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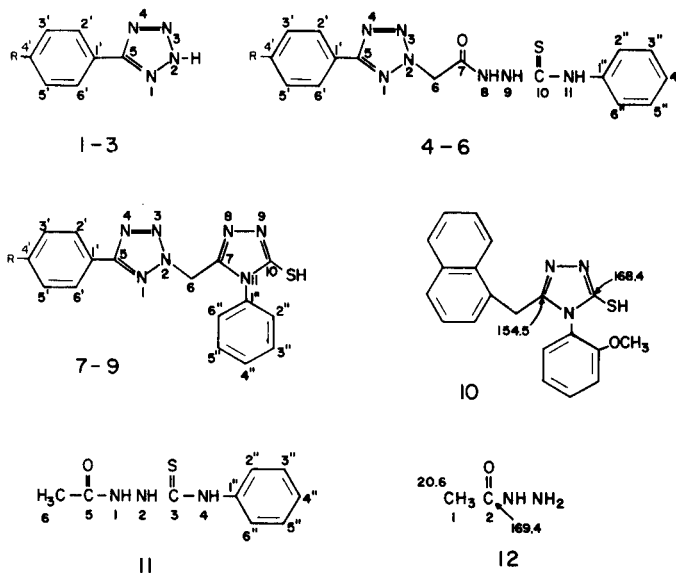
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The natural abundance carbon-13 nuclear magnetic resonance spectra of various 5-aryltetrazoles, 1-(5-aryltetrazol-2-ylacetyl)-4-phenyl thiosemicarbazides and 5-(5-aryltetrazol-2-ylmethyl)-4-phenyl-s-triazole-3-thiols were recorded using Fourier transform techniques. The chemical shifts of various carbon resonances have been assigned on the basis of chemical shift theory, the signal multiplicity observed in the single-frequency off-resonance decoupled (SFORD) spectra and comparison with the chemical shifts of the model compounds.

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The compounds containing tetrazole and triazole moieties are receiving significant importance because of their various biological properties (1-4). Recently, we have reported the synthesis of several 1-(5-aryltetrazole-2-ylacetyl)-4-substituted thiosemicarbazides and 5-(5-aryltetrazole-2-ylmethyl)-4-substituted-s-triazole-3-thiols and their antiproteolytic and antihemolytic properties (5). Our continuing interest to assign the carbon-13 nmr chemical shifts of various classes to therapeutic agents (6-13), initiated the study of the carbon-13 nmr spectra of these compounds which are of theoretical interest for organic chemists.

The natural abundance  $^{13}\text{C}$  nmr spectra of **1-9**, **11** and **12** were recorded on JEOL FX-60 spectrometer operating at 15.00 KHz using deuterated dimethylsulfoxide as a solvent and tetramethylsilane as a reference. In all cases, both proton noise decoupled and single-frequency off-resonance (SFORD) decoupled spectra were obtained. The signal multiplicities observed in SFORD spectra differentiated the methyl, methylene, methine and nonprotonated carbon resonances. In some cases the multiplicity was not clear due to very close chemical shifts. The carbon resonances have been assigned on the basis of chemical shift theory, signal multiplicity and comparison with the carbon chemical shifts of the model compounds.



### 5-Aryltetrazoles (1-3).

The carbon-13 nmr chemical shifts of various 5-aryltetrazoles are listed in Table III. A total of five signals account for the seven carbon resonances of **1-3**. The singlets observed at 155.6 and 124.4 ppm are assigned to C-5 and C-1' of **1**, respectively, on the basis of chemical

Table I  
Physical Constants of 1-(5-Aryltetrazol-2-ylacetyl)-4-phenylthiosemicarbazides 4-6

| Compound No. | R  | M.p. °C | Yield | Formula  | Analysis % |       |       | Ir Absorption Bands (a) $\text{cm}^{-1}$ |      |       | Nmr Chemical Shifts (b) $\delta$                 |          |             |          |
|--------------|----|---------|-------|--|------------|-------|-------|--|------|-------|--|----------|-------------|----------|
|              |    |         |       |  | Calculated | Found |       |  |      |       |  |          |             |          |
|              |    |         |       |  | C          | H     | N     | C  | H    | N     | -CH <sub>2</sub> -                               | Aromatic | NH          |          |
| 4            | H  | 203-204 | 97    | C <sub>11</sub> H <sub>13</sub> N <sub>5</sub> OS  | 54.39      | 4.25  | 27.76 | 54.25                                    | 4.16 | 27.73 | 3280, 3200, 1700, 1600<br>1535, 1410             | 5.66 (s) | 7.1-8.3 (m) | 9.73 (s) |
| 5            | Cl | 210 (d) | 95    | C <sub>10</sub> H <sub>9</sub> ClN <sub>5</sub> OS | 49.54      | 3.61  | 25.29 | 49.57                                    | 3.56 | 25.32 | 3220, 1724, 1610, 1560                           | 5.66 (s) | 7.0-8.2 (m) | 9.80 (s) |
| 6            | Br | 210 (d) | 95    | C <sub>10</sub> H <sub>9</sub> BrN <sub>5</sub> OS | 44.54      | 3.24  | 22.74 | 44.53                                    | 3.37 | 22.84 | 3280, 3200, 1705, 1610<br>1600, 1540, 1500, 1420 | 5.66 (s) | 7.1-8.2 (m) | 9.73 (s) |

(a) Infrared spectra of these compounds were recorded on a Beckman Model-33 spectrophotometer as a suspension in nujol mull. (b) Nuclear magnetic resonance spectra were obtained on a Varian Associates 90 MHz EM-390 instrument using tetramethylsilane as an internal standard and deuterated dimethyl sulfoxide as solvent.

Table II

Physical Constants of 5-(5-Aryltetrazol-2-ylmethyl)-4-phenyl-s-triazole-3-thiols **7-9**

| Compound No. | R  | M.p. °C | Yield | Formula  | Calcd. |      | Analysis % |       | Found |       | Ir Absorption Bands (a)                              | Nmr Chemical Shifts (b) $\delta$ |             |
|--------------|----|---------|-------|--|--------|------|------------|-------|-------|-------|--|----------------------------------|-------------|
|              |    |         |       |  | C      | H    | N          | C     | H     | N     |  | CH <sub>2</sub>                  | Aromatic    |
| 7            | H  | 191-192 | 88    | C <sub>15</sub> H <sub>13</sub> N <sub>7</sub> S   | 57.31  | 3.88 | 29.25      | 57.29 | 3.75  | 29.35 | 3100, 3060, 1600, 1585, 1540, 1510, 1440, 1425, 1320 | 6.0 (s)                          | 7.1-8.0 (m) |
| 8            | Cl | 233-234 | 83    | C <sub>15</sub> H <sub>12</sub> ClN <sub>7</sub> S | 51.96  | 3.24 | 26.52      | 51.65 | 3.31  | 26.41 | 3110, 3060, 1610, 1585, 1500, 1490, 1325             | 6.03 (s)                         | 7.1-8.0 (m) |
| 9            | Br | 218-219 | 95    | C <sub>15</sub> H <sub>12</sub> BrN <sub>7</sub> S | 46.49  | 2.91 | 23.72      | 46.35 | 3.15  | 23.56 | 3120, 3070, 1610, 1590, 1570, 1495, 1440, 1420, 1330 | 6.03 (s)                         | 7.2-8.1 (m) |

(a,b) See footnotes in Table I.

shift theory and comparing the corresponding carbon chemical shift of **10**. The assignment of C-5 is further supported by the presence of singlets about 155 ppm in compounds **2** and **3**, where the substituents present on the benzene nucleus do not influence the electronic environment of C-5. Since a nitrile group on a benzene nucleus, which is analogous to the tetrazole nucleus in part, causes a 3.6, 3.9 and 0.6 ppm downfield shift at the *ortho*-, *para* and *meta*-positions, respectively, the doublet centered at 131.2 ppm is attributed C-4' on the basis of chemical shift theory and signal intensity. The remaining two doublets centered at 129.4 and 127.2 ppm are represented by C-2', C-6' and C-3', C-5', respectively. The various carbon resonances of **2** and **3** have been assigned by considering the substituent effect of chloro- or bromo- group on the phenyl ring.

#### 4-Phenyl-3-Acetylthiosemicarbazide (**11**).

The proton noise decoupled spectrum of **11** exhibited three singlets and three doublets in downfield region and one quartet in the upfield region (Table IV). The quartet centered at 21.1 ppm is assigned to C-6. The three singlets at 181.1, 169.3 and 139.2 ppm are attributed to C-3, C-5 and C-1", respectively, on the basis of chemical shift theory and comparing the carbon resonances of carbonyl group of acetylthiosemicarbazide **12**. The amino group in the aniline causes 18.0 and 0.9 ppm downfield shift to its *ipso*- and *meta*-carbons, respectively, and 13.3 and 9.8 ppm upfield shift to *ortho*- and *para*-carbons, respectively. Hence, the doublets centered at 128.1, 125.5 and 125.1 ppm are represented by the carbon resonances of C-3"-C-5", C-2"-C-6", and C-4", respectively. However, the assignments of C-2", C-6" and C-4" may be interchanged.

#### 1-(5-Aryltetrazol-2-ylacetyl)-4-phenylthiosemicarbazides (**4-6**).

The chemical shift of the various carbon resonances of **4-6** are recorded in Table V. The triplet centered at 53.8 ppm is assigned to C-6 of **4**. Two singlets at 181.1 and

Table III

Carbon-13 Nmr Chemical Shifts of 5-Aryltetrazoles **1-3**

| Assignment (a) | Chemical Shift (ppm) |       |       |
|----------------|----------------------|-------|-------|
|                | H                    | Cl    | Br    |
| C-1'           | 124.4                | 123.4 | 123.7 |
| C-2', C-6'     | 129.4                | 129.4 | 132.4 |
| C-3', C-5'     | 127.2                | 128.7 | 128.8 |
| C-4'           | 131.2                | 136.1 | 124.8 |
| C-5            | 155.6                | 155.2 | 155.2 |

(a) Numbering of carbons is shown in the structure **1-3**.

Table IV

Carbon-13 Nmr Chemical Shifts of 4-Phenyl-3-acetylthiosemicarbazide **11**

| Assignment (a) | Chemical Shift (ppm) |
|----------------|----------------------|
| C-6            | 21.1                 |
| C-5            | 169.3                |
| C-3            | 181.1                |
| C-1"           | 139.2                |
| C-2" (b), C-6" | 125.5                |
| C-3", C-5"     | 128.1                |
| C-4" (b)       | 125.1                |

(a) Numbering of carbons is shown in structure **11**. (b) May be interchanged.

164.3 ppm are attributed to C-10 and both C-5 and C-7, respectively, on the basis of chemical shift theory and comparison with the carbon chemical shifts of model compounds **1**, **11** and **12**. Here the signal of C-5 is observed at lower field as compared to the C-5 of **1** due to the deshielding effect of the functional group at N-2 on **4-6** which decreases the electronegativity of the tetrazole nucleus. The singlet at 139.0 ppm is due to the carbon resonance of C-1" which is well comparable with corresponding carbon chemical shift of **11**. Three unresolved signals at 128.2, 126.4 and 125.8 ppm in single-frequency

Table V

Carbon-13 Nmr Chemical Shifts of 1-(5-Aryltetrazol-2-ylacetyl)-4-phenylthiosemicarbazides **4-6**

| Assignment (a) | Chemical Shift (ppm) |         |           |
|----------------|----------------------|---------|-----------|
|                | H                    | R<br>Cl | Br        |
| C-1'           | 125.5 (b)            | 125.7   | 124.2     |
| C-2', C-6'     | 129.3                | 129.5   | 132.5     |
| C-3', C-5'     | 126.8 (c)            | 128.3   | 128.3     |
| C-4'           | 130.7                | 135.5   | 125.5 (b) |
| C-1''          | 139.0                | 139.0   | 139.0     |
| C-2'', C-6''   | 126.4 (c)            | 125.7   | 126.0     |
| C-3'', C-5''   | 128.2                | 128.3   | 128.3     |
| C-4''          | 125.8 (b)            | 125.7   | 125.9 (b) |
| C-5            | 164.3                | 163.5   | 163.5     |
| C-6            | 53.8                 | 53.8    | 53.9      |
| C-7            | 164.3                | 164.4   | 164.4     |
| C-10           | 181.1                | 181.1   | 181.1     |

(a) Numbering of carbons is shown in the structure **4-6**. (b,c) May be interchanged in the same compound.

Table VI

Carbon-13 Nmr Chemical Shifts of 5-(5-Aryltetrazol-2-ylmethyl)-4-phenyl-s-triazole-3-thiols **7-9**

| Assignment (a) | Chemical Shift (ppm) |         |           |
|----------------|----------------------|---------|-----------|
|                | H                    | R<br>Cl | Br        |
| C-1'           | 126.5                | 125.1   | 124.2 (b) |
| C-2', C-6'     | 129.4 (b)            | 129.7   | 132.3     |
| C-3', C-5'     | 126.5                | 128.1   | 128.3     |
| C-4'           | 130.8                | 135.4   | 125.5 (b) |
| C-1''          | 145.7                | 145.5   | 145.5     |
| C-2'', C-6''   | 127.9                | 127.7   | 127.8     |
| C-3'', C-5''   | 129.3 (b)            | 129.4   | 129.3     |
| C-4''          | 132.7                | 132.5   | 132.6     |
| C-5            | 164.3                | 163.5   | 163.4     |
| C-6            | 47.6                 | 47.6    | 47.7      |
| C-7            | 145.7                | 145.5   | 145.5     |
| C-10           | 169.1                | 168.9   | 169.0     |

(a) Numbering of carbons is shown in structure **7-9**. (b) May be interchanged in the same compound.

off-resonance decoupled spectra are assigned to C-3''-C-5'', C-2''-C-6'', and C-4'', respectively. These assignments have been made on the basis of chemical shift theory, signal intensity and comparing the carbon chemical shifts of **11**. The signals at 129.3, 126.8, 130.7 and 125.5 ppm are represented by the carbon resonances of C-2'-C-6', C-3'-C-5', C-4' and C-1', respectively. These assignments have been made on the basis of chemical shift theory signal intensity and comparing the corresponding carbon chemical shifts of **1**. However, signals of C-1' and C-4'' could be interchanged. Similarly, the carbon resonances of C-2'', C-6'', C-3' and C-5' may be interchanged. The various carbon resonances of **5** and **6** have been

assigned by considering the effects of chloro- or bromo-group on benzene nucleus attached at position 5 of **4** and comparing the carbon chemical shift of corresponding carbons of **2**, **3** and **4**.

5-(5-Aryltetrazol-2-ylmethyl)-4-phenyl-s-triazole-3-thiols (**7-9**).

The chemical shifts of the carbon resonances of **7-9** obtained from their proton noise decoupled spectra are recorded in Table VI. The triplet centered at 47.6 ppm is assigned to C-6 of **7**. The singlets observed in downfield region at 169.1, 164.3 and 145.7 ppm are represented by the carbon resonances of C-10, C-5 and both C-7, C-1'', respectively, on the basis of chemical shift theory and signal intensity. These assignments are further supported by the corresponding carbon chemical shifts of **4** and **10**. The phenyl group attached to the N-11 of the triazole nucleus is in the same electronic environment in all the three compounds (**7-9**), hence the carbon resonances of this phenyl ring will be almost in the same position. The signals at 127.9, 129.3 and 132.7 ppm in **7** are assigned to C-2''-C-6'', C-3''-C-5'', and C-4'', respectively, on the basis of chemical shift theory, signal intensity and by comparing the chemical shift of corresponding carbons of **8** and **9**. The remaining signals at 126.5, 129.4 and 130.8 ppm have been represented by the carbon resonances of C-1', C-3'-C-5'; C-2'-C-6'; and C-4', respectively. The above assignments have been made on the basis of chemical shift theory, signal intensity and by comparing the chemical shift of the corresponding carbons of **4**. Similarly, the carbon resonances of **8** and **9** have been assigned by considering the effect of chloro- or bromo-substituent on the phenyl ring of the tetrazole moiety, signal intensity and comparison of corresponding carbon chemical shifts of **5** and **6**.

## EXPERIMENTAL

### 5-Aryltetrazoles (**1-3**).

These compounds were prepared according to the method reported earlier (14).

### Acethydrazide (**12**).

Acethydrazide was synthesized following the method of Lindgren and Niemann (15).

### 4-Phenyl-3-acetylthiosemicarbazide (**11**).

This compound was prepared according to the method reported by Kendall, *et al.* (16).

### 1-(5-Aryltetrazol-2-ylacetyl)-4-phenylthiosemicarbazides (**4-6**).

The appropriate 5-aryltetrazole **1-3** (0.1 mole) was dissolved in a solution of sodium (0.1 g.-atom) in 200 ml. of absolute ethanol and to this ethylbromoacetate (0.1 mole) was added with stirring. The reaction mixture was refluxed for 16 hours, filtered while hot, and the excess of solvent was removed under reduced pressure. The solid mass of the ethyl-(5-aryltetrazol-2-yl)acetate which separated out was filtered and recrystallized from ethanol-water. Ethyl-(5-aryltetrazol-2-yl)acetate (0.1 mole) was then refluxed with hydrazine hydrate (0.15 mole, 99%) in 150 ml. of absolute ethanol for 8 hours to obtain the (5-aryltetrazol-2-yl)acethydrazide

which was recrystallized from ethanol-water. Equimolar quantities of the appropriate (5-aryltetrazol-2-yl)acetylhydrazide (0.01 mole) and phenylisothiocyanate (0.01 mole) were refluxed in 50 ml. of absolute ethanol. The excess of solvent was removed under reduced pressure and solid mass thus obtained was recrystallized from dimethylformamide-water. These compounds were characterized by their sharp melting points and elemental and spectral analysis (Table I).

#### 5-(5-Aryltetrazol-2-ylmethyl)-4-phenyl-*s*-triazole-3-thiols (7-9).

The suitable 1-(5-aryltetrazol-2-ylacetyl)-4-phenylthiosemicarbazide **4-6** were cyclized into **7-9** by refluxing in 50 ml. of 2*N* sodium hydroxide for 2-3 hours. The reaction mixture was cooled, filtered, and the filtrate was acidified to pH 2 with 2*N* hydrochloric acid. The precipitate thus obtained was filtered, washed with cold water, and recrystallized from dimethylformamide-water. These compounds were characterized by their sharp melting points and elemental and spectral analysis (Table II).

The <sup>13</sup>C nmr spectra of **1-9**, **11** and **12** were obtained on a JEOL FX-60 spectrometer operating at 15.00 KHz. The compounds were run in 10 mm tubes using deuterated dimethylsulfoxide (30% w/v) as an internal lock and tetramethylsilane as a reference. Spectrometer settings were: spectral width, 4 KHz; pulse width, 6 μseconds (30°) and data points, 8 K.

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