   | 3.33<br>t | 4.69<br>ddd  | 5.84<br>ddd  | 5.40<br>ddt  | 4.57<br>ddd  | 6.04<br>dt   | 0.7               | 7.8                | 7.8       | 4.01, 5.17, 5.61 (N-allyl)<br>m m m                 | 334 (M <sup>+</sup> )               |
| <b>13</b> 1760, 1690,<br>1660       | 5.15<br>s                                                                | 3.64<br>d    | 3.40<br>t | 4.70<br>ddd  | 5.91<br>ddd  | 5.44<br>ddt  | 4.54<br>ddd  | 6.09<br>dt   | 0                 | 7.9                | 7.9       | 2.92 (N-Me), 6.58, 7.38, 7.64<br>s (furoyl-H) dd dd | 298 (M <sup>+</sup> )               |
| <b>14</b> 1770, 1705,<br>1670       | 5.29<br>d                                                                | 3.82<br>dd   | 3.53<br>t | 4.82<br>ddd  | 5.98<br>ddd  | 5.51<br>ddt  | 4.62<br>ddd  | 6.16<br>dd   | 0.5               | 7.9                | 7.9       | 2.37 (p-Me), 6.58, 7.38, 7.64<br>s (furoyl-H) dd dd | 374 (M <sup>+</sup> )<br>a)         |
| <b>15</b> 1780, 1720,<br>1710       | 4.51<br>s                                                                | 3.91<br>d    | 3.33<br>t | 4.79<br>ddd  | 5.8—<br>ddd  | 5.48<br>ddt  | 4.31<br>ddd  | 5.8—<br>6.1m | 0                 | 7.9                | 7.9       | 2.28 (COMe), 2.32 (p-Me),<br>s s                    |                                     |
| <b>16</b> 1780, 1740,<br>1710       | 4.59<br>s                                                                | 3.71<br>d    | 3.44<br>t | 4.6—<br>4.9m | 5.8—<br>6.1m | 5.4—<br>5.6m | 4.6—<br>4.8m | 5.8—<br>6.1m | 0                 | 8.0                | 8.0       | 2.32 (p-Me), 3.74 (COOMe)<br>s s                    | 338 (M <sup>+</sup> )               |
| <b>17</b> 1775, 1730,<br>1705       | 4.57<br>s                                                                | 3.73<br>d    | 3.45<br>t | 4.6—<br>4.9m | 5.8—<br>6.2m | 5.4—<br>5.6m | 4.6—<br>4.9m | 5.8—<br>6.2m | 0                 | 8.0                | 8.0       | 1.29, 4.18 (COOEt), 2.32 (p-Me)<br>t q s            | 352 (M <sup>+</sup> )               |
| <b>18</b> 1780, 1720,<br>1710       | 4.80<br>s                                                                | 3.62<br>d    | 3.47<br>t | 4.97<br>ddd  | 5.8—<br>6.2m | 5.72<br>ddt  | 4.70<br>ddd  | 5.8—<br>6.2m | 0                 | 7.8                | 7.8       | 2.37 (p-Me)<br>s                                    |                                     |
| <b>19</b> 1770, 1720,<br>1705       | 5.30<br>d                                                                | 3.65<br>dd   | 3.38<br>t | 4.83<br>ddd  | 5.99<br>ddd  | 5.60<br>ddt  | 4.63<br>ddd  | 6.10<br>dt   | 0.8               | 8.0                | 8.0       | 2.37 (p-Me)<br>s                                    | 401 (M <sup>+</sup> )               |
| <b>20</b> 1770, 1710,<br>1690       | 5.80<br>d                                                                | 3.74<br>dd   | 3.41<br>t | 4.83<br>ddd  | 5.37<br>ddd  | 5.89<br>ddd  | 4.71<br>dt   | —            | 0.7               | 8.0                | 8.0       | 1.81 (6-Me), 2.37 (p-Me)<br>s s                     | 398 (M <sup>+</sup> )               |
| <b>21</b> 1770, 1710 <sup>e)</sup>  | 5.42<br>s                                                                | 3.91<br>br.d | 3.44<br>t | 4.38<br>dd   | 5.5—6.0<br>m | —            | —            | 5.8—<br>6.0m | 0                 | 8.0                | 8.0       | 1.60 (7-Me), 2.37 (p-Me)<br>s s                     | 398 <sup>b)</sup> (M <sup>+</sup> ) |
| <b>22</b> 1770, 1700                | 5.50<br>d                                                                | 4.00<br>dd   | 3.59<br>t | 4.18<br>d    | —            | 5.77<br>d    | 4.88<br>dd   | 6.04<br>d    | 0.8               | 8.0                | 8.0       | 1.85 (9-Me), 2.37 (p-Me)<br>s s                     | 398 (M <sup>+</sup> )               |

TABLE 2. (Continued)

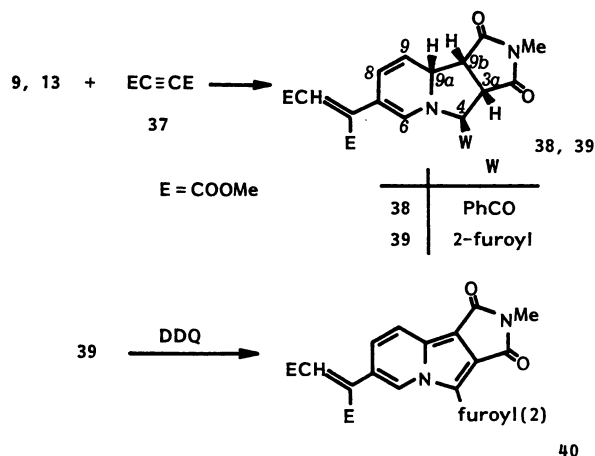
| <sup>1</sup> H-NMR spectra measured in CDCl <sub>3</sub> (δ, ppm and Hz) |                     |            |            |             |            |              |              |              |                     |                     |                      |                                              | MS<br>m/z                          |
|--------------------------------------------------------------------------|---------------------|------------|------------|-------------|------------|--------------|--------------|--------------|---------------------|---------------------|----------------------|----------------------------------------------|------------------------------------|
| IR<br>cm <sup>-1</sup>                                                   | 4-H                 | 3a-H       | 9b-H       | 9a-H        | 9-H        | 8-H          | 7-H          | 6-H          | J <sub>4-3a</sub>   | J <sub>3a-9b</sub>  | J <sub>9b-9a</sub>   |                                              |                                    |
| <b>23</b> 1780, 1710                                                     | 5.48<br>d           | 3.94<br>dd | 3.44<br>t  | 4.27<br>ddd | 5.25<br>m  | —            | 4.76<br>dd   | 6.12<br>br.d | 0.8                 | 7.8                 | 7.8                  | 1.72 (8-Me), 2.37 ( <i>p</i> -Me)<br>s       | 398 (M <sup>+</sup> )              |
| <b>24</b> 1780, 1700                                                     | 5.47<br>s           | 3.98<br>d  | 3.55<br>t  | 4.07<br>d   | —          | 5.68<br>br.s | —            | 5.80<br>br.s | 0                   | 8.0                 | 8.0                  | 1.60 (7-Me), 1.87 (9-Me), 2.36<br>s          | 412 (M <sup>+</sup> )              |
| <b>25</b> 2200, 1780,<br>1710                                            | 5.48<br>s           | 3.80<br>d  | 3.45<br>t  | 4.77<br>dd  | 6.10<br>dd | —            | 4.83<br>dd   | 6.22<br>d    | 0                   | 8.0                 | 8.0                  | ( <i>p</i> -Me)<br>2.37 ( <i>p</i> -Me)<br>s | 409 (M <sup>+</sup> )              |
| <b>26</b> 1780, 1700,<br>1130-1180,<br>810 <sup>c</sup>                  | 5.51<br>s           | 3.73<br>dd | 3.40<br>t  | 4.78<br>m   | 5.51<br>m  | 6.02<br>br.d | —            | 6.65<br>br.s | 0.8                 | 8.0                 | 8.0                  | 2.30 ( <i>p</i> -Me)<br>s                    | 452 <sup>b</sup> (M <sup>+</sup> ) |
| <b>27</b>                                                                | 5.51<br>s           | 3.90<br>dd | 3.45<br>t  | 4.39<br>dd  | —          | 10.0<br>d    | 4.90<br>dd   | 6.49<br>d    | 0.8                 | 8.0                 | 8.0                  | 2.30 ( <i>p</i> -Me)<br>s                    |                                    |
| <b>28</b>                                                                | 5.60<br>d           | 3.77<br>dd | 3.65<br>t  | 4.87<br>m   | 4.90<br>m  | 5.40<br>dd   | 7.3<br>dd    | 6.5<br>d     | 1.0                 | 8.0                 | 8.0                  | 2.32 ( <i>p</i> -Me), 3.63 (COOMe)<br>s      |                                    |
| <b>29</b>                                                                | 5.52<br>d           | 3.97<br>dd | 3.52<br>t  | 4.8—<br>m   | —          | 6.3—<br>6.5m | 4.8—<br>5.0m | 6.3—<br>6.5m | 1.0                 | 8.0                 | 8.0                  | 2.32 ( <i>p</i> -Me), 3.72 (COOMe)<br>s      |                                    |
| <b>30</b>                                                                | 1770, 1700,<br>1670 | 8-H        | 8a-H       | 11a-H       | 11b-H      | 5-H          | 6-H          |              | J <sub>8-8a</sub>   | J <sub>8a-11a</sub> | J <sub>11a-11b</sub> |                                              | 448 (M <sup>+</sup> )              |
|                                                                          |                     | —          | 4.44<br>d  | 3.43<br>t   | 4.64<br>d  | 5.44<br>d    | 6.48<br>d    |              | —                   | 8.0                 | 8.0                  | 1.96 (8-Me), 2.18 ( <i>p</i> -Me)<br>s       |                                    |
| <b>31</b>                                                                | 1780, 1700,<br>1680 | 10-H       | 9b-H       | 6b-H        | 6a-H       | 6-H          | 5-H          |              | J <sub>10-9b</sub>  | J <sub>9b-9b</sub>  | J <sub>6b-6a</sub>   |                                              | 434 (M <sup>+</sup> )              |
|                                                                          |                     | 5.80<br>d  | 3.78<br>dd | 3.51<br>t   | 5.17<br>dt | 6.43<br>dd   | 6.03<br>dd   |              | 1.0                 | 8.0                 | 8.0                  | 2.35 ( <i>p</i> -Me)<br>s                    |                                    |
| <b>32</b>                                                                | 1780, 1720,<br>1710 | 5-H        | 5a-H       | 8a-H        | 8b-H       | 2-H          | 3-H          |              | J <sub>5-5a</sub>   | J <sub>5a-8a</sub>  | J <sub>8a-8b</sub>   |                                              | 390 (M <sup>+</sup> )              |
|                                                                          |                     | 5.72<br>s  | 3.84<br>d  | 3.57<br>t   | 5.37<br>d  | 5.67<br>d    | 5.24<br>d    |              | 0                   | 9.0                 | 9.0                  | 2.32 ( <i>p</i> -Me)<br>s                    |                                    |
| <b>33</b>                                                                | 1770, 1705,<br>1680 | 5.48<br>s  | 3.63<br>d  | 3.51<br>t   | 5.34<br>d  | 5.89<br>d    | 5.19<br>d    |              | 0                   | 8.0                 | 8.0                  | 2.90 ( <i>N</i> -Me), 6.59, 7.41, 7.61<br>dd | 304 (M <sup>+</sup> )<br>a)        |
|                                                                          |                     |            |            |             |            | 4.3<br>d     |              |              |                     |                     |                      | (furoyl-H)                                   |                                    |
| <b>34</b>                                                                | 1780, 1700,<br>1680 | 10-H       | 10a-H      | 3a-H        | 3b-H       |              |              |              | J <sub>10-10a</sub> | J <sub>10a-3a</sub> | J <sub>3a-3b</sub>   |                                              | 456 (M <sup>+</sup> )<br>a, c)     |
|                                                                          |                     | 6.05<br>d  | 4.03<br>dd | 3.59<br>t   | 5.41<br>d  |              |              |              | 0.5                 | 7.9                 | 7.9                  | 3.73 ( <i>p</i> -MeO)<br>s                   |                                    |
| <b>36</b>                                                                | 1850, 1780,<br>1680 | 6.02<br>d  | 4.23<br>dd | 3.73<br>t   | 5.33<br>d  |              |              |              | 1.0                 | 8.6                 | 8.6                  |                                              | 351 (M <sup>+</sup> )<br>a, c)     |

a) <sup>13</sup>C-NMR spectrum is available in Experimental Section. b) Measured as a mixture with its stereoisomer. c) Satisfactory elemental analysis is available in Experimental Section.

**3**, **4**, **6**, and **7** with *N*-substituted maleimides **8** gave each single isomers of the 3+2 cycloadducts **30–34** in quantitative yields (Scheme 3 and Table 1). Their structures were assigned as the endo cycloadducts to the anti ylides on the basis of the spectral data shown in Table 2, especially of the close resemblance of coupling patterns of the methine hydrogens on the newly formed five-membered rings between **9–29** and **30–34**. The configuration at the 8-position of **30** was confirmed by the low field shift of 8-Me (1.96 ppm) owing to an anisotropy from the adjacent maleimide carbonyl, and by the comparison of chemical shifts of 8a-, 11a-, and 11b-H (4.44, 3.43, and 4.64 ppm, respectively) with those of the corresponding methine hydrogens in the endo 3+2 cycloadduct between the anti form of isoquinolinium *p*-nitrophenacylide and *N*-phenylmaleimide (8a-H: 4.11, 10a-H: 3.63, and 10b-H: 4.78 ppm).<sup>30</sup> The low field shift of 6-H of **31** is consistent with the assigned endo structure (6-H: 6.43 and 5-H: 6.03 ppm). A similar 3+2 cycloadduct **36** was obtained in the reaction of **7** with maleic anhydride **35**.

The heteroaromatic ring which has been incorporated from the heteroaromatic *N*-ylides into cycloadducts as a dihydro form tends to recover its aromaticity. This tendency induces the C–C bond cleavage into a betain intermediary and brings about further decomposition with the elimination of heteroaromatic ring.<sup>31,32</sup> Instability of these cycloadducts will be reduced if the remaining unsaturation on the incorporated heterocycles is consumed in another reaction.

With the aim of the formation of Diels-Alder cycloadducts, reactions of the 3+2 cycloadducts **9** and **13** with dimethyl acetylenedicarboxylate **37** were carried out. However, the 1:1 adducts **38** and **39** obtained were not the expected Diels-Alder cycloadducts but the Michael type adducts at the 7-position as shown in Scheme 4. Although **38** was



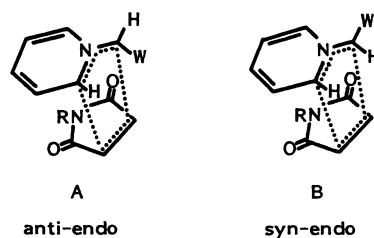
Scheme 4.

found stable enough to be purified without serious decomposition, **39** was still unstable. So it was dehydrogenated with DDQ into the indolizine derivative **40**.

As described above, the cycloaddition reactions of heteroaromatic *N*-ylides to cyclic cis olefins proceed in a highly stereoselective manner giving quantitative yields of the endo 3+2 cycloadducts to the anti form of ylides. The reaction of a pyridinium methylide **1** carrying *W* as a ylide-stabilizing substituent with a maleimide is illustrated in Fig. 1 as an example. There is an attractive interaction working between the  $\pi$  conjugation on the pyridine nucleus and the additional unsaturations (carbonyls) of maleimide, only the endo approach of these reagents being preferred. The exclusive participation of the anti form of **1** may be partly because the endo approach toward the anti ylide **A** leads to a sterically less hindered transition state than that toward the syn ylide **B**. If the anti and syn forms of heteroaromatic *N*-ylides are energetically unidentical, unlike the pyridinium methylides such as **1a–g**, there should be some difference of stability between these two ylidic forms. It will be discussed later that the anti form of ylide is more stabilized than the syn form when the ylide is carrying a ylide-stabilizing substituent of carbonyl type.

*Cycloaddition to Acyclic cis Olefins.* In the reactions of the pyridinium phenacylide **1a** with such acyclic cis olefins as (*Z*)-1,2-dibenzoyl ethene **41b** and dimethyl maleate **41c**, the corresponding 3+2 cycloadducts could not be isolated because of their instability, only the pyridine-eliminated products being obtained.<sup>32</sup> However, maleonitrile **41a** produced a fairly stable cycloadduct **42** as a single stereoisomer in a quantitative yield as shown in Scheme 5 and Table 3.

It is clear that the cis geometry of the olefin **41a** has been retained in the cycloadduct **42**, for a similar stereospecific reaction of **1a** with fumaronitrile **55a**, the trans isomer of **41a**, provides two stereoisomeric 3+2 cycloadducts neither of which is identical with **42** as discussed later. The structure of **42** was independently assigned to be the endo 3+2 cycloadduct to the anti form of **1a** on the basis of the spectral data shown in Table 4, especially of a small

Fig. 1. Two endo approaches between **1** and a maleimide.

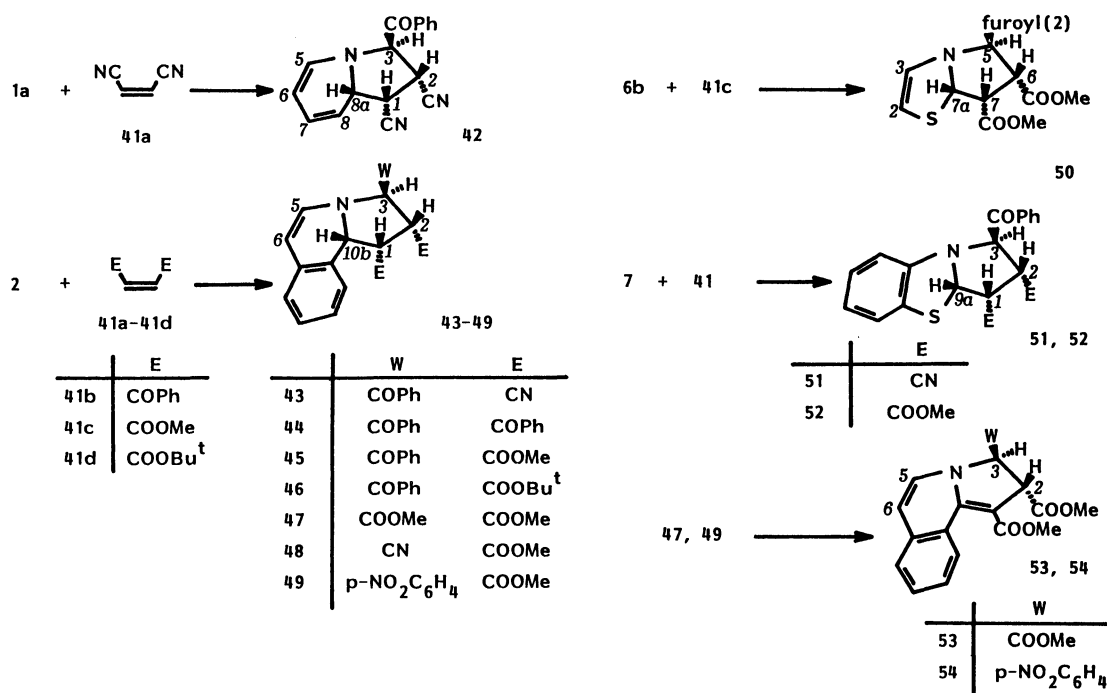
coupling constant between 2-H and 3-H (3.2 Hz).

Expecting the formation of stable 3+2 cycloadducts to acyclic cis olefins, several isoquinolinium methylides **2a**–**c** were allowed to react with **41a**–**d**, at room temperature in chloroform for less than an hour, to give only the endo cycloadducts **43**–**48** to the anti forms of **2** (Scheme 5 and Table 3). Similarly the thiazolium **6b** and benzothiazolium methylides **7** afforded the endo cycloadducts **50**–**52** in the stereoselective and stereospecific reactions with **41**.

The cycloadducts derived from the esteric dipolarophiles **41c** and **41d** are usually sensitive to dehydrogenation at one of the bonds newly formed in a cycloaddition step. In these cases, it is not easy to

purify the crude cycloadducts since they undergo ready dehydrogenation during the purification by chromatography over silica gel or when warmed for a while in solution. Thus, the chromatographic treatment of **47** gave *trans*-2,3-dihydro-1,2,3-tris(methoxycarbonyl)pyrrolo[2,1-*a*]isoquinoline **53** in a fair yield. When isoquinolinium *p*-nitrobenzylide **2d** which was found not so highly reactive toward **41c** at room temperature in chloroform was allowed to react with **41c** under reflux in acetonitrile for 1 h, was obtained none of the cycloadduct **49** but the dehydrogenated product **54** as a single isomer.

All the spectral data for the stereoselective 3+2 cycloadducts **42**–**52** to the acyclic cis olefins **41** are



Scheme 5.

TABLE 3. CYCLOADDITIONS TO ACYCLIC CIS OLEFINS

| Ylide     | Olefin     | Reaction conditions <sup>a)</sup> |      |          | Product   | Mp<br>θ <sub>m</sub> /°C | Yield/% <sup>b)</sup> |
|-----------|------------|-----------------------------------|------|----------|-----------|--------------------------|-----------------------|
|           |            | Solvent <sup>c)</sup>             | Temp | Time/min |           |                          |                       |
| <b>1a</b> | <b>41a</b> | CF                                | rt   | 1 h      | <b>42</b> | 118–121 (d)              | 100                   |
| <b>2a</b> | <b>41a</b> | CF                                | rt   | 10       | <b>43</b> | 181–183 (d)              | 99                    |
| <b>2a</b> | <b>41b</b> | CF                                | rt   | 10       | <b>44</b> | 130–132 (d)              | 100                   |
| <b>2a</b> | <b>41c</b> | CF                                | rt   | 10       | <b>45</b> | 146–148                  | 91                    |
| <b>2a</b> | <b>41d</b> | CF                                | rt   | 30       | <b>46</b> | oil                      | 100                   |
| <b>2b</b> | <b>41c</b> | CF                                | rt   | 10       | <b>47</b> | 147–149                  | 93                    |
| <b>2c</b> | <b>41c</b> | CF                                | rt   | 10       | <b>48</b> | oil                      | 100                   |
| <b>6b</b> | <b>41c</b> | CF                                | rt   | 10       | <b>50</b> | oil                      | 92                    |
| <b>7</b>  | <b>41a</b> | CF                                | rt   | 10       | <b>51</b> | 181–183 (d)              | 100                   |
| <b>7</b>  | <b>41c</b> | CF                                | rt   | 20       | <b>52</b> | 119–122                  | 100                   |

a) All the ylides were generated *in situ* from the corresponding precursors and triethylamine. b) Isolated yields.

c) CF: chloroform.

TABLE 4. SPECTRAL DATA FOR THE CYCLOADDUCTS TO ACYCLIC CIS OLEFINS

|    | IR<br>cm <sup>-1</sup>    | <sup>1</sup> H-NMR spectra measured in CDCl <sub>3</sub> (δ, ppm and Hz) <sup>a)</sup> |                |            |             |             |             |             |            |                  |                  | MS<br>m/z         |                                |
|----|---------------------------|----------------------------------------------------------------------------------------|----------------|------------|-------------|-------------|-------------|-------------|------------|------------------|------------------|-------------------|--------------------------------|
|    |                           | 3-H                                                                                    | 2-H            | 1-H        | 8a-H        | 8-H         | 7-H         | 6-H         | 5-H        | J <sub>3-2</sub> | J <sub>2-1</sub> |                   | J <sub>1-8a</sub>              |
| 42 | 2225, 1695                | 5.44<br>d                                                                              | 3.99<br>dd     | 3.59<br>dd | 4.31<br>ddd | 5.32<br>ddt | 6.10<br>ddt | 4.97<br>ddd | 6.14<br>dt | 3.2              | 8.8              | 6.0               | 275 (M <sup>+</sup> )          |
|    |                           |                                                                                        |                |            | 4.3         | 10.0        | 6.0         | 7.2         |            |                  |                  |                   |                                |
| 43 | 2240, 1680,<br>1625       | 5.77<br>d                                                                              | 4.23<br>dd     | 3.97<br>dd | 4.68<br>d   |             | 5.48<br>d   | 6.50<br>d   |            | 3.2              | 9.0              | 6.8               | 325 (M <sup>+</sup> )<br>b)    |
|    |                           | 6.08<br>d                                                                              | 4.28<br>m      |            | 4.63<br>d   |             | 5.42<br>d   | 6.69<br>d   | 7.5        |                  |                  |                   |                                |
| 44 | 1700, 1690,<br>1680, 1640 | 5.42<br>d                                                                              | 5.16<br>dd     | 4.78<br>m  |             |             | 5.54<br>d   | 6.32<br>d   |            | 3.6              | 8.0              | c)                | 483 (M <sup>+</sup> )<br>b)    |
|    |                           |                                                                                        |                |            |             |             | 5.02<br>d   | 6.08<br>d   | 7.5        |                  |                  |                   |                                |
| 45 | 1730, 1690,<br>1630       | 5.70<br>d                                                                              | 3.98<br>dd     | 3.60<br>dd | 5.24<br>d   |             | 4.93<br>d   | 6.03<br>d   | 8.0        | 6.4              | 7.4              | 5.3               | 391 (M <sup>+</sup> )<br>d)    |
|    |                           |                                                                                        |                |            |             |             | 5.04<br>d   | 6.12<br>d   | 7.3        |                  |                  |                   |                                |
| 46 | 1730, 1670,<br>1620       | 5.63<br>d                                                                              | 3.83<br>t      | 3.49<br>dd | 5.32<br>d   |             | 4.93<br>d   | 6.03<br>d   |            | 7.0              | 7.0              | 5.2               |                                |
|    |                           |                                                                                        |                |            |             |             | 5.04<br>d   | 6.12<br>d   | 7.6        |                  |                  |                   |                                |
| 47 | 1760—1720,<br>1620        | 4.71<br>d                                                                              | 3.50—3.85<br>m | 3.85<br>m  | 5.34<br>d   |             | 5.04<br>d   | 6.12<br>d   |            | 7.0              | b)               | 5.0               | 345 (M <sup>+</sup> )<br>b, d) |
|    |                           |                                                                                        |                |            |             |             | 5.19<br>d   | 6.07<br>d   | 7.8        |                  |                  |                   |                                |
| 48 | 1760—1720,<br>1630        | 5.00<br>d                                                                              | 3.50—3.85<br>m | 3.85<br>m  | 5.40<br>d   |             | 5.19<br>d   | 6.07<br>d   |            | 7.8              | b)               | 4.8               | 312 (M <sup>+</sup> )<br>d)    |
|    |                           |                                                                                        |                |            |             |             | 5.98<br>d   | 5.53<br>d   | 4.0        |                  |                  |                   |                                |
| 50 | 1730, 1670,<br>1600       | 5.16<br>s                                                                              | 3.52<br>d      | 4.01<br>t  | 5.27<br>d   |             | 5.98<br>d   | 5.53<br>d   |            | 8.0              | 7.8              | 6.0               | e)                             |
|    |                           |                                                                                        |                |            |             |             | 5.98<br>d   | 5.53<br>d   | 4.0        |                  |                  |                   |                                |
| 51 | 2230, 1670                | 5.68<br>d                                                                              | 4.04<br>m      | 3.95<br>t  | 5.36<br>d   |             |             |             |            | J <sub>3-2</sub> | J <sub>2-1</sub> | J <sub>1-8a</sub> | 331 (M <sup>+</sup> )          |
| 52 | 1780, 1680                | 5.67<br>d                                                                              | 3.94<br>dd     | 3.65<br>t  | 5.88<br>d   |             |             |             |            | 7.3              | 7.3              | 5.5               | 397 (M <sup>+</sup> )          |
|    |                           |                                                                                        |                |            |             |             |             |             |            | 3.53             | 3.59             |                   |                                |

a) The only exception is **43** which was measured in acetonitrile-d<sub>3</sub> (the upper column) or in dimethyl-d<sub>6</sub> sulfoxide (the lower). b) Satisfactory elemental analysis is available in Experimental Section. c) No clear coupling was given because of the signal overlapping. d) Satisfactory high mass spectrum is available in Experimental Section. e) No parent ion peak was observed.

collected in Table 4. The assignment of signals in the  $^1\text{H}$ -NMR spectra was based upon the decoupling of coupled signals by irradiation or deuterium labeling. The use of the monodeuterated derivative of **2a** in the reaction with **41c** succeeded in the introduction of a deuterium at the 3-position of **45**. The cycloadducts **45**–**48** are carrying two endo ester groups introduced from the esteric dipolarophiles **41c** and **41d**. The ones at the 1-position (3.30–3.33 ppm for COOMe and 1.12 ppm for COOBu<sup>t</sup>) are more extensively shielded by the fused benzene ring than the others at the 2-position (3.65–3.75 ppm for COOMe and 1.39 ppm for COOBu<sup>t</sup>), the assigned endo structures being confirmed.

As described above, the endo cycloadducts **9**–**36** to maleimides showed very small vicinal couplings (0–1.0 Hz) from a terminal methine hydrogen of ylidic origin. Although the cycloadducts **42**–**52** possess the same configuration to **9**–**36**, their coupling patterns are quite different. The corresponding vicinal couplings are varying in some wide range (3.2 to 8.0 Hz).

Figure 2 illustrates the conformations of pyrrolidine rings included as a part of the endo 3+2 cycloadducts to cyclic and acyclic cis olefins. A molecular model inspection indicates that the cycloadduct **C** to a maleimide is conformationally rigid. The cycloadduct **D** which carries such sterically small substituents as cyano moiety ( $\text{E}=\text{CN}$ ) may take a conformation of close resemblance to **C**, since the gauche repulsion among substituents seems not critical. In these cases (cycloadducts **42**, **43**, and **51**), small coupling constants (3.2–3.5 Hz) were observed between 2-H and 3-H. When the substituents in **D** are bulky and therefore the gauche conformation becomes unstable, a rotation around

C–C bonds takes place in a way to minimize the steric repulsion leading to **E**. The coupling constant between 2-H and 3-H becomes larger (6.4–8.0 Hz) and that between 1-H and 2-H slightly smaller (7.0–8.0 Hz) in the cycloadducts derived from the olefins **41b**–**d**.

The exclusive formation of endo cycloadducts to the anti forms of ylides in the reactions with acyclic cis olefins shows that the attractive interaction between the heteroaromatic plane of ylides and the additional unsaturations of olefins has overwhelmed the steric repulsion of all sorts. It is quite surprising that no any exo cycloadduct was formed in the reaction with **41d** which bears two bulky ester groups (COOBu<sup>t</sup>).

The thermal stability for some of these cycloadducts will be discussed in the following section.

*Cycloaddition to Acyclic trans Olefins.* The reaction of **1a** with fumaronitrile **55a** in chloroform

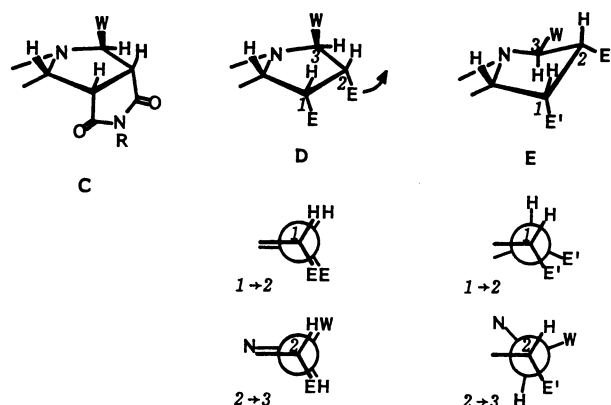
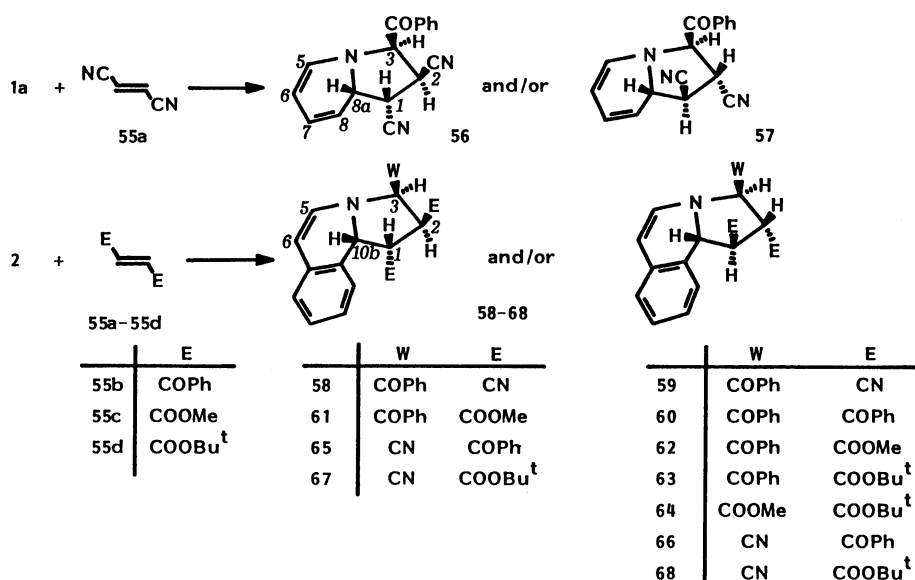


Fig. 2. Stable conformations for the newly formed five-membered rings.



Scheme 6.

at 0°C for 5 min furnished a mixture of two stereoisomeric cycloadducts **56** and **57** (7:3), and for 1 h at the same temperature only **57**, both in quantitative yields (Scheme 6 and Table 5). On standing in solution (chloroform) at room temperature, **56** gradually changed into **57** and this clean isomerization was completed in 1 h, indicating that **56** and **57** are kinetically and thermodynamically controlled products, respectively. Although chromatographic separation of the kinetical cycloadduct **56** from the mixture with **57** was unsuccessful, the reaction of **1a** with **55a** in dimethyl sulfoxide under similar conditions precipitated almost pure **56** out of the solution.

Based upon the spectral data listed in Table 6, the structures of **56** and **57** were assigned to be the 1-endo-2-exo and 1-exo-2-endo cycloadducts to the anti form of **1a**, respectively. The isomer **57** shows a small coupling constant (2.8 Hz) between 2-H and 3-H which are in a trans relationship. This cycloaddition is highly stereospecific, so neither **56** nor **57** is identical with the cycloadduct **42** which was obtained as a single isomer from the cis olefin **41a** (Scheme 5). The stereospecific isomerization of **56** into **57** proceeds through a retro cycloaddition

pathway as evidenced below. These facts were also helpful for the structural determination of **56** and **57**.

A similar reaction of isoquinolinium phenacylide **2a** with **55a** in dimethyl sulfoxide precipitated out the kinetically controlled cycloadduct **58** in a pure form together with **58**+**59** as a solution, and in chloroform the thermodynamically controlled 1-exo-2-endo isomer **59** was a major product in an equilibrium with **58** (Table 5). This equilibration can be achieved within a few minutes at room temperature in chloroform.

It was found that the isomerization of the 1-endo-2-exo cycloadducts into the 1-exo-2-endo cycloadducts was deeply related with thermal instability of these cycloadducts. They have a tendency of going back to the starting components, the heteroaromatic *N*-ylide and the dipolarophile, when heated or dissolved in solvent. This retro cycloaddition proceeds in a highly stereospecific fashion and is facilitated if both of the ylide and dipolarophile are carrying strongly electron-withdrawing substituents such as cyano and benzoyl moieties. Thus, the isomerization of **56** into **57** has taken place in the following way: The kinetic cycloadduct **56** is cleaved into **1a** and **55a** even at room temperature and then the dissociated species are

TABLE 5. CYCLOADDITIONS TO ACYCLIC TRANS OLEFINS

| Ylide     | Olefin     | Reaction conditions <sup>a)</sup> |        |          | Product (yield/%) <sup>b)</sup> |                                                  |
|-----------|------------|-----------------------------------|--------|----------|---------------------------------|--------------------------------------------------|
|           |            | Solvent <sup>c)</sup>             | Temp   | Time/min |                                 |                                                  |
| <b>1a</b> | <b>55a</b> | CF                                | 0 °C   | 5        | <b>56</b> (70)                  | <b>57</b> (30)                                   |
|           |            | CF                                | 0 °C   | 1 h      |                                 | <b>57</b> (100)                                  |
| <b>2a</b> | <b>55a</b> | DMSO                              | rt     | 5        | <b>58</b> (67)                  | <b>59</b> (33)                                   |
|           |            | CF                                | rt     | 5        | <b>58</b> (14)                  | <b>59</b> (86)                                   |
|           |            | CF                                | rt     | 18 h     | <b>58</b> (14)                  | <b>59</b> (86)                                   |
| <b>2a</b> | <b>55b</b> | CF or AN                          | rt     | 10       |                                 | <b>60</b> (100)                                  |
| <b>2a</b> | <b>55c</b> | CF or AN                          | rt     | 10       | <b>61</b> (50)                  | <b>62</b> (50)                                   |
| <b>2a</b> | <b>55d</b> | CF                                | rt     | 2 h      |                                 | <b>63</b> (100)                                  |
| <b>2c</b> | <b>55d</b> | CF                                | rt     | 20       |                                 | <b>64</b> (91)                                   |
| <b>2d</b> | <b>55b</b> | CF                                | rt     | 20       | <b>65</b> (50)                  | <b>66</b> (50)                                   |
|           |            | DMSO                              | rt     | 13 h     | <b>65</b> (33)                  | <b>66</b> (67)                                   |
|           |            | AN                                | rt     | 6 h      | <b>65</b> (25)                  | <b>66</b> (75)                                   |
| <b>2d</b> | <b>55d</b> | CF or DMSO                        | rt     | 20       | <b>67</b> (50)                  | <b>68</b> (13) another isomer (37) <sup>d)</sup> |
| <b>5</b>  | <b>55c</b> | CF                                | rt     | 10       |                                 | <b>69</b> (100)                                  |
| <b>5</b>  | <b>55d</b> | CF                                | rt     | 5        |                                 | <b>70</b> (99)                                   |
| <b>6a</b> | <b>55c</b> | CF                                | rt     | 10       | <b>71</b> (50)                  | <b>72</b> (50)                                   |
| <b>7</b>  | <b>55a</b> | CF                                | rt     | 10       | <b>73</b> (68)                  | <b>74</b> (32)                                   |
| <b>7</b>  | <b>55b</b> | DM                                | rt     | 10       | <b>75</b> (45)                  | <b>76</b> (45)                                   |
| <b>7</b>  | <b>55c</b> | CF                                | rt     | 3 h      | <b>77</b> (82)                  |                                                  |
| <b>7</b>  | <b>55d</b> | DM                                | rt     | 20       |                                 | <b>78</b> (97)                                   |
| <b>2d</b> | <b>55b</b> | AN                                | rt     | 12 h     |                                 | <b>79</b> (100)                                  |
| <b>2d</b> | <b>55c</b> | AN                                | reflux | 3        |                                 | <b>80</b> (71) <sup>e)</sup>                     |
| <b>2d</b> | <b>55d</b> | AN                                | rt     | 17 h     |                                 | <b>81</b> (97)                                   |

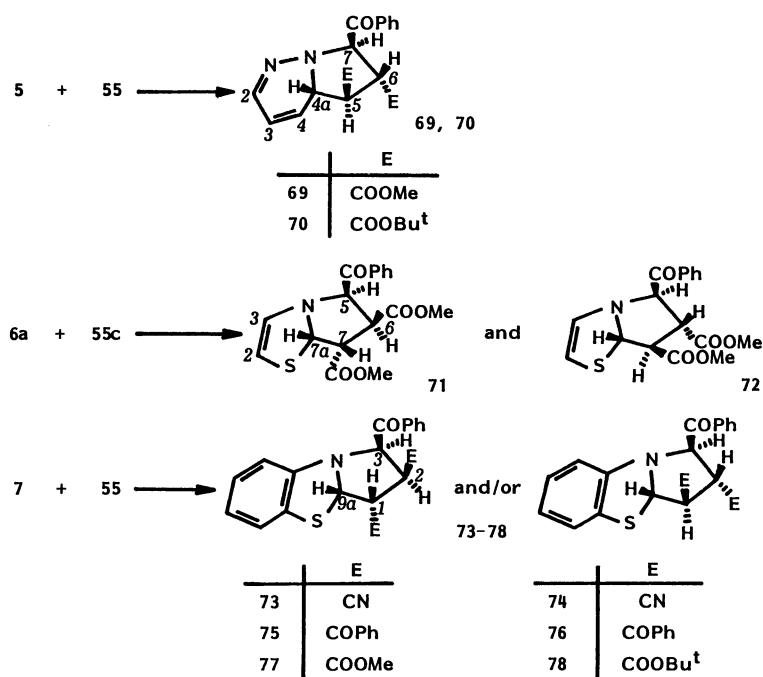
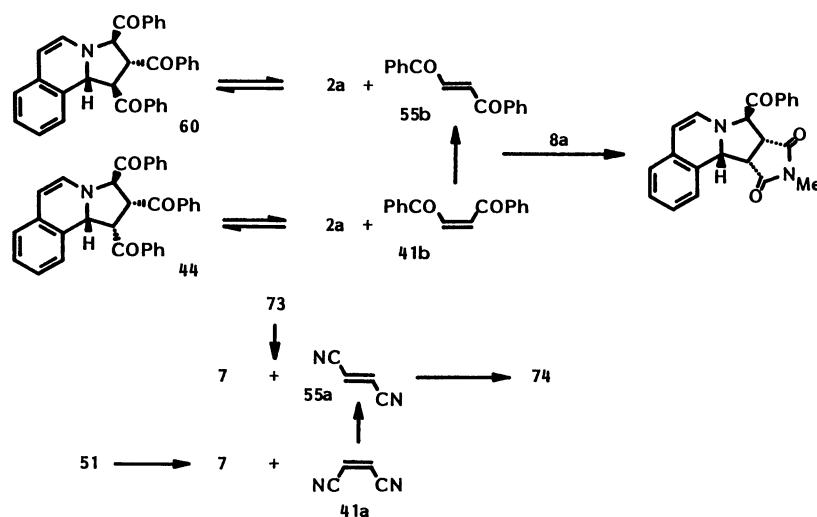
a) All the ylides were generated *in situ* from the corresponding precursors and triethylamine. b) Isolated yields as single cycloadducts or mixtures of stereoisomeric cycloadducts. The isomer ratios were determined on the basis of the <sup>1</sup>H-NMR spectra of crude products. c) CF: chloroform; DMSO: dimethyl sulfoxide; AN: acetonitrile; DM: dichloromethane. d) Tentatively assigned as a cycloadduct to the syn form of **2d**. e) Containing 17% of the 1,10b-dehydrogenated derivative of **37**.

recombined into the thermodynamic isomer **57**, both processes being highly stereospecific.

When the 1-exo-2-endo cycloadduct **60**, the only product in the reaction of **2a** with (*E*)-1,2-dibenzoyl-ethene **55b** at room temperature for 10 min, was warmed at 50–60 °C in dimethyl sulfoxide in the presence of *N*-methylmaleimide **8a**, the endo 3+2 cycloadduct of **8a** to the anti form of **2a** was formed in an excellent yield (Scheme 7). This result as an evidence for the retro cycloaddition process indicates that even the thermodynamically controlled cycloadducts may be readily dissociated into the starting ylide and olefin. An unusual isomerization of **44**, the cycloadduct of **2a** to (*Z*)-1,2-dibenzoyl-ethene **41b**,

occurred leading to **60** when warmed in dimethyl sulfoxide at 50–60 °C for 1 h. This reaction is also stereospecific, but with the complete inversion of stereochemistry of olefin part (from *Z* to *E*). As **41b** was found to isomerize into **55b** with comparable easiness under the reaction conditions, it can be concluded that this isomerization has been caused through the similar retro cycloaddition pathway and the additional olefin isomerization.

The cycloadducts carrying at least one esteric substituent, which were obtained in the reactions of **2b** or **55c** and **55d** as shown in Scheme 6 and Table 5, resist their dissociation into the starting ylides and olefins. Neither the incorporation of maleimide nor



the change of isomer ratio was observed on their heating in the presence or absence of a maleimide. It was found, however, that the isomerization was catalyzed by palladium on charcoal. Thus, the mixture between **61** and **62** or among **67**, **68**, and their isomer<sup>33)</sup> could isomerize into **62** or **68** in almost quantitative yield, respectively, when heated under reflux in benzene in the presence of palladium on charcoal.

Similar cycloadditions of other heteroaromatic *N*-ylides **5**, **6a**, and **7** with symmetrically substituted olefins **55** are shown in Scheme 8, the results in Table 5, and the spectral data of cycloadducts obtained in Table 6.

The first nine cycloadducts in Table 6 (compounds **55** to **77**) as kinetical products have the same stereochemistry as to the newly formed five-membered rings whose four consecutive methine hydrogens are in a *cis-trans-cis* relationship. The small *trans* coupling constants of **58**, **61**, **65**, and **67** (3.5–4.8 Hz) and the upfield shift of COOMe in **61** (3.14 ppm) and COOBu<sup>t</sup> in **67** (1.08 ppm) at the 1-*endo* position are consistent with the proposed structures. On the other hand, the large *trans* couplings of **56**, **71**, **73**, **75**, and **77** will be because of the increase of dihedral angle by the rotation around the corresponding bonds. In the kinetic cycloadducts to **2**, for example **61**, such rotation is inhibited by the growing steric repulsion between the substituent at the 1-position and the extruding hydrogen at the 10-position.

The other fourteen cycloadducts (compounds **57** to **78**) as thermodynamic products have another stereochemistry on the five-membered rings whose four methine hydrogens are in a *trans-trans-trans* relationship that is thermodynamically more stable than the above *cis-trans-cis* succession. All the cycloadducts of

this category show a similar coupling pattern. The *trans* couplings from the ylide hydrogen are generally small (2.8–5.8 ppm) and no strong shielding towards the substituents of olefins from the fused heterocyclic rings has been observed, the proposed structures being again confirmed.

As described above, the attractive interaction between the heteroaromatic ring of ylides and the substituents of olefins have determined the structures of cycloadducts in the 1,3-dipolar cycloadditions of heteroaromatic *N*-ylides to both cyclic and acyclic *cis* olefins. With *trans* olefins, the similar interaction also plays an important role as shown in Fig. 3 which illustrates the reaction of an isoquinolinium ylide as an example. One of the electron-withdrawing substituents E of *trans* olefin positively interacts with the heteroaromatic plane of the anti form of ylide, through the approach **F**, leading to the 1-*endo*-2-*exo* cycloadduct **H** as a kinetically controlled product. When both E and W are strongly electron-withdrawing, **H** is readily dissociated into the starting ylide and olefin, which are then recombined giving the thermodynamically more favored cycloadduct **I**, both in a highly stereospecific manner. Such dissociation of cycloadduct is inhibited under the conditions of cycloaddition reaction if it carries at least one esteric substituent. In this case, the formation of **H** and/or **I** is a result from the competition between the 1-*endo*-2-*exo* **F** and 1-*exo*-2-*endo* approach **G**, and hence from a cycloaddition path of kinetically controlled type. When E is small in size, the attractive interaction of E toward the ring in **F** is predominant, the cycloadduct **H** being the major product. However, when E is bulky, such interaction in **F** is reduced and instead the repulsion between the other E and W is increased. In the other approach **G**, an attractive interaction works between E and the edge of heteroaromatic plane, so that steric repulsion is not critical. This is the reason why the 1-*exo*-2-*endo* cycloadduct **I** was the only cycloadduct formed when both E and W are sterically crowded.

It is surprising that, in the approach **F**, the substituent W from the ylide has been sitting in such a direction as it causes some steric repulsion toward E. As shown by the exclusive participation of the anti form of ylide in the cycloadditions to *cis* olefins, there is no important attractive interaction working between E and W. Accordingly a reasonable explanation is that the anti ylide **J** is better stabilized than the syn ylide **K** so as to get a chance of participating to the cycloadditions. This stabilization may be caused by a proximate interaction of the both poles of 1,5-dipole **L** which arises from an extended conjugation of 1,3-dipole with the carbonyl. It is not confirmed so far, however, whether cyano moiety can act in the same manner or not.

Isoquinolinium *p*-nitrobenzylide **2d** might exist

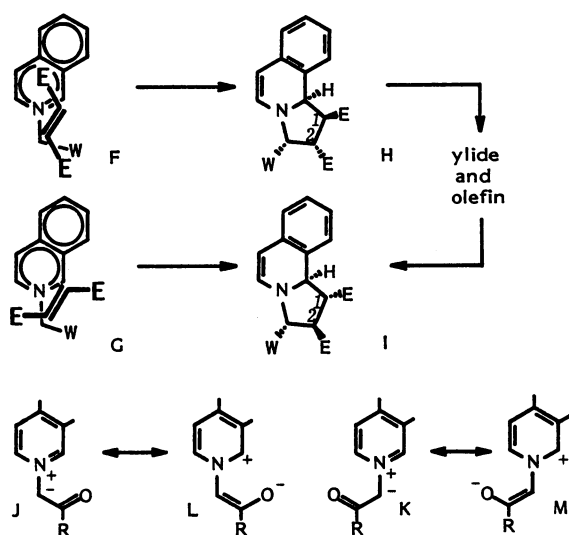


Fig. 3. Approaches of *trans* olefins to the anti form of heteroaromatic *N*-ylides.

TABLE 6. SPECTRAL DATA FOR THE CYCLOADDUCTS TO ACYCLIC TRANS OLEFINS

| IR<br>cm <sup>-1</sup>                               | <sup>1</sup> H-NMR spectra measured in CDCl <sub>3</sub> (δ, ppm and Hz) <sup>a)</sup> |                   |                   |                   |                    |                         |                    |            |                         |                          | MS<br>m/z                |                                                                                      |
|------------------------------------------------------|----------------------------------------------------------------------------------------|-------------------|-------------------|-------------------|--------------------|-------------------------|--------------------|------------|-------------------------|--------------------------|--------------------------|--------------------------------------------------------------------------------------|
|                                                      | 3-H                                                                                    | 2-H               | 1-H               | 8a-H              | 8-H                | 7-H                     | 6-H                | 5-H        | J <sub>3-2</sub>        | J <sub>2-1</sub>         |                          | J <sub>1-8a</sub>                                                                    |
| <b>56</b><br>2250, 1690,<br>1640                     | 5.41<br>d                                                                              | 3.16<br>dd        | 3.82<br>t         | 4.72<br>ddd       | 5.36<br>ddd<br>4.0 | 6.18<br>ddt<br>9.5      | 5.02<br>ddd<br>7.5 | 6.07<br>dt | 6.8                     | 7.8                      | 7.8                      | 275 (M <sup>+</sup> )<br>b)                                                          |
| <b>58</b><br>2240, 1690,<br>1630                     | 6.00<br>d                                                                              | 4.25<br>dd        | 4.43<br>dd        | 5.06<br>d         |                    | 5.37<br>d               | 6.44<br>d<br>7.9   |            | 7.5                     | 4.8                      | 6.4                      | 325 (M <sup>+</sup> )<br>b)                                                          |
| <b>61</b><br>1740, 1730,<br>1670, 1620 <sup>e)</sup> | 5.56<br>d                                                                              | 3.60—4.02<br>m    | 5.00<br>d         |                   | 5.36<br>d          | 6.24<br>d<br>7.4        |                    |            | 7.0                     | —                        | 8.4                      | 391 (M <sup>+</sup> ) <sup>e)</sup><br>3.14, 3.58 (COOMe)<br>s s                     |
| <b>65</b><br>1680, 1660,<br>1590 <sup>e)</sup>       | 4.75<br>d                                                                              | 4.31<br>dd        | 4.80—4.95<br>m    |                   | 5.37<br>d          |                         |                    |            | 7.8                     | 3.5                      | —                        | 404 (M <sup>+</sup> ) <sup>e)</sup><br>d)                                            |
| <b>67</b><br>2250, 2240,<br>1720, 1630 <sup>e)</sup> | 4.31<br>d                                                                              | 3.35<br>dd        | 3.53<br>dd        | 4.90<br>d         | 5.34<br>d          | 6.19<br>d<br>7.5        |                    |            | 7.0                     | 4.0                      | 7.4                      | 396 (M <sup>+</sup> ) <sup>e)</sup><br>d)<br>1.08, 1.50 (COOBu <sup>t</sup> )<br>s s |
| <b>71</b>                                            | 5-H<br>5.37<br>d                                                                       | 6-H<br>3.67<br>dd | 7-H<br>4.15<br>dd | 7a-H<br>5.64<br>d | 2-H<br>5.90<br>d   | 3-H<br>5.34<br>d<br>4.2 |                    |            | J <sub>5-6</sub><br>7.0 | J <sub>6-7</sub><br>10.2 | J <sub>7-7a</sub><br>9.0 | 3.51, 3.72 (COOMe)<br>s s                                                            |
| <b>73</b><br>2240, 1680                              | 3-H<br>5.70<br>d                                                                       | 2-H<br>3.42<br>dd | 1-H<br>4.17<br>dd | 9a-H<br>5.58<br>d |                    |                         |                    |            | J <sub>3-2</sub><br>7.0 | J <sub>2-1</sub><br>9.2  | J <sub>1-9a</sub><br>7.5 | 331 (M <sup>+</sup> )<br>c)                                                          |
| <b>75</b><br>1680, 1650 <sup>e)</sup>                | 6.33<br>d                                                                              | 5.20<br>dd        | 4.96<br>dd        | 5.75<br>d         |                    |                         |                    |            | 8.0                     | 9.5                      | 8.0                      | 489 (M <sup>+</sup> ) <sup>e)</sup><br>d)                                            |
| <b>77</b><br>1780, 1680                              | 5.50<br>d                                                                              | 3.77<br>dd        | 4.26<br>dd        | 5.89<br>d         |                    |                         |                    |            | 7.4                     | 9.8                      | 7.9                      | 397 (M <sup>+</sup> )<br>c)<br>3.42, 3.73 (COOMe)<br>s s                             |

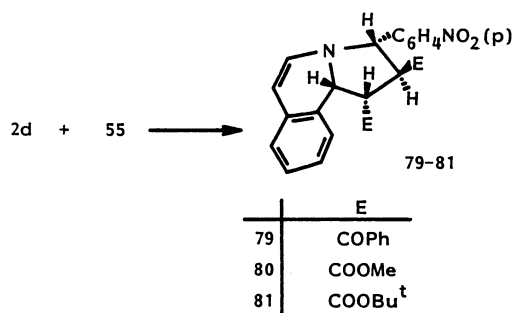
TABLE 6. (Continued)

| IR<br>cm <sup>-1</sup>                               | <sup>1</sup> H-NMR spectra measured in CDCl <sub>3</sub> (δ, ppm and Hz) <sup>a)</sup> |             |            |             |                    |                    |                    |                   |                  |                  | MS<br>m/z |                                                                                    |
|------------------------------------------------------|----------------------------------------------------------------------------------------|-------------|------------|-------------|--------------------|--------------------|--------------------|-------------------|------------------|------------------|-----------|------------------------------------------------------------------------------------|
|                                                      | 3-H                                                                                    | 2-H         | 1-H        | 8a-H        | 8-H                | 7-H                | 6-H                | 5-H               | J <sub>3-2</sub> | J <sub>2-1</sub> |           | J <sub>1-8a</sub>                                                                  |
| <b>57</b><br>2240, 1690<br>1630                      | 5.37<br>d                                                                              | 3.98<br>dd  | 3.31<br>dd | 3.95<br>ddd | 5.56<br>ddt<br>4.8 | 6.12<br>ddt<br>9.5 | 5.08<br>ddd<br>6.0 | 6.23<br>dt<br>7.3 | 2.8              | 7.3              | 9.0       | 275 (M <sup>+</sup> )                                                              |
| <b>59</b><br>2240, 1690,<br>1630                     | 5.42<br>d                                                                              | 4.26<br>dd  | 3.38<br>dd | 4.33<br>d   |                    | 5.68<br>d<br>7.8   | 6.30<br>d          |                   | 2.8              | 8.0              | 9.5       | 325 (M <sup>+</sup> )                                                              |
| <b>60</b><br>1670, 1600                              | 6.07<br>d                                                                              | 4.28<br>dd  | 3.79<br>dd | 4.33<br>d   |                    | 5.63<br>d<br>7.8   | 6.77<br>d          |                   | 2.8              | 8.0              | 9.5       | 483 (M <sup>+</sup> )<br>e)                                                        |
| <b>62</b><br>1740, 1730,<br>1670, 1620 <sup>e)</sup> | 5.57<br>d                                                                              | 5.07<br>ddd | 4.80<br>dd | 4.63<br>dd  |                    | 5.52<br>d<br>7.8   | 6.44<br>d          |                   | 3.0              | 7.8              | 9.2       | 391 (M <sup>+</sup> ) <sup>e)</sup>                                                |
| <b>63</b><br>1720, 1690,<br>1620                     | 5.43<br>d                                                                              | 4.08<br>dd  | 3.64<br>dd | 4.67<br>d   |                    | 5.46<br>d<br>7.6   | 6.23<br>d          |                   | 3.7              | 8.0              | 9.5       | 3.68 (COOMe)                                                                       |
| <b>64</b><br>1720, 1670                              | 5.41<br>d                                                                              | 3.75<br>dd  | 3.34<br>dd | 4.67<br>d   |                    | 5.44<br>d<br>7.4   | 6.17<br>d          |                   | 4.0              | 8.8              | 9.5       | 1.41, 1.43 (COOBu <sup>t</sup> )<br>s                                              |
| <b>66</b><br>1680, 1660,<br>1590 <sup>e)</sup>       | 4.57<br>d                                                                              | 3.58<br>dd  | 3.27<br>dd | 4.76<br>d   |                    | 5.37<br>d<br>7.7   | 6.05<br>d          |                   | 4.0              | 8.8              | 9.5       | 1.44, 1.46 (COOBu <sup>t</sup> )<br>s<br>3.78 (COOMe)<br>s                         |
| <b>68</b><br>2240, 2250,<br>1720, 1630 <sup>e)</sup> | 5.09<br>d                                                                              | 4.83<br>dd  | 4.46<br>dd | 4.96<br>d   |                    | 5.53<br>d<br>7.8   | 6.12<br>d          |                   | 3.0              | 7.9              | 9.2       | 404 (M <sup>+</sup> ) <sup>e)</sup><br>d)                                          |
| <b>68</b><br>2240, 2250,<br>1720, 1630 <sup>e)</sup> | 4.84<br>d                                                                              | 3.64<br>dd  | 3.25<br>dd | 4.77<br>d   |                    | 5.52<br>d<br>7.8   | 6.07<br>d          |                   | 3.7              | 8.0              | 9.2       | 1.44, 1.49 (COOBu <sup>t</sup> )<br>s<br>396 (M <sup>+</sup> ) <sup>e)</sup><br>d) |

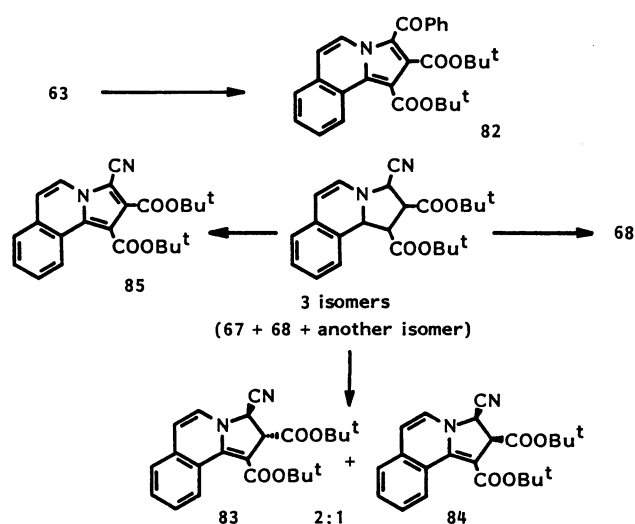
TABLE 6. (Continued)

| IR<br>cm <sup>-1</sup>                 | <sup>1</sup> H-NMR spectra measured in CDCl <sub>3</sub> (δ, ppm and Hz) <sup>a)</sup> |            |            |             |                |                |     |                  |                  |                    | MS<br>m/z                                 |
|----------------------------------------|----------------------------------------------------------------------------------------|------------|------------|-------------|----------------|----------------|-----|------------------|------------------|--------------------|-------------------------------------------|
|                                        | 7-H                                                                                    | 6-H        | 5-H        | 4a-H        | 4-H            | 3-H            | 2-H | J <sub>7-6</sub> | J <sub>6-5</sub> | J <sub>5-4a</sub>  |                                           |
| <b>69</b><br>1740, 1730,<br>1600       | 5.83<br>d                                                                              | 3.69<br>dd | 3.80<br>dd | 4.27<br>dd  | 5.65—6.03<br>m | 6.64—6.80<br>m |     | 3.2              | 7.5              | 9.0                | 342 (M <sup>+</sup> )<br>d)               |
| <b>70</b><br>2300, 1740,<br>1730       | 5.68<br>d                                                                              | 3.84<br>dd | 3.50<br>dd | 3.92<br>ddd | 5.82<br>ddd    | 6.80<br>dd     | 3.5 | 4.0              | 8.0              | 10.4               | 426 (M <sup>+</sup> )<br>d)               |
| <b>72</b>                              | 5.50<br>d                                                                              | 3.93<br>dd | 3.65<br>dd | 5.15<br>d   | 5.96<br>d      | 5.28<br>d      | 4.2 | 4.3              | 7.8              | 7.8                | 3.73 (COOMe)<br>s                         |
| <b>74</b><br>2240, 1680                | 5.73<br>d                                                                              | 4.16<br>dd | 3.25<br>dd | 4.95<br>d   |                |                |     | J <sub>3-2</sub> | J <sub>2-1</sub> | J <sub>1-9a</sub>  | 331 (M <sup>+</sup> )<br>e)               |
| <b>76</b><br>1680, 1650 <sup>e)</sup>  | 5.77<br>d                                                                              | 5.02<br>dd | 4.57<br>dd | 5.42<br>d   |                |                |     | 4.5              | 8.1              | 8.0                | 489 (M <sup>+</sup> ) <sup>e)</sup><br>d) |
| <b>78</b><br>1720, 1700                | 5.44<br>d                                                                              | 3.68<br>dd | 3.45<br>dd | 5.56<br>d   |                |                |     | 5.8              | 8.5              | 7.5                | 481 (M <sup>+</sup> )<br>e)               |
| <b>79</b><br>1670, 1600,<br>1520, 1340 | 5.37<br>d                                                                              | 4.61<br>dd | 4.80<br>t  | 5.10<br>d   | 6-H            | 5-H            |     | J <sub>3-2</sub> | J <sub>2-1</sub> | J <sub>1-10a</sub> | 496 (M <sup>+</sup> )<br>b)               |
| <b>80</b><br>1740                      | 5.06<br>d                                                                              | 3.38<br>dd | f)         | 4.92<br>d   | 5.49<br>d      | 5.22<br>d      | 7.4 | 6.0              | 10.0             | 9.0                | 3.71, 3.97 (COOMe)<br>s                   |
| <b>81</b><br>1720, 1520,<br>1340, 1150 | 5.03<br>d                                                                              | 3.29<br>dd | 3.52<br>dd | 4.90<br>d   | 5.36<br>d      | 5.98<br>d      | 7.6 | 6.0              | 10.0             | 9.2                | 492 (M <sup>+</sup> )<br>b)               |

a) The following compounds were measured in other solvents: **58**, **59** (the upper column), **60** (the upper): in dimethyl-d<sub>6</sub> sulfoxide; **75**, **60** (the lower), **76**: in acetonitrile-d<sub>3</sub>. b) Satisfactory high mass spectrum is available in Experimental Section. c) Measured as a mixture with its stereoisomer. d) Satisfactory elemental analysis for the mixture of two stereoisomers is available in Experimental Section. e) Satisfactory elemental analysis is available in Experimental Section. f) Overlapping with other signals.



Scheme 9.



Scheme 10.

both as the anti and syn forms since no stabilization of anti ylide is expected in this case. Therefore, its cycloadditions to trans olefins will lead to the 1-endo-2-exo cycloadducts to the syn form, which are the most feasible products from the analysis of all possible attractive interactions and steric repulsions. As expected, the corresponding cycloadducts **79–81** were obtained as single stereoisomers (Scheme 9) and assigned as the 1-endo-2-exo cycloadducts to the syn form of **2d** on the basis of the spectral data shown in Table 6 and of the reaction mode of **2d** toward unsymmetrically substituted trans olefins.<sup>34)</sup>

As shown in Scheme 10, some of the cycloadducts to trans olefinic esters undergo dehydrogenation reactions. The cycloadduct **63** was dehydrogenated into a pyrrolo[2,1-*a*]isoquinoline **82** when heated under reflux in benzene in the presence of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). A mixture of three isomers formed from **2c** and **55d**, which was found to isomerize into the thermodynamically most stable cycloadduct **68** on heating in benzene in the presence of palladium on charcoal, was similarly dehydrogenated into the pyrrolo[2,1-*a*]isoquinoline **85** or the 2:1 mixture of stereoisomeric

dihydropyrrolo[2,1-*a*]isoquinolines **83+84** when heated in ethanol or chromatographed over silica gel using benzene as an eluent, respectively.

## Experimental

**General.** Melting points were determined on a Yanagimoto micro melting point apparatus and uncorrected. IR spectra were taken with a JASCO IRA-1 or a JASCO A-702 spectrometer. <sup>1</sup>H-NMR spectra were recorded on a Hitachi R-40 or a JEOL FX-100 instrument and <sup>13</sup>C-NMR spectra on a JEOL FX-100 spectrometer at 25.05 MHz. Chemical shifts are expressed in parts per million downfield from tetramethylsilane. Mass spectra were measured with a JEOL JMS-01SG-2 spectrometer at 70 eV of ionization energy. Elementary analyses were performed on a Hitachi 026 CHN analyzer. Thin-layer chromatography (TLC) was accomplished on 0.2 mm precoated plates of silica gel 60 F-254 (Merck) or of aluminum oxide 60 F-254 type-E (Merck). Visualization was with ultraviolet light (254 and 365 nm) and iodine. Wakogel C200 and C300 (Wako) and Silicagel 60 (Merck) were used for preparative column chromatography. Flash chromatography was carried out on an EYELA EF-10 apparatus using a column (20×180 mm) packed with Silicagel 60 (Merck, size: 0.04–0.063 mm). Solvents were evaporated with a Tokyo Rikakikai rotary evaporator type V.

**Materials.** The following olefins are commercially available and were used without further purification: *N*-methylmaleimide **8a**, maleic anhydride **35**, dimethyl maleate **41c**, fumalonitrile **55a**, and dimethyl fumarate **55c**. *N*-Substituted maleimides such as *N*-phenyl- **8b** (mp 89–90 °C), *N*-(*p*-methylphenyl)- **8c** (mp 152–153 °C), *N*-(2-propenyl)- **8d** (mp 52–53 °C), and *N*-(*p*-methoxyphenyl)-maleimide **8e** (mp 149–150 °C) were all prepared according to the reported method<sup>35)</sup> which involves the aminolysis of **35** with the corresponding primary amines in ether at room temperature and the followed cyclization of the maleamic acids with acetic anhydride at 110–120 °C. *trans*-1,2-Dibenzoyl ethene **55b** was obtained by the Friedel-Crafts reaction of fumaroyl dichloride with benzene in the presence of aluminum chloride (**55b**: mp 108–110 °C).<sup>36)</sup> Di-*t*-butyl fumarate **55d** was synthesized by the reaction of fumaroyl dichloride with 2 equivalents of *t*-butyl alcohol under reflux in ether for 2 h in the presence of *N,N*-dimethylaniline (**55d**: bp 113–115 °C/400 Pa; mp 59–60 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ=1.50 (18H, s, COOBu<sup>t</sup>) and 6.63 ppm (2H, s, =CH)). Maleonitrile **41** (bp 105–110 °C/2260 Pa) was prepared from the trans isomer **55a** according to the known method.<sup>37)</sup> *cis*-1,2-Dibenzoyl ethene **41b** (mp 128–129 °C)<sup>38)</sup> was given by a photochemical isomerization from **55b**, and similarly di-*t*-butyl maleate **41d** from **55d** (**41d**: mp 64–65 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ=1.50 (18H, s, COOBu<sup>t</sup>) and 6.03 ppm (2H, s, =CH)).

**Preparation of Quaternary Salts as the Precursors of Heteroaromatic *N*-Ylides.**

A mixture of heteroaromatic compound and slightly excess of alkylating reagent in dry ether was allowed to stir at room temperature for a few hours to a day precipitating the corresponding quaternary salt which was collected on a filter and washed with ether. The filtrate was again stirred at the same temperature

giving another portion of the precipitate of quaternary salt. The precursors of heteroaromatic *N*-ylides thus synthesized are as follows: *N*-phenacylpyridinium bromide:<sup>39,40</sup> mp 204–206 °C. *N*-(2-furoylmethyl)pyridinium bromide: mp 208–209 °C (IR (KBr) 1692 cm<sup>-1</sup>; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>) δ=6.38 (2H, s, CH<sub>2</sub>), 6.87, 7.72, 8.20 (each 1H, dd, furoyl-H), 8.30 (2H), 8.72 (1H), and 9.07 ppm (2H, each dd, pyridyl-H); Found: C, 49.14; H, 3.84; N, 5.25%. Calcd for C<sub>11</sub>H<sub>10</sub>O<sub>2</sub>NBr: C, 49.25; H, 3.73; N, 5.22%). *N*-acetylpyridinium bromide:<sup>39,40,41</sup> hygroscopic solid (no melting point was measured). *N*-(methoxycarbonylmethyl)pyridinium chloride:<sup>42</sup> mp 170–173 °C. *N*-(ethoxycarbonylmethyl)pyridinium bromide:<sup>40,43,44</sup> mp 120–123 °C. *N*-(cyanomethyl)pyridinium bromide: mp 166–167 °C (Found: C, 42.07; H, 3.56; N, 14.26%. Calcd for C<sub>7</sub>H<sub>7</sub>N<sub>2</sub>Br: C, 42.21; H, 3.52; N, 14.07%). *N*-(*p*-nitrobenzyl)pyridinium bromide:<sup>44,45</sup> mp 224–225 °C. *N*-phenacyl-2-methylpyridinium bromide:<sup>46</sup> mp 229–231 °C (dec). *N*-phenacyl-3-methylpyridinium bromide:<sup>47</sup> mp 185–187 °C. *N*-phenacyl-4-methylpyridinium bromide:<sup>48</sup> mp 274–276 °C (dec). *N*-phenacyl-3,5-dimethylpyridinium bromide: mp 200–203 °C (Found: C, 58.56; H, 5.33; N, 4.54%. Calcd for C<sub>15</sub>H<sub>16</sub>ONBr: C, 58.82; H, 5.23; N, 4.58%). *N*-phenacyl-4-cyanopyridinium bromide: mp 224–227 °C (dec) (Found: C, 55.22; H, 3.71; N, 9.42%. Calcd for C<sub>14</sub>H<sub>11</sub>ON<sub>2</sub>Br: C, 55.43; H, 3.63; N, 9.24%). *N*-phenacyl-3-(trifluoromethyl)pyridinium bromide: mp 197–198 °C (Found: C, 48.39; H, 3.25; N, 4.18%. Calcd for C<sub>14</sub>H<sub>11</sub>ONF<sub>3</sub>: C, 48.55; H, 3.18; N, 4.05%). *N*-phenacyl-3-(methoxycarbonyl)pyridinium bromide:<sup>49</sup> mp 183–185 °C. *N*-phenacylisoquinolinium bromide:<sup>39</sup> mp 209–210 °C. *N*-(methoxycarbonylmethyl)isoquinolinium bromide:<sup>50</sup> mp 159–160 °C (dec). *N*-(cyanomethyl)isoquinolinium bromide: mp 215–218 °C (dec) (Found: C, 52.64; H, 3.75; N, 11.39%. Calcd for C<sub>11</sub>H<sub>9</sub>N<sub>2</sub>Br: C, 52.82; H, 3.63; N, 11.29%). *N*-(*p*-nitrobenzyl)isoquinolinium bromide:<sup>39,40,51</sup> mp 207–208 °C. *N*-(1-benzoylthyl)isoquinolinium bromide: mp 183–184 °C (Found: C, 63.30; H, 4.72; N, 4.07%. Calcd for C<sub>18</sub>H<sub>16</sub>ONBr: C, 63.16; H, 4.68; N, 4.09%). *N*-phenacylquinolinium bromide:<sup>39,40</sup> mp 173–175 °C (dec). *N*-phenacylpyridazinium bromide: mp 227–228 °C (dec) (Found: C, 51.42; H, 4.04; N, 10.04%. Calcd for C<sub>12</sub>H<sub>11</sub>ON<sub>2</sub>Br: C, 51.61; H, 3.94; N, 10.04%). *N*-phenacylthiazolium bromide: mp 215–216 °C (Found: C, 46.39; H, 3.67; N, 5.20%. Calcd for C<sub>11</sub>H<sub>14</sub>ONSBr: C, 46.48; H, 3.52; N, 4.93%). *N*-(2-furoylmethyl)thiazolium bromide: mp 204–205 °C (IR (KBr) 1690 cm<sup>-1</sup>; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>) δ=6.37 (2H, s, CH<sub>2</sub>), 6.88, 7.72, 8.20 (each 1H, dd, furoyl-H), 8.44, 8.61, and 10.34 ppm (each 1H, dd, thiazolium-H); <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>) δ=59.36, 113.13, 120.41, 126.40, 138.14, 148.95, 161.68, 178.77, and 203.61 ppm; MS (rel intensity) *m/z* 190 (23), 95 (base peak), and 81 (8); Found: C, 39.43; H, 3.17; N, 5.04%. Calcd for C<sub>9</sub>H<sub>8</sub>O<sub>2</sub>NBr: C, 39.43; H, 2.94; N, 5.11%). *N*-phenacylbenzothiazolium bromide:<sup>53</sup> mp 249–250 °C (dec).

#### General Procedure for the Cycloadditions to Cyclic *cis* Olefins.

To the suspension of a quaternary salt was added an equivalent of *cis* olefin and then slowly a slight excess (1.1–1.2 equivalent) of triethylamine at 0 °C or room temperature. The resulting mixture was stirred at room temperature until all the salt dissolved into a clear solution. The solvent and time for each reaction are listed

in Table 1. After the completion of reaction, the solution was poured into ice water and extracted with dichloromethane or chloroform. The extract was dried over MgSO<sub>4</sub> and evaporated under vacuum at or below room temperature. Mostly the residue solidified on the trituration with ether or petr. ether or their mixture. If the product is an oily material, the residue was subjected to an operation for the complete elimination of reaction and extraction solvents under high vacuum at or below room temperature for at least a few hours. The yield as well as the melting point of each cycloadduct is given in Table 1. In most cases the purification of cycloadduct was unsuccessful affording no analytical samples of authentic purity because of their lability. Therefore the unpurified products were subjected to the spectral measurement whose results are listed in Table 2. Other data for the cycloadducts are given as follows: **9**: <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ=25.41 (q, *N*-Me), 45.47, 51.30 (each d, 3a- and 9b-C), 59.24 (d, 9a-C), 70.59 (d, 4-C), 98.24 (d, 7-C), 114.13 (d, 9-C), 124.01, 128.95, 129.13, 129.30, 134.18 (each d), 134.07 (s), 176.07, 178.19 (each s, CON), and 194.19 ppm (COPh). **14**: <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ=21.25 (*p*-Me), 44.56, 52.49 (3a- and 9b-C), 59.53 (9a-C), 71.86 (4-C), 97.69 (7-C), 112.78, 114.42, 119.71, 123.70, 125.99, 129.28, 129.81, 134.39, 147.54, 174.72 (CON), 176.89 (CON), and 177.71 ppm (furyl-CO). **26+27**: F-NMR (CDCl<sub>3</sub>) δ=31.28 (7-CF<sub>3</sub>) and 34.39 ppm (9-CF<sub>3</sub>) with the ratio of 1:2. **33**: <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ=24.78 (*N*-Me), 46.91, 51.25 (5a- and 8a-C), 67.52 (5-C), 70.98 (8b-C), 97.16, 112.72, 121.06, 132.92, 148.83, 149.42, 174.37 (CON), 176.80 (CON), and 183.06 ppm (furyl-CO). **34**: <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ=47.60, 50.59 (each d, 3a- and 10a-C), 55.27 (q, OMe), 68.43 (d, 3b-C), 71.89 (d, 10-C), 173.30, 176.48 (each s, CON), and 194.02 ppm (s, CPh); Found: C, 68.54; H, 4.39; N, 6.15%. Calcd for C<sub>26</sub>H<sub>20</sub>O<sub>4</sub>N<sub>2</sub>S: C, 68.41; H, 4.42; N, 6.14%. **36**: <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ=47.88, 51.09 (each d, 3a- and 10a-C), 69.32 (d, 3b-C), 71.93 (d, 10-C), 167.64, 172.08 (each d, CON), and 193.22 ppm (s, CPh); Found: C, 65.02; H, 3.68; N, 3.96%. Calcd for C<sub>19</sub>H<sub>13</sub>O<sub>4</sub>NS: C, 64.96; H, 3.73; N, 3.99%.

**Reaction of 9 with 37 Leading to 38.** A mixture of each equivalents of the cycloadduct **9** and dimethyl acetylenedicarboxylate **37** in dichloromethane was refluxed for 10 min and the solvent was removed under vacuum. The residue was chromatographed over silica gel using hexane/ethyl acetate (3:1) to give 67% of **38**: pale yellow prisms; mp 200 °C; IR (KBr) 1780, 1720–1700, 1620, 1600, and 1580 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CD<sub>3</sub>CN) δ=2.95, 3.47, 3.68 (each 3H, s, *N*-Me and COOMe), 3.54 (1H, dd, *J*<sub>9b-9a</sub>=9.8 and *J*<sub>9b-3a</sub>=7.4 Hz, 9b-H), 3.63 (1H, dd, *J*<sub>3a-9b</sub>=7.4 and *J*<sub>3a-4</sub>=0.5 Hz, 3a-H), 5.63 (1H, dd, *J*<sub>9a-9b</sub>=9.8 and *J*<sub>9a-9</sub>=8.0 Hz, 9a-H), 5.73 (1H, d, *J*<sub>4-3a</sub>=0.5 Hz, 4-H), 5.79 (1H, ddd, *J*<sub>9-8</sub>=9.8, *J*<sub>9-9a</sub>=8.0, and *J*<sub>9-6</sub>=1.0 Hz, 9-H), 6.57 (1H, dd, *J*<sub>8-9</sub>=9.8 and *J*<sub>8-6</sub>=3.4 Hz, 8-H), 6.84 (1H, dd, *J*<sub>6-8</sub>=3.4 and *J*<sub>6-9</sub>=1.0 Hz, 6-H), 7.36 (1H, br. s, HC=), 7.40–7.80, and 8.05–8.25 ppm (5H, m, CPh); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ=25.25 (q, *N*-Me), 51.31, 52.19 (each q, COOMe), 47.79 (d, 2×C, 3a- and 9b-C), 57.59 (d, 9a-C), 67.75 (d, 4-C), 102.04 (s, 7-C), 129.05 (d), 130.57 (d), 132.62 (d), 132.74 (s), 134.33 (d), 134.92 (d), 135.39 (d), 144.48 (d, CH=), 167.85 (s, 2×C, COOMe), 174.60, 176.07 (each s, CON), and 194.92 ppm (s, CPh); MS (rel intensity) *m/z* 450 (M<sup>+</sup>, 22), 105 (base peak), and 77 (79).

Found: C, 63.85; H, 5.01; N, 6.34%. Calcd for  $C_{24}H_{22}O_7N_2$ : C, 63.99; H, 4.92; N, 6.22%.

**Reaction of 13 with 37 Leading to 39.** The similar procedure described above gave 70% of **39**: yellow solid; mp 117–118 °C; IR (KBr) 1770, 1720, and 1690  $cm^{-1}$ ;  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ =3.07, 3.58, 3.72 (each 3H, s, *N*-Me and COOMe), 3.48 (1H, dd,  $J_{3a-9b}$ =8.7 and  $J_{3a-4}$ =2.0 Hz, 3a-H), 3.76 (1H, t,  $J_{9b-9a}$ = $J_{9b-3a}$ =8.7 Hz, 9b-H), 5.22 (1H, d,  $J_{4-3a}$ =2.0 Hz, 4-H), 5.25–5.80 (2H, m, 9- and 9a-H), 6.60 (1H, dd,  $J_{8-9}$ =9.4 and  $J_{8-6}$ =3.5 Hz, 8-H), 6.63 (1H, dd,  $J$ =3.8 and 1.7 Hz, 4-H of furyl), 6.93 (1H, dd,  $J_{6-8}$ =3.5 and  $J_{6-9}$ =0.8 Hz, 6-H), 7.34 (1H, br. s, CH=), 7.50 (1H, dd,  $J$ =3.8 and 0.8 Hz, 5-H of furyl), and 7.72 ppm (1H, dd,  $J$ =1.7 and 0.8 Hz, 2-H of furyl);  $^1H$ -NMR ( $CD_3CN$ )  $\delta$ =2.96, 3.48, 3.67 (each 3H, s, *N*-Me and COOMe), 3.53 (1H, dd,  $J_{3a-9b}$ =8.5 and  $J_{3a-4}$ =2.4 Hz, 3a-H), 3.77 (1H, dd,  $J_{9b-9a}$ =9.5 and  $J_{9b-3a}$ =8.5 Hz, 9b-H), 5.36 (1H, d,  $J_{4-3a}$ =2.4 Hz, 4-H), 5.63 (1H, dd,  $J_{9a-9b}$ =9.5 and  $J_{9a-9}$ =8.5 Hz, 9a-H), 5.80 (1H, ddd,  $J_{9-8}$ =10.4,  $J_{9-9a}$ =8.5, and  $J_{9-6}$ =1.0 Hz, 9-H), 6.58 (1H,  $J_{8-9}$ =10.4 and  $J_{8-6}$ =3.4 Hz, 8-H), 6.69 (1H, dd,  $J$ =4.0 and 1.7 Hz, 4-H of furyl), 6.83 (1H, dd,  $J_{6-8}$ =3.4 and  $J_{6-9}$ =1.0 Hz, 6-H), 7.33 (1H, br. s, CH=), 7.64 (1H, dd,  $J$ =1.7 and 0.8 Hz, 5-H of furyl), and 7.83 ppm (1H, dd,  $J$ =4.0 and 0.8 Hz, 3-H of furyl);  $^{13}C$ -NMR ( $CDCl_3$ )  $\delta$ =25.19 (q, *N*-Me), 51.31, 52.13 (each q, COOMe), 47.79, 48.08 (each d, 3a- and 9b-C), 57.65 (d, 9a-C), 67.05 (d, 4-C), 102.56 (s, 7-C), 112.96 (d), 120.59 (d), 130.39 (d), 132.45 (s), 135.15 (d), 135.38 (d), 144.07 (d), 149.30 (s), 148.30 (d, CH=), 167.73 (s, 2×C, COOMe), 174.72, 175.83 (each s, CON), and 184.05 ppm (s, furyl-CO).

Purification of **39** in order to get the authentic sample failed due to its instability.

**Dehydrogenation of 39 into 40.** An equimolar mixture of **39** (347 mg, 0.79 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 179 mg, 0.79 mmol) in 10 ml of dry benzene was heated under reflux for 21 h. The solvent was evaporated *in vacuo* and the residue was chromatographed over silica gel using ethyl acetate/hexane (1:1) giving 211 mg (61%) of **40**: pale yellow needles from ethyl acetate/hexane; mp 204 °C; IR (KBr) 1780, 1730, 1710, 1670, 1640, and 1270  $cm^{-1}$ ;  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ =3.03, 3.72, 3.78 (each 3H, s, *N*-Me and COOMe), 6.54 (1H, dd,  $J_{7-8}$ =12.0 and  $J_{7-5}$ =3.3 Hz, 7-H), 6.62 (1H, dd,  $J$ =3.8 and 2.0 Hz, 4-H of furyl), 6.70 (1H, d,  $J_{8-7}$ =12.0 Hz, 8-H), 7.38 (1H, d,  $J_{5-7}$ =3.3 Hz, 5-H), 7.39 (1H, dd,  $J$ =3.8 and 0.9 Hz, 5-H of furyl), 7.67 (1H, dd,  $J$ =2.0 and 0.9 Hz, 3-H of furyl), and 7.98 ppm (1H, s, CH=);  $^{13}C$ -NMR ( $CDCl_3$ )  $\delta$ =24.35 (q, *N*-Me), 52.71 (q, 2×C, COOMe), 113.01 (d), 121.16 (d), 121.60 (d), 126.07 (s), 127.77 (s), 127.77 (s), 129.20 (s), 132.30 (s), 135.71 (d), 138.25 (d), 141.07 (d), 148.54 (d), 151.54 (s), 162.36, 163.07, 164.60, 164.78 (each s, CON and COOMe), and 170.48 ppm (s, furyl-CO); MS (rel intensity)  $m/z$  436 ( $M^+$ , base peak), 320 (75), and 95 (76); Found: C, 60.55; H, 3.81; N, 6.56%. Calcd for  $C_{22}H_{16}O_8N_2$ : C, 60.55; H, 3.70; N, 6.42%.

**General Procedure for the Cycloadditions to Acyclic cis Olefins.**

To the suspension of a quaternary salt in dry chloroform was added an equivalent of acyclic cis olefin and then slowly a slight excess (1.1–1.2 equivalent) of triethylamine at 0 °C. The cooling bath was removed and the reaction mixture was stirred at room temperature until all the suspension disappeared. After the reaction was complete, the mixture was poured into ice water and

extracted with dichloromethane (twice). The combined extract was evaporated *in vacuo* below room temperature. The residue, in most cases, solidified on the trituration with ether, petr. ether, or their mixture. If the product is an oily material, the residue was evacuated below room temperature for a few hours. The yield and melting point of each cycloadduct is given in Table 3. The crude cycloadducts were all submitted for the  $^1H$ -NMR spectral measurement from which the isomer formation was judged. Although some of the cycloadducts were successfully purified by crystallization below room temperature (down to –78 °C), the purification of the other failed because of their instability. The IR,  $^1H$ -NMR, and mass spectra of each cycloadduct are listed in Table 4. Other data for the cycloadducts are given as follows: **43**: yellow needles from  $CHCl_3$ ; Found: C, 77.28; H, 4.62; N, 12.85%. Calcd for  $C_{21}H_{15}ON_3$ : 77.52; H, 4.65; N, 12.92%. **44**: yellow grains from ether; Found: C, 81.90; H, 5.19; N, 3.15%. Calcd for  $C_{33}H_{25}O_3N$ : C, 81.96; H, 5.21; N, 2.90%. **45**: yellow prisms from ether; Found:  $m/z$  391.1412. Calcd for  $C_{23}H_{21}O_5N$ : M, 391.1418. **47**: yellow needles from ether–petr. ether; Found: C, 62.33; H, 5.55; N, 4.09%. Calcd for  $C_{18}H_{19}O_6N$ : C, 62.60; H, 5.55; N, 4.06%; Found:  $m/z$  345.1220. Calcd for  $C_{18}H_{19}O_6N$ : C, 345.1211. **48**: Found:  $m/z$  312.1108. Calcd for  $C_{17}H_{16}O_4N_2$ : M, 312.1108. **51**: colorless plates from ethanol; Found: C, 68.71; H, 3.81; N, 12.51%. Calcd for  $C_{19}H_{13}ON_3S$ : C, 68.86; H, 3.95; N, 12.68%. **52**: pale yellow needles from benzene–hexane; Found: C, 63.47; H, 4.82; N, 3.53%. Calcd for  $C_{21}H_{19}O_5NS$ : C, 63.37; H, 4.79; N, 3.67%.

The crude cycloadduct **47** was dehydrogenated when chromatographed over silica gel using benzene as an eluent to give **53** in 36% yield: **53**: colorless needles from ether; mp 156 °C (lit.<sup>54</sup>) mp 156–157 °C).

The reaction between each equivalent amounts of **2d** and **41c** in chloroform at room temperature for 10 h was carried out and the crude product which showed no clean formation of the cycloadduct **49** in its  $^1H$ -NMR spectrum was subjected to a chromatography over silica gel using benzene as an eluent. The product **54** obtained in 40% yield was colored viscous oil whose purification by the repeated chromatography failed. **54**: IR (neat) 1760  $cm^{-1}$ ;  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ =3.64, 3.78 (each 3H, s, COOMe), 3.97 (1H, d,  $J_{3-2}$ =4.7 Hz, 3-H), 5.38 (1H, d,  $J_{2-3}$ =4.7 Hz, 2-H), 6.23 (1H, d,  $J_{6-5}$ =6.9 Hz, 6-H), 6.57 (1H, d,  $J_{5-6}$ =6.9 Hz, 5-H), 7.20–8.30 (7H, m, ArH), and 9.89 ppm (1H, br. d,  $J_{10-9}$ =8.0 Hz, 10-H).

**General Procedure for the Cycloadditions to Acyclic trans Olefins.**

To the suspension of a quaternary salt was added an equivalent of trans olefin and then slowly a slight excess (1.1–1.2 equivalent) of triethylamine at 0 °C. The resulting mixture was stirred at 0 °C or room temperature until all the salt disappeared. The solvent and time for each reaction are listed in Table 5. After the completion of reaction, the mixture was poured into ice water and extracted with dichloromethane (twice). The extract was dried over  $MgSO_4$  and evaporated under vacuum at or below room temperature. The crude product was submitted, after the complete elimination of the reaction and extraction solvents *in vacuo* below room temperature, for the  $^1H$ -NMR measurement. The  $^1H$ -NMR spectrum was inspected in order to know the isomer formation and

isomer ratio. The yield as well as the isomer ratio of each reaction is given in Table 5 and the IR,  $^1\text{H-NMR}$ , and mass spectra in Table 6. Sometimes the crude cycloadducts solidified when triturated with ether, petr. ether, or their mixture. They were purified by crystallization below room temperature (down to  $-78^\circ\text{C}$ ). However, in most cases not only the purification but the separation of isomers was unsuccessful because the cycloadducts were too labile against heating and chromatographic treatment. The unstable cycloadducts or the unseparable mixture of isomeric cycloadducts were assigned only on the basis of the spectral data. Other data and exceptional procedures for the cycloadducts are given as follows:

The reaction between **1a** and **55a**, 1 mmol each, in 10 ml of chloroform or dimethyl sulfoxide at  $0^\circ\text{C}$  for 5 min precipitated almost pure **56**, whereas the same reaction in 50 ml of chloroform for 1 h gave a clean solution of **57**. **56**: pale yellow needles from chloroform; mp  $120\text{--}121^\circ\text{C}$  (dec); Found:  $m/z$  275.1034. Calcd for  $\text{C}_{17}\text{H}_{13}\text{ON}_3$ : M, 275.1058. **57**: yellow viscous oil.

The reaction between **2a** and **55a**, 1 mmol each, in 10 ml of dimethyl sulfoxide at room temperature for 5 min precipitated almost pure **58** which was collected on a filter and washed with ether, whereas the same reaction in 50 ml of chloroform gave a clean solution of **59** which was contaminated with a small amount of **58**. **58**: colorless prisms from acetonitrile; mp  $179\text{--}182^\circ\text{C}$  (dec); Found:  $m/z$  325.1210. Calcd for  $\text{C}_{21}\text{H}_{15}\text{ON}_3$ : M, 325.1214. **59**: yellow needles from chloroform-ether; mp  $127^\circ\text{C}$ .

Other data are shown as follows: **60**: yellow needles from ether; mp  $173^\circ\text{C}$  (dec); Found: C, 81.96; H, 5.21; N, 2.90%. Calcd for  $\text{C}_{33}\text{H}_{25}\text{O}_3\text{N}$ : C, 81.75; H, 5.15; N, 3.18%. **61+62**: viscous yellow oil. **63**: yellow prisms from ether; mp  $84\text{--}86^\circ\text{C}$  (dec); Found:  $m/z$  475.2373. Calcd for  $\text{C}_{29}\text{H}_{35}\text{O}_5\text{N}$ : M, 475.2357. **64**: viscous yellow oil. **65+66**: yellow solid from ether; mp  $138\text{--}142^\circ\text{C}$ ; Found: C, 80.18; H, 4.98; N, 6.92%. Calcd for  $\text{C}_{27}\text{H}_{20}\text{O}_2\text{N}_2$ : C, 79.90; H, 4.98; N, 6.92%. **67+68**+another isomer: yellow solid from ether; mp  $67\text{--}70^\circ\text{C}$ ; Found: C, 69.39; H, 7.06; N, 6.99%. Calcd for  $\text{C}_{23}\text{H}_{28}\text{O}_4\text{N}_2$ : C, 69.67; H, 7.12; N, 7.07%. **69**: colorless plates from ether; mp  $130\text{--}132^\circ\text{C}$  (dec); Found: C, 62.98; H, 5.33; N, 8.29%. Calcd for  $\text{C}_{18}\text{H}_{18}\text{O}_5\text{N}_2$ : C, 63.15; H, 5.30; N, 8.18%. **70**: yellow viscous oil; Found: C, 67.36; H, 7.02; N, 6.50%. Calcd for  $\text{C}_{24}\text{H}_{30}\text{O}_5\text{N}_2$ : C, 67.58; H, 7.09; N, 6.59%. **71+72**: orange viscous oil. **73**: colorless needles from ethanol-hexane; mp  $190\text{--}191^\circ\text{C}$ ; Found: C, 69.05; H, 3.90; N, 12.44%. Calcd for  $\text{C}_{19}\text{H}_{13}\text{ON}_3\text{S}$ : C, 68.87; H, 3.96; N, 12.68%. **74**: colorless prisms from ethanol-hexane; mp  $133\text{--}135^\circ\text{C}$  (dec); Found: C, 68.82; H, 4.09; N, 12.60%. Calcd for  $\text{C}_{19}\text{H}_{13}\text{ON}_3\text{S}$ : C, 68.87; H, 3.96; N, 12.68%. **75+76**: yellow prisms from ether; mp  $64^\circ\text{C}$ ; Found: C, 75.77; H, 5.00; N, 3.15%. Calcd for  $\text{C}_{31}\text{H}_{23}\text{O}_3\text{NS}$ : C, 76.07; H, 4.70; N, 2.86%. **77**: colorless needles from carbon tetrachloride; mp  $104\text{--}105^\circ\text{C}$  (dec); Found: C, 63.14; H, 4.74; N, 3.50%. Calcd for  $\text{C}_{21}\text{H}_{19}\text{O}_5\text{NS}$ : C, 63.47; H, 4.82; N, 3.53%. **78**: pale yellow prisms from ether; mp  $50^\circ\text{C}$ ; Found: C, 67.66; H, 6.25; N, 3.26%. Calcd for  $\text{C}_{27}\text{H}_{31}\text{O}_5\text{NS}$ : C, 67.36; H, 6.44; N, 2.91%. **79**: pale yellow grains from ether; mp  $93^\circ\text{C}$ ; Found:  $m/z$  496.1462. Calcd for  $\text{C}_{32}\text{H}_{20}\text{O}_4\text{N}_2$ : M, 496.1421. **80**: yellow solid; mp  $80\text{--}82^\circ\text{C}$ . **81**: pale yellow grains from ether; mp  $75\text{--}77^\circ\text{C}$ ; Found:  $m/z$  492.2258. Calcd for  $\text{C}_{28}\text{H}_{32}\text{O}_6\text{N}_2$ : M, 492.2258.

*Isomerization of 44 into 60 and of 41b into 55b.* The cycloadduct **44** was dissolved in dimethyl- $d_6$  sulfoxide in an NMR sample tube. The  $^1\text{H-NMR}$  spectrum of the solution after 1 h at  $50\text{--}60^\circ\text{C}$  showed the quantitative formation of **60**. Under the same conditions, **41b** was found to isomerize into **55b**.

*The Retro Cycloaddition of 60.* The solution of each equivalent amounts of **60** and **8a** in dimethyl- $d_6$  sulfoxide was warmed at  $50\text{--}60^\circ\text{C}$  for 24 h in an NMR tube. The quantitative formation of the endo cycloadduct of **8a** to the anti form of **2a** and the eliminated olefin **55b** was confirmed in the  $^1\text{H-NMR}$  spectrum.

*Isomerization of 73 and 51 into 74 and of 41a into 55a.* The cycloadduct **73** or **51** was dissolved in acetonitrile- $d_3$  in an NMR tube. The  $^1\text{H-NMR}$  spectrum of the solution after 24 h at room temperature showed the clean isomerization into **74**. Under the same conditions **41a** was found to isomerize completely into **55a**.

*Dehydrogenation of 63 Leading to 82.* A mixture of each equivalent amounts of **63** and DDQ in benzene was heated under reflux for 23 h. The residue obtained by the removal of the benzene *in vacuo* was chromatographed over silica gel using benzene as an eluent giving 31% of **82**: pale yellow prisms from hexane; mp  $153\text{--}154^\circ\text{C}$ ; IR (KBr)  $1720, 1710$ , and  $1630\text{ cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta=1.05, 1.67$  (each 9H, s,  $\text{COOBU}^t$ ),  $6.98$  (1H, d,  $J=8.0\text{ Hz}$ , 6-H)  $7.30\text{--}7.93$  (8H, m, ArH), and  $8.52\text{ ppm}$  (2H, m, 5- and 10-H); MS (rel intensity)  $m/z$  471 ( $\text{M}^+$ , 34) and 359 (base peak).

Found: C, 73.68; H, 6.27; N, 2.99%. Calcd for  $\text{C}_{29}\text{H}_{29}\text{O}_5\text{N}$ : C, 73.86; H, 6.20; N, 2.97%.

*Isomerization of a Mixture of 67, 68, and Another Isomer into 68.* The solution of 1.0 mmol of the mixture among **67**, **68**, and another isomer in 20 ml of dry benzene was heated under reflux in the presence of palladium on charcoal (10 mg) for 24 h. The benzene was evaporated *in vacuo* leaving the residue whose  $^1\text{H-NMR}$  in  $\text{CDCl}_3$  was identical with that of **68**.

*Dehydrogenation of a Mixture of 67, 68, and Another Isomer into the Dihydropyrrolo[2,1-a]isoquinolines 83+84 or the Pyrrolo[2,1-a]isoquinoline 85.* The mixture of three isomers was heated under reflux in ethanol for 48 h and the residue after the evaporation of the ethanol *in vacuo* was chromatographed over silica gel using benzene as an eluent giving 40% of **85**: colorless needles from ether; mp  $212^\circ\text{C}$  (dec); IR (KBr)  $2220$  and  $1720\text{ cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta=1.63, 1.66$  (each 9H, s,  $\text{COOBU}^t$ ),  $7.13$  (1H, br. d,  $J=7.5\text{ Hz}$ , 6-H),  $7.44\text{--}7.73$  (3H, m, ArH),  $8.39$  (1H, m, 10-H), and  $8.88\text{ ppm}$  (1H, d,  $J=7.5\text{ Hz}$ , 5-H); MS (rel intensity)  $m/z$  347 ( $\text{M}^+$ , base peak).

Found: C, 70.68; H, 6.33; N, 6.87%. Calcd for  $\text{C}_{23}\text{H}_{24}\text{O}_4\text{N}_2$ : C, 70.39; H, 6.16; N, 7.14%.

The above mixture was subjected to a column chromatography over silica gel using benzene affording the eluent containing 2:1 mixture of **83** and **84** in 25% yield. Their separation by repeated chromatography failed. **83+84**: yellow oil; IR (neat)  $2210, 1710$ , and  $1680\text{ cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ) **83**:  $\delta=1.48, 1.52$  (each 9H, s,  $\text{COOBU}^t$ ),  $4.20$  (1H, d,  $J_{2-3}=4.0\text{ Hz}$ , 2-H),  $5.02$  (1H, d,  $J_{3-2}=4.0\text{ Hz}$ , 3-H),  $6.16$  (1H, d,  $J_{6-5}=7.4\text{ Hz}$ , 6-H), and  $6.70\text{ ppm}$  (1H, d,  $J_{5-6}=7.4\text{ Hz}$ , 5-H); **84**:  $\delta=1.48, 1.51$  (each 9H, s,  $\text{COOBU}^t$ ),  $4.10$  (1H, d,  $J_{2-3}=11.8\text{ Hz}$ , 2-H),  $5.13$  (1H, d,  $J_{3-2}=11.8\text{ Hz}$ , 3-H),  $6.13$  (1H, d,  $J_{6-5}=7.4\text{ Hz}$ , 6-H), and  $6.72\text{ ppm}$  (1H, d,  $J_{5-6}=7.4$

Hz, 5-H).

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