

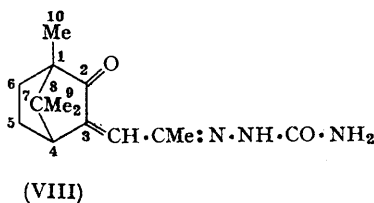
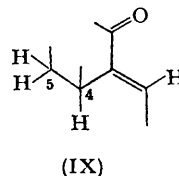
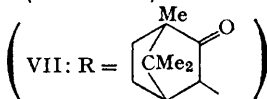
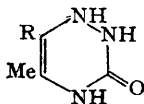
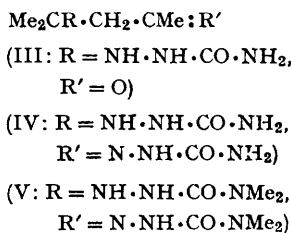
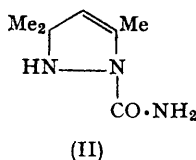
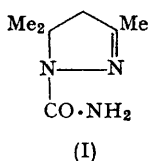
**1167.** *The Constitutions of Scholtz's Base and an "Analogue" from Camphorylideneacetone, as Indicated by Proton Magnetic Resonance.*

By J. A. ELVIDGE and V. A. MOSS.

Proton magnetic resonance studies indicate the pyrazoline structure (I) for Scholtz's base (a thermal isomer of mesityl oxide semicarbazone) and show that an "analogue" from 3-camphorylideneacetone is merely the semicarbazone (VIII): neither is a triazine, as has been suggested.

Allylic couplings and other data are given and discussed for the semicarbazone (VIII), 3-camphorylideneacetone, 3-camphorylideneacetic acid, and the semicarbazone and amidinohydrazone of mesityl oxide. Heating the last-named derivative gives 3,5,5-trimethyl- $\Delta^2$ -pyrazoline, the fine structure of which is confirmed by proton magnetic resonance.

ABOVE its melting point, mesityl oxide semicarbazone isomerises to a base (as Scholtz first observed),<sup>1</sup> for which the pyrazoline structures (I) and (II) were suggested.<sup>2</sup> These possibilities were supported but not differentiated by formation of the base from 4-methyl-4-semicarbazidopentan-2-one (III) in water, and from a boiling aqueous solution of the



derived semicarbazone<sup>3</sup> (IV). The resistance of Scholtz's base to alkaline hydrolysis<sup>3</sup> led Rupe and his co-workers<sup>4</sup> to suggest a 1,2,4-triazine formulation (VI), with (VII) for an analogous product from 3-camphorylideneacetone and semicarbazide. Positionally isomeric structures would have been more logical, or 7-membered ring structures derived by 1,4-addition.

<sup>1</sup> M. Scholtz, *Ber.*, 1896, **29**, 610.

<sup>2</sup> C. Harries and F. Kaiser, *Ber.*, 1899, **32**, 1338; cf. H. Rupe and P. Schlochoff, *ibid.*, 1903, **36**, 4377.

<sup>3</sup> H. Rupe and S. Kessler, *Ber.*, 1909, **42**, 4503.

<sup>4</sup> H. Rupe, M. Werder, and K. Takagi, *Helv. Chim. Acta*. 1918, **1**, 309.

However, Locquin and Heilmann<sup>5</sup> later prepared the base from 3,5,5-trimethyl- $\Delta^2$ -pyrazoline and cyanic acid, and this is now confirmed by us: taking the structure of the pyrazoline as known, they regarded (I) as proved. Neither this information nor the similarity of the ultraviolet absorption of Scholtz's base to that of the parent pyrazoline<sup>6</sup> were reported by Erickson, Wiley, and Wystrach in a review of triazines<sup>7</sup> which included (VI) and (VII).

We find that the proton magnetic resonance (p.m.r.) spectrum of Scholtz's base shows no olefinic-proton signal and no signal from an isopropyl group, so that structures (II) and (VI) are eliminated. There is a singlet from a geminal methyl group, and signals from a methylene and from an olefinic methyl group which appear as a fine quartet and triplet, respectively, because of weak coupling (see data in Experimental section). These findings, with the u.v. absorption, conclusively indicate structure (I). P.m.r. observations confirm also the structure of 3,5,5-trimethyl- $\Delta^2$ -pyrazoline, and of mesityl oxide semicarbazone. The spectrum of the latter in the methyl region (see Experimental section) closely resembles that of the ketone itself,<sup>8</sup> the lower-field signal from a geminal methyl group being obscured by the line from the lone methyl group. The unobserved higher-field signal from one of the geminal methyls is split by 1.3 c./sec. This is presumably the magnitude of the cisoid allylic coupling. Furthermore, the product from 3-camphorylideneacetone and semicarbazide is shown by the p.m.r. spectrum to be the semicarbazone (VIII) and not a triazine (Experimental section). Although reported to be stable to alkali,<sup>4</sup> this product is readily hydrolysed by acid. The p.m.r. spectra of the intermediates, 3-camphorylideneacetic acid and 3-camphorylideneacetone, like that of the semicarbazone (VIII), show a fine doublet signal from the olefinic proton. In each case this long-range coupling must be to the 4-proton in the allylic position,<sup>9</sup> the small magnitudes resulting from the unfavourable transoid coplanar configurations which scale models indicate (see IX). The models also show that the 4-proton, in each case, makes dihedral angles of about 85° and 45° with the protons at C-5, and in agreement, the spectra show that the 4-proton (a slightly broadened doublet), is appreciably coupled ( $J$  4 c./sec.) to only one of the 5-protons.<sup>10</sup>

The resistance of the amide (I) to degradation remains puzzling. We confirmed that boiling alkali acts only very slowly. Cold aqueous nitrous acid, and 50% nitric acid at 100°, had no effect. Nitrosyl chloride in acetic anhydride at 30° attacked Scholtz's base slowly but gave no identifiable product; nor did fuming nitric acid. Rupe and Kessler,<sup>3</sup> however, obtained carbamoyl azide and mesityl oxide using nitrite.

In related experiments we examined the cyclisation of the more strongly basic amidino-hydrazone of mesityl oxide. This distilled unchanged under reduced pressure, but at atmospheric pressure afforded 3,5,5-trimethyl- $\Delta^2$ -pyrazoline by elimination of cyanamide or its equivalent.

The p.m.r. spectrum of mesityl oxide amidinohydrazone was well resolved, both doublet signals from the geminal methyl groups being unobserved—unlike the oxide and semicarbazone. The higher-field signal was split by 1.1 c./sec. and the lower-field signal by 1.4 c./sec. If the higher-field doublet is assigned to that geminal methyl group which is *trans* to the rest of the chain—which is reasonable because of the unsaturation—then it follows that the *cis* allylic coupling is smaller than the *trans* coupling in this molecule. This is not in accord with general findings,<sup>9</sup> although exceptions have previously been noted, e.g., methacraldehyde and methacryloyl chloride.<sup>11</sup>

Attempts to obtain mesityl oxide 4,4-dimethylsemicarbazone (for other cyclisation attempts) by direct interaction of the components gave a liquid product which appeared

<sup>5</sup> R. Locquin and R. Heilmann, *Bull. Soc. chim. France*, 1929, **45**, 553.

<sup>6</sup> K. Dimroth and O. Lüderitz, *Chem. Ber.*, 1948, **81**, 242.

<sup>7</sup> J. G. Erickson, P. F. Wiley, and V. P. Wystrach, "The 1,2,3- and 1,2,4-Triazines, Tetrazines, and Pentazines," ed. A. Weissberger, Interscience New York, 1956, pp. 64—65.

<sup>8</sup> L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry." Pergamon, London, 1959, p. 84.

<sup>9</sup> S. Sternhell, *Rev. Pure Appl. Chem. (Australia)*, 1964, **14**, 15.

<sup>10</sup> H. Conroy *Adv. Org. Chem.*, 1960, **2**, 265.

<sup>11</sup> L. M. Jackman and R. H. Wiley, *J.*, 1960, 2881.

from its p.m.r. spectrum to contain a little of the required product, together with the compound (V) and acetone 4,4-dimethylsemicarbazone. Distillation of the mixture afforded the acetone derivative only and there were no indications of formation of an analogue of (I). The compound (V) was separately obtained from mesityl oxide and 1 equivalent of 4,4-dimethylsemicarbazide in aqueous solution. Its p.m.r. spectrum indicated that it was a mixture of *syn*- and *anti*-forms in approximately equal proportions, the signals from the methylene group and the olefinic-methyl being doubled, although of the correct total relative intensities.

#### EXPERIMENTAL

The integrated intensities of all the p.m.r. bands were measured, and were consistent with the assignments given below.

Mesityl oxide semicarbazone had m. p. 163° (plates from ethanol) [Found: C, 54.1; H, 8.5; N, 27.4%; *M* (ebullioscopic in MeOH), 159. Calc. for C<sub>7</sub>H<sub>13</sub>N<sub>3</sub>O: C, 54.2; H, 8.4; N, 27.1%; *M*, 155],  $\lambda_{\max}$  (in EtOH) 267 m $\mu$  ( $\epsilon$  15,500);  $\nu_{\max}$  (in CHCl<sub>3</sub>) 3497, 3378, 3226bd (NH<sub>2</sub>, NH), 2940 (CH), 1685s (CO), 1650sh, 1553s, and 1421 cm.<sup>-1</sup>;  $\nu_{\max}$  (Nujol) 3390, 3250—3050 (NH<sub>2</sub>, NH), 1684s (CO), 1669, 1640, 1574s, 1351, 1253s, 1194, 1098, 974, 900, 837, 815w, 758, 720bd, and 676 cm.<sup>-1</sup>;  $\tau$  (in CDCl<sub>3</sub>) 8.15, 8.03 (*gem*-Me<sub>2</sub>, doublets, higher-field doublet, *J* 1.3 c./sec.), 8.04 (:CMe, singlet), 4.33 (:CH, multiplet), 4.28 (NH<sub>2</sub>, broad, 0.5 p.p.m.), and 1.43 p.p.m. (NH, broadened, 0.17 p.p.m.).

*Cyclisation*.—Sublimation of the semicarbazone under high vacuum, or distillation at 170°/50 mm., gave the isomeric 1-carbamoyl-3,5,5-trimethyl- $\Delta^2$ -pyrazoline (I) (*ca.* 30%) which crystallised from light petroleum (b. p. 60—80°) as prisms, m. p. 129° [identical (m. p., u.v., and i.r.) with the product<sup>5</sup> from 3,5,5-trimethyl- $\Delta^2$ -pyrazoline and cyanate] [Found: C, 54.6; H, 8.7; N, 27.15%; *M* (ebullioscopic in benzene), 157],  $\lambda_{\max}$  (in EtOH) 240 m $\mu$  ( $\epsilon$  11,400);  $\nu_{\max}$  (in CCl<sub>4</sub>) 3555, 3500 (NH<sub>2</sub>), 3430 (NH, bonded intramolecularly to -N-?), 3350—3100 (NH, bonded intermolecularly), and 3000—2800 cm.<sup>-1</sup> (CH);  $\nu_{\max}$  (Nujol) 3410, 3210, 3130 (NH<sub>2</sub>, NH), 1606s (CO), 1590s, 1330, 1250, 1173, 1124w, 965, 855w, 755, 736w, and 689bd cm.<sup>-1</sup>,  $\tau$  (in CDCl<sub>3</sub>) 8.47 (5-Me<sub>2</sub>), 8.06 (3-Me; triplet), 7.35 (4-H<sub>2</sub>; quartet, *J*<sub>Me, H<sub>2</sub></sub> 1.05 c./sec.), and 4.80 p.p.m. (NH<sub>2</sub>, broad, 0.6 p.p.m.).

*Attempted Degradation*.—(a) When Scholtz's base (I) (150 mg.) was boiled with 15% aqueous potassium hydroxide (3 c.c.) for 30 hr., ammonia was slowly evolved. Extraction of the solution with ether and evaporation gave an oil (20 mg.) identified (i.r. spectrum) as mesityl oxide. (b) The base (I) (150 mg.) was treated with 2*N*-hydrochloric acid (0.6 ml.) and sodium nitrite (76 mg.) at 0°. After 30 min. at room temperature, the solution was warmed to 60° and extracted with chloroform to give the starting material (mixed m. p. and i.r. spectrum). (c) Compound (I) (400 mg.) was similarly recovered (70%) after being heated with 1:1 aqueous nitric acid (3 ml.) at 100° for 30 min. (d) Compound (I) was recovered by evaporation after treatment in acetic anhydride with nitrosyl chloride at -20° for 3 hr. Similar treatment of (I) at 30° for 2 hr. led to a brown gum, as also did treatment with fuming nitric acid.

3,5,5-Trimethyl- $\Delta^2$ -pyrazoline<sup>12</sup> had b. p. 62—64°/23 mm.,  $n_D^{23}$  1.4538,  $\lambda_{\max}$  (in EtOH) 238 m $\mu$  ( $\epsilon$  12,000);  $\nu_{\max}$  (film) 3230 (NH), 2900s (CH), 1624w (C-N), 1461w, 1435, 1375s, 1362, 1321s, 1262w, 1228, 1210w, 1171, 1112w, 1049bd, 935s, 908, 862w, 830s, and 729bd cm.<sup>-1</sup>;  $\tau$  (in CCl<sub>4</sub>) 8.81 (5-Me<sub>2</sub>), 8.15 (3-Me, triplet, *J*<sub>Me, H<sub>2</sub></sub> 1.1 c./sec.), 7.70 (4-H<sub>2</sub>, quartet), and 5.15 p.p.m. (NH).

3-Camphorylideneacetone.—(+)-Camphor was converted<sup>13,4</sup> into 3-carboxymethylencamphor,  $\nu_{\max}$  (Nujol) 2700—2450 (OH), 1733s (CO), and 1687s cm.<sup>-1</sup> (CO of carboxyl);  $\tau$  (in CDCl<sub>3</sub>) 9.18, 8.96 (9-H<sub>3</sub>, 8-H<sub>3</sub>), 8.96 (10-H<sub>3</sub>), 8.80—7.43 (5-H<sub>2</sub>, 6-H<sub>2</sub>, complex), 6.42 (4-H, *ca.* doublet, *J*<sub>4,5</sub> 4 c./sec.), 3.62 (:CH, doublet, coupled to 4-H, *J* 0.95 c./sec.), and -0.83 p.p.m. (CO<sub>2</sub>H), and thence into 3-camphorylideneacetone,<sup>4</sup>  $\nu_{\max}$  (film) 2885 (CH), 1733s (CO), 1685s (CO), and 1637 cm.<sup>-1</sup> (C-C);  $\tau$  (in CCl<sub>4</sub>) 9.23, 9.03 (9-H<sub>3</sub>, 8-H<sub>3</sub>), 9.00 (10-H<sub>3</sub>), 8.82—7.78 (5-H<sub>2</sub>, 6-H<sub>2</sub>, complex), 7.73 (Ac), 6.51 (4-H, *ca.* doublet, *J*<sub>4,5</sub> 4 c./sec.), and 3.46 p.p.m. (-CH, doublet, coupled to 4-H, *J* 0.6 c./sec.).

3-Camphorylideneacetone semicarbazone<sup>4</sup> (83%) crystallised from aqueous ethanol as prisms, m. p. 231° (Found: C, 63.9; H, 8.0; N, 16.0. C<sub>14</sub>H<sub>21</sub>N<sub>3</sub>O<sub>2</sub> requires C, 63.85; H, 8.0; N, 16.0%),  $\lambda_{\max}$  310 and 216 m $\mu$  ( $\epsilon$  22,750 and 7900);  $\nu_{\max}$  (Nujol) 3410, 3260—3050 (NH<sub>2</sub>, NH), 1718s (C), 1690s (Amide I), 1632 (C-C), 1340, 1320, 1285, 1251, 1208w, 1192, 1152s, 1123, 1107s, 1064s,

<sup>12</sup> T. Curtius and F. Wirsing, *J. prakt. Chem.*, 1894, **50**, 531; A. P. Meshcheryakov, L. V. Petrova, and Yu. P. Egerov, *Zhur. obshchei Khim.*, 1958, **28**, 2588.

<sup>13</sup> A. W. Bishop, L. Claisen, and W. Sinclair, *Annalen*, 1894, **281**, 389.

1037w, 1013, 954, 912w, 860w, 823, 798, and 760s  $\text{cm}^{-1}$ ;  $\tau$  (in  $\text{CDCl}_3$ ) 9.19, 9.01 (9-H<sub>3</sub>, 8-H<sub>3</sub>), 8.99 (10-H<sub>3</sub>), 8.76—8.09 (5-H<sub>2</sub>, 6-H<sub>2</sub>, complex), 7.93 (:CMe), 6.90 (4-H,  $J_4$ , 5.3.6 c./sec.), 4.27 (NH<sub>2</sub>, broad, 0.5 p.p.m.), 3.30 (=CH, doublet, coupled to 4-H,  $J$  0.9 c./sec.), and 1.08 p.p.m. (NH, broadened, 0.1 p.p.m.).

The semicarbazone (17 mg.) was warmed on a steam-bath with concentrated hydrochloric acid (2 ml.) for 30 min. Isolation with ether (3  $\times$  1 ml.) gave an oil, identified (i.r. spectrum) as 3-camphorylideneacetone (8 mg., 35%).

*Mesityl Oxide Amidinohydrazone*.—To 50% acetic acid (12 ml.), aminoguanidine hydrogen carbonate (13.6 g.) was added, followed by mesityl oxide (9.8 g.). The mixture was clarified by addition of ethanol, and sodium acetate (10 g.) was dissolved in the solution by warming. After 2 days, the aminohydrazone acetate (19.3 g.), m. p. 214°, was collected and dissolved in *N*-sodium hydroxide. Evaporation of an ether extract, and crystallisation of the residue from light petroleum (b. p. 40—60°) gave *mesityl oxide amidinohydrazone*, m. p. 72° (Found: C, 54.9; H, 8.95; N, 36.5.  $\text{C}_7\text{H}_{14}\text{N}_4$  requires C, 54.5; H, 9.15; N, 36.3%),  $\lambda_{\text{max}}$  235  $\text{m}\mu$  ( $\epsilon$  10,000);  $\tau$  (in  $\text{CDCl}_3$ ) 8.26, 8.17 (*gem*-Me<sub>2</sub>, doublets coupled to :CH,  $J$  1.1, 1.4 c./sec., respectively), 7.91 (:CMe, singlet), 5.06 (NH<sub>2</sub> and 2NH), and 3.81 p.p.m. (:CH, multiplet). The derived *picrate* crystallised from ethanol as needles, m. p. 193° (Found: C, 41.2; H, 4.6; N, 25.2.  $\text{C}_{13}\text{H}_{17}\text{N}_7\text{O}_7$  requires C, 40.7; H, 4.5; N, 25.6%).

The amidinohydrazone distilled unchanged at 20 mm. (m. p. and mixed m. p. 72°) but at atmospheric pressure gave an oil (55%), b. p. 158—161°, identified as 3,5,5-trimethyl- $\Delta^2$ -pyrazoline from the i.r. and u.v. spectra.

*Reactions with 4,4-Dimethylsemicarbazide*.—(a) 4,4-Dimethylsemicarbazide<sup>14</sup> (1 g.) was heated with mesityl oxide (1.2 g.) for 3—4 hr. on a steam-bath. Distillation afforded a viscous oil, b. p. 105°/0.1 mm.,  $n_D^{25}$  1.5145, which solidified, m. p. ca. 72°, and which was identified as acetone 4,4-dimethylsemicarbazone,  $\tau$  (in  $\text{CDCl}_3$ ) 8.12, 7.98 (*gem*-Me<sub>2</sub>, singlets), 6.99 (NMe<sub>2</sub>), and 3.34 p.p.m. (NH, broad, 0.4 p.p.m.) (identical with the spectrum of an authentic sample). (b) Mesityl oxide (1 g.) was added to 4,4-dimethylsemicarbazide (1.04 g.) in water and the mixture clarified with ethanol. After 20 hr. at 0°, the product was isolated by extraction with chloroform and evaporation. Trituration with ether gave 4-(4,4-dimethylsemicarbazido)-4-methylpentan-2-one 4,4-dimethylsemicarbazone (V), m. p. 159° (decomp.) (prisms from chloroform-ether) (Found: C, 50.2; H, 9.1.  $\text{C}_{12}\text{H}_{26}\text{N}_6\text{O}_2$  requires C, 50.3; H, 9.15%),  $\lambda_{\text{max}}$  233  $\text{m}\mu$ ;  $\tau$  (in  $\text{CDCl}_3$ ) 8.87, 8.80 (*gem*-Me<sub>2</sub>, singlets), 8.05, 7.92 (:CMe, singlets, *anti* and *syn*), 7.61, 7.59 (CH<sub>2</sub>, singlets, *anti* and *syn*), 7.09, 7.03, and 7.00 p.p.m. (2NMe<sub>2</sub>).

*Addendum*.—A referee suggested that the infrared spectrum of Scholtz's base (I) in carbon tetrachloride might indicate a tautomeric mixture of structures (I) and (II). There is no evidence for this, however, from the p.m.r. spectrum, determined for a solution in deuteriochloroform. If a second form showed in the infrared spectrum, then it would certainly show in the p.m.r. spectrum, because the sensitivity of the methods is similar. There is no sign at all of an olefinic proton signal or of any doubling of the methyl signals. This is supported by the integral trace. The compound therefore does not show tautomerism, rapid or slow, with long residence times for the two forms. Moreover, rapid tautomerism with short residence times is precluded by the quartet and triplet splitting of the methylene and lone methyl signals, respectively, in the p.m.r. spectrum. The latter is not an averaged one, as indeed the chemical shift of the methylene protons also shows. The multiplets were recorded with a scale of 5 mm. per c./sec.

It is appropriate to state, also, that the p.m.r. spectrum of the parent pyrazoline, 3,5,5-trimethyl- $\Delta^2$ -pyrazoline, similarly shows no sign of being a mixture of tautomers in carbon tetrachloride solution.

We acknowledge the award of a State Scholarship (to V. A. M.) and thank Professor D. H. R. Barton, Sc.D., F.R.S., for access to a Varian Associates A-60 spectrometer on permanent loan to him from the Wellcome Trustees.

CHEMISTRY DEPARTMENT, IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,  
SOUTH KENSINGTON, LONDON, S.W.7.

[Received, September 7th, 1964.]

<sup>14</sup> C. Vogelsang, *Rec. Trav. chim.*, 1943, **62**, 5.