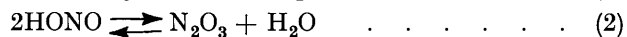
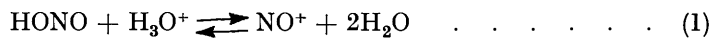


## NOTES.

**482.** *Nitrous Acid Equilibria in Perchloric Acid.*

By T. A. TURNEY and G. A. WRIGHT.

THE following equilibria are of interest in considering the reactivity of nitrous acid in acidic media:



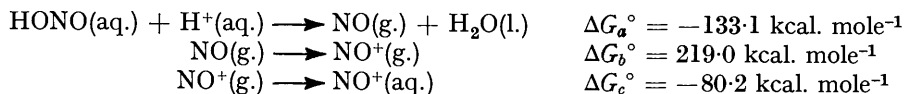
Recently,<sup>1</sup> the proportion of nitrosonium ion present in solutions of sodium nitrite in concentrated perchloric acid was measured spectrophotometrically, but no equilibrium constant was found. We have now estimated the equilibrium constants of the two reactions by considering thermodynamic cycles, and determined the equilibrium constant for reaction (1) spectrophotometrically.

*Thermodynamic Calculations.*—Two cycles of hypothetical reactions were used involving

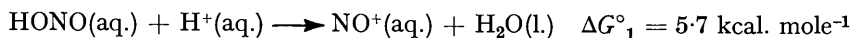
<sup>1</sup> Singer and Vamplew, *J.*, 1956, 3971.

the gas phase in which the ionisation potential of nitric oxide and the free energy of formation of dinitrogen trioxide are known.

(1) *Nitrosonium ion.*

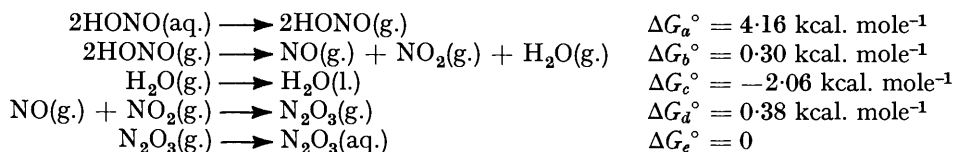


Hence,

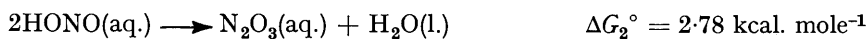


Thus  $K_1 = 7 \times 10^{-5}$  (25°).  $\Delta G_a^\circ$  was obtained from the standard free energies of formation of the substances involved.<sup>2</sup>  $\Delta G_b^\circ$  was calculated from the ionisation energy of nitric oxide.<sup>3</sup>  $\Delta G_c^\circ$  was interpolated from the data for the alkali-metal ions,<sup>4</sup> by assuming that the nitrosonium ion is approximately a sphere of radius 1.11 Å<sup>3</sup> and correcting to a standard pressure of 1 atm. The uncertainty in this interpolation is the limitation on the accuracy of the calculation.

(2) *Dinitrogen trioxide.*



Hence



Thus  $K_2 = 9 \times 10^{-3}$  (25°).  $\Delta G_a^\circ$  and  $\Delta G_b^\circ$  were obtained from Wayne and Yost's calculations.<sup>5</sup>  $\Delta G_c^\circ$  was found from the standard free energies of formation.<sup>2</sup>  $\Delta G_d^\circ$  has been measured experimentally.<sup>6</sup>  $\Delta G_e^\circ$  cannot be found exactly but was estimated approximately by plotting the hydration energies of similar molecules against their parachors (a convenient measure of molecular volume) and extrapolating to find the value for dinitrogen trioxide.

*Experimental.*—Solutions of nitrous acid were made by dissolving "AnalaR" sodium nitrite in aqueous "AnalaR" perchloric acid. Absorption was measured on a Beckman model D.U. spectrophotometer with a hydrogen lamp and photomultiplier attachment. The total concentration of all the nitrous acid species present was determined colorimetrically<sup>7</sup> through the diazotisation of sulphanilic acid and coupling with  $\alpha$ -naphthylamine. Dilute solutions of nitrous acid in 50% perchloric acid solution decompose steadily. The extent of this decomposition was measured by recording the change of optical density with time. Also, the additional decomposition due to disturbance of the solution during transfer by pipette was estimated similarly. The sum of these errors in the 3 min. required to complete the absorbance readings and commence the analysis was not greater than 4%. The procedure used was rapidly to measure the optical densities of the solution at four selected wavelengths, then immediately transfer 1 ml. of the solution to a flask containing 1 ml. of the sulphanilic acid reagent. This strongly acidic mixture diazotises rapidly, so minimising errors due to decomposition.

<sup>2</sup> Latimer, "Oxidation Potentials," Prentice-Hall, New York, 1952.

<sup>3</sup> Addison and Lewis, *Quart. Rev.*, 1955, **9**, 115.

<sup>4</sup> Robinson and Stokes, "Electrolyte Solutions," Butterworths, London, 1955.

<sup>5</sup> Wayne and Yost, *J. Chem. Phys.*, 1951, **19**, 41.

<sup>6</sup> Beattie and Bell, *J.*, 1957, 1686.

<sup>7</sup> Rider and Mellon, *Ind. Eng. Chem. Anal.*, 1946, **18**, 96.

*Results and Discussion.*—In 10% perchloric acid the known spectrum of the nitrous acid molecule was observed.<sup>8, 9, 10</sup> Four main absorption peaks occurred at 347 m $\mu$  ( $\epsilon_1$  39), 358 m $\mu$  ( $\epsilon_1$  54), 372 m $\mu$  ( $\epsilon_1$  55), and 386 m $\mu$  ( $\epsilon_1$  33). The spectrum persisted unchanged in up to 40% perchloric acid. Above 55% perchloric acid a single intense, broad band with a maximum at 260 m $\mu$  ( $\epsilon$  ca. 4000) appeared and was taken to be the spectrum of the nitrosonium ion. This spectrum remained constant in shape but the extinction coefficients varied considerably as the perchloric acid concentration or the nitrous acid concentration changed. This may be due to some hydration effect of the nitrosonium ion. In the region 45–55% perchloric acid the spectra corresponded to a mixture of molecular nitrous acid and nitrosonium ions. There was no sign of dinitrogen trioxide in these dilute solutions of nitrous acid ( $10^{-3}$  mole l.<sup>-1</sup>); this is as expected from the calculated equilibrium constants. These results generally agree with those of previous workers,<sup>1</sup> but there are some differences of detail.

To determine  $K_1$  from the absorption spectra the ratio  $R = [\text{NO}^+]/[\text{HNO}_2]$  in the region of the mixed spectra must be determined, so the four main absorption peaks of molecular nitrous acid were measured, these being reliably known. The spectrum of the nitrosonium ion is unsuitable because it does not obey Beer's law. However, the shape of the absorption curve of nitrosonium ion is fixed and the extinction coefficients in any solution are given by  $x\epsilon_2$ , where  $x$  is a factor for that solution and  $\epsilon_2$  is the value for 60% perchloric acid, e.g., at 347 m $\mu$  ( $\epsilon_2$  131), 358 m $\mu$  ( $\epsilon_2$  53), 372 m $\mu$  ( $\epsilon_2$  18), and 386 m $\mu$  ( $\epsilon_2$  6). At any wavelength,  $D = \epsilon_1[\text{HNO}_2] + x\epsilon_2[\text{NO}^+]$ . Also, since  $C = [\text{HNO}_2] + [\text{NO}^+]$ , then  $D/C = (\epsilon_1 + x\epsilon_2R)/(1 + R)$ . If the optical density  $D$  is measured at the four selected wavelengths, then there are four such equations which can be solved in pairs to eliminate  $x$  and give  $R$ . The mean values of  $R$  so determined are given for six solutions in Table 1.

TABLE 1. Typical determinations of  $R$  at  $[\text{HClO}_4] = 10.40\text{m}$ .

10 <sup>4</sup> C (M)	D/C					R
	347 m $\mu$	358 m $\mu$	372 m $\mu$	386 m $\mu$		
25.0	60.4	48.8	36.8	22.0	0.65	
29.2	60.6	47.3	35.6	21.6	0.69	
33.2	62.0	49.1	37.1	22.6	0.62	
40.9	65.3	50.6	37.9	23.5	0.58	
41.1	64.5	50.1	36.7	23.1	0.62	
44.8	69.6	55.6	40.9	24.6	0.49	

TABLE 2. Determination of  $\text{p}K_1$  for various molalities,  $m$ , of perchloric acid.

$m$	$H_0$	$J_0''$	$R$	$\text{p}K_1$
10.20	-3.74	-4.73	0.26	7.05
10.40	-3.79	-4.82	0.61	6.77
10.50	-3.81	-4.86	0.97	6.61
10.71	-3.90	-5.03	1.01	6.77
10.86	-3.94	-5.10	1.46	6.68
10.99	-4.00	-5.22	1.81	6.70

The values of  $R$  (mean  $0.61 \pm 0.05$ ) show some scatter and for this reason six determinations were carried out at each concentration of perchloric acid used. By this method  $R$  could be measured conveniently over only a small range of perchloric acid concentrations (50–53%). There is no systematic variation of  $R$  with nitrous acid concentration.

The most satisfactory method of finding  $K_1$  is to use the acidity function<sup>11</sup>  $J_0 = -\text{p}K_1 - \log R$ .  $J_0$  is not known for perchloric acid but a reasonable approximation to it has been suggested:<sup>12</sup>

$$J_0'' = 2H_0 + \log [\text{H}_3\text{O}^+]_N + 1.74$$

$H_0$  is known for perchloric acid,<sup>11</sup> and hence  $\text{p}K_1$  can be found as shown in Table 2. The subscript  $N$  indicates (see ref. 12) that  $\text{H}_3\text{O}^+$  is measured in mole-fraction units.

Values of  $\text{p}K_1$  (mean 6.76) are reasonably constant, giving  $K_1 = 2 \times 10^{-7}$  (20°). Singer and Vamplew's results<sup>1</sup> can be treated in a similar fashion, yielding  $K_1 = 3 \times 10^{-7}$ . The disagreement with the predicted constant is due partly to the uncertainty of the free

<sup>8</sup> Kortum, *Z. phys. Chem.*, 1939, **43**, B, 418.

<sup>9</sup> Bayliss and Watts, *Austral. J. Chem.*, 1956, **9**, 319.

<sup>10</sup> Longstaff and Singer, *J.*, 1954, 2604.

<sup>11</sup> Paul and Long, *Chem. Rev.*, 1957, **57**, 1.

<sup>12</sup> Gold, *J.*, 1955, 1263.

energy of hydration of the nitrosonium ion and partly to the fact that the approximate  $J_0''$  values have uncertain absolute magnitudes although their variation with acid concentration is satisfactory.

One of us (T. A. T.) thanks the New Zealand University Research Grants Committee for a grant.

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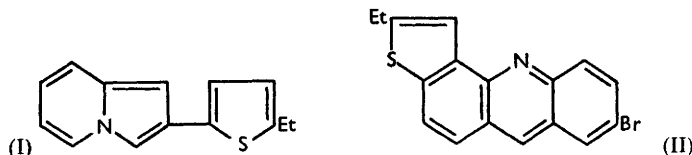
[Received, October 2nd, 1957.]

### 483. Thiophen Derivatives. Part XII.\* Some Derivatives of 2-Ethylthiophen.

By NG. PH. BUU-HOÏ.

2-ETHYLTHIOPHEN was a convenient intermediate for the synthesis of thiophen compounds required for evaluation of the potential carcinogenic or choleric activity. The present Note records the preparation of these new compounds, mostly ketones and nitrogen heterocyclic derivatives therefrom, none of which proved of biological interest.

2-Acetyl-5-ethylthiophen gave 2-(5-ethyl-2-thienyl)indole, and condensation of 2-bromoacetyl-5-ethylthiophen with  $\alpha$ -picoline, followed by a Tschitschibabin cyclisation<sup>1</sup> of the quaternary picolinium salt, furnished 2-(5-ethyl-2-thienyl)pyrrocoline (I). Pfitzinger reaction of 5-bromoisatin with 2-acetyl-5-ethyl- and 2-ethyl-5-propionylthiophen afforded the 6-bromocinchoninic acids, which gave 6-bromoquinolines on thermal decarboxylation;  $\alpha$ -naphthisatin<sup>2</sup> reacted with 2-acetyl-5-ethyl- but not with 2-ethyl-5-propionylthiophen under the same conditions.



Pfitzinger reaction of 5-bromoisatin with 2-ethyl-4 : 5 : 6 : 7-tetrahydro-4-oxothio-naphthen<sup>3</sup> yielded 3-bromo-6 : 7-dihydro-5'-ethylthieno(2' : 3'-8 : 9)acridine-5-carboxylic acid which, when heated above its m. p., underwent both decarboxylation and dehydrogenation, to give compound (II). Friedel-Crafts condensation of 2-ethylthiophen with phthalic anhydride afforded *o*-(5-ethyl-2-thienyl)benzoic acid; similar Friedel-Crafts reactions with various aliphatic, aromatic, and thiophen acid chlorides yielded ketones listed in the Table.

*Experimental.*—2-(5-Ethyl-2-thienyl)indole. 2-Acetyl-5-ethylthiophen<sup>4</sup> (3 g.) was heated with phenylhydrazine (3 g.) at 120° until steam ceased to be evolved; to the crude phenylhydrazone, powdered fused zinc chloride (7 g.) was added, and the mixture heated above 200°, upon which a vigorous reaction set in. After cooling, aqueous acetic acid was added, the indole taken up in benzene, washed with water, and dried ( $\text{Na}_2\text{SO}_4$ ), the solvent distilled off, and the residue fractionated *in vacuo*. The distillate (b. p. 240—250°/18 mm.) crystallised as prisms (2.5 g.), m. p. 130°, from light petroleum (Found: C, 73.7; H, 6.0.  $\text{C}_{14}\text{H}_{13}\text{NS}$  requires C, 74.0; H, 5.8%). A similar reaction with 2-ethyl-5-propionylthiophen<sup>5</sup> gave 2-(5-ethyl-2-thienyl)-3-methylindole, a yellow oil, which gave a *picrate*, brown-violet needles, m. p. 126°, from light petroleum (Found: N, 11.6.  $\text{C}_{21}\text{H}_{18}\text{O}_7\text{N}_4\text{S}$  requires N, 11.9%).

\* Part XI, Buu-Hoï and Lavit, *J.*, 1958, 1721.

<sup>1</sup> Cf. Borrows and Holland, *Chem. Rev.*, 1948, **42**, 612; Buu-Hoï and Hoán, *Rec. Trav. chim.*, 1949, **68**, 454.

<sup>2</sup> Cf. Buu-Hoï and Cagniant, *Bull. Soc. chim. France*, 1946, **13**, 134.

<sup>3</sup> Buu-Hoï, Hoán, and Khôi, *J. Org. Chem.*, 1950, **15**, 957.

<sup>4</sup> Schleicher, *Ber.*, 1886, **19**, 660; Steinkopf, Frömmel, and Leo, *Annalen*, 1941, **546**, 199.

<sup>5</sup> Steinkopf, *Annalen*, 1923, **430**, 78.

2-(5-Ethyl-2-thienyl)pyrrocoline (I). 2-Acetyl-5-ethylthiophen (13 g.) with bromine (12.7 g.) in chloroform gave a bromo-ketone which decomposed on distillation *in vacuo*. A mixture of this compound (8 g.) and 2-picoline (4 g.) was heated in ethanol (10 c.c.) at 70° for a few minutes, and the picolinium salt obtained was precipitated by ether. An aqueous solution of this salt was brought to the boil with sodium hydrogen carbonate and the cyclisation product formed was collected and recrystallised from light petroleum, giving colourless prisms (5 g.), m. p. 119° (Found: N, 6.2. C<sub>14</sub>H<sub>13</sub>NS requires N, 6.2%).

6-Bromo-2-(5-ethyl-2-thienyl)cinchoninic acid. 2-Acetyl-5-ethylthiophen<sup>6</sup> (3 g.) and 5-bromoisatin (4.4 g.) were heated with potassium hydroxide (3.5 g.) in ethanol (40 c.c.) for 5 hr.; after dilution with water and removal of the neutral impurities by ether the aqueous layer was acidified with acetic acid, and the precipitate recrystallised from ethanol as yellowish prisms (4 g.), m. p. 238° (Found: C, 52.8; H, 3.4. C<sub>16</sub>H<sub>12</sub>O<sub>2</sub>NSBr requires C, 53.0; H, 3.3%). 6-Bromo-2-(5-ethyl-2-thienyl)quinoline, prepared by heating this acid above its m. p., was purified *via* its picrate (deep yellow prisms, m. p. 188°, from ethanol), and formed yellowish leaflets, m. p. 107°, from ethanol (Found: C, 56.3; H, 3.9. C<sub>15</sub>H<sub>12</sub>NSBr requires C, 56.6; H, 3.8%).

6-Bromo-2-(5-ethyl-2-thienyl)-3-methylcinchoninic acid. Prepared analogously (10 hours' refluxing), this acid (4.5 g.) formed pale yellow, sublimable needles, m. p. 239°, from ethanol (Found: C, 54.0; H, 3.5. C<sub>17</sub>H<sub>14</sub>O<sub>2</sub>NSBr requires C, 54.3; H, 3.7%). 6-Bromo-2-(5-ethyl-2-thienyl)-3-methylquinoline formed yellowish prisms, m. p. 80°, from ethanol (Found: C, 57.7; H, 4.5. C<sub>16</sub>H<sub>14</sub>NSBr requires C, 57.8; H, 4.2%).

2-(5-Ethyl-2-thienyl)-7:8-benzocinchoninic acid. This acid (3 g.), similarly prepared, formed pale yellow, sublimable needles, m. p. 241°, from ethanol (Found: C, 71.8; H, 4.4. C<sub>20</sub>H<sub>16</sub>O<sub>2</sub>NS requires C, 72.1; H, 4.5%).

3-Bromo-6:7-dihydro-5'-ethylthieno(2':3'-8:9)acridine-5-carboxylic acid, similarly prepared, formed yellowish prisms, m. p. 242°, from ethanol (Found: C, 55.5; H, 3.5. C<sub>18</sub>H<sub>14</sub>O<sub>2</sub>NSBr requires C, 55.7; H, 3.6%). Thermal decarboxylation of the acid (1.5 g.), and distillation of the product *in vacuo*, gave a resin which was converted into a picrate, forming orange-yellow prisms, m. p. 265° (decomp.), from ethanol (Found: N, 9.6. C<sub>23</sub>H<sub>15</sub>O<sub>7</sub>N<sub>4</sub>SBr requires N, 9.8%). Basification of this picrate with ammonia yielded 3-bromo-5'-ethylthieno(2':3'-8:9)acridine (II), crystallising as yellow prisms (0.2 g.), m. p. 150°, from ethanol (Found: C, 59.8; H, 3.4. C<sub>17</sub>H<sub>12</sub>NSBr requires C, 59.6; H, 3.5%). That dehydrogenation had occurred was further shown by recovery of the base from treatment with chloranil in boiling xylene for 16 hr. This spontaneous dehydrogenation is in contrast with the relative stability of the analogous dihydrobenzocridines, which undergo dehydrogenation only when heated with chloranil.<sup>7</sup>

#### Ketones derived from 2-ethylthiophen.

Acyl deriv. of 2-ethylthiophen	B. p./mm.	M. p.	Formula	Found (%)		Reqd. (%)	
				C	H	C	H
isoButyroyl .....	146—148°/20	—	C <sub>10</sub> H <sub>14</sub> OS	65.8	7.5	65.9	7.7
Octanoyl .....	196—198°/21	—	C <sub>14</sub> H <sub>22</sub> OS	70.3	9.2	70.6	9.3
<i>p</i> -Anisoyl <sup>a</sup> .....	241—243°/21	48°	C <sub>14</sub> H <sub>14</sub> O <sub>2</sub> S	68.2	5.9	68.3	5.7
<i>p</i> -Hydroxybenzoyl <sup>b</sup> .....	—	126	C <sub>13</sub> H <sub>12</sub> O <sub>2</sub> S	67.3	5.5	67.2	5.2
3-Allyl-4-hydroxybenzoyl <sup>c</sup> .....	—	84	C <sub>16</sub> H <sub>16</sub> O <sub>2</sub> S	70.8	6.1	70.6	5.9
<i>p</i> -Toluoyl .....	—	69	C <sub>14</sub> H <sub>14</sub> OS	73.2	6.3	73.0	6.1
<i>p</i> -Ethylbenzoyl .....	—	56	C <sub>15</sub> H <sub>16</sub> OS	73.6	6.5	73.8	6.6
2-Thenoyl .....	—	41	C <sub>11</sub> H <sub>10</sub> OS <sub>2</sub>	59.5	4.8	59.5	4.5
5-Chloro-2-thenoyl <sup>d</sup> .....	228—230°/23	—	C <sub>11</sub> H <sub>9</sub> OS <sub>2</sub> Cl	51.8	3.3	51.5	3.5
5-Bromo-2-thenoyl .....	—	44	C <sub>11</sub> H <sub>9</sub> OS <sub>2</sub> Br	44.1	3.2	43.9	3.0
5-Ethyl-2-thenoyl .....	—	81	C <sub>13</sub> H <sub>14</sub> OS <sub>2</sub>	62.5	5.6	62.4	5.6
Fluorene-2-carbonyl <sup>e</sup> .....	—	89	C <sub>20</sub> H <sub>16</sub> OS	78.6	5.2	78.9	5.3
2-Furoyl .....	195—197°/20	—	C <sub>11</sub> H <sub>10</sub> O <sub>2</sub> S	64.3	5.2	64.1	4.9

<sup>a</sup> All the solid ketones formed colourless prisms or leaflets from ligroin or benzene-ligroin. <sup>b</sup> Prepared by demethylation of the preceding ketone (10 g.) with boiling pyridine hydrochloride (30 g.), and recrystallised from benzene-ligroin. <sup>c</sup> Obtained by Claisen rearrangement of the allyl ether of the foregoing ketone (24 hours' boiling in dimethylaniline), and recrystallised from benzene-ligroin. <sup>d</sup> Solidified at room temperature. <sup>e</sup> Oxidised by sodium dichromate in acetic acid to a mixture of fluorenone-2-carboxylic acid and a compound which formed yellow prisms, m. p. 164°, from ethanol.

o-(5-Ethyl-2-thenoyl)benzoic acid. To a stirred mixture of 2-ethylthiophen (1.2 g.) and phthalic anhydride (1.5 g.) in carbon disulphide, aluminium chloride (1.5 g.) was added in small

<sup>6</sup> For other Pfitzinger reactions, see Cagniant and Cagniant, *Bull. Soc. chim. France*, 1952, 713.

<sup>7</sup> Buu-Hoi, Hoán, and Xuong, *J.*, 1952, 279.

portions at room temperature, and stirring was continued for 4 more hours. After decomposition with ice, the product was purified *via* its sodium salt; recrystallisation from *cyclohexane* yielded fine, colourless prisms (0.5 g.), m. p. 103° (Found: C, 64.5; H, 4.8. C<sub>14</sub>H<sub>12</sub>O<sub>3</sub>S requires C, 64.6; H, 4.6%). With phenylhydrazine in boiling acetic acid, this *acid* gave a condensation product, m. p. 135°.

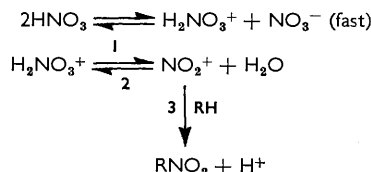
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[Received, December 30th, 1957.]

#### 484. Oxygen Exchange between Nitric Acid and Water. Part IV.\* The Nitration of 2-Mesitylethanesulphonic Acid.

By C. A. BUNTON and G. STEDMAN.

IN Part II of this series<sup>1</sup> it was shown that the nitronium ion was an intermediate in both oxygen-exchange and aromatic nitration in aqueous nitric acid, and that the rate of the former was the rates of formation and hydration of the nitronium ion<sup>2</sup> (reactions 1 and 2):



As the reactivities (or concentrations) of the aromatic compounds are increased they will capture an increasing proportion of the nitronium ions (reaction 3). Then the rate of nitration will approach that of oxygen exchange, and the kinetic order, which is first with respect to the aromatic compound when most of the nitronium ions are captured by water ( $v_2 \gg v_3$ ), will decrease towards zero.

When the bulk reactivity of the aromatic compound is sufficiently greater than that of the water for sensibly all the nitronium ions to be captured by the aromatic compound ( $v_3 \gg v_2$ ), the rate of nitration will be the rate of formation of nitronium ions and of oxygen-exchange, and independent of the nature or concentration of the aromatic compound. This is the well-known zero-order kinetic form for electrophilic aromatic substitution.<sup>3</sup>

In our earlier experiments<sup>1</sup> the aromatic compounds studied were not sufficiently reactive for the rate of nitration to equal that of oxygen exchange; the maximum nitration rates (observed for mesitylene- $\alpha$ - and *isodurene*- $\alpha^2$ -sulphonic acid) were *ca.* 80% of those of oxygen exchange. 2-Mesitylethanesulphonic acid, in which the deactivating sulphonate group is further removed from the aromatic ring, was therefore synthesised, and its nitration followed dilatometrically.

The kinetic form, for most of the reaction (see Figure), was of zero order with respect to the aromatic compound. This region was followed by a very slow volume change, probably due to dinitration or demethylation, which did not interfere with determination of the nitration rate.

The zero-order rates are tabulated together with some data on *isodurene*- $\alpha^2$ -sulphonic acid, and compared with the extrapolated rates of oxygen exchange. It was possible to obtain first-order nitration rates for all the compounds discussed in Part II,<sup>1</sup> but 2-mesitylethanesulphonic acid is too reactive for first-order nitrations to be studied.

\* Part III, *J.*, 1953, 2653.

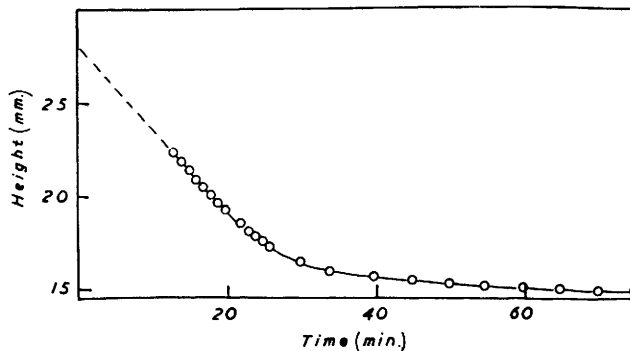
<sup>1</sup> Bunton and Halevi, *J.*, 1952, 4917.

<sup>2</sup> Bunton, Halevi, and Llewellyn, *J.*, 1952, 4913.

<sup>3</sup> Hughes, Ingold, and Reed, *J.*, 1950, 2400; de la Mare, Ketley, and Vernon, *J.*, 1954, 1290.

The zero-order nitration rates ( $k_0$ ) for 2-mesitylethanesulphonic acid are *ca.* 15% greater than those of oxygen exchange ( $R$ ). However the uncertainty in these extrapolated exchange rates<sup>2</sup> is of this order of magnitude, and the ionic-strength effect of the

Nitration at 0°.  $[\text{HNO}_3] = 37.32$  mole %.  $[\text{ArH}] = 0.244$  mole %.



sodium 2-mesitylethanesulphonate will increase the rate of formation of the nitronium ion and hence of nitration.<sup>1,4</sup>

*Experimental.—Preparation of materials.* Mesitylene was chloromethylated, and the chloride converted into mesitylacetic acid *via* the cyanide.<sup>5</sup> The acid was reduced by lithium aluminium hydride and the 2-mesitylethyl alcohol brominated with phosphorus tribromide in dry benzene, to give 2-mesitylethyl bromide, m. p. 74° (Found: C, 58.4; H, 6.6; Br, 35.0.  $\text{C}_{11}\text{H}_{15}\text{Br}$  requires C, 58.2; H, 6.7; Br, 35.2%). The bromide was then converted into the sodium salt of the sulphonic acid by boiling aqueous sodium sulphite. It was characterised as its *S*-benzylthiuronium salt, m. p. 206° (Found: C, 58.1; H, 7.0; N, 7.4.  $\text{C}_{15}\text{H}_{26}\text{O}_3\text{N}_2\text{S}_2$  requires C, 57.8; H, 6.6; N, 7.1%).

*Kinetic measurements.* The procedure was that described in Part II of this series.<sup>1</sup> The acid was used as its sodium salt.

*Nitration of 2-mesitylethanesulphonic acid and isodurene- $\alpha^2$ -sulphonic acid at 0°.*

	2-Mesitylethanesulphonic acid					<i>iso</i> Durene- $\alpha^2$ -sulphonic acid	
$[\text{HNO}_3]$ (mole %) ...	36.37	37.32	38.73	39.04	39.40	38.02	38.98
$10^4 k_0$ (mole % sec. <sup>-1</sup> )	0.98	1.28	1.78	2.11	2.42	1.15	1.57
$10^4 R$ " "	0.81	1.10	1.74	1.92	2.15	1.44	1.82

The concentration of the aromatic compound was varied between 0.170 and 0.300 mole %.

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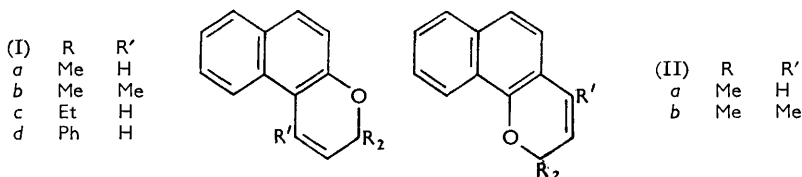
<sup>4</sup> Halberstadt, Hughes, and Ingold, *J.*, 1950, 2441.

<sup>5</sup> *Org. Synth.*, 1945, **25**, 65.

## 485. Preparation of Some Naphthopyrans.

By R. LIVINGSTONE, D. MILLER, and R. B. WATSON.

THE action of anhydrous formic acid on a number of 6:6-disubstituted chromens was recently compared with the dimerisation of lapachenole<sup>1</sup> under similar conditions. The dimethylnaphthopyrans<sup>2</sup> (Ia) and (IIa) gave dimers when treated with anhydrous formic or methanolic sulphuric acid, unlike the analogues (IIb)<sup>2</sup> and (Ib)<sup>3</sup> which were inert. The 4-methyl group may hinder dimerisation sterically.<sup>1</sup> 6:6-Diethylnaphtho(2':1'-2:3)pyran (Ic), the corresponding 6:6-diphenyl compound (Id), and the 4-chloro-derivative<sup>2</sup> of (IIb) also failed to dimerise when treated with formic acid or methanolic hydrogen chloride.



6:6-Dimethylnaphtho(2':1'-2:3)pyran (Ia) with 2:4-dinitrophenylhydrazine in butanolic sulphuric acid<sup>2</sup> gave 2:2-dimethyl-5:6-benzochroman-4-one 2:4-dinitrophenylhydrazone. The authentic benzochromanone was prepared by the Fries rearrangement<sup>4</sup> of the  $\beta\beta$ -dimethylacryloyl ester.<sup>5</sup> The other analogues (Ib), (Ic), (Id), and (IIb), unlike (IIa),<sup>2</sup> failed to react with 2:4-dinitrophenylhydrazine.

*Experimental.*—Preparation of 6:6-dialkyl- and 6:6-diaryl-naphtho(2':1'-2:3)pyrans.<sup>6</sup> The benzocoumarin (0.077 mole) in dry benzene (250 c.c.) was added in 1½ hr. to a stirred Grignard solution from alkyl or aryl iodide (0.2 mole), magnesium (0.2 g.-atom), and ether (75 c.c.). The solution was refluxed for 1 hr. and set aside overnight. Decomposition with 22% ammonium chloride solution (300 c.c.) and extraction with ether gave an ethereal solution, which was washed with water and dried (Na<sub>2</sub>SO<sub>4</sub>). The alcohol was cyclised by refluxing glacial acetic acid (50 c.c.) for ½ hr., and the solution poured into water, and extracted with ether. The ethereal solution was washed with dilute sodium hydroxide solution, then water, and dried (Na<sub>2</sub>SO<sub>4</sub>). Removal of the solvent and distillation gave the naphthopyran.

6:6-Dimethylnaphtho(2':1'-2:3)pyran (Ia) (from 5:6-benzocoumarin<sup>7</sup>), b. p. 164°/3 mm. (75%), on crystallisation from dilute acetic acid, gave plates, m. p. 45° (Found: C, 85.5; H, 6.2. C<sub>15</sub>H<sub>14</sub>O requires C, 85.7; H, 6.7%); it gave a picrate, red needles, m. p. 115°. The alcohol crystallised from methanol as needles, m. p. 130°.

The 6:6-diethyl analogue (Ic) (from 5:6-benzocoumarin<sup>7</sup>) had b. p. 180—182°/15 mm. (30%) (Found: C, 85.8; H, 7.4. C<sub>17</sub>H<sub>18</sub>O requires C, 85.7; H, 7.6%).

6:6-Diphenylnaphtho(2':1'-2:3)pyran (Id) (from 5:6-benzocoumarin<sup>7,8</sup>). After decomposition of the Grignard complex with ammonium chloride solution the product was steam-distilled and extracted with ether from the non-volatile portion. Removal of the solvent and crystallisation from ethanol afforded needles of the pyran, m. p. 159—160° (20%) (Found: C, 89.3; H, 5.4. C<sub>25</sub>H<sub>18</sub>O requires C, 89.9; H, 5.4%).

The 4:6:6-trimethyl analogue (Ib) (from 4-methyl-5:6-benzocoumarin), b. p. 188—190°/15 mm. (35%), crystallised from dilute acetic acid as plates, m. p. 74—76° (Found: C, 86.1; H, 7.2. C<sub>16</sub>H<sub>16</sub>O requires C, 85.7; H, 7.1%).

<sup>1</sup> Livingstone and Whiting, *J.*, 1955, 3631.

<sup>2</sup> Livingstone and Watson, *J.*, 1957, 1509.

<sup>3</sup> Hendry, Sandrock, and Robertson, *J.*, 1931, 2426.

<sup>4</sup> Cavill, Dean, McGookin, Marshall, and Robertson, *J.*, 1954, 4573.

<sup>5</sup> Arima, *J. Chem. Soc. Japan*, 1932, 53, 715.

<sup>6</sup> Smith and Ruoff, *J. Amer. Chem. Soc.*, 1940, 62, 145.

<sup>7</sup> Kauffman, *Ber.*, 1883, 16, 685; Boehm and Profft, *Ann. Chim.*, 1931, 16.

<sup>8</sup> Löwenbein, *Ber.*, 1924, 57, 1517.



*Preparation of dimethylnaphthopyran dimers.* The dimethylnaphthopyran (0.01 mole) was boiled with formic acid (75 c.c.; *d* 1.2) for 2 hr. The mixture was cooled, and the precipitate separated by filtration, washed with sodium hydrogen carbonate solution, then water, and dried. The dimer was recrystallised from a suitable solvent.

(a) *The 6:6-dimethylnaphtho(2':1'-2:3)pyran dimer*, crystallised from ethyl acetate, had m. p. 204° (50%) [Found: C, 85.7; H, 6.6%; *M*, 433. (C<sub>15</sub>H<sub>14</sub>O)<sub>2</sub> requires C, 85.7; H, 6.8%; *M*, 420].

(b) *The 6:6-dimethylnaphtho(1':2'-2:3)pyran dimer* crystallised as plates (from ethanol), m. p. 132–134° (Found: C, 85.9; H, 6.9%; *M*, 395).

*6:6-Dimethylnaphtho(2':1'-2:3)pyran 2:4-dinitrophenylhydrazine derivative.* The naphthopyran (1 mol.), 2:4-dinitrophenylhydrazine (2.2 mols.), butan-1-ol (3.5 l./mole), and sulphuric acid (0.38 l./mole) were refluxed for 3 hr. The residue afforded by the removal of the solvent and excess of hydrazine was purified by chromatography on alumina from benzene. The derivative, recrystallised from glacial acetic acid, had m. p. 254° alone or mixed with 2:2-dimethyl-5:6-benzochroman-4-one 2:4-dinitrophenylhydrazone.

*2:2-Dimethyl-5:6-benzochroman-4-one.* ββ-Dimethylacryloyl chloride (3.6 g.) was added to a solution of 2-naphthol (4 g.) in nitrobenzene (31 c.c.). Anhydrous aluminium chloride (3.8 g.) was added in small portions to the cooled solution, and the mixture set aside for 12 days.<sup>8</sup> The mixture was poured on ice and 3*N*-hydrochloric acid, the nitrobenzene removed by steam-distillation, and the residue extracted with ether. The ethereal extract was washed with dilute sodium hydroxide solution and water. Evaporation of the dried (MgSO<sub>4</sub>) extract gave a brown oil (2.8 g.) which was chromatographed on alumina from benzene solution. Removal of the solvent and crystallisation from light petroleum (b. p. 40–60°) afforded 2:2-dimethyl-5:6-benzochroman-4-one as prisms, m. p. 81° (Found: C, 79.7; H, 6.4. C<sub>15</sub>H<sub>14</sub>O<sub>2</sub> requires C, 79.65; H, 6.2%).

The crude dinitrophenylhydrazone, obtained by treating a warm ethanolic solution of the chroman-4-one with an excess of Brady's reagent, was purified by chromatography on alumina from benzene. Crystallisation from benzene afforded crimson plates, m. p. 254°.

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## 486. Reactions of Amino-acids with Acetic Acid.

By E. A. BELL.

AMINO-ACIDS with acetic anhydride<sup>1</sup> and keten<sup>2</sup> have given optically active acetamido-acids, racemic acetamido-acids, oxazolones, and acetamidoacetone derivatives, depending on the amino-acid,<sup>3</sup> the choice and concentration of acetylating agent, the temperature,<sup>4</sup> and the pH<sup>5</sup> at which the reaction is carried out.

As briefly reported,<sup>6</sup> ornithine and citrulline have been converted into 3-acetamido-2-piperidone by refluxing acetic acid. The ease with which these reactions proceed suggested that other amino-acids might be readily acetylated under the same conditions. Leucine, valine, alanine, and α-aminobutyric and α-amino-α-methylpropionic acid have now been found to be acetylated smoothly and in good yield in this way. However, glutamic acid is dehydrated rapidly to 5-oxopyrrolidine-2-carboxylic acid, and ornithine and citrulline undergo both acetylation and dehydration.

<sup>1</sup> Bergmann and Zervas, *Biochem. Z.*, 1928, **203**, 280.

<sup>2</sup> Bergmann and Stern, *Ber.*, 1930, **63**, 437.

<sup>3</sup> Wolf and Berger, *J. Amer. Chem. Soc.*, 1951, **73**, 3533; du Vigneau and Meyer, *J. Biol. Chem.*, 1932, **98**, 295.

<sup>4</sup> Neuberger, *Biochem. J.*, 1938, **32**, 1452; Dakin and West, *J. Biol. Chem.*, 1928, **78**, 745.

<sup>5</sup> Jackson and Cahill, *ibid.*, 1938, **126**, 37; Cahill and Burton, *ibid.*, 1940, **132**, 161.

<sup>6</sup> Bell, *Chem. and Ind.*, 1956, 1143.

Optically active alanine, valine, leucine, and glutamic acid as well as the racemic forms were refluxed with acetic acid; racemic derivatives were obtained in every case.

Glutamic acid was refluxed with butan-1-ol to establish that its rapid dehydration by boiling acetic acid is not merely a temperature effect (butanol was chosen because of its similarity to acetic acid in respect of its boiling point and its properties as a solvent for 5-oxopyrrolidine-2-carboxylic and glutamic acid—the former is readily soluble in both liquids, and the latter in neither). 5-Oxopyrrolidine-2-carboxylic acid was formed under these conditions, but only in low yield and after prolonged refluxing.

*Experimental.*—In each of the following reactions the amino-acid was refluxed in the free state with acetic acid. The excess of acetic acid and water were then distilled off under reduced pressure and the product was recrystallised.

Comparison of  $R_F$  values was carried out by downward chromatography on paper (Whatman No. 1) in phenol-water (4 : 1 w/v). Whatman No. 3 MM. paper, phosphate buffer (pH 8), and 2.5—5 v/cm. were used for ionophoresis.

TABLE 1. *Dehydration of glutamic acid.*

No.	Acid	Refluxed with	Time (hr.)	Yield (%)	M. p.	$[\alpha]_D^{20}$ (in H <sub>2</sub> O)
1	DL	AcOH	20	100	178—180°	0
2	L	"	2	68	175—177	0
3	DL	BuOH	20	9	174—176	0

No.	C <sub>5</sub> H <sub>7</sub> O <sub>3</sub> N	Found (%)			Calculated (%)			Acid equiv.	
		C	H	N	C	H	N	Found	Calc.
1		46.4	5.34	10.9	46.5	5.43	10.9	128	129
2	"	46.5	5.33	10.7	"	"	"	127	"

Anderlini<sup>9</sup> gives m. p. 176—180° for racemic 4-oxopyrrolidine-2-carboxylic acid, and Menozzi and Appiani<sup>10</sup> give m. p. 159—160° and  $[\alpha]_D^{23}$  -7.2° (in H<sub>2</sub>O) for the *lævo*-isomer.

TABLE 2. *Acetylation of amino-acids.*

No.	Amino-acid	Reflux time (hr.)	Yield (%)	M. p.	M. p. (lit.) *
1	DL-Valine	20	74	145—146°	144—146° <sup>a</sup>
2	L-Valine	22	74	144—145	"
3	DL-Alanine	8	44	134—136	136°
4	L-Alanine	22	61	134—136	"
5	DL-Leucine	20	75	156—158	155—157° <sup>b</sup>
6	L-Leucine	22	75	154—156	"
7	DL-Norleucine	20	87	106	104.5—105.5° <sup>b</sup>
8	DL- $\alpha$ -Aminobutyric	20	90	128—130	129—131° <sup>a</sup>
9	$\alpha$ -Amino- $\alpha$ -methylpropionic	20	21	191	195—196° <sup>c</sup>

No.	C <sub>7</sub> H <sub>13</sub> O <sub>3</sub> N	Found (%)			Calculated (%)			Acid equiv.	
		C	H	N	C	H	N	Found	Calc.
1		52.92	8.31	8.9	52.84	8.2	8.8	160	159
3	C <sub>7</sub> H <sub>9</sub> O <sub>3</sub> N	45.65	6.99	10.9	45.8	6.87	10.7	132	131
5	C <sub>8</sub> H <sub>15</sub> O <sub>3</sub> N	55.38	8.7	8.2	55.5	8.68	8.2	173	173
7	"	55.48	9.02	8.4	"	"	"	172	"
8	C <sub>8</sub> H <sub>11</sub> O <sub>3</sub> N	49.27	7.44	10.1	49.6	7.58	9.65	145	145
9	"	49.6	7.67	9.79	"	"	"	148	"

\* The m. p. values from the literature are for the DL-acetamido-acids. The values for the relevant optically active acids are acetyl-L-valine, m. p. 157—158°,  $[\alpha]_D^{20}$  +5.8 (in EtOH),<sup>a</sup> acetyl-L-alanine, m. p. 116°,  $[\alpha]_D^{19}$  -45.6 (in H<sub>2</sub>O) (Karrer, Escher, and Widmer, *Helv. Chim. Acta*, 1929, **9**, 301), acetyl-L-leucine, m. p. 167°,  $[\alpha]_D^{19}$  -12.1 (in EtOH) (*idem, ibid.*). Determinations of  $[\alpha]$  on products 2, 4, and 6 were carried out in the appropriate solvents.

<sup>a</sup> Syngé, *Biochem. J.*, 1939, **33**, 1913. <sup>b</sup> Synder, Shekleton, and Lewis, *J. Amer. Chem. Soc.*, 1945, **67**, 310. <sup>c</sup> Levene and Steiger, *J. Biol. Chem.*, 1931, **93**, 581.

**3-Acetamido-2-piperidone.** DL-Ornithine (1.2 g.) was refluxed with acetic acid (100 ml.) for 13 hr. The product was obtained from aqueous acetone in needles (0.9 g.), m. p. 185—186°

alone or mixed with 3-acetamido-2-piperidone prepared from triacetylanhydro-DL-arginine<sup>7</sup> (Found: C, 54.1; H, 7.7; N, 17.5. Calc. for C<sub>7</sub>H<sub>12</sub>O<sub>2</sub>N<sub>2</sub>: C, 53.8; H, 7.7; N, 17.9%). Hydrolysis for 3 hr. at 100° with 20% hydrochloric acid regenerated DL-ornithine.

*5-Oxopyrrolidine-2-carboxylic acid.* (a) DL-Glutamic acid (2.0 g.) was refluxed with acetic acid (100 ml.) and in a second experiment with butan-1-ol (100 ml.). (b) L-Glutamic acid (2.0 g.) was refluxed with acetic acid (100 ml.).

The results of these three experiments are set out in Table 1. The identity of each product with authentic acid (prepared by the method of Abderhalden and Kautzsch<sup>8</sup>) was confirmed by chromatography, ionophoresis, and mixed m. p. The spots of acid on the dried chromatography and ionophoresis papers were developed by exposure to iodine vapour.

*Acetyl-DL-amino-acids.* Each amino-acid was refluxed in the free state with acetic acid (50 ml./g.), and the product recrystallised from ethanol. The results are set out in Table 2.

The derivatives of the three optically active amino-acids were not analysed as they showed no optical activity and no depression of m. p. when mixed with the acetyl derivatives of the corresponding racemic amino-acids.

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<sup>7</sup> Bergmann and Koster, *Z. physiol. Chem.*, 1926, **159**, 179.

<sup>8</sup> Abderhalden and Kautzsch, *ibid.*, 1910, **68**, 487.

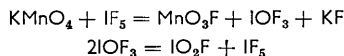
<sup>9</sup> Anderlini, *Gazzetta*, 1889, **19**, 100.

<sup>10</sup> Menozzi and Appiani, *ibid.*, 1894, **24**, I, 370.

## 487. *The Oxyfluorides of Manganese and Iodine.*

By E. E. AYNLEY.

PURE manganese trioxyfluoride (permanganyl fluoride, MnO<sub>3</sub>F) was prepared by Engelbrecht and Grosse<sup>1</sup> from potassium permanganate and fluorosulphuric acid and Aynley, Nichols, and Robinson,<sup>2</sup> using iodine pentoxide and iodine pentafluoride, succeeded in isolating iodine oxytrifluoride IOF<sub>3</sub> and iodyl fluoride IO<sub>2</sub>F. This communication describes the preparation of all three oxyfluorides by the reaction of potassium permanganate with excess of iodine pentafluoride. The reactions involved are:



In the preparation iodine pentafluoride must always be in large excess, otherwise there is the risk of a violent explosion when the temperature is raised to about 60°.

*Experimental.—Preparation of manganese trioxyfluoride.* About 50 ml. of iodine pentafluoride, prepared by burning dry iodine in a fluorine-nitrogen stream (4 : 6, by vol.), was fractionated in a vacuum to free it from fluorine and iodine heptafluoride, and was then poured under the same conditions, on 5 g. of finely powdered potassium permanganate. No change was observed at room temperature but at *ca.* 40° reaction occurred and the permanganate rapidly dissolved to form a deep green solution. When the temperature was gradually raised further, green gaseous manganese trioxyfluoride was rapidly evolved: it was condensed into a trap cooled to -80°. Since manganese trioxyfluoride begins to decompose at 0°, there was appreciable evolution of oxygen and deposition of a brown mixture of the dioxide and difluoride of manganese on the walls of the reaction vessel. To complete the separation of manganese trioxyfluoride from its decomposition products and from a small amount of iodine pentafluoride, the crude oxyfluoride was distilled into a trap containing pellets of anhydrous potassium fluoride and for final purification the product was redistilled three times and collected as dark green crystals at -80° (Found: Mn, 44.9; F, 15.4. Calc. for MnO<sub>3</sub>F: Mn, 45.1; F, 15.6%). The product had m. p. -38.2° in good agreement with that given by Engelbrecht and Grosse.<sup>1</sup>

<sup>1</sup> Engelbrecht and Grosse, *J. Amer. Chem. Soc.*, 1954, **76**, 2042.

<sup>2</sup> Aynley, Nichols, and Robinson, *J.*, 1953, 623.

Near the entrance to the first of the three traps used in the final distillation there collected a small amount of a brown solid which contained manganese and fluorine but was not manganese difluoride (cf. Engelbrecht and Grosse <sup>1</sup>). The yield of this substance was too small to allow it to be identified with certainty but the author regards it as manganese trifluoride.

*Preparation of iodine oxytrifluoride.* The brown liquid left in the reaction vessel consisted of unchanged iodine pentafluoride containing dissolved iodine oxytrifluoride, mixed with potassium fluoride and the dioxide and difluoride of manganese. This liquid was filtered through a fritted-glass filter and the filtrate was evaporated to dryness, leaving crude iodine oxytrifluoride. This recrystallised from fresh boiling iodine pentafluoride as white needles from which the mother-liquor was removed by decantation, and the excess of iodine pentafluoride by evaporation under a vacuum at room temperature for 1 hr. (Found: I, 63.9; F, 28.2. Calc. for IOF<sub>3</sub>: I, 63.6; F, 28.5%).

*Preparation of iodyl fluoride.* Iodine oxytrifluoride was heated to 110° in a stream of dry nitrogen. The crystals fell to a white powder, and elsewhere in the apparatus iodine pentafluoride collected. To remove the last traces of the latter, the solid was kept at 110°, the vessel being subjected to continuous exhaustion for 1 hr. The residue of iodyl fluoride was a fine white powder (Found: I, 71.5; F, 10.5. Calc. for IO<sub>2</sub>F: I, 71.3; F, 10.7%).

*Analytical methods.* Manganese trioxyfluoride was first hydrolysed with water in a Polythene flask to permanganic acid and hydrogen fluoride, and the manganese determined by titrating the resulting solution with standard potassium oxalate solution. The oxyfluorides of iodine were decomposed by water to iodic acid and hydrogen fluoride. The iodine was then determined by acidification, addition of potassium iodide, and titration of the liberated iodine with standard sodium thiosulphate solution. Fluorine was determined by the methods of Willard and Winter <sup>3</sup> and Offerman <sup>4</sup> and as lead chlorofluoride.

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<sup>3</sup> Willard and Winter, *Ind. Eng. Chem. Analyt.*, 1933, **5**, 7.

<sup>4</sup> Offerman, *Z. angew. Chem.*, 1890, **3**, 615; cf. Adolph, *J. Amer. Chem. Soc.*, 1915, **37**, 2500.

## 488. 5-Nitro- and 5-Amino-2-benzylbenziminazole.

By B. N. FEITELSON and R. ROTHSTEIN.

2-BENZYL-4 : 5-DIHYDROGLYOXALINE (I), theophylline, 8-benzyltheophylline, and 5-nitro-(II; X = NO<sub>2</sub>) and 5-amino-2 : 3-dialkylindoles (II; X = NH<sub>2</sub>) are known <sup>1</sup> to be capable of preventing the rise in blood-pressure normally obtained on introduction of a vasoconstrictor in dogs. It appeared of interest therefore to examine the effect on blood-pressure of the benziminazole analogue (III; X = H) of compound (I), and of 2-benzyl-5-nitro-(III; X = NO<sub>2</sub>) and 5-amino-2-benzyl-benziminazole (III; X = NH<sub>2</sub>), which show certain structural similarities with the above-mentioned theophylline and indole derivatives.

2-Benzyl-5-nitrobenziminazole (III; X = NO<sub>2</sub>) was prepared by addition of nitric-sulphuric acid to a sulphuric acid solution of 2-benzylbenziminazole. Potassium nitrate in sulphuric acid failed to effect nitration, whereas the addition of a nitric acid suspension of 2-benzylbenziminazole to sulphuric acid, as in Bamberger's preparation <sup>2</sup> of 5-nitrobenziminazole, gave a benzyldinitrobenziminazole. The orientation of the nitro-group in the product (III) was confirmed by the identity of this substance with that obtained by synthesis, albeit in low yield, from 4-nitro-*o*-phenylenediamine and phenylacetic acid. Catalytic hydrogenation in the presence of Raney nickel provided the corresponding amine (III; X = NH<sub>2</sub>).

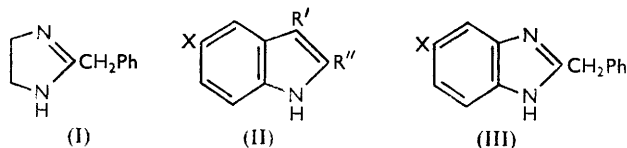
The dinitration product is 5-nitro-2-*p*-nitrobenzylbenziminazole since it is also obtained from 4-nitro-*o*-phenylenediamine and *p*-nitrophenylacetic acid. It is noteworthy that this reaction proceeded more smoothly and in higher yield than that with phenylacetic acid.

<sup>1</sup> Hager, Krantz, and Harmon, *J. Amer. Pharm. Assoc.*, 1953, **42**, 36; Shaw and Woolley, *J. Amer. Chem. Soc.*, 1952, **74**, 2948; 1953, **75**, 1877.

<sup>2</sup> Bamberger, *Annalen*, 1893, **273**, 303.

The same 5-nitro-2-*p*-nitrobenzylbenziminazole was also obtained by nitration of 2-4'-nitrobenzylbenziminazole.

Preliminary biological examination indicated that 5-amino-2-benzylbenziminazole (III; X = NH<sub>2</sub>) caused a greater depression of arterial blood-pressure than the unsubstituted



compound (III; X = H) when administered intravenously in rabbits, whilst the 5-nitro-derivative (III; X = NO<sub>2</sub>) proved too sparingly soluble for examination by this route.

*Experimental.*—2-Benzylbenziminazole. *o*-Phenylenediamine (5.4 g.), phenylacetic acid (6.8 g.), and 4*N*-hydrochloric acid (100 ml.) were heated under reflux for 7 hr. The mixture was cooled and made alkaline, and the precipitated solids were collected. The product recrystallised from benzene as needles (8.1 g., 72%), m. p. 187°. 2-Benzylbenziminazole hydrochloride formed needles (from dilute hydrochloric acid), m. p. 175° (Found: Cl, 14.7. C<sub>14</sub>H<sub>13</sub>N<sub>2</sub>Cl requires Cl, 14.5%).

2-Benzyl-5-nitrobenziminazole. (a) To 2-benzylbenziminazole (5.7 g.), dissolved in concentrated sulphuric acid (50 ml.) at 0°, was added dropwise, with cooling and stirring, a mixture of concentrated nitric acid (1.6 ml.) and concentrated sulphuric acid (2.3 ml.) and stirring was continued for 1 hr. The mixture was poured on crushed ice, and the precipitated sticky solid was collected. This was taken up in ethanol, the solvent removed, and the residue, dissolved in anhydrous ethanol, neutralised with alcoholic sodium hydroxide. After removal of mineral salts, the solution was saturated with hydrogen chloride. On cooling, the solution deposited 2-benzyl-5-nitrobenziminazole hydrochloride (3.1 g.), m. p. 186–188°. Recrystallisation from 80 volumes of absolute alcohol yielded needles (2.5 g.), m. p. 191°.

(b) 4-Nitro-*o*-phenylenediamine (5.1 g.), phenylacetic acid (4.6 g.), and 4*N*-hydrochloric acid (50 ml.) were heated under reflux for 5 hr. The dark solids (5.2 g.) which had separated were removed and the filtrate was heated under reflux for 6 hr., whereafter a further quantity of product (1.6 g.) was removed. The combined solids (6.8 g.) were purified by dissolution in 20% sodium hydroxide solution and precipitation by mineral acid. This operation was repeated and the product recrystallised twice from aqueous ethanol, to give a small quantity of 2-benzyl-5-nitrobenziminazole, white needles, m. p. 184° (Found: C, 65.9; H, 4.4; N, 17.2. C<sub>14</sub>H<sub>11</sub>O<sub>2</sub>N<sub>3</sub> requires C, 66.4; H, 4.4; N, 16.2%). The hydrochloride, needles (from alcohol), had m. p. 192° alone or in admixture with the specimen obtained by nitration (Found: Cl, 11.9. C<sub>14</sub>H<sub>12</sub>O<sub>2</sub>N<sub>3</sub>Cl requires Cl, 12.2%).

5-Amino-2-benzylbenziminazole dihydrochloride. 2-Benzyl-5-nitrobenziminazole (0.86 g.) in ethanol (50 ml.) was hydrogenated in the presence of Raney nickel. After removal of the catalyst, the solution was taken to dryness, the residue dissolved in absolute ethanol (15 ml.) and the solution saturated with hydrogen chloride. The product (0.85 g.), m. p. 206–207°, which separated, was collected and recrystallised from methanol, to yield 5-amino-2-benzylbenziminazole dihydrochloride (0.65 g.), m. p. 207° (Found: C, 56.8; H, 5.2; N, 13.6. C<sub>14</sub>H<sub>15</sub>N<sub>3</sub>Cl<sub>2</sub> requires C, 56.7; H, 5.1; N, 14.2%).

5-Nitro-2-*p*-nitrobenzylbenziminazole. (a) A mixture of 2-benzylbenziminazole (5 g.) and nitric acid (*d* 1.41; 20 ml.) was added portionwise, with stirring and cooling in ice-salt, to concentrated sulphuric acid (20 ml.). Stirring was continued for 1 hr., the mixture was poured on crushed ice, and the precipitated solids were collected. The dried material was taken up in hot absolute alcohol and neutralised by alcoholic sodium hydroxide, and the filtrate concentrated to small volume. On cooling, a yellow crystalline product (2.8 g.), m. p. 219–220°, was obtained. After 3 recrystallisations from alcohol the m. p. rose to 227–228° (Found: C, 56.6; H, 3.4; N, 18.8; O, 21.4. C<sub>14</sub>H<sub>10</sub>O<sub>4</sub>N<sub>4</sub> requires C, 56.4; H, 3.4; N, 18.8; O, 21.4%). No hydrochloride could be obtained from this product.

(b) 4-Nitro-*o*-phenylenediamine (7.6 g.), *p*-nitrophenylacetic acid<sup>3</sup> (9 g.), and 4*N*-hydrochloric acid (90 ml.) were heated under reflux for 24 hr. and left overnight. The resulting

<sup>3</sup> Vogel, "Practical Organic Chemistry," Longmans, 1951, p. 723.

crystals were collected, washed with water, ground with sodium carbonate solution to remove unchanged acid, and dried, to give 11 g. of product, m. p. 219°. Recrystallisation from alcohol yielded 2-benzyl-4':5-dinitrobenzimidazole (7.8 g.), m. p. 227—228°, alone or in admixture with the product described above. The acid mother-liquors, on neutralisation, yielded unchanged diamine (2.3 g.), and from the alkaline extract of the crude product 4-nitrophenyl-acetic acid (2.3 g.) was recovered.

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### 489. *m*-Hydrazinostyrene.

By C. L. ARCUS and R. E. SCHAFFER.

In an investigation of the reactivity of groups attached to macromolecules<sup>1</sup> a monomer was required containing the hydrazino-group and the vinyl group; *m*-hydrazinostyrene has therefore been prepared.

*m*-Nitrostyrene is stated to be formed from *m*-nitrocinnamic acid, quinoline, and copper powder in 55% yield,<sup>2</sup> but we obtained yields of only 14 and 15%. Accordingly, preparation by dehydration of  $\alpha$ -methyl-*m*-nitrobenzyl alcohol was investigated. Boiling with acetic anhydride-sulphuric acid is reported by Smets and Reckers<sup>3</sup> to give a 70% yield of *m*-nitrostyrene. However, we found that: (a) such treatment, with subsequent dilution and washing with water, gave  $\alpha$ -methyl-*m*-nitrobenzyl acetate in good yield; (b) direct distillation gave a little acetate, and a gum; and (c) use, as in (a), of acetic acid in place of the anhydride, yielded a mixture of acetate and unchanged alcohol.

Marvel and his co-workers<sup>4</sup> have prepared *m*-nitrostyrene in 25% yield by thrice heating  $\alpha$ -methyl-*m*-nitrobenzyl alcohol with phosphoric oxide in benzene and distillation in steam. It is more satisfactory to heat the benzyl alcohol with excess of phosphoric acid for a short time at above 100°, a 45% yield of *m*-nitrostyrene being obtained.

*m*-Nitrostyrene has been reduced to *m*-aminostyrene by stannous chloride and hydrochloric acid<sup>5</sup> and by tin and hydrochloric acid (giving 41% yield);<sup>6</sup> Wiley and Smith,<sup>7</sup> who used zinc and hydrochloric acid, obtained 84% of a polymer of the hydrochloride.

Reduction by hydrazine hydrate and Raney nickel<sup>8</sup> gave a 12% yield and by stannous chloride and ethanolic hydrochloric acid a 48% yield, both of monomer.

Diazotisation of *m*-aminostyrene proceeded smoothly. Attempted reduction with sodium hydrogen sulphite gave sulphur-containing products (cf. ref. 9); however, reduction of the diazonium chloride solution with stannous chloride and hydrochloric acid gave *m*-hydrazinostyrene in 39% yield.

*Experimental*.—M. p.s are corrected.

*m*-Nitroacetophenone<sup>10</sup> (75 g.), reduced by Lund's method<sup>11</sup> with aluminium isopropoxide [from aluminium (6.3 g.) and propan-2-ol (256 ml.)], gave  $\alpha$ -methyl-*m*-nitrobenzyl alcohol [44 g.; from benzene-light petroleum (b. p. 60—80°)], m. p. 62°, and further crops (17 g.), m. p. 59—61°.

*Dehydration*. (a)  $\alpha$ -Methyl-*m*-nitrobenzyl alcohol (6.3 g.), acetic anhydride (25 ml.), and

<sup>1</sup> Arcus, J., 1949, 2732; *J. Polymer Sci.*, 1952, **8**, 365.

<sup>2</sup> *Org. Synth.*, 1953, **33**, 62.

<sup>3</sup> Smets and Reckers, *Rec. Trav. chim.*, 1949, **68**, 983.

<sup>4</sup> Marvel, Overberger, Allen, and Saunders, *J. Amer. Chem. Soc.*, 1946, **68**, 736.

<sup>5</sup> Komppa, Dissertation, Helsingfors, 1893; Beilstein, Hauptwerk, **12**, 1187.

<sup>6</sup> Matsui, *J. Soc. Chem. Ind. Japan*, 1942, **45**, Suppl., 437; *Chem. Abs.*, 1950, **44**, 9187.

<sup>7</sup> Wiley and Smith, *J. Amer. Chem. Soc.*, 1948, **70**, 2295.

<sup>8</sup> Balcom and Furst, *ibid.*, 1953, **75**, 4334.

<sup>9</sup> Kharasch, May, and Mayo, *J. Org. Chem.*, 1938, **3**, 175; Kharasch, Schenk, and Mayo, *J. Amer. Chem. Soc.*, 1939, **61**, 3092.

<sup>10</sup> *Org. Synth.*, Coll. Vol. II, 1st Edn., p. 434; Morgan and Watson, *J. Soc. Chem. Ind.*, 1936, **55**, 29T.

<sup>11</sup> Lund, *Ber.*, 1937, **70**, 1520.

sulphuric acid ( $d$  1.84; 15 drops) were refluxed for 10 min., and then poured into water (500 ml.); the oil which separated was extracted with ether, and the extract was washed with water, dried ( $K_2CO_3$ ), and distilled. The product (5.2 g.), b. p. 176—180°/16 mm., on redistillation yielded  $\alpha$ -methyl-*m*-nitrobenzyl acetate, b. p. 112.5—114.5°/0.8 mm.,  $n_D^{25}$  1.5260 (Found: C, 58.1; H, 5.4; N, 6.95.  $C_{10}H_{11}O_4N$  requires C, 57.4; H, 5.3; N, 6.7%).

(b)  $\alpha$ -Methyl-*m*-nitrobenzyl alcohol (5.00 g.) and phosphoric acid ("AnalaR";  $d$  1.74; 40 ml.) were heated with mechanical stirring to 125° (bath temp.) during 12 min. and kept at that temperature for 1 min. The mixture was poured into water (500 ml.), and the yellow oil which separated was extracted with benzene. The extract was washed with water, dried ( $K_2CO_3$ ), and, after the addition of quinol (0.05 g.), distilled. The yield of *m*-nitrostyrene,  $n_D^{25}$  1.5810, b. p. of main fraction 81°/1.2 mm., was 45%.

*Reduction.* *m*-Nitrostyrene (6.95 g.), hydrazine hydrate (5.8 g.), and ethanol (70 ml.) were heated for 1 hr. at 70°, Raney nickel (approx. 0.5 g.) being added at 30°, and then boiled for 10 min., a little more catalyst having been added to decompose excess of hydrazine. The mixture was filtered and evaporated, and a benzene solution of the product extracted with 1.5*N*-hydrochloric acid; the extract, together with aqueous washings, was made alkaline (3*N*-sodium hydroxide) and extracted with benzene. The extract was washed with brine, dried ( $K_2CO_3$ ), and distilled. It yielded *m*-aminostyrene (0.67 g.; 12%), b. p. 68—72°/0.8 mm. (Found: C, 79.25; H, 7.7; N, 11.85. Calc. for  $C_8H_9N$ : C, 80.6; H, 7.6; N, 11.75%).

*m*-Nitrostyrene (7.65 g.), stannous chloride dihydrate (46 g.), concentrated hydrochloric acid (46 ml.), and ethanol (23 ml.) were refluxed for 15 min., cooled, then poured into aqueous sodium hydroxide (68 g. in 230 ml.). The oil which separated from the steam-distillate was extracted with benzene, the extract was dried ( $K_2CO_3$ ), and the benzene distilled after the addition of a little quinol; distillation of the product under oxygen-free nitrogen gave *m*-aminostyrene (2.93 g.; 48%), b. p. 68°/0.8 mm.

To *m*-aminostyrene (3.04 g.) hydrochloric acid ( $d$  1.18; 31 ml.) was added at <0°; to the resulting slurry sodium nitrite (1.81 g.) in water (14 ml.) was added dropwise at <3°. After 5 min. stannous chloride dihydrate (11.5 g.) in hydrochloric acid (10 ml.) was added dropwise at 0—2°, and, after a further 10 min., the tin double salt was collected and dissolved in water (50 ml.) at 35°. The solution was poured into aqueous sodium hydroxide (8 g. in 40 ml.) in the presence of benzene (30 ml.) at 0°. The mixture was shaken, then separated and the aqueous layer further extracted. The combined extracts were washed once with water and dried ( $Na_2SO_4$ ), and after the addition of quinol (15 mg.) the benzene was distilled off. The product, on distillation under oxygen-free nitrogen, yielded *m*-hydrazinostyrene (1.32 g.), b. p. 104—105°/0.3 mm.,  $n_D^{25}$  1.6200 (Found: C, 69.75; H, 7.4; N, 19.45.  $C_8H_{10}N_2$  requires C, 71.65; H, 7.5; N, 20.9%). It (0.55 g.) was dissolved in aqueous acetic acid containing sodium acetate, and benzaldehyde (0.44 g.) in ethanol was added; the whole was heated on a steam-bath for 1 min., cooled, and filtered. The product (0.88 g.) gave benzaldehyde *m*-vinylphenylhydrazone, needles (from ethanol), m. p. 123.5° (Found: C, 81.1; H, 6.5; N, 12.2.  $C_{15}H_{14}N_2$  requires C, 81.05; H, 6.35; N, 12.6%).

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## 490. *Pyrolysis of Phenylmercuric Iodide.*

By M. COWPERTHWAIT and E. WARHURST.

CARTER, CHAPPELL, and WARHURST<sup>1</sup> showed that thermal decompositions of organo-mercury compounds fall into two classes. Class I is characterised by frequency factors in the "normal" range (*i.e.*,  $A = 10^{13}$ — $10^{14}$  sec.<sup>-1</sup>) and activation energies identifiable with values of the dissociation energy,  $D_1$ , of the first mercury-carbon bond. Dimethyl- and diethyl-mercury and phenylmercuric chloride and bromide are of this class. Class II is characterised by high frequency factors ( $10^{15}$ — $10^{16}$  sec.<sup>-1</sup>) and activation energies approximately equal to the sum of the first and second bond-dissociation energies (*i.e.*,

<sup>1</sup> Carter, Chappell, and Warhurst, *J.*, 1956, 106.

$D_1 + D_2$ ). Di-*n*- and di*iso*-propylmercury and diphenylmercury are of this class. These characteristics are suggested to arise from a difference in the nature of the first step in the thermal decomposition.<sup>1,2,3</sup> In members of class I only one bond is broken, producing two fragments, whereas in those of class II both bonds break simultaneously, giving three fragments.

There is little doubt that an essential requirement (though not the only one; see ref. 1) for class II behaviour is that  $D_2$  should be small. Phenylmercuric iodide is an interesting and critical example for the classification since  $D_2$  [*i.e.*,  $D(\text{Hg-I}) = 8 \pm 1$  kcal. mole<sup>-1</sup>] is very small and approximately equal to  $D_2$  for the  $\cdot\text{Hg}\cdot\text{CH}_3$  and  $\cdot\text{Hg}\cdot\text{C}_2\text{H}_5$  radicals.

*Experimental.—Materials.* Phenylmercuric iodide, precipitated by adding an equimolar amount of B.D.H. diphenylmercury to red "AnalaR" mercuric iodide dissolved in hot acetone, was washed with chloroform and hot acetone and recrystallised (m. p. 271°) from hot acetone. The carrier gas, nitrogen, was purified as described by Morantz and Warhurst.<sup>4</sup> Toluene was purified as previously described.<sup>1</sup>

*Apparatus and technique.* As previously described,<sup>1,5</sup> a circulating stream of carrier gas introduces known partial pressures of toluene and substrate into a hot reaction vessel for known contact times. In the pyrolysis of phenylmercuric iodide all the substances issuing therefrom, except for a small fraction of the mercuric iodide, were condensed from the carrier gas stream in a U-tube at  $-80^\circ$ . Determinations of the percentage decomposition were based on the amounts of undecomposed phenylmercuric iodide. Free mercury and mercurous iodide were removed as insoluble residues by treating the contents of the U-tube with hot acetone. Acetone and toluene were completely removed by careful evaporation. All remaining hydrocarbons were dissolved in the minimum of ice-cold carbon tetrachloride. Mercuric iodide was then removed as the soluble complex  $\text{K}_2\text{HgI}_4$  by treatment with aqueous potassium iodide, leaving only undecomposed phenylmercuric iodide.

*Results.* Pyrolyses were done within the following range of conditions: total pressure =  $8.5 \pm 0.5$  mm.; time of contact = 0.23–0.45 sec.; decomposition = 12–84%; toluene : PhHgI ratio = 19–43; toluene pressure =  $3.0 \pm 0.2$  mm. Velocity constants were determined twice at 575°, twice at 598°, three times at 624°, and twice at 651°. They were calculated from  $k = (1/\tau) \ln [100/(100 - f)]$ , where  $\tau$  is the time of contact (sec.) and  $f$  is the percentage decomposition. The activation energy obtained from the Arrhenius plot by the method of least squares is  $E = 63 \pm 2$  kcal. mole<sup>-1</sup> and the frequency factor  $A = 10^{15.7}$  sec.<sup>-1</sup>. The average deviation from the least-squares line was 0.01, and the maximum deviation 0.03, in units of  $\log_{10} k$ . We estimate a limit of accuracy of  $\pm 2$  kcal. mole<sup>-1</sup> mainly from our general experience of this technique and the small number of experiments.

*Discussion.*—The determination of  $k$  from values of  $f$  from the amounts of undecomposed substrate is valid whatever the mechanism after the first dissociative step, provided that no free-radical intermediate reacts appreciably with the substrate. This seems very improbable because pyrolyses of phenylmercuric chloride and bromide and diphenylmercury, investigated in more detail than the present one, are free from such complications. Comparisons of estimates of the heats of likely reactions between radical intermediates and these four substrates indicate that such reactions should be even less likely in the phenylmercuric iodide system. We do not consider that there can be an appreciable heterogeneous contribution to the decomposition since pyrolyses of other mercury alkyls at temperatures lower than the one used here are predominantly homogeneous.

Our value of  $10^{15.7}$  sec.<sup>-1</sup> for the frequency factor for the decomposition of phenylmercuric iodide is large and lies in the class II range.<sup>1</sup> Our value for the activation energy,  $63 \pm 2$  kcal. mole<sup>-1</sup>, lies in the possible range of values for  $D_1 + D_2$  obtained<sup>6</sup> from thermochemistry and spectroscopy [based on  $D(\text{Ph-H}) = 97.8$ :  $D_1 + D_2 = 63.2 \pm 3$ ;

<sup>2</sup> Chilton and Gowenlock, *Trans. Faraday Soc.*, 1953, **49**, 1451; 1954, **50**, 824.

<sup>3</sup> Pritchard, *J. Chem. Phys.*, 1956, **25**, 267.

<sup>4</sup> Morantz and Warhurst, *Trans. Faraday Soc.*, 1955, **51**, 1375.

<sup>5</sup> Gowenlock, Polanyi, and Warhurst, *Proc. Roy. Soc.*, 1953, *A*, **218**, 269.

<sup>6</sup> Pritchard, Ph.D. Thesis, Manchester, 1951.



$D_2 = 8 \pm 1$ ;  $D_1 = 55.2 \pm 4$ : based on  $D(\text{Ph-H}) = 102$ ;  $D_1 + D_2 = 67.4 \pm 3$ ;  $D_2 = 8 \pm 1$ ;  $D_1 = 59.4 \pm 4$  kcal. mole<sup>-1</sup>], so we conclude that this compound is a genuine member of class II.

It appears that the interdependence of the extension energies of the Hg-Ph and Hg-I bonds of the molecule is such that the potential-energy surface for the various nuclear configurations possesses a pronounced "diagonal basin" (ref. 1). Consequently the most probable mode of decomposition is that corresponding to simultaneous stretching of both bonds yielding three fragments in a single step. The very low value of  $D_2$  contributes to this effect.

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#### 491. The C-Benzylolation of Phenols by Use of Sodium Hydride.

By F. M. ELKOBASI and W. J. HICKINBOTTOM.

It is known that a benzyl group can be introduced directly into the *ortho*-position of a phenol by reaction of a suspension of its sodium salt in benzene or toluene with benzyl chloride.<sup>a</sup> In the course of other work, it was observed that the suspension of the sodium salt can be obtained more cleanly and conveniently if sodium hydride, suspended in toluene, was used instead of sodium as described by Claisen.

#### EXPERIMENTAL

The following general conditions were found to be satisfactory. The phenol (1 mole) diluted with specially dried toluene (200 c.c.) was added dropwise to a warmed and stirred suspension of finely powdered sodium hydride (1 mole) in toluene. The addition of the phenol required about 1 hr. and the reaction was completed by stirring and heating the mixture under reflux for another hour. The result was a thick pasty suspension of the sodium salt of the phenol.

To this suspension, benzyl chloride (1 mole), diluted with some toluene, was added steadily. With *ortho*-substituted phenols, it was more satisfactory to use 1.2—1.3 moles of benzyl chloride. As the reaction proceeded, the suspension became thinner owing to the formation of sodium chloride; it was completed by 2 hours' heating under reflux after all the chloride had been

Substituted phenol	B. p./mm.	M. p.	Found (%)		Formula	Calc. (%)		Derivative, m. p.
			C	H		C	H	
2-Benzyl <sup>a</sup>	170°/15	—	84.8	6.5	C <sub>13</sub> H <sub>12</sub> O	84.7	6.6	Phenylurethane, 117°
2 : 4-Dibenzyl <sup>b</sup>	260°/15	48—49°	87.1	6.7	C <sub>20</sub> H <sub>18</sub> O	87.6	6.6	α-Naphthylurethane, 148—149°
2 : 6-Dibenzyl <sup>c</sup>	240°/15	—	87.6	6.5	C <sub>20</sub> H <sub>18</sub> O	87.6	6.6	α-Naphthylurethane, 168°
2-Benzyl-6-methyl <sup>d</sup>	143°/1	52	84.5	7.1	C <sub>14</sub> H <sub>14</sub> O	84.8	7.1	<i>p</i> -Bromo-compound, 66°
2-Benzyl-4-methyl <sup>e</sup>	186°/15	36	84.8	7.4	C <sub>14</sub> H <sub>14</sub> O	84.8	7.1	Phenylurethane, 146°
2-Benzyl-4-chloro	204°/15	53	{ 71.4 Cl, 16.2	{ 5.0 Cl, 16.2	{ C <sub>13</sub> H <sub>11</sub> OCl Cl, 16.2	{ 71.4 Cl, 16.2	{ 5.0 Cl, 16.2	{ Phenylurethane, 165°

<sup>a</sup> Claisen (*Annalen*, 1925, **442**, 238) gives m. p. 21°, b. p. 171°/13 mm. (phenylurethane, m. p. 117.5—118°). <sup>b</sup> Prepared from *p*-benzylphenol. Short and Stewart (*J.*, 1929, 558) give for 2 : 4-dibenzylphenol, b. p. 252—254°/10 mm. (α-naphthylurethane, m. p. 144°). <sup>c</sup> Prepared from *o*-benzylphenol. Short and Stewart (*loc. cit.*) give for 2 : 6-dibenzylphenol, b. p. 237.5—238°/10 mm. (α-naphthylurethane, m. p. 165—166°). <sup>d</sup> Schorigin (*Ber.*, 1925, **58**, 2033) gives b. p. 187—188°/15 mm., m. p. 51—52°; Huston, Swartout, and Wardwell (*J. Amer. Chem. Soc.*, 1930, **52**, 4484) give *p*-bromo-compound, m. p. 63—64°. <sup>e</sup> Claisen (*Annalen*, 1925, **442**, 241) gives b. p. 180—182°/12 mm. (phenylurethane, m. p. 144.5—145°); Huston and Lewis (*J. Amer. Chem. Soc.*, 1931, **53**, 2379) give m. p. 35—36°.

added and then storage overnight. The clear toluene solution was washed with water, dried, and distilled to remove solvent. The residual oil was dissolved in 5 times its volume of methylalcoholic potassium hydroxide (Claisen's solution) and freed from neutral matter by repeated

extractions with light petroleum. The residual alkaline solution was concentrated to remove alcohol, then acidified, and the phenols were taken up in ether.

The Table summarises the constants of phenols prepared in this way; the yields were generally 80—90%.

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#### 492. *Alkaloids of Rauwolfia Species. Part IV.*<sup>1</sup> *Rauwolfia cambodiana* Pierre.

By D. A. A. KIDD.

ALTHOUGH no detailed chemical study had been published, *Rauwolfia cambodiana*<sup>2</sup> was included by Maison<sup>3</sup> in a group reported to be free from reserpine. Since that alkaloid is an almost invariable constituent of *Rauwolfia* species, a quantity of *R. cambodiana* roots was extracted with methanol, subsequent fractionation of the extract being carried out by a method similar to that used by Hochstein, Murai, and Boegemann<sup>4</sup> for *R. heterophylla*.

The greater part of the alkaloids (3.4% of powdered root) separated in the weakly basic fraction, which was shown by paper electrophoresis to contain two major components. As already indicated<sup>1</sup> one of these is reserpine, which was isolated by chromatography and identified by direct comparison with an authentic specimen. The second, which gave a strongly fluorescent brownish-yellow spot and presumably corresponded to that described by Dillemann and Paris,<sup>5</sup> had properties (see Table) resembling those described for *isoreserpiline*, already encountered in *R. canescens*,<sup>6</sup> *R. vomitoria*,<sup>7</sup> and *R. schueli*.<sup>8</sup> Some minor differences between the infrared spectra of the *cambodiana* alkaloid and that published for *isoreserpiline*<sup>6</sup> were evidently due to the different method of determination, since a direct comparison of its methanesulphonate with an authentic sample of *isoreserpiline* methanesulphonate established their identity.

From the mother-liquors of *isoreserpiline*, a third alkaloid was isolated as its di-*p*-toluoyl-L-tartrate but the quantity of free base obtained from it was too small for further identification.

The strongly basic fraction, of which unusually little was obtained, gave a complex electrophoresis pattern. A strongly fluorescing blue spot corresponding in mobility with that of serpentine was present, together with a strong greenish spot distinct from that of reserpine and five or six weaker spots. Spotting with concentrated nitric acid gave a red colour in the position expected for ajmaline; this alkaloid normally separates with the weaker bases but the persistence of traces in the strongly basic fraction has been previously noted with *R. sellowii*.

For pharmacological purposes, it was important to know more accurately the content of reserpine in *R. cambodiana*, and the method of isolation used was unsuitable for this purpose. The countercurrent distribution method<sup>9</sup> described for *R. serpentina* and *R. vomitoria* gave inadequate resolution between reserpine and *isoreserpiline* in the small number of transfers involved, and an alternative method of extraction was therefore adopted, which had earlier been found reliable for the quantitative isolation of reserpine

<sup>1</sup> Part III, *Chem. and Ind.*, 1957, 1013.

<sup>2</sup> Craib, *Florae Siamensis Enumeratio*, 1939, 2, 428.

<sup>3</sup> Maison, *Lancet*, 1955, 268, 866.

<sup>4</sup> Hochstein, Murai, and Boegemann, *J. Amer. Chem. Soc.*, 1955, 77, 3551.

<sup>5</sup> Dillemann and Paris, *Compt. rend.*, 1957, 244, 1254.

<sup>6</sup> Stoll, Hofmann, and Brunner, *Helv. Chim. Acta*, 1955, 38, 270.

<sup>7</sup> Poisson and Goutarel, *Bull. Soc. chim. France*, 1956, 1703.

<sup>8</sup> Iacobucci and Deulofeu, *J. Org. Chem.*, 1957, 22, 94.

<sup>9</sup> Kidd and Scott, *J. Pharm. Pharmacol.*, 1957, 9, 176.

in other species. The content of reserpine in powdered whole *R. cambodiana* root containing 11% of moisture was 0.01%.

*Experimental.*—All melting points were determined in evacuated capillaries, and infrared spectra in potassium bromide discs.

*Extraction.* Finely ground roots (2 kg., containing 11% of moisture), collected during late summer in Bangkok, Thailand, were percolated slowly with cold methanol (40 l.) and finally extracted with boiling methanol (15 l.). The combined extracts were evaporated *in vacuo* and the soft residue poured into 5% acetic acid (1 l.) to give a turbid mixture which was defatted with light petroleum and filtered through kieselguhr. The chilled filtrate was basified with ammonia (s.g. 0.88) below 10° and the bulky precipitate collected. Extraction of a small additional quantity from the liquor with chloroform gave a combined weakly basic fraction (68.25 g.; 3.4% on powdered root). Further basification of the aqueous phase with sodium hydroxide followed by chloroform extraction gave a strongly basic fraction (0.3 g.). The aqueous layer, after adjustment of pH, was treated with saturated ammonium reineckate solution and a reineckate fraction obtained (18.75 g.).

*Purification of weak bases.* A part (30 g.) of the weakly basic fraction was repeatedly extracted with cold chloroform, and the insoluble residue adsorbed on kieselguhr and then extracted with 1*N*-acetic acid. Evaporation of the chloroform extract gave fraction *A* (6.65 g.) and basification of the acid phase an amorphous precipitate [fraction *B* (12.6 g.)]. Paper electrophoresis in 3*N*-acetic acid (400 v) of fraction *B* gave only one, yellowish-brown fluorescent spot, which was also obtained from fraction *A* together with a yellowish-green spot corresponding to reserpine.

Chromatography of fraction *A* on alumina (150 g.) in benzene, elution with benzene-acetone (9 : 1), and crystallisation of the amorphous residues from methanol containing a little water, gave flat prisms of *isoreserpiline*, m. p. 211—212° (0.29 g.),  $[\alpha]_D^{21} - 111^\circ$  ( $c = 2.1$  in chloroform) (Found: N, 6.9. Calc. for  $C_{23}H_{28}O_5N_2$ : N, 6.8%).

Treatment of the mother-liquors with di-*p*-toluoyl-*L*-tartaric acid gave a crystalline di-*p*-toluoyl-*L*-tartrate, minute prisms (from aqueous methanol), m. p. 213° (decomp.) (Found: C, 63.6; H, 7.2; N, 4.7%). The free base had m. p. 226—227° and is so far unidentified. Pale mauve colours were obtained in the Keller and the Fröhde reaction.

Subsequent elution of the column with benzene-acetone (3 : 1) gave a small quantity of reserpine, m. p. and mixed m. p. 277—278°; its infrared spectra, electrophoretic mobility, and Fröhde colour reactions also agreed with those of authentic material.

Fraction *B* was insoluble in the usual chromatographic solvents and no crystalline substance could be isolated from it.

*isoreserpiline methanesulphonate.* This salt, prepared in methanol, separated when ether was added to incipient turbidity and was recrystallised from the same solvent. The needles, which were dried at 100°/0.01 mm., had m. p. and mixed m. p. 294—295° (decomp.). This value is higher than that (282—284°) recorded by Stoll, Hofmann, and Brunner,<sup>6</sup> but the difference must be due to the conditions of measurement since the same value was obtained on the pure sample provided by Dr. Hofmann. Our sample had infrared and ultraviolet spectra indistinguishable from those of authentic material (Found: N, 5.2. Calc. for  $C_{23}H_{28}O_5N_2 \cdot CH_3 \cdot SO_3H$ : N, 5.5%).

	M.p.	$[\alpha]_D$ in $CHCl_3$	$\lambda_{max}$ . (log E)
<i>isoreserpiline</i> .....	211—212° <sup>6,8</sup>	-102°, <sup>7</sup> -112° <sup>8</sup>	229, 304 (4.56, 4.02) <sup>6</sup>
<i>R. cambodiana</i> Alkaloid .....	211—212°	-111°	230, 303 (4.59, 4.05)

*Quantitative isolation of reserpine.* Concentrated methanolic extract of powdered root (500 g.) was adsorbed on kieselguhr, washed with cold water (3 × 1 l.), and extracted with 15% acetic acid. The acid extract was repeatedly shaken with chloroform, the combined chloroform layers were washed with 10% aqueous sodium carbonate (100 ml.) and water and evaporated to dryness, and the residue (0.87 g.) chromatographed on alumina in benzene. Elution with benzene-chloroform (3 : 1) and crystallisation of the residues gave reserpine, m. p. 274—275°,  $[\alpha]_D^{19} - 122^\circ$  (0.052 g., 0.01% yield on powdered root).

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specimen of *isoreserpiline* methanesulphonate, and the Directors of May & Baker Ltd. for permission to publish this Note.

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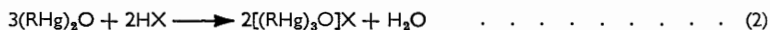
### 493. *Trismethylmercurisulphonium Nitrate and Dichromate.*

By D. GRDENIĆ and B. MARKUŠIĆ.

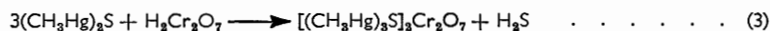
It was reported recently that trismethylmercurioxonium fluoroborate was obtained by neutralization of an alcoholic solution of methylmercuric hydroxide with fluoroboric acid,<sup>1</sup> and the reaction was interpreted<sup>2</sup> as addition of methylmercuric fluoroborate to methylmercuric oxide.<sup>2</sup> It was shown that methylmercuric hydroxide, prepared by Slotta and Jacobi's method, was a mixture of oxide and hydroxide, so that the pure oxide was obtained by dehydration of the crude material. This class of oxonium compounds can be prepared by addition:



or by partial neutralization:



The present note deals with the application of reaction (2) to the preparation of the sulphonium compounds. When a solution of bismethylmercuric sulphide in benzene is shaken with an aqueous solution of chromium(vi) oxide or potassium dichromate, yellow crystalline trismethylmercurisulphonium dichromate is deposited immediately and quantitatively. This is insoluble in benzene, ether, or chloroform, and scarcely soluble in



ethanol, but recrystallizes from water. Double decomposition with lead nitrate in ethanol gives the sulphonium nitrate which crystallizes in colourless needles. Both the nitrate and the dichromate are fairly stable except that they are slightly sensitive to light.

Bismethylmercuric sulphide was prepared previously<sup>4</sup> by the action of hydrogen sulphide on methylmercuric chloride in alcohol.<sup>4</sup> We found this method unsatisfactory and elaborated a convenient preparation by use of sodium sulphide.

*Experimental.*—*Trismethylmercurisulphonium dichromate.* An aqueous solution (40 ml.) of chromium(vi) oxide (1.6 g.) was added to a solution of bismethylmercuric sulphide (5 g.) in warm benzene (150 ml.) and the mixture shaken. The brownish-yellow *dichromate* was collected (filtrate I), washed with water, and recrystallized from boiling water (600 ml.; 4 or 5 times). The golden-yellow leaflets (5 g.) decompose at 200°, are stable in air but darken on exposure to light (Found: Hg, 76.7; Cr, 6.6; S, 3.9.  $\text{C}_6\text{H}_{18}\text{O}_7\text{S}_2\text{Cr}_2\text{Hg}_6$  requires Hg, 76.7; Cr, 6.6; S, 4.0%). Solutions in cold and hot water give reactions for dichromate and chromate respectively.

The benzene component of the filtrate (I) contained insignificant quantities of sulphur and bismethylmercuric sulphide. The aqueous part did not contain mercury but gave the reaction for sulphate ion which resulted from the oxidation of hydrogen sulphide. According to the equation (3), each mol. of bismethylmercuric sulphide evolves 1/3 mol. of hydrogen sulphide, which on its turn uses 8/9 mol. of chromium(vi) oxide for complete oxidation to sulphuric acid. The corresponding quantity of chromium(III) ions was found by analysis in the remaining aqueous solution, so reaction (3) is established.

*Trismethylmercurisulphonium nitrate.* Trismethylmercurisulphonium dichromate (1.5 g.,

<sup>1</sup> Grdenić, XVth Internat. Congr. Pure Appl. Chem., 1957, Congress Handbook, Vol. II, p. 112.

<sup>2</sup> Grdenić and Zado, *Croat. Chem. Acta*, 1957, **29**, 425.

<sup>3</sup> Slotta and Jacobi, *J. prakt. Chem.*, 1929, **120**, 249.

<sup>4</sup> Hilpert and Ditmar, *Ber.*, 1913, **46**, 3738; A. Perret and R. Perrot, *Helv. Chim. Acta*, 1933, **16**, 848.

1 mol.) and lead nitrate (0.32 g., 2 mol.) were moistened with a little ethanol and thoroughly mixed by means of a pestle and mortar (1 hr.). The yellow solid was collected and extracted (small Buchner funnel) with ethanol (60 ml.). The filtrate was evaporated *in vacuo*, the crystalline residue (1.2 g.) dissolved in ethanol, the solution filtered, and the filtrate treated with twice its volume of dry ether and cooled overnight. Colourless needles of the *nitrate* were formed, very soluble in water or ethanol, decomposing at 160° (Found: NO<sub>3</sub>, 8.4; Hg, 81.1. C<sub>3</sub>H<sub>9</sub>O<sub>3</sub>NSHg<sub>3</sub> requires NO<sub>3</sub>, 8.4; Hg, 81.2%) (the nitrate ion was determined in aqueous solution by means of nitron acetate).

*Bismethylmercuric sulphide.* A warm solution of methylmercuric bromide (10 g.) in acetone (200 ml.) was divided into two equal parts. A solution of sodium sulphide (20 g. of nonahydrate in 250 ml. of ethanol) was added gradually to one part until the white precipitate just dissolved. To this solution, which apparently contains sodium methylmercuric sulphide, the second part of the methylmercuric bromide solution was added and the mixture cooled. The white crystalline precipitate of bismethylmercuric sulphide was collected (7.7 g.), and recrystallized from benzene (200 ml.) as leaflets, m. p. 144° (lit., 143°), becoming grey on long exposure to light.

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#### 494. *The Hunsdiecker Reaction in the Pyrazole Series.*

By E. G. BRAIN and I. L. FINAR.

IN an attempt to discover a relation between the orientation of pyrazolecarboxylic acids and their behaviour in the Hunsdiecker reaction ( $R\cdot CO_2Ag + Br_2 \longrightarrow RBr + AgBr + CO_2$ ), several silver pyrazolecarboxylates were subjected to the action of anhydrous bromine in carbon tetrachloride. Silver 1-phenylpyrazole-4-carboxylate gave 4-bromo-1-phenylpyrazole with some 4-bromo-1-*p*-bromophenylpyrazole. The latter compound was shown to be the normal product of further bromination of 4-bromo-1-phenylpyrazole.<sup>1</sup>

Silver 4-bromo-1:3-dimethylpyrazole-5-carboxylate yielded 4:5-dibromo-1:3-dimethylpyrazole, but silver 4-bromo-1:5-dimethylpyrazole-3-carboxylate was unaffected by bromine under the same conditions. Two other pyrazole-3-carboxylates which were investigated also failed to give the Hunsdiecker reaction. Silver 1:4-dimethylpyrazole-3-carboxylate was unaffected by the reagent: silver 1:5-diphenylpyrazole-3-carboxylate was brominated to give silver 4-bromo-1:5-diphenylpyrazole-3-carboxylate, on which an excess of bromine had no further action.

From this limited number of experiments it appears that the carboxyl group in position 3 of the pyrazole nucleus is resistant to the Hunsdiecker reaction.

*Experimental.*—Bromine and carbon tetrachloride were dried over phosphoric oxide. Silver salts were precipitated from neutral aqueous solutions of the ammonium salts by the addition of silver nitrate solution. With one exception they were dried for several hours at 120°.

*4-Bromo-1-phenylpyrazole.* Silver 1-phenylpyrazole-4-carboxylate (4.35 g., 1 mol.) was suspended in boiling carbon tetrachloride (30 c.c.), and bromine (1 mol.) in carbon tetrachloride was slowly added. This was rapidly decolorised except for the last drops. The solution was then filtered from silver bromide, and the filtrate was washed with dilute aqueous ammonia, then with water; when dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated, this gave 4-bromo-1-phenylpyrazole<sup>1</sup> (2.0 g., 59%), m. p. 70—72°. Pure 4-bromo-1-phenylpyrazole (0.5 g., 15%) was obtained from this by chromatography on alumina with benzene–light petroleum and had m. p. and mixed m. p. 81.5—82.5°. No other compound was isolated by this method or by fractional crystallisation

<sup>1</sup> Balbiano, *Gazzetta*, 1889, **19**, 128.

from dilute ethanol. The infrared absorption spectrum of the crude product in  $\text{CCl}_4$  and  $\text{CS}_2$  showed bands due to both 4-bromo-1-phenylpyrazole and 4-bromo-1-*p*-bromophenylpyrazole.

*4-Bromo-1-p-bromophenylpyrazole.* 1-*p*-Bromophenylpyrazole was treated with 1 mol. of bromine in chloroform. The product, twice recrystallised from dilute ethanol, gave elongated platelets, m. p. 84.5—85°, identical with dibromo-1-phenylpyrazole obtained by brominating 4-bromo-1-phenylpyrazole<sup>1</sup> (mixed m. p.; infrared spectra).

*4 : 5-Dibromo-1 : 3-dimethylpyrazole.* Silver 4-bromo-1 : 3-dimethylpyrazole-5-carboxylate<sup>2</sup> was dried by washing it with dry methanol and then heating it at 60—70° for 3 hr. since it decomposed at 120°. When treated with bromine in the usual way the silver salt decolorised about 1 mol. of bromine. The mixture was worked up as for 4-bromo-1-phenylpyrazole but the residue on evaporation was an oil. Pure 4 : 5-dibromo-1 : 3-dimethylpyrazole was obtained by chromatography on alumina with light petroleum, and had m. p. 74—75° (50%) (Found: N, 10.8; Br, 63.2.  $\text{C}_8\text{H}_8\text{N}_2\text{Br}_2$  requires N, 11.05; Br, 63.0%).

*Action of bromine on silver 1 : 5-diphenylpyrazole-3-carboxylate.* The silver salt was obtained from the acid<sup>3</sup> by the usual method, and when treated with bromine in carbon tetrachloride by the previous method gave no residue on evaporation of the filtrate. The reaction residue was boiled again with excess of bromine solution for 90 min. and again filtered off, etc. This filtrate also left no residue on evaporation. Free 4-bromo-1 : 5-diphenylpyrazole-3-carboxylic acid was liberated from the insoluble reaction residue by refluxing it with 1 : 1 3N-hydrochloric acid-ethanol. The mixture was filtered, the filtrate evaporated, and after recrystallisation from dilute ethanol crystals, m. p. 221—222.5°, were obtained. The mixed m. p. with the bromo-acid (m. p. 223°) obtained by brominating 1 : 5-diphenylpyrazole-3-carboxylic acid in carbon tetrachloride was not depressed (Found: C, 56.3; H, 3.1; N, 8.3; Br, 23.3.  $\text{C}_{16}\text{H}_{11}\text{O}_2\text{N}_2\text{Br}$  requires C, 56.0; H, 3.2; N, 8.2; Br, 23.3%).

*Action of bromine on silver 4-bromo-1 : 5-dimethylpyrazole-3-carboxylate.*<sup>2</sup> When this silver salt was treated with bromine under the usual conditions no decolorisation was observed after 6 hours' refluxing, and the filtrate left no residue on evaporation. A small amount of 4-bromo-1 : 5-dimethylpyrazole-3-carboxylic acid, m. p. and mixed m. p. 194°, was recovered from the silver salt by means of hydrochloric acid-ethanol.

*Action of bromine on silver 1 : 4-dimethylpyrazole-3-carboxylate:* 1 : 4-Dimethylpyrazole-3-carboxylic acid<sup>4</sup> was obtained by hypobromite oxidation of 3-acetyl-1 : 4-dimethylpyrazole.<sup>5</sup> The silver salt was treated by the usual method. No residue was obtained on evaporating the filtrate, and unchanged 1 : 4-dimethylpyrazole-3-carboxylic acid, m. p. and mixed m. p. 165—169°, was recovered from the silver salt.

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<sup>2</sup> von Auwers and Beyhan, *J. prakt. Chem.*, 1935, **143**, 259.

<sup>3</sup> Claisen and Beyer, *Ber.*, 1887, **20**, 2186.

<sup>4</sup> von Auwers and Ungemach, *Ber.*, 1933, **66**, 1208.

<sup>5</sup> Brain and Finar, *J.*, 1957, 2356.