

1-Phenyl-3,3,4-trialkyl-1,2,4-triazolidin-5-ones via  
Cycloisomerization of Ketone 4-Alkyl-2-phenylsemicarbazones

Kurt Pilgram, Richard D. Skiles and Glenn E. Pollard

Biological Sciences Research Center, Shell Development Company, Modesto, California 95352

Received August 5, 1976

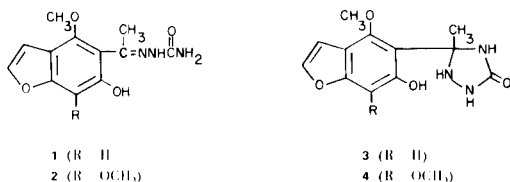
Acetone 2-phenylsemicarbazone undergoes reversible cyclotautomerization to 3,3-dimethyl-1-phenyl-1,2,4-triazolidin-5-one in the presence of hydrochloric acid. Ketone 4-alkyl-2-phenylsemicarbazones derived from aliphatic and alicyclic ketones also undergo cycloisomerization in the presence of catalytic amounts of hydrochloric acid to the ring-tautomeric 1-phenyl-3,3,4-trialkyl-1,2,4-triazolidin-5-ones; the presence of a tertiary butyl group in the 4-position retarded cyclization. Unlike most 4-alkyl-2-phenylsemicarbazones benzaldehyde 2-phenylsemicarbazones do not cyclize. Infrared and nmr data supporting the structural assignments are discussed.

*J. Heterocyclic Chem.*, **13**, 1257 (1976).

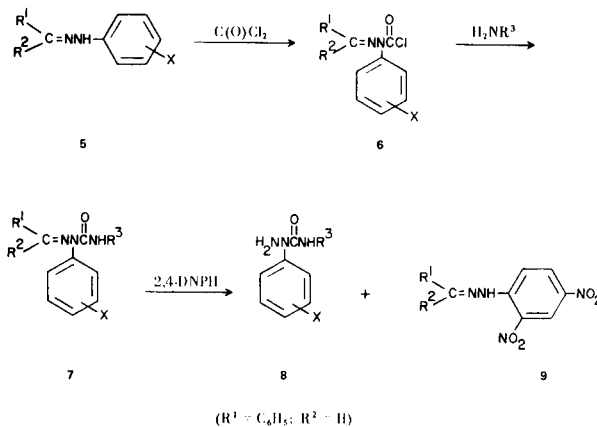
Isomerism amongst the two semicarbazones of Visnaginone, **1**, and Khellinone, **2**, has recently been shown (1) not to be due to the presence of *syn* and *anti* forms, but rather to the presence of cyclic tautomers **3** and **4**. A compound at first formulated as acetone 2-phenylsemicarbazone (2,3), **7a**, and more recently as 3,3-dimethyl-1-phenyl-1,2,4-triazolidin-5-one (4), **10a**, is formed by the addition of cyanic acid to acetone phenylhydrazone (2,3,4) and is hydrolyzed in aqueous acid to 2-phenylsemicarbazide (3,4,5), **8a**. These results led us to follow other workers (3,4) into the field of ring-chain tautomerism of semicarbazones, and we report here our observations on some aldehyde and ketone 4-alkyl-2-phenylsemicarbazones.

mary amine. In this sequence (Scheme I), the reaction of **5** with phosgene was carried out in benzene at ambient temperature and in the presence of equimolar amounts of collidine as acceptor for hydrogen chloride. The **6** compounds, obtained in almost quantitative yield of viscous amber oils that showed no tendency to crystallize, reacted exothermically with primary amines in solution to give **7a-7k** in high yields.

Reaction of **7a-7k** with one molar equivalent of 2,4-dinitrophenylhydrazine (2,4-DNPH) afforded the desired 2-phenylsemicarbazides, **8a-8k** (Table II). This reaction was carried out in warm ethanol (60-80°, 2-18 hours) containing small amounts (*ca.* 1%) of concentrated sulfuric



Scheme I

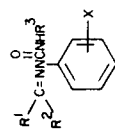


## Results and Discussion

### Preparation of Starting Materials.

The benzaldehyde 2-phenylsemicarbazones, **7a-7k** (Table I), were prepared by treating a benzaldehyde phenylhydrazone, **5**, with phosgene, and then the resulting *N*-(benzylideneamino)carbanilic acid chloride, **6**, with a pri-

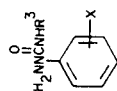
Table I  
2-Phenylsemicarbazones, 7



Compound	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	X	% Yield	M.p., °C	Formula	Infrared Absorption (b) (in cm <sup>-1</sup> )		Nmr Data (c)	Carbon		Hydrogen		Nitrogen		
								ν NH	ν C=O		Calcd.	Found	Calcd.	Found	Calcd.	Found	
7a	C <sub>6</sub> H <sub>5</sub>	H	CH <sub>3</sub>	H	92	140-142	C <sub>15</sub> H <sub>15</sub> N <sub>3</sub> O	3440	1695	1520	7.5 (1, CH=), 6.7 (1, NH), 3.0 (3, CH <sub>3</sub> )	71.0	71.0	5.9	5.9	16.6	16.5
7b	C <sub>6</sub> H <sub>5</sub>	H	CH <sub>3</sub>	3-CF <sub>3</sub> ,4-F	29	168-170	C <sub>16</sub> H <sub>13</sub> F <sub>4</sub> N <sub>3</sub> O	3380	1685	1510	7.2, 7.4 (9, CH=), 6.8 (1, NH), 3.0 (3, CH <sub>3</sub> )	56.6	56.6	3.8	3.9	12.4	12.7
7c	C <sub>6</sub> H <sub>5</sub>	H	CH <sub>3</sub>	3-Cl,4-F	65	158-161	C <sub>15</sub> H <sub>13</sub> ClFN <sub>3</sub> O	3440	1695	1520	7.3 (9, CH=), 6.7 (1, NH), 2.95 (3, CH <sub>3</sub> )	58.9	59.4	4.3	4.4	13.7	13.3
7d	C <sub>6</sub> H <sub>5</sub>	H		3-Cl,4-F	99	161-163	C <sub>17</sub> H <sub>15</sub> ClFN <sub>3</sub> O	3420	1690	1500	6.7-7.7 (10, CH=, NH), 0.8 (4, CH <sub>2</sub> CH <sub>2</sub> ), 2.8 (1, CH)	61.5	61.4	4.5	4.5	12.7	12.6
7e	C <sub>6</sub> H <sub>5</sub>	H	CH <sub>3</sub>	3,4-Cl <sub>2</sub>	60	174-177	C <sub>15</sub> H <sub>13</sub> Cl <sub>2</sub> N <sub>3</sub> O	3440	1695	1510	7.5 (10, CH=, NH), 2.7 (3, CH <sub>3</sub> )	55.9	55.9	4.0	4.1	13.1	13.3
7f	C <sub>6</sub> H <sub>5</sub>	H		3,4-Cl <sub>2</sub>	79	175-177	C <sub>17</sub> H <sub>15</sub> Cl <sub>2</sub> N <sub>3</sub> O	3420	1700	1500	6.7-8.0 (10, CH=, NH), 0.8 (4, CH <sub>2</sub> CH <sub>2</sub> ), 2.8 (1, CH)	58.6	58.7	4.3	4.3	12.1	12.0
7g	C <sub>6</sub> H <sub>5</sub>	H	n-C <sub>4</sub> H <sub>9</sub>	3,4-Cl <sub>2</sub>	85	122-123	C <sub>18</sub> H <sub>19</sub> Cl <sub>2</sub> N <sub>3</sub> O	3430	1685	1505	7.3 (10, CH=, NH), 0.8-1.8 (7, CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> ), 3.2 (2, CH <sub>2</sub> N)	59.3	59.3	5.2	5.2	11.5	11.7
7h	C <sub>6</sub> H <sub>5</sub>	H	(CH <sub>3</sub> ) <sub>2</sub> CHCH <sub>2</sub>	3,4-Cl <sub>2</sub>	96	144-145	C <sub>18</sub> H <sub>19</sub> Cl <sub>2</sub> N <sub>3</sub> O	3440	1690	1515	6.6-7.7 (10, CH=, NH), 1.0 (6, (CH <sub>3</sub> ) <sub>2</sub> ), 1.85 (1, CH), 3.2 (2, CH <sub>2</sub> N)	59.3	59.4	5.2	5.3	11.5	11.4
7i	C <sub>6</sub> H <sub>5</sub>	H	(CH <sub>3</sub> ) <sub>3</sub> C	3,4-Cl <sub>2</sub>	90	133-136	C <sub>18</sub> H <sub>19</sub> Cl <sub>2</sub> N <sub>3</sub> O	3410	1690	1510	7.8 (9, CH=), 6.8 (1, NH), 1.5 (9, (CH <sub>3</sub> ) <sub>3</sub> )	59.3	59.4	5.2	5.4	11.5	11.6
7j	C <sub>6</sub> H <sub>5</sub>	H	n-C <sub>8</sub> H <sub>17</sub>	3,4-Cl <sub>2</sub>	81	105-107	C <sub>22</sub> H <sub>27</sub> Cl <sub>2</sub> N <sub>3</sub> O	3420	1685	1500	7.4 (10, CH=, NH), 0.5-1.0 (15, CH <sub>2</sub> CH <sub>2</sub> ), 3.4 (2, CH <sub>2</sub> N)	62.9	63.0	6.4	6.5	10.0	9.8
7k	C <sub>6</sub> H <sub>5</sub>	H	CH <sub>2</sub> CH <sub>2</sub> OH	3,4-Cl <sub>2</sub>	93	150-152	C <sub>16</sub> H <sub>15</sub> Cl <sub>2</sub> N <sub>3</sub> O <sub>2</sub>	3400	1690	1525	7.8 (10, CH=, NH), 3.4 (4, CH <sub>2</sub> CH <sub>2</sub> ), 4.8 (1, OH)	54.5	54.7	4.3	4.3	11.9	11.7 (r)
7l	CH <sub>3</sub>	CH <sub>3</sub>	H	H	33	157-159 (a)	C <sub>10</sub> H <sub>13</sub> N <sub>3</sub> O	3600-3100	1695	1560	7.1 (5, CH=), 6.2 (2, NH <sub>2</sub> ), 2.1 (3, CH <sub>3</sub> ), 1.6 (3, CH <sub>3</sub> )	62.8	63.0	6.8	6.9	22.0	21.7
7m	C <sub>6</sub> H <sub>5</sub>	H	H	H	95	149-152	C <sub>14</sub> H <sub>13</sub> N <sub>3</sub> O	3400	1700	1560	ca. 7.3 (CH= and NH <sub>2</sub> )	70.3	70.2	5.4	5.5	17.6	17.3
7n	CH <sub>3</sub>	CH <sub>3</sub>	(CH <sub>3</sub> ) <sub>2</sub> CHCH <sub>2</sub>	3,4-Cl <sub>2</sub>	91	69-71	C <sub>14</sub> H <sub>19</sub> Cl <sub>2</sub> N <sub>3</sub> O	3340	1660	1530	7.3 (3, CH=), 6.0 (1, NH), 2.1 (3, CH <sub>3</sub> ), 1.6 (3, CH <sub>3</sub> ), 0.9 (6, (CH <sub>3</sub> ) <sub>2</sub> ), 1.8 (1, CH), 3.05 (2, CH <sub>2</sub> )	53.2	53.1	6.0	6.0	13.3	13.2
7o	CH <sub>3</sub>	CH <sub>3</sub>	(CH <sub>3</sub> ) <sub>3</sub> C	3,4-Cl <sub>2</sub>	82	116-119	C <sub>14</sub> H <sub>19</sub> Cl <sub>2</sub> N <sub>3</sub> O	3350	1680	1505	7.3 (3, CH=), 5.9 (1, NH), 2.1 (3, CH <sub>3</sub> ), 1.65 (3, CH <sub>3</sub> ), 1.35 (9, (CH <sub>3</sub> ) <sub>3</sub> )	53.2	52.9	6.0	5.9	13.3	13.6

(a) Lit. (4) m.p. 154-156°. (b) Potassium bromide pellet. (c) In parts per million (number of protons, assignment). (d) D = DMSO-d<sub>6</sub>; C = deuteriochloroform. (r) Compound 7k: *Anal.* Calcd. for Cl: 20.2. Found: 20.0.

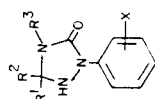
Table II  
2-Phenylsemicarbazides, **8**



Compound	R <sup>3</sup>	X	% Yield	M.p., °C	Formula	Infrared Absorption (b) (in cm <sup>-1</sup> )		Nmr Data (c)	Solvent (d)	Carbon		Hydrogen		Nitrogen	
						ν NH	ν C=O			Calcd.	Found	Calcd.	Found	Calcd.	Found
<b>8a</b>	H	H	70	115-118 (a)	C <sub>7</sub> H <sub>9</sub> N <sub>3</sub> O	3500-3200	1660	7.8 (5, CH=), 6.5 (2, NH <sub>2</sub> ), 5.2 (2, NH <sub>2</sub> )	D	55.6	55.8	6.0	6.1	27.8	28.1
<b>8b</b>	CH <sub>3</sub>	H	53	106-108	C <sub>8</sub> H <sub>11</sub> N <sub>3</sub> O	3430-3260	1680	7.3(5, CH=, NH), 5.1(2, NH <sub>2</sub> ), 2.6(3, CH <sub>3</sub> )	D	58.2	57.8	6.7	6.7	24.5	24.3
<b>8c</b>	CH <sub>3</sub>	3-CF <sub>3</sub> , 4-F	100	123-125	C <sub>9</sub> H <sub>9</sub> F <sub>4</sub> N <sub>3</sub> O	3420-3360	1670	6.5-3.0 (4, CH=, NH), 4.1 (2, NH <sub>2</sub> ), 2.8 (3, CH <sub>3</sub> )	C	43.0	43.1	3.6	3.6	16.7	16.8
<b>8d</b>	CH <sub>3</sub>	3-Cl, 4-F	29	192-194	C <sub>8</sub> H <sub>9</sub> ClFN <sub>3</sub> O	3430-3190	1675	7.8(4, CH=, NH), 5.3(2, NH <sub>2</sub> ), 2.7(3, CH <sub>3</sub> )	D	44.1	44.1	4.1	4.1	19.3	19.3
<b>8e</b>		3-Cl, 4-F	77	124-127	C <sub>10</sub> H <sub>11</sub> ClFN <sub>3</sub> O	3390-3220	1660	7.5 (4, CH=, NH), 5.2 (2, NH <sub>2</sub> ), 2.1 (1, CH), 0.6 (4, (CH <sub>2</sub> ) <sub>2</sub> )	D	49.3	49.4	4.5	4.6	17.2	17.1
<b>8f</b>	CH <sub>3</sub>	3,4-Cl <sub>2</sub>	25	174-176	C <sub>8</sub> H <sub>9</sub> Cl <sub>2</sub> N <sub>3</sub> O	3400	1670	7.5(4, CH=, NH), 5.05(2, NH <sub>2</sub> ), 2.5(3, CH <sub>3</sub> )	D	41.0	41.1	3.8	3.8	17.9	17.9
<b>8g</b>		3,4-Cl <sub>2</sub>	94	140-143	C <sub>10</sub> H <sub>11</sub> Cl <sub>2</sub> N <sub>3</sub> O	3400-3210	1670	7.8 (3, CH=), 6.9 (1, NH), 3.85 (2, NH <sub>2</sub> ), 2.6 (1, CH), 0.3-1.3 (4, (CH <sub>2</sub> ) <sub>2</sub> )	C	46.2	46.6	4.2	4.4	16.2	16.2
<b>8h</b>	n-C <sub>4</sub> H <sub>9</sub>	3,4-Cl <sub>2</sub>	91	69-72	C <sub>11</sub> H <sub>15</sub> Cl <sub>2</sub> N <sub>3</sub> O	3410-3200	1665	7.0-7.5 (3, CH=), 6.7 (1, NH), 4.2 (2, NH <sub>2</sub> ), 3.15 (2, CH <sub>2</sub> N), 0.7-1.8 (7, (CH <sub>2</sub> ) <sub>2</sub> CH <sub>3</sub> )	C	47.8	47.6	5.4	5.5	15.2	15.4
<b>8i</b>	(CH <sub>3</sub> ) <sub>2</sub> CHCH <sub>2</sub>	3,4-Cl <sub>2</sub>	82	121-123	C <sub>11</sub> H <sub>15</sub> Cl <sub>2</sub> N <sub>3</sub> O	3400-3210	1670	7.3-7.7 (3, CH=), 6.8 (1, NH), 4.0 (1, NH <sub>2</sub> ), 3.05 (2, CH <sub>2</sub> ), 1.8 (1, CH), 0.9 (6, (CH <sub>3</sub> ) <sub>2</sub> )	C	47.8	47.7	5.4	5.3	15.2	15.3
<b>8j</b>	CH <sub>2</sub> CH <sub>2</sub> OH	3,4-Cl <sub>2</sub>	100	(e)	C <sub>9</sub> H <sub>11</sub> Cl <sub>2</sub> N <sub>3</sub> O <sub>2</sub>	3400	1650	7.5 (4, CH=, NH), 5.4 (2, NH <sub>2</sub> ), 3.4 (2, CH <sub>2</sub> O), 1.3 (2, CH <sub>2</sub> N)	D	40.9	40.7	4.2	4.5		
<b>8k</b>	(CH <sub>3</sub> ) <sub>3</sub> C	3,4-Cl <sub>2</sub>	90	134-136	C <sub>11</sub> H <sub>15</sub> Cl <sub>2</sub> N <sub>3</sub> O	3370-3210	1665	7.8 (4, CH=, NH), 5.3 (2, NH <sub>2</sub> ), 1.3 (9, (CH <sub>3</sub> ) <sub>3</sub> )	D	47.8	47.4	5.4	5.4	15.2	15.2 (f)

(a) Lit. (3,5) m.p. 118-119° (Reference 3) and 120° (Reference 5). (b) Potassium bromide pellet. (c) In parts per million (number of protons, assignment). (d) D = DMSO-d<sub>6</sub>; C = deuteriochloroform. (e) Amber syrup. (f) Compound **8k**: Anal. Calcd. for Cl: 25.7. Found: 25.8.

Table III  
1-Phenyl-1,2,4-triazolidin-5-ones, 10



Compound	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	X	% Yield	M.p., °C	Formula	Infrared Absorption (c)		Nmr Data (d)	Solvent (e)		Carbon		Hydrogen		Nitrogen	
								$\nu$ NH	$\nu$ C=O		Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
10a	CH <sub>3</sub>	CH <sub>3</sub>	H	H	84	138-140(a)	C <sub>10</sub> H <sub>13</sub> N <sub>3</sub> O	3420-3220	1720	6.6-7.8(7, CH=, NH), 6.05(1, NH), 1.3(6, (CH <sub>3</sub> ) <sub>2</sub> )	D	62.8	62.8	6.8	6.8	22.0	21.9	
10b	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	H	100	78-80	C <sub>11</sub> H <sub>15</sub> N <sub>3</sub> O	3220	1720	6.9-8.0(5, CH=), 4.3(1, NH), 2.7(3, (CH <sub>3</sub> ), 1.4(6, (CH <sub>3</sub> ) <sub>2</sub> )	C	64.4	64.4	7.3	7.4	20.5	20.6	
10c	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	3,4-F <sub>3,4</sub> F	67	161-163	C <sub>12</sub> H <sub>13</sub> F <sub>4</sub> N <sub>3</sub> O	3190	1700	7.8(3, CH=), 6.2(1, NH), 2.7(3, CH <sub>3</sub> ), 1.3(6, (CH <sub>3</sub> ) <sub>2</sub> )	D	49.5	49.6	4.5	4.5	14.4	14.5	
10d	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	3-Cl,4-F	28	115-118	C <sub>11</sub> H <sub>13</sub> ClN <sub>3</sub> O	3230	1715	6.8-8.0(3, CH=), 4.2(1, NH), 2.7(3, (CH <sub>3</sub> ), 1.35(6, (CH <sub>3</sub> ) <sub>2</sub> )	C	51.3	51.4	5.0	5.2	16.3	16.2	
10e	CH <sub>3</sub>	CH <sub>3</sub>		3-Cl,4-F	74	114-117	C <sub>13</sub> H <sub>15</sub> ClFN <sub>3</sub> O	3230	1705	6.6-8.0(3, CH=), 4.3(1, NH), 2.2(1, Cl), 1.45(6, (CH <sub>3</sub> ) <sub>2</sub> ), 0.75(4, (CH <sub>2</sub> ) <sub>2</sub> )	C	55.0	55.0	5.3	5.2	14.8	14.7	
10f	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	3,4-Cl <sub>2</sub>	48	123-126	C <sub>11</sub> H <sub>13</sub> Cl <sub>2</sub> N <sub>3</sub> O	3230	1725	7.7(3, CH=), 6.2(1, NH), 2.7(3, CH <sub>3</sub> ), 1.3(6, (CH <sub>3</sub> ) <sub>2</sub> )	D	48.7	48.5	4.7	5.1	15.3	14.9	
10g	CH <sub>3</sub>	CH <sub>3</sub>		3,4-Cl <sub>2</sub>	71	149-151	C <sub>13</sub> H <sub>15</sub> Cl <sub>2</sub> N <sub>3</sub> O	3230	1710	7.5(3, CH=), 4.2(1, NH), 2.1(Cl), 1.4(6, (CH <sub>3</sub> ) <sub>2</sub> ), 0.7(4, (CH <sub>2</sub> ) <sub>2</sub> )	C	52.0	52.0	5.0	5.0	14.0	14.1	
10h	CH <sub>3</sub>	CH <sub>3</sub>	n-C <sub>4</sub> H <sub>9</sub>	3,4-Cl <sub>2</sub>	75	98-100	C <sub>14</sub> H <sub>19</sub> Cl <sub>2</sub> N <sub>3</sub> O	3180	1695	7.8(3, CH=), 4.0(1, NH), 3.1(2, CH <sub>2</sub> N), 0.8-2.0(3, (CH <sub>3</sub> ) <sub>2</sub> , (CH <sub>2</sub> ) <sub>2</sub> )	C	53.2	53.1	6.0	6.1	13.3	13.4(f)	
10i	CH <sub>3</sub>	CH <sub>3</sub>	(CH <sub>3</sub> ) <sub>2</sub> CHCH <sub>2</sub>	3,4-Cl <sub>2</sub>	70	110-112	C <sub>14</sub> H <sub>19</sub> Cl <sub>2</sub> N <sub>3</sub> O	3230	1715	7.8(3, CH=), 4.4(1, NH), 2.9(2, CH <sub>2</sub> ), 1.9(1, Cl), 1.4(6, (CH <sub>3</sub> ) <sub>2</sub> ), 1.0(6, (CH <sub>2</sub> ) <sub>2</sub> )	C	53.2	53.3	6.0	5.9	13.3	13.1	
10j	CH <sub>3</sub>	CH <sub>3</sub>	n-C <sub>8</sub> H <sub>17</sub>	3,4-Cl <sub>2</sub>	86	68-70	C <sub>18</sub> H <sub>27</sub> Cl <sub>2</sub> N <sub>3</sub> O	3200	1700	7.8(3, CH=), 4.7(1, NH), 0.5-1.7(23, (CH <sub>3</sub> ) <sub>2</sub> , (CH <sub>2</sub> ) <sub>2</sub> , CH <sub>3</sub> )	C	58.1	58.2	7.2	6.9	11.3	11.3	
10k	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>2</sub> CH <sub>2</sub> OH	3,4-Cl <sub>2</sub>	76	(b)	C <sub>12</sub> H <sub>15</sub> Cl <sub>2</sub> N <sub>3</sub> O <sub>2</sub>	3420	1710	7.7(3, CH=), 4.0(1, NH), 4.0(1, OH), 3.3(4, (CH <sub>2</sub> ) <sub>2</sub> ), 1.35(6, (CH <sub>3</sub> ) <sub>2</sub> )	D	47.4	47.1	4.9	5.1	13.8	13.7	
10l	CH <sub>3</sub>		CH <sub>3</sub>	3,4-Cl <sub>2</sub>	67	136-138	C <sub>13</sub> H <sub>15</sub> Cl <sub>2</sub> N <sub>3</sub> O	3190	1715	7.7(3, CH=), 6.1(1, NH), 2.8(3, CH <sub>3</sub> ), 1.3(3, CH <sub>3</sub> ), 1.1(1, Cl), 0.3(4, (CH <sub>2</sub> ) <sub>2</sub> )	D	52.0	51.9	5.0	5.0	14.0	14.0	
10m	-CH <sub>2</sub> (CH <sub>2</sub> ) <sub>2</sub> CH <sub>2</sub> -	CH <sub>3</sub>	CH <sub>3</sub>	3,4-Cl <sub>2</sub>	86	146-147	C <sub>13</sub> H <sub>15</sub> Cl <sub>2</sub> N <sub>3</sub> O	3200	1720	7.7(3, CH=), 6.1(1, NH), 2.7(3, CH <sub>3</sub> ), 1.7(8, (CH <sub>2</sub> ) <sub>4</sub> )	D	52.0	52.1	5.0	5.0	14.0	13.9	
10n	-CH <sub>2</sub> (CH <sub>2</sub> ) <sub>3</sub> CH <sub>2</sub> -	CH <sub>3</sub>	CH <sub>3</sub>	3,4-Cl <sub>2</sub>	90	166	C <sub>14</sub> H <sub>17</sub> Cl <sub>2</sub> N <sub>3</sub> O	3100	1720	7.8(3, CH=), 4.2(1, NH), 2.7(3, CH <sub>3</sub> ), 1.7(10, (CH <sub>2</sub> ) <sub>5</sub> )	C	53.5	53.7	5.4	5.3	13.4	13.6	

(a) Lit. (3,4) m.p. 140° (Reference 3) and 138-140° (Reference 4). (b) Amber syrup. (c) Potassium bromide pellet. (d) In parts per million (number of protons, assignment). (e) D = DMSO-d<sub>6</sub>; C = deuteriochloroform. (f) Compound 10h: Anal. Calcd. for Cl: 22.5, Found: 22.2.

acid; no reaction takes place in the absence of sulfuric acid. The co-product, benzaldehyde 2,4-dinitrophenylhydrazone, **9**, is insoluble in the chilled (5–15°) reaction mixture containing **8** in solution and was conveniently removed by filtration.

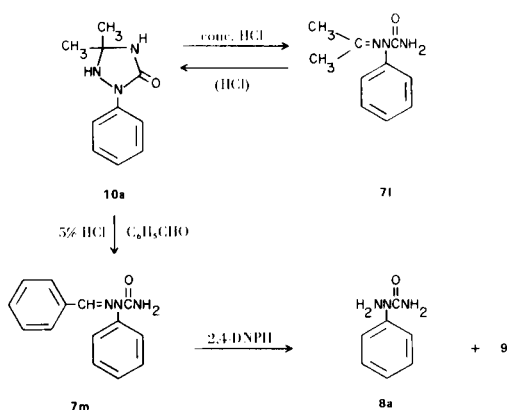
#### Cycloisomerization.

We confirm the report (4) that the product obtained in 86% yield from acetone phenylhydrazone with potassium cyanate in 75% acetic acid is 3,3-dimethyl-1-phenyl-1,2,4-triazolidin-5-one, **10a**. There is reason to believe that **10a** and **71** are readily interconverted. During a study of the hydrolysis of **10a**, we observed that warm concentrated hydrochloric acid unexpectedly isomerized it to **71** (Scheme II). Although isomerization of **10a** to **71** proceeded cleanly, the percent conversion was lower (ca. 33%) than for the reverse reaction, **71** → **10a**, which proceeded quantitatively in refluxing ethanol or acetone containing **71** and a catalytic amount of hydrogen chloride.

Structures **71** and **10a** were proven unequivocally, both having nmr spectra consistent with their assigned structures. The protons of the methyl groups of **71** appeared as two singlets (8) ( $\delta$  1.6 and 2.3 ppm), whereas the methyl protons of **10a** gave only one signal at 1.3 ppm (6, s,  $(\text{CH}_3)_2$ ). Furthermore, the  $\text{NH}_2$  protons appeared as one singlet in the spectrum of **71**, whereas two singlets in the spectrum of **10a** have been assigned to NH signals (4).

Benzaldehyde 2-phenylsemicarbazone, **7m**, was obtained in 95% yield from the reaction of **10a** with benzaldehyde in 5% hydrochloric acid (80°, 1 hour). Treatment of **7m** with 2,4-dinitrophenylhydrazine gave 2-phenylsemicarbazide, **8a**, in 70% yield.

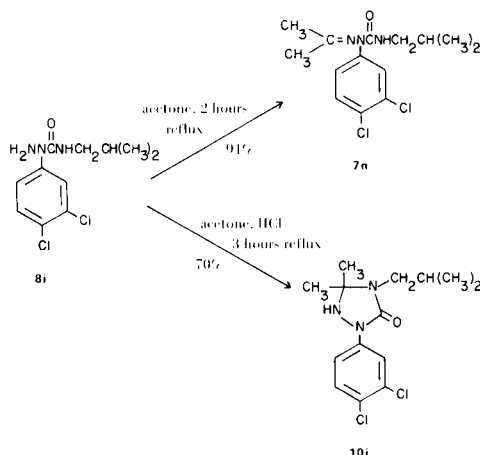
Scheme II



In order to assess whether cyclotautomerization is limited to acetone 2-phenylsemicarbazone, several 2-phenylsemicarbazides, **8b–8k** (Table II), in which the phenyl ring was substituted and the amide nitrogen ( $\text{N}^4$ ) atom was alkylated were allowed to react with an aliphatic or

alicyclic ketone or with benzaldehyde. In general, the 4-alkyl (and cyclopropyl)-2-phenylsemicarbazides, **8b–8j**, reacted readily in refluxing acetone containing small amounts of concentrated hydrochloric acid, in the presence or in the absence of anhydrous magnesium sulfate, to give the 3,3-dimethyl-4-alkyl (and cyclopropyl)-1-phenyl-1,2,4-triazolidin-5-ones, **10b–10k** (Table III). Cyclopropyl methyl ketone, cyclopentanone and cyclohexanone reacted analogously with **8f** in refluxing ethanol containing catalytic amounts of hydrochloric acid to give the respective triazolidinones **10l**, **10m**, and **10n** (Table III).

The following experiments illustrate the importance, in several instances, of the catalyst hydrogen chloride in these cycloisomerizations. With 2-(3,4-dichlorophenyl)-4-isobutylsemicarbazide, **8i**, and acetone, the following results were obtained: when **8i** was refluxed in acetone (2 hours), the corresponding semicarbazone, **7n**, was isolated in 91% yield as the only detectable reaction product. A solution containing **7n** in glacial acetic acid was unchanged after two days at ambient temperature. However, when several drops of concentrated hydrochloric acid were added to a solution containing **8i** in acetone, the triazolidinone **10i** was isolated in 70% yield after three hours reflux.



Acetone 2-(3,4-dichlorophenyl)-4-(*t*-butyl)semicarbazone, **7o**, obtained in 82% yield from 2-(3,4-dichlorophenyl)-4-(*tert* butyl)semicarbazide, **8k**, in refluxing acetone (1 hour), failed to undergo cycloisomerization, giving only starting material after prolonged heating in acetone containing hydrochloric acid. A solution of **7o** in glacial acetic acid showed no change after three days at ambient temperature; decomposition occurred when this solution was refluxed for eighteen hours. The reluctance of **7o** to undergo cycloisomerization is presumably due to the presence of the *tert* butyl group in the 4-position on nitrogen. The bulk of this group induces increased steric resistance, thus preventing cyclization. Benzaldehyde 4-alkyl-2-phenylsemicarbazones, **7a–7k**, also failed to cy-

clize to the ring-tautomeric triazolidinone structure when heated in the presence of small amounts of hydrochloric acid.

Relevant nmr and infrared data for 2-phenylsemicarbazones, **7**, 2-phenylsemicarbazides, **8**, and 1-phenyl-1,2,4-triazolidin-5-ones, **10**, are collected in Tables I, II, and III, respectively. As with **7i**, the structure assignment of **7n** and **7o** (Table I) follows from their nmr spectra in which the protons of the two methyl groups appear as two singlets ( $\delta$  1.6-1.65 and 2.1 ppm). For the triazolidinones **10a-10k**, the two methyl groups in position 3 appear as one singlet at 1.3-1.45 ppm.

From the infrared data, several conclusions can be drawn that are pertinent to structural assignments. All semicarbazides, **8**, and semicarbazones, **7**, show the amide II absorption in the infrared at 1535-1500  $\text{cm}^{-1}$ . Cycloisomerization of semicarbazones, **7**, in which  $\text{R}^3$  equals alkyl or cyclopropyl, into ring-tautomeric triazolidinones, **10b-10n**, is accompanied by the disappearance of the amide II band, which is absent from the spectra of tertiary amides and also from those of cyclic lactams (**10**). The presence or absence of the amide II band in the **7** and **10** compounds may be used for structural assignments.

#### EXPERIMENTAL

Representative methods for the preparation of benzaldehyde and acetone 2-phenylsemicarbazones, **7**, 2-phenylsemicarbazides, **8**, and 1-phenyl-1,2,4-triazolidin-5-ones, **10**, are described.

##### 3,3-Dimethyl-1-phenyl-1,2,4-triazolidin-5-one (**10a**).

Potassium cyanate, 90 g. (1.11 moles), was added portionwise within 30 minutes to a stirred solution of 148 g. (1.0 mole) of acetone phenylhydrazone in 600 ml. of 75% aqueous acetic acid. The resulting mixture was heated at 60° for one hour, cooled to 10° and filtered. The filtrate was diluted 1200 ml. with water and made alkaline with ammonium hydroxide. The solid that precipitated was filtered and dried to give 164 g. (85.9%) of **10a**; a colorless, crystalline solid; mass spectrum: (70 eV),  $m/e$  191 ( $\text{M}^+$ ), 176, 149, 133, 108, 107, 106, 92, 84, 77, 65, 56, 51, 43, 42.

##### Acetone 2-Phenylsemicarbazone (**7i**).

A solution containing 159 g. (0.832 mole) of **10a** in 725 ml. of water and 75 ml. of concentrated hydrochloric acid was concentrated to dryness at 30° under reduced pressure. A sample treated with ammonium hydroxide gave starting material ( $\text{R}_F$ -value, m.p.). The residual solid was suspended in 200 ml. of concentrated hydrochloric acid and warmed (steam bath) until a clear solution resulted. After cooling to 10-15°, the solution was made alkaline with ammonium hydroxide and extracted with chloroform. The combined extracts were dried (magnesium sulfate) and concentrated to give a mixture of **7i** and **10a**. Recrystallization from methanol gave 52 g. (32.7%) of pure **7i**; mass spectrum: (70 eV),  $m/e$  191 ( $\text{M}^+$ ), 148, 133, 106, 92, 77, 65, 56, 51, 44, 43, 42, 41, 39, 28.

##### Benzaldehyde 2-Phenylsemicarbazone (**7m**).

To a mixture containing 164 g. (0.859 mole) of **10a** in 1 liter of water and 86 ml. of concentrated hydrochloric acid was added, at 35°, 92 g. (0.859 mole) of benzaldehyde. The mixture was

stirred and heated at 80° for one hour while a light yellow solid began to precipitate. The reaction mixture was cooled and filtered. The filter cake was washed well with water and dried to give 194 g. (94.6%) of **7m**.

##### 2-Phenylsemicarbazide (**8a**).

To a solution of 194 g. (0.812 mole) of **7m** in 2 liters of ethanol was added 161 g. (0.812 mole) of 2,4-dinitrophenylhydrazine and 5 ml. of concentrated sulfuric acid. The mixture was stirred and heated at 60-70° for 4 hours, cooled to 18° and filtered. The filtrate was concentrated to dryness to leave 150 g. of a brown syrup that crystallized from methanol to give 86 g. (70%) of **8a** as light yellow solid.

##### Benzaldehyde 2-(3,4-Dichlorophenyl)-4-methylsemicarbazone (**7e**).

To a solution containing 97 g. (0.366 mole) of benzaldehyde 3,4-dichlorophenylhydrazone and 45 g. (0.366 mole) of collidine in 1000 ml. of benzene was added, with stirring and external cooling at 25-30°, 49 g. (0.495 mole) of phosgene in 300 ml. of benzene. The mixture was stirred at room temperature for 45 minutes and filtered. The filtrate was used in the next reaction step without isolation of the carbanilic acid chloride, **6** ( $\text{R}^1 = \text{H}$ ,  $\text{R}^2 = \text{C}_6\text{H}_5$ ,  $\text{X} = 3,4\text{-Cl}_2$ ).

Anhydrous methylamine was introduced into 315 ml. of the filtrate containing 20.8 g. (0.064 mole) of the above carbanilic acid chloride. The mixture was filtered, washed with dilute hydrochloric acid, dried and concentrated to dryness. The residual oil was recrystallized from ether to give 12.0 g. (60%) of **7e** as an off-white solid.

##### 2-(3,4-Dichlorophenyl)-4-methylsemicarbazide (**8f**).

To a mixture of 11.0 g. (0.0342 mole) of **7e** in 200 ml. of ethanol was added with stirring at 60°, 7.0 g. (0.035 mole) of 2,4-dinitrophenylhydrazine and five drops of concentrated sulfuric acid. The clear solution was stirred at 60-65° for 18 hours, chilled (20°), filtered and concentrated. The residual solid crystallized from methanol to give 4.0 g. (50%) of **8f**, a light-orange solid, m.p. 161-163°; purification by silica chromatography gave 2.0 g. (25%) of pure **8f**, m.p. 174-176°.

In a second experiment, **8f** was isolated in 98.7% yield, m.p. 168-171°.

##### 2-(3,4-Dichlorophenyl)-4-methyl-1,2,4-triazaspiro[4.4]nonan-3-one (**10m**).

A solution containing 5.0 g. (0.0214 mole) of **8f**, 4.2 g. (0.05 mole) of cyclopentanone, and three drops of concentrated hydrochloric acid in 50 ml. of ethanol was refluxed for 24 hours and chilled to 5°. A yellow solid was filtered and recrystallized from methanol to give 5.5 g. (85.9%) of **10m** as a light-yellow crystalline solid.

##### Benzaldehyde 4-Isobutyl-2-(3,4-dichlorophenyl)semicarbazone (**7h**).

To a stirred solution containing 47 g. (0.144 mole) of *N*-(benzylideneamino)-3',4'-dichlorocarbanilic acid chloride in 400 ml. of benzene was added dropwise 21 g. (0.288 mole) of isobutylamine, causing the temperature to rise to 50°. After 1 hour, water was added. The benzene layer was washed with dilute hydrochloric acid, dried (magnesium sulfate), and concentrated to dryness to give 50.2 g. (95.8%) of **7h**.

##### 2-(3,4-Dichlorophenyl)-4-isobutylsemicarbazide (**8i**).

A mixture consisting of 48.4 g. (0.133 mole) of **7h** and 26.3 g. (0.133 mole) of 2,4-dinitrophenylhydrazine in 350 ml. of ethanol

containing 1 ml. of concentrated sulfuric acid was refluxed (70-80°) for 1 hour, cooled (10°) and filtered. The filtrate was cooled to -45°, and the resultant solid was filtered to give 30 g. (81.7%) of **8i**, an off-white solid.

Acetone 2-(3,4-Dichlorophenyl)-4-isobutylsemicarbazone (**7n**).

A suspension of 10 g. of anhydrous magnesium sulfate in 200 ml. of acetone containing 23 g. (0.0833 mole) of **8i** was refluxed for 2 hours and filtered. Evaporation of the filtrate left a solid that was recrystallized from hexane to give 24 g. (91.3%) of **7n**, as colorless crystals.

1-(3,4-Dichlorophenyl)-3,3-dimethyl-4-isobutyl-1,2,4-triazolidin-5-one (**10i**).

A solution containing 20 g. (0.0633 mole) of **7n** in 200 ml. of acetone containing 3 drops of concentrated hydrochloric acid was refluxed for 3 hours and concentrated to dryness. The residual solid was recrystallized from methanol to give 8.0 g. (70.2%) of **10i**, a light-tan solid, m.p. 90-92°, resolidifies and melts at 110-112°.

Benzaldehyde 4-Methyl-2-phenylsemicarbazone (**7a**) Method A.

To a solution of benzaldehyde phenylhydrazone, 330 g. (1.68 moles), and collidine, 204 g. (1.68 moles) in 2.5 l. of benzene was added rapidly a solution of 225 g. (2.28 moles) of phosgene in 1 l. of benzene. The mixture was stirred for 2 hours at room temperature and filtered. Evaporation of the solvent gave 434 g. (99.7%) of a syrup that was used without purification. A solution containing 384 g. (1.49 moles) of the carbanilic acid chloride syrup in 800 ml. of benzene was saturated with methylamine. The reaction mixture was filtered and the filtrate was concentrated to dryness to give 345.4 g. (91.6%) of amber syrup that crystallized on standing. Recrystallization from ether gave a crystalline product, m.p. 140-142°, identical with the product obtained by Method B (below).

Method B.

A glass cylinder was charged with 15.7 g. (0.08 mole) of benzaldehyde phenylhydrazone, 15 ml. of methyl isocyanate, 75 ml. of tetrahydrofuran and 3 drops of triethylamine. The sealed cylinder was placed on a steam bath and heated at 100° for 5 days. The reaction mixture was evaporated to dryness and purified by silica chromatography to give 15.4 g. (51%) of **7a** as colorless solid, m.p. 138-140°.

A second fraction that emerged from the column, 2.5 g., m.p. 172-175°, was identified as methyl isocyanate trimer.

*Anal.* Calcd. for C<sub>6</sub>H<sub>9</sub>N<sub>3</sub>O<sub>3</sub>: C, 42.2; H, 5.3; N, 24.6. Found: C, 42.3; H, 5.0; N, 24.6.

4-Methyl-2-phenylsemicarbazide (**8b**).

A mixture containing 345 g. (1.36 moles) of **7a** and 269 g. (1.36 moles) of 2,4-dinitrophenylhydrazine in 2.5 l. of ethanol containing 5 ml. of concentrated sulfuric acid was stirred and heated at 60-70° for 5 days. The mixture was cooled (15°) and filtered. The filtrate was concentrated to dryness leaving 259 g. of a red, viscous oil. Crystallization from ether-methanol gave 118 g. (52.7%) of **8b** as a light-yellow crystalline solid; mass spectrum: (70 eV) m/e 165 (M<sup>+</sup>), 150, 149, 135, 136, 119, 108, 93, 92, 91, 79, 78, 77, 65, 58, 39, 29, 28.

1-Phenyl-3,3,4-trimethyl-1,2,4-triazolidin-5-one (**10b**).

A suspension of 10 g. of anhydrous magnesium sulfate in 150 ml. of acetone containing 8.3 g. (0.05 mole) of **8b** was stirred and refluxed for 3 hours and filtered. Evaporation of the filtrate to dryness gave 10.2 g. (100%) of **10b**.

REFERENCES AND NOTES

- (1) M. Anteunis, F. Borremans, W. Tadros, A. H. A. Zaher, and S. S. Gliobrial, *J. Chem. Soc., Perkin Trans. I*, 616 (1972).
- (2) A. Arnold, *Ber.*, **30**, 1015 (1897).
- (3) R. C. Goodwin and J. R. Bailey, *J. Am. Chem. Soc.*, **46**, 2827 (1924).
- (4) H. Schildknecht and G. Hatzmann, *Ann. Chem.*, **724**, 226 (1969).
- (5) A. Fischer, D. A. R. Happer, and J. Vaughan, *J. Chem. Soc.*, 7444 (1965).
- (6) K. Pilgram, *German Patent* 2,342,688; *Chem. Abstr.*, **80**, 145845r (1974).
- (7) To our knowledge the tautomerization of **6** to **5** has not yet been described.
- (8) The nmr spectrum of the unsubstituted acetone semicarbazone (**9**) shows two singlets for the protons of the two methyl groups at 1.85 and 2.0 ppm (in chloroform).
- (9) G. J. Karabatsos, F. M. Vane, R. A. Taller, and N. Hsi, *J. Am. Chem. Soc.*, **86**, 3351 (1964).
- (10) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Chapter 12 (4), 216, John Wiley, New York, 1957.