

The Photochemical Synthesis of Novel Heterocyclic Compounds from  
*s*-Triazolo[4,3-*b*]pyridazine (I)

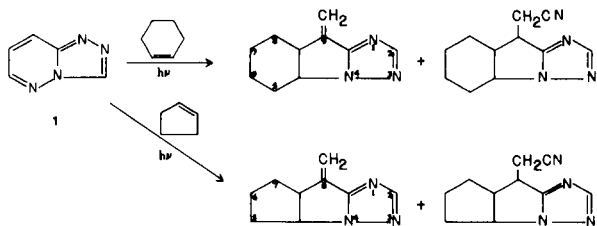
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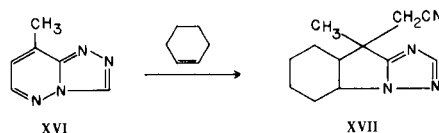
*s*-Triazolo[4,3-*b*]pyridazine (I) photochemically reacted with cyclooctene, cyclododecene, bicyclo[2.2.2]oct-2-ene, bicyclo[2.2.1]hept-2-ene and indene to form tri and tetracyclic triazoles (II-X). Generally, two or more products were formed. For example the reaction with cyclooctene gave 4a,5,7,8,9,10,10a,11-octahydro-11-methylene-6*H*-cycloocta[4,5]-pyrrolo[1,2-*b*]-*s*-triazole (II) and the corresponding 11-cyanomethyl product (III). When I was reacted with open chain alkenes, various isomers of the substituted pyrrolo[1,2-*b*]triazoles (XI-XV) were formed. Since the reaction was not stereospecific, cycloaddition must be a two step process.

We have previously reported the unusual [3 + 2] photocycloaddition of cyclopentene and cyclohexene to *s*-triazolo[4,3-*b*]pyridazine (I) (3,4). The products of those reactions resulted from the addition of the alkene to the 1 and 8 positions of I with a concurrent opening of the pyridazine ring.



This reaction has been extended to include a number of other cyclic and open chain alkenes. The following compounds have been prepared from I: 4a,5,7,8,9,10,10a,11-octahydro-11-methylene-6*H*-cycloocta[4,5]pyrrolo[1,2-*b*]-*s*-triazole (II) and the corresponding 11-cyanomethyl product III from cyclooctene; 15-cyanomethyl-4a,5,7,8,9,10,11,12,13,14,14a,15-dodecahydro-6*H*-cyclo-dodeca[4,5]pyrrolo[1,2-*b*]-*s*-triazole (IV) from cyclododecene; 4a,5,7,8,8a,9-hexahydro-9-methylene-5,8-ethano-6*H*-*s*-triazolo[1,5-*a*]indole (V) and the corresponding 9-cyanomethyl product VI from bicyclo[2.2.2]oct-2-ene; the *endo* and *exo* isomers of 4a,5,7,8,8a,9-hexahydro-9-methylene-5,8-methano-6*H*-*s*-triazolo[1,5-*a*]indole (VII) and the corresponding 9-cyanomethyl product VIII from bicyclo[2.2.1]hept-2-ene; 10-methylene-4a,5,9b,10-tetrahydroindeno[1',2':4,5]pyrrolo[1,2-*b*]-*s*-triazole (IX) and the corresponding 10-cyanomethyl product X from indene; 6-*n*-butyl-6,7-dihydro-7-methylene-5*H*-pyrrolo[1,2-*b*]-*s*-triazole XI, 5-*n*-butyl-7-cyanomethyl-6,7-dihydro-5*H*-pyrrolo-

[1,2-*b*]-*s*-triazole XII, and the *cis* and *trans*- isomers of the 6-*n*-butyl-7-cyanomethyl compound XIII from 1-hexene; and all possible geometric isomers of 5,6-diethyl-6,7-dihydro-7-methylene (and 7-cyanomethyl)-5*H*-pyrrolo[1,2-*b*]-*s*-triazole (XIV and XV) from *cis* and *trans*-3-hexene (5). We have also isolated the 9-cyanomethyl-4a,5,7,8,8a,9-hexahydro-9-methyl-6*H*-*s*-triazolo[1,5-*a*]indole (XVII) from the reaction of 8-methyl-*s*-triazolo[4,3-*b*]pyridazine XVI with cyclohexene.



#### Results and Discussion.

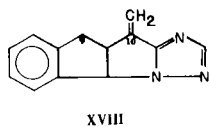
The pyridazine starting material and the appropriate alkene were dissolved in methylene chloride and irradiated through pyrex. The resulting mixtures were separated on a vapor phase chromatograph (vpc). The products were subjected to analyses by ir, nmr, high resolution mass spectrometry (ms) and where possible elemental analysis.

The products all exhibited the expected analyses (4). Thus the methylene compounds (II, V, VII, XI and XIV) all exhibited nmr peaks at  $7.9 \pm 0.1 \delta$  ( $H_2$ ),  $5.9 \pm 0.2$  and  $5.3 \pm 0.2 \delta$  (methylene hydrogens),  $4.25 \pm 0.2 \delta$  ( $H_{4a}$  or  $H_5$ ) and  $3.3 \pm 0.3 \delta$  which is the other hydrogen on the pyrrole ring [ $H_{10a}$  (II),  $H_{8a}$  (V and VII) etc.]. The usual nmr peaks mentioned above for compound IX were shifted down field due to the presence of the benzene ring. The cyanomethyl compounds (III, IV, VI, VIII, X, XII, XIII, XV and XVII) all exhibited a cyano band in the ir as well as nmr peaks at  $7.9 \pm 0.1 \delta$  ( $H_2$ ),  $4.25 \pm$

0.3  $\delta$  ( $H_{4a}$  or  $H_5$ ) and  $2.8 \pm 0.2 \delta$  (usually a doublet,  $CH_2CN$ ).

Products VII and to a lesser extent IX proved to be mixtures of isomers. The nmr spectrum for VII showed two methylene and  $H_{4a}$  peaks as follows: VIIa: 5.97  $\delta$  (d, 1H, methylene H), 5.23  $\delta$  (d, 1H, methylene H) and 4.66  $\delta$  (dd; 1H;  $J_{8a,4a} = 9.8$  Hz;  $J_{5,4a} = 4$  Hz;  $H_{4a}$ ); and VIIb: 5.86  $\delta$  (d, 1H, methylene H), 5.31  $\delta$  (d, 1H, methylene H) and 4.25  $\delta$  (d; 1H;  $J_{8a,4a} = 6$  Hz;  $J_{5,4a} < 0.3$  Hz;  $H_{4a}$ ). The ratio of these peaks was 1 VIIa to 2 VIIb. These same peaks in the nmr spectrum (including coupling constants) for V were almost identical to VIIa [6.0  $\delta$  (d, 1H, methylene); 5.25  $\delta$  (d, 1H, methylene) and 4.45  $\delta$  (dd;  $J_{8a,4a} = 8.5$  Hz;  $J_{5,4a} = 4$  Hz;  $H_{4a}$ )]. Since  $H_{4a}$  and  $H_{8a}$  in V are *endo* to an ethano bridge, this similarity in the nmr spectra of VIIa and V indicates that  $H_{4a}$  and  $H_{8a}$  in VIIa are likewise *endo* to the ethano bridge. Product VIIb must be the *exo* isomer. The cyanomethyl product VIII must also have the *exo* configuration since the nmr peak for  $H_{4a}$  is exactly like that in the spectrum for VIIb. A third peak was observed in the vpc but it could not be isolated in sufficient quantity for nmr analysis. This may have been the *endo* cyano-methyl product.

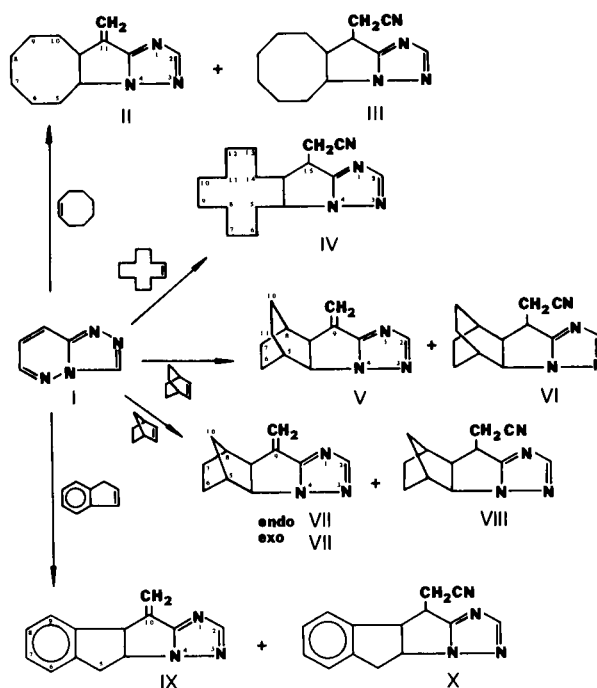
The indene product IX also has a small amount of another isomer. The nmr spectrum of IX shows the methylene hydrogens as doublets at 5.90 and 5.61  $\delta$ . Two smaller doublets (10% of the total) appear at 5.82 and 5.34  $\delta$ . There is also a doublet at 3.20  $\delta$  which can be attributed to a different isomer. The major product is considered to be structure IX since the nmr peak for  $H_{9b}$  has been shifted from about 3.7 to 4.83  $\delta$ . This is because  $H_{9b}$  is now benzylic as well as allylic. The nmr spectrum for the other possible structure (XVIII) would have peaks at about 4-4.2  $\delta$  ( $H_{9a}$ ) and nearly 6  $\delta$  ( $H_{4a}$ , now  $\alpha$  to both benzene and triazole). There are minor peaks with those chemical shifts in the nmr of IX.



The 5*H*-pyrrolo[1,2-*b*]-s-triazole products (XI-XV) from the reaction of open chain alkenes proved to be very interesting. In the case of the reaction of I with 1-hexene, 4 products were isolated. On the basis of their spectra, these proved to be the methylene product XI, the 5-*n*-butyl product XII and the *cis* and *trans*-6-*n*-butyl products (XIII). No attempt was made to distinguish between the *cis* and *trans* isomers.

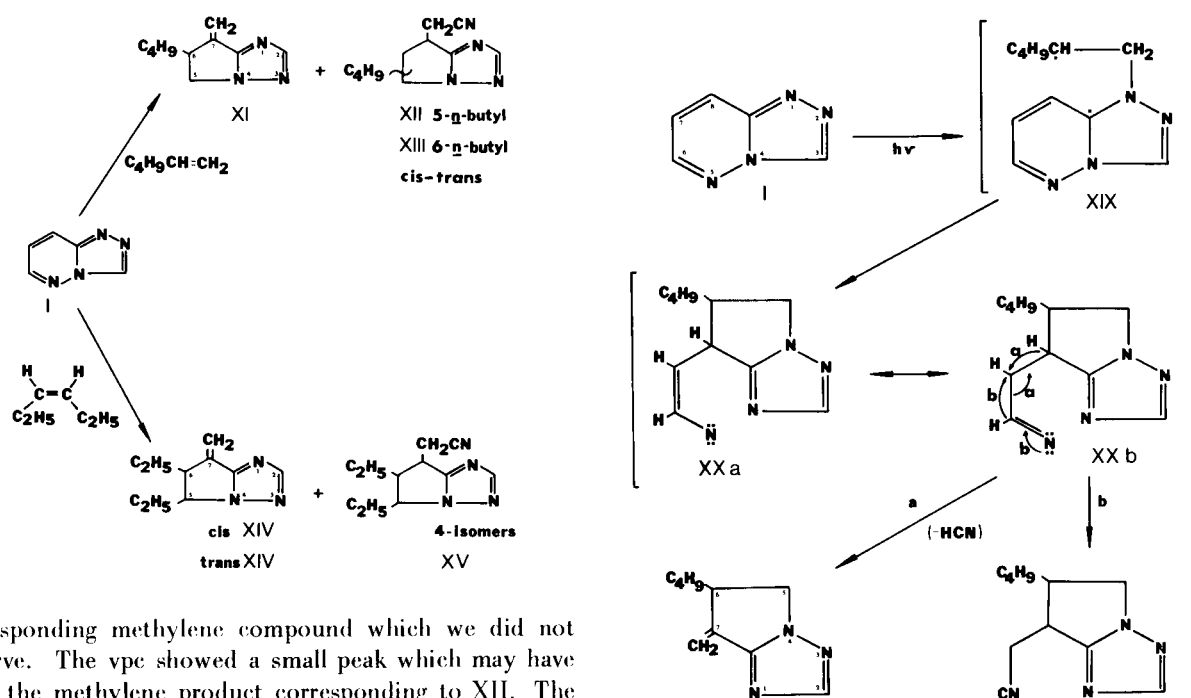
Products XIV and XV from the reaction of I with *cis*-3-hexene (5) are geometrical isomers. A careful separation and analysis using nmr decoupling experiments have

shown the 6 products to be *cis* and *trans*-5,6-diethyl-7-methylene products XIV and the four geometrical isomers of 5,6-diethyl-7-cyanomethyl products XV (5) (see Figure 1). Anet and Muchowski (6) have shown that the  $J_{cis}$  of the ring protons of a five membered ring which cannot deviate from planarity was always appreciably larger than the  $J_{trans}$ . As shown in Figure 1, our J values were either small (2 Hz or less) or nearly 6 Hz; The configuration assignments are based on the J values.



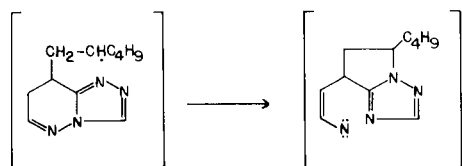
The multiple products obtained in these latter two reactions indicate that there is more than one intermediate in the photocycloaddition reaction. The loss of stereochemistry also shows that the reaction is not concerted. The fact that products XI and XIII in the 1-hexene reaction predominate indicates that the major initial reaction is addition to the nitrogen in position 1 giving the most stable diradical intermediate (XIX in Scheme 1). This diradical could add to position 8 with a concurrent opening of the  $N_4-N_5$  bond to form the vinyl nitrene intermediate XXa. Vinyl nitrenes are known to form cyano compounds (7), perhaps by process b. This would form the cyanomethyl product XIII. A hydride transfer by the ring hydrogen followed by a loss of hydrogen cyanide (process a) would form the methylene product XI.

The formation of compound XII indicates that the alkene is also adding to carbon 8 on the pyrrolo ring to form intermediate XXI. The resulting diradical would close to form the vinyl nitrene intermediate (XXIIa) which would react as in Scheme 1 to give XII as well as a



SCHEME I

corresponding methylene compound which we did not observe. The vpc showed a small peak which may have been the methylene product corresponding to XII. The loss of stereochemistry in the 3-hexene reaction (products



XIV and XV) shows the reaction to be in steps as we have postulated in Scheme I. A one step process would have resulted in a retention of stereochemistry.

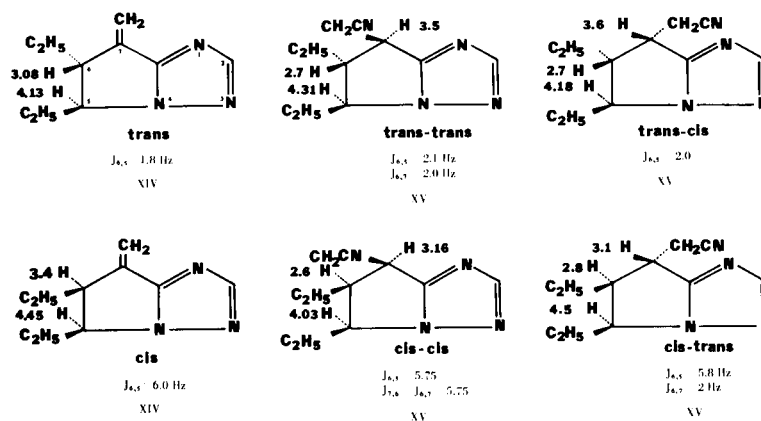
Since most of the isolated yields were XI and XIII, the addition to nitrogen 1 is the favored reaction. This was

also evident when 2,3-dimethylbutadiene was added to 1 (4). In that case, only the 6-substituted compounds were formed.

## EXPERIMENTAL

All ir spectra were obtained on a Hilger and Watts H1200 Infragraph. The nmr spectra were obtained on a Varian A60-A spectrometer and the decoupling experiments were performed in a

FIGURE I



Varian XL-100 spectrometer. Varian model 202B and 1700 vapor phase chromatographs were used to isolate all products. A 6' x 1/4" copper tube packed with 10% SE-30 on 60/100 mesh on 60/100 mesh chromasorb G/AW was used except where noted. The mass spectra (MS) were obtained on a CEC-20-110C high resolution mass spectrometer. Elemental analyses were performed by MIW Laboratories, Garden City, Michigan.

All reactions were carried out in pyrex tubes placed next to a Hanovia 450-W lamp in a water cooled immersion reaction. In most cases, 200 mg. of compound I (8) and about 1 ml. of the appropriate alkene were dissolved in 10 ml. of reagent methylene chloride. The irradiation was continued until no starting compound I was observed when the mixture was subjected to tlc (4). The solvent was then removed under vacuum and the products separated by vpc at 225°. Each reaction and products are given as follows:

#### Cyclooctene Photoproducts.

Two peaks were isolated on the vpc. Peak 1 (35% of the total proved to be compound II, nmr ( $\delta$ ): 1.2-2.2 (m, 12H, H<sub>5-10</sub>), 3.2-3.7 (m, 1H, H<sub>10a</sub>), 4.45 (dt, 1H, J = 8.5 Hz, H<sub>4a</sub>), 5.25 (d, 1H, J = 2 Hz, methylene H), 5.90 (d, 1H, J = 2 Hz, methylene H), 7.95 (s, 1H, H<sub>2</sub>); molecular weight: Calcd. for C<sub>12</sub>H<sub>17</sub>N<sub>3</sub>: 203.1423. Found: 203.1413.

Peak 2 (compound III) exhibited the following spectra: ir: 2230 cm<sup>-1</sup> (CN); nmr ( $\delta$ ): 1.5-2.2 (m, 13H, H<sub>5-10a</sub>), 2.9 (m, 3H, H<sub>11</sub> and CH<sub>2</sub>CN), 4.55 (m, 1H, H<sub>4a</sub>), 7.90 (s, 1H, H<sub>2</sub>).

Anal. Calcd. for C<sub>13</sub>H<sub>18</sub>N<sub>4</sub>: C, 67.80; H, 7.88; N, 24.32. Found: C, 67.66; H, 7.75; N, 24.48.

#### Cyclododecene Photoproduct.

The vpc analysis (2 ft. column of 10% SE30) of the photoproducts from the irradiation of cyclododecene showed one major (80%) and 3 minor peaks. The major peak exhibited the following spectra: ir: 2220 cm<sup>-1</sup> (CN); nmr ( $\delta$ ): 1.2-1.8 (m, 21H, H<sub>5-14a</sub>), 2.7-2.9 (m, 3H, H<sub>15</sub> and CH<sub>2</sub>CN), 4.3 (m, 1H, H<sub>4a</sub>), 7.9 (s, 1H, H<sub>2</sub>).

Anal. Calcd. for C<sub>17</sub>H<sub>26</sub>N<sub>4</sub>: C, 71.29; H, 9.15; N, 19.56. Found: C, 71.27; H, 8.96; N, 19.34.

#### Bicyclo[2.2.2]oct-2-ene Photoproducts.

Three peaks were isolated from the vpc. Peak 1 (15%, compound V) exhibited the following spectra: nmr ( $\delta$ ): 1.0-2.3 (m, 10H, H<sub>5-8</sub> and H<sub>10,11</sub>), 3.55 (m, 1H, H<sub>11a</sub>), 4.45 (dd, 1H; J<sub>8a,4a</sub> = 8.5 Hz; J<sub>5,4a</sub> = 4 Hz; H<sub>4a</sub>), 5.25 (d, 1H, J = 2 Hz, methylene H), 6.0 (d, 1H, J = 2 Hz, methylene H), 8.02 (s, 1H, H<sub>2</sub>); M<sup>+</sup> = 201.

Peak 2 (75%, compound VI) exhibited the following spectra: ir: 2240 cm<sup>-1</sup> (CN); nmr ( $\delta$ ): 1.2-2.0 (m, 11H, H<sub>5-8a</sub> and H<sub>10,11</sub>), 2.2-3.2 (m, 3H, H<sub>9</sub> and CH<sub>2</sub>CN), 4.4 (m, 1H, H<sub>4a</sub>), 7.9 (s, 1H, H<sub>2a</sub>).

Anal. Calcd. for C<sub>13</sub>H<sub>16</sub>N<sub>4</sub>: C, 68.39; H, 7.07; N, 24.54. Found: C, 68.13; H, 6.96; N, 24.42.

The ir spectrum of peak 3 (<10%) was very similar to that for compound VI.

#### Bicyclo[2.2.1]hept-2-ene Photoproducts.

Two peaks were isolated from the vpc. A third (<5% could not be isolated for analyses. Peak 1 (35%, compound VII) exhibited the following spectra: nmr ( $\delta$ ): 1.0-1.8 (m, 6H, H<sub>6,7,10</sub>), 2.3 (m, 2/3H, H<sub>5</sub> and 8) 2.7 (m, 1/3H, H<sub>5</sub> and 8), 3.35 (d, 2/3H, J = 6 Hz, H<sub>8a</sub>), 3.75 (m, 1/3H, H<sub>8a</sub>), 4.25 (d, 2/3H, J<sub>8a,4a</sub> = 6 Hz, J<sub>5,4a</sub> < 0.3 Hz, H<sub>4a</sub>), 4.66 (dd, 1/3H,

J<sub>8a,4a</sub> = 9.8 Hz, J<sub>5,4a</sub> = 4 Hz, H<sub>4a</sub>), 5.23 (d, 1/3H, J = 2 Hz, methylene H), 5.31 (d, 2/3H, J = 2 Hz, methylene H), 5.86 (d, 2/3H, J = 2 Hz, methylene H), 5.97 (d, 1/3H, J = 2 Hz, methylene H), 7.94 (s, 1H, H<sub>2</sub>); M<sup>+</sup> 187.

Peak 2 (61%, compound VIII) exhibited the following spectra: ir: 2250 cm<sup>-1</sup> (CN); nmr ( $\delta$ ): 1.0-1.8 (m, 6H, H<sub>6,7,10</sub>), 2.2-3.2 (m, 6H, H<sub>5,8,8a,9</sub> and CH<sub>2</sub>CN) 4.30 (d, 1H, J = 6 Hz, H<sub>4a</sub>), 7.92 (s, 1H, H<sub>2</sub>).

Anal. Calcd. for C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>: C, 67.28; H, 6.57; N, 26.15. Found: C, 67.17; H, 6.34; N, 26.03.

#### Indene Photoproducts.

The vpc of the photoproducts from the indene reaction showed three peaks. Peak 3 (<6%) could not be isolated. Peak 1 (68%, compound IX) exhibited the following nmr spectrum ( $\delta$ ): 3.5 (d, 2H, J = 4 Hz, H<sub>5</sub>), 4.83 (d, 1H, J = 6 Hz, H<sub>9b</sub>), 5.09 (dt, 1H, J = 6 Hz, H<sub>4a</sub>), 5.60 (d, 1H, J = 2 Hz, methylene H), 5.90 (d, 1H, J = 2 Hz, methylene H), 7.17 (m, 4H, benzene H), 7.93 (s, 1H, H<sub>2</sub>). The nmr spectrum contained small peaks (10% of those above) at ( $\delta$ ): 3.20 (d) 5.34 (d, J = 2 Hz) and 5.82 (d). The molecular weight was as follows: Calcd. for C<sub>13</sub>H<sub>11</sub>N<sub>3</sub>: 209.095293. found: 209.095043.

Peak 2 (26%, compound X) exhibited the following spectra: ir: 2230 cm<sup>-1</sup> (CN); nmr ( $\delta$ ): 2.7-3.2 (m, 3H, H<sub>10</sub> and CH<sub>2</sub>CN), 2.4-2.7 (m, 3H, H<sub>5,9b</sub>), 4.5 (m, 1H, H<sub>4a</sub>), 7.25 (m, 4H, benzene H), 7.90 (s, 1H, H<sub>2</sub>). This material could not be isolated in enough quantity for further analysis.

#### 1-Hexene Photoproducts.

The photoproducts were isolated on the vpc using a 6' x 1/4" column packed with 5% FFAP on chromasorb G/AW. Five peaks were observed but only peaks 2-5 could be isolated. Peak 2 (<3%, compound XI) exhibited the following spectra: nmr ( $\delta$ ): 0.9-1.9 (m, 9H, n-butyl H), 3.0 (m, 1H, H<sub>6</sub>), 3.90 (m, 1H, H<sub>5</sub>), 4.30 (m, 1H, H<sub>5</sub>), 5.25 (d, 1H, J = 2 Hz, methylene H), 5.90 (d, 1H, J = 2 Hz, methylene H); molecular weight: Calcd. for C<sub>10</sub>H<sub>15</sub>N<sub>3</sub>: 177.12659. Found: 177.1273.

Peak 3 (27%, compound XII) exhibited the following spectra: ir: 2200 cm<sup>-1</sup> (CN); nmr ( $\delta$ ): 0.9 (m, 3H, CH<sub>3</sub>), 1.4 (m, 6H, CH<sub>2</sub>), 2.8 (d, 2H, CH<sub>2</sub>CN), 2.9 (m, 2H, H<sub>6</sub>), 3.50 (m, 1H, H<sub>7</sub>), 4.25 (m, 1H, H<sub>5</sub>), 7.9 (s, 1H, H<sub>2</sub>); molecular weight: Calcd. for C<sub>11</sub>H<sub>16</sub>N<sub>4</sub>: 204.13749. Found: 204.1365.

Peak 4 [33%, compound XIII (cis or trans)] exhibited the following spectra: ir: 2250 cm<sup>-1</sup> (CN); nmr ( $\delta$ ): 0.95 (t, 3H, CH<sub>3</sub>), 1.45 (m, 6H, CH<sub>2</sub>), 1.75 (m, 1H, H<sub>6</sub>), 2.90 (m, 3H, H<sub>7</sub> and CH<sub>2</sub>CN), 3.78 (m, 1H, H<sub>5</sub>), 4.40 (m, 1H, H<sub>5</sub>) 7.95 (s, 1H, H<sub>2</sub>); molecular weight: Calcd. for C<sub>11</sub>H<sub>16</sub>N<sub>4</sub>: 204.13749. Found: 204.1362.

Peak 5 (38%, compound XII cis or trans) gave the following spectra: ir: 2240 cm<sup>-1</sup> (CN); nmr ( $\delta$ ): 0.95 (t, 3H, CH<sub>3</sub>), 1.40 (m, 6H, CH<sub>2</sub>), 1.75 (m, 1H, H<sub>6</sub>), 2.75 (d, 2H, CH<sub>2</sub>CN), 3.30 (m, 1H, H<sub>7</sub>), 4.05 (m, 1H, H<sub>5</sub>), 4.25 (m, 1H, H<sub>5</sub>), 7.95 (s, 1H, H<sub>2</sub>); molecular weight: Calcd. for C<sub>11</sub>H<sub>16</sub>N<sub>4</sub>: 204.13749. Found: 204.1366.

#### Irradiation of Compound XVI and Cyclohexene.

Compound XVI (9) was irradiated in the presence of cyclohexene in methylene chloride as described above. Only one peak was observed on the vpc; ir: 2250 cm<sup>-1</sup> (CN); nmr ( $\delta$ ): 0.8-2.0 (m, 11H, H<sub>5-8</sub> and CH<sub>3</sub>), 2.5-3.0 (m, 3H, H<sub>9</sub> and CH<sub>2</sub>CN), 4.5 (m, 1H, H<sub>4a</sub>), 7.91 (s, 1H, H<sub>2</sub>).

Anal. Calcd. for C<sub>12</sub>H<sub>16</sub>N<sub>4</sub>: C, 66.63; H, 7.46; N, 25.90. Found: C, 66.43; H, 7.32; N, 26.14.

## Acknowledgements.

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## REFERENCES

- (1) Presented at the Fifth International Congress of Heterocyclic Chemistry, Ljubljana, Yugoslavia, July 1975.
- (2) To whom inquiries should be sent.
- (3) J. S. Bradshaw, B. Stanovnik and M. Tišler, *Tetrahedron Letters*, 2199 (1973).
- (4) J. S. Bradshaw, B. Stanovnik and M. Tišler, *J. Heterocyclic Chem.*, **10**, 801 (1973).
- (5) J. T. Carlock, J. S. Bradshaw and W. Zmolek, *Tetrahedron Letters*, 2049 (1975).
- (6) F. A. L. Anet and J. M. Muchowski, *Chem. Ind. (London)*, 81 (1963).
- (7) J. H. Boyer, W. E. Kreuger and G. J. Mikol, *J. Am. Chem. Soc.*, **89**, 5505 (1967).
- (8) N. Takahayashi, *J. Pharm. Soc. Japan*, **76**, 765 (1956).
- (9) M. Japelj, B. Stanovnik and M. Tišler, *Monatsh. Chem.*, **100**, 671 (1969).