

AMINOMETHYLATION OF 4,5-SUBSTITUTED  
1,2,4-TRIAZOLE-3-THIONES

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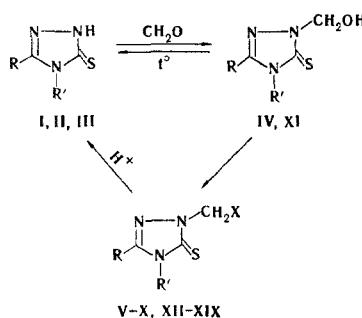
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4,5-Disubstituted 1,2,4-triazole-3-thiones are hydroxymethylated and aminomethylated in the 2 position.

It is known [1] that the aminomethylation of S-alkyl-substituted  $\Delta^2$ -1,2,4-triazole-3-thiones gives N-aminomethyl derivatives.

We have carried out the aminomethylation of the previously unstudied derivatives of 4,5-diphenyl-1,2,4-triazole-3-thione (I), 4-allyl-5-phenyl-1,2,4-triazole-3-thione (II), and 4-phenyl-5-benzyl-1,2,4-triazole-3-thione (III). Piperidine, morpholine, dimethyl(diethyl)-amine, diethanolamine, and N-methylaniline were subjected to the Mannich reaction with I-III. We were unable to obtain aminomethyl derivatives with p-hydroxyaniline.

Hydroxymethyl derivatives of I-III are not formed in aqueous or alcohol media. We obtained compounds of this sort (IV, XI) by reaction of I and II with a fourfold excess of 30% formalin in acetone. Compounds IV and XI are unstable and decompose on heating in water or alcohol to give starting triazoles I and II. Compound IV is also converted to I on heating above its melting point. Compounds IV and XI also react with secondary amines in acetone at room temperature to give aminomethyl derivatives V-X and XII-XVI. Compounds XVII-XIX (see Table 1) were obtained, without isolation of the hydroxymethyl derivative, from triazole-3-thione III and secondary amines. The aminomethyl derivatives obtained from XI and dimethylamine and from III and dimethyl(diethyl)amine and methylphenylamine proved to be oily compounds that could not be identified. The synthesized Mannich bases are colorless



substances that are practically insoluble in water; they decompose in acidic media to give the starting triazolethiones.

The UV spectra of I and its N-cyanoethyl derivative [2] have absorption maxima at 254 and 270 nm. As seen from Table 1, the UV spectra of 2-unsubstituted 1,2,4-triazole-3-thiones and their cyanoethyl derivatives and of the aminomethylation products are similar, and this serves as a confirmation of their identical electronic structures, i.e., 4,5-disubstituted 1,2,4-triazole-3-thiones are aminomethylated at the N(2) nitrogen atom.

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## EXPERIMENTAL

The UV spectra of ethanol solutions of the compounds were recorded with an SF-4 spectrophotometer.

2-Hydroxymethyl-4,5-diphenyl-1,2,4-triazole-3-thione (IV). A fourfold excess of a 30% solution of formalin was added to a suspension of 5 g (0.02 mole) of 4,5-diphenyl-1,2,4-triazole-3-thione (I) in 75 ml of hot acetone, after which the mixture was stirred thoroughly and allowed to stand for 2 h. The solvent was then evaporated or the product was precipitated by the addition of water. Compound XI was similarly obtained (see Table 1).

2-Piperidylmethyl-4,5-diphenyl-1,2,4-triazole-3-thione (V). A 0.28-g (0.001 mole) sample of IV was dissolved in acetone at room temperature, after which 0.1 g (0.0012 mole) of piperidine was added, and the mixture was stirred for 5 min. The resulting precipitate was then removed by filtration. Compounds VI-X and XII-XVI were similarly obtained. Compounds XII-XVI were isolated as oils that gradually began to crystallize.

2-Piperidylmethyl-4-phenyl-5-benzyl-1,2,4-triazole-3-thione (XVII). A fourfold excess of 30% formalin was added to a suspension of 0.27 g (0.001 mole) of 4-phenyl-5-benzyl-1,2,4-triazole-3-thione (III) in hot acetone, after which the mixture was homogenized by shaking and allowed to stand for 30 min. The solvent was evaporated, and the resulting oil was washed with cold water and dissolved in acetone. A 0.1-g (0.0012 mole) sample of piperidine was added to the solution, and the mixture was shaken for 5 min. The acetone was evaporated, and the oily product gradually began to crystallize. Compounds XVIII and XIX were similarly obtained.

## LITERATURE CITED

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2. M. M. Tsitsika, S. M. Khripak, and I. V. Smolanka, Khim. Geterotsikl. Soedin., 851 (1974).

TABLE 1. Characteristics of IV-XIX

Compound	R	R'	X	mp, °C	Empirical formula	N, % found	N, % calc.	UV spectrum λ <sub>m,α</sub>	Yield, %
IV	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	OH NC <sub>6</sub> H <sub>10</sub> NC <sub>4</sub> H <sub>8</sub> O	185–187 206–207 197–198	C <sub>15</sub> H <sub>13</sub> N <sub>3</sub> OS C <sub>20</sub> H <sub>22</sub> N <sub>4</sub> S C <sub>19</sub> H <sub>20</sub> N <sub>4</sub> OS	14.9 16.0 15.9	14.8 16.1 15.9	245, 270, 285 246, 265, 285, 305	4.01; 3.86; 3.88 4.03; 3.99 3.73; 3.83; 3.81; 3.53
V	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	N(CH <sub>3</sub> ) <sub>2</sub>	166–167	C <sub>17</sub> H <sub>18</sub> N <sub>4</sub> S	18.1	18.1	240, 265, 295 240, 260, 295 240, 265, 295	4.03; 4.00; 3.96 4.17; 4.22; 3.97 4.06; 4.00; 3.95
VI	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	N(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	170	C <sub>19</sub> H <sub>22</sub> N <sub>4</sub> S	16.5	16.6	240, 265, 295	4.03; 4.00; 3.96
VII	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	N(C <sub>2</sub> H <sub>4</sub> OH) <sub>2</sub>	157–158	C <sub>19</sub> H <sub>22</sub> N <sub>4</sub> O <sub>2</sub> S	15.1	15.1	240, 265, 295	4.03; 4.00; 3.96
VIII	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	N(C <sub>2</sub> H <sub>5</sub> )C <sub>6</sub> H <sub>5</sub>	168–169	C <sub>22</sub> H <sub>26</sub> N <sub>4</sub> S	14.9	15.0	240, 265, 295	4.03; 4.00; 3.96
IX	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	OH	140–141	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> OS	17.0	17.0	255	4.27
X	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	N(CH <sub>3</sub> ) <sub>2</sub>	58–59	C <sub>17</sub> H <sub>22</sub> N <sub>4</sub> S	17.8	17.8	255, 300	4.45; 3.57
XI	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	NC <sub>6</sub> H <sub>10</sub>	58–59	C <sub>17</sub> H <sub>22</sub> N <sub>4</sub> S	17.8	17.8	255, 300	4.26
XII	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	CH <sub>2</sub> =CH—CH <sub>2</sub>	58–60	C <sub>16</sub> H <sub>20</sub> N <sub>4</sub> OS	17.7	17.7	260	6.67
XIII	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	CH <sub>2</sub> =CH—CH <sub>2</sub>	58–60	C <sub>16</sub> H <sub>20</sub> N <sub>4</sub> OS	18.6	18.6	255, 300	4.16; 3.47
XIV	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	CH <sub>2</sub> =CH—CH <sub>2</sub>	37–38	C <sub>16</sub> H <sub>20</sub> N <sub>4</sub> OS	16.9	16.8	260	6.67
XV	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	N(C <sub>2</sub> H <sub>5</sub> ) <sub>2</sub>	115–116	C <sub>16</sub> H <sub>22</sub> N <sub>4</sub> O <sub>2</sub> S	16.8	16.7	265	8.11
XVI	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	N(CH <sub>3</sub> ) <sub>2</sub> —C <sub>6</sub> H <sub>5</sub>	114–115	C <sub>19</sub> H <sub>20</sub> N <sub>4</sub> S	15.4	15.4	265	3.92
XVII	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	NC <sub>6</sub> H <sub>10</sub>	76–77	C <sub>20</sub> H <sub>22</sub> N <sub>4</sub> OS	15.3	15.3	265	5.50
XVIII	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	NC <sub>6</sub> H <sub>8</sub> O	110–112	C <sub>20</sub> H <sub>22</sub> N <sub>4</sub> OS	15.3	14.5	265	4.04
XIX	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	N(C <sub>2</sub> H <sub>4</sub> OH) <sub>2</sub>	62–63	C <sub>20</sub> H <sub>24</sub> N <sub>4</sub> O <sub>2</sub> S	15.3	14.6	265	5.50