## The Reactions of Some 1,4-Diketones with 2,4-Dinitrophenylhydrazine

By T. D. Binns and R. Brettle

The 1,4-diketones MeCO·CH<sub>2</sub>·CH<sub>2</sub>·COMe, MeCO·CH<sub>2</sub>·CH(CO<sub>2</sub>Et)·COMe, and

 $MeCO \cdot CH(CO_2Et) \cdot CH(CO_2Et) \cdot COMe$  each react with 2,4-dinitrophenylhydrazine to give a mixture of the corresponding N-(2,4-dinitroanilino)pyrrole and the bis-2,4-dinitrophenylhydrazone.

In connection with other studies,<sup>1</sup> we have investigated the reaction of diethyl  $\alpha \alpha'$ -diacetylsuccinate (I; R = R' = CO<sub>2</sub>Et) with 2,4-dinitrophenylhydrazine. This 1,4-diketone has been reported to react with arylhydr-

## ${\sf MeCO}{\boldsymbol{\cdot}}{\sf CHR}{\boldsymbol{\cdot}}{\sf CHR}{\boldsymbol{\cdot}}{\sf COMe}~(I)$

azines <sup>2,3</sup> to give products which have been formulated either as *N*-anilinopyrroles <sup>2</sup> or as *N*-aryldihydropyridazines.<sup>3</sup> The related diketone acetonylacetone (I; R = R' = H) has frequently been characterised as its bis-2,4-dinitrophenylhydrazone,<sup>4a</sup> but two mono-2,4-dinitrophenylhydrazones have also been reported,<sup>5,6</sup> and it seemed necessary to reinvestigate these also.

The pale yellow crystalline solid obtained in high yield from diethyl  $\alpha\alpha'$ -diacetylsuccinate (I;  $R = R' = CO_2Et$ ) and Brady's reagent was shown by the analytical data and its infrared spectrum, which showed a band at 3270 cm.<sup>-1</sup> (NH), to be either diethyl 1-(2,4-dinitro-anilino)-2,5-dimethylpyrrole-3,4-dicarboxylate (II;  $R = R' = CO_2Et$ ) or diethyl 1-(2,4-dinitrophenyl)-1,2-dihydro-3,6-dimethylpyridazine-4,5-dicarboxylate (III;  $R = R' = CO_2Et$ ). The nuclear magnetic resonance (n.m.r.) spectrum of this product showed the equivalence of the two ring-methyl groups and of the two ester-ethyl groups, and hence indicated that the product is the N-

<sup>1</sup> T. D. Binns and R. Brettle, preceding Paper.

<sup>2</sup> L. Knorr, Annalen, 1886, 236, 290.

<sup>3</sup> S. Kawai and S. Tanaka, Bull. Chem. Soc. Japan, 1960, **33**, 674.

anilinopyrrole (II;  $R = R' = CO_2Et$ ). This structure was confirmed by the synthesis of (II;  $R = R' = CO_2Et$ ) by the reaction of the corresponding aminopyrrole (IV;  $R = CO_2Et$ )<sup>7</sup> with 1-fluoro-2,4-dinitrobenzene.



Surprisingly, this reaction only took place when the reactants were heated for 20 hours at 100° in the absence of a solvent. The *N*-aminopyrrole structure for (IV;  $R = CO_2Et$ ), one of the products obtained by the reaction of diethyl  $\alpha \alpha'$ -diacetylsuccinate (I;  $R = R' = CO_2Et$ ) with hydrazine,<sup>7</sup> has been fully established. This compound (IV;  $R = CO_2Et$ ) with nitrous acid gives diethyl 2,5-dimethylpyrrole-3,4-dicarboxylate.<sup>8</sup> On hydrolysis and decarboxylation it gives the *N*-aminopyrrole (IV; R = H),<sup>7</sup> which on hydrogenation gives *cis*-1-amino-2,5-dimethylpyrrolidine, identical with

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  - 7 C. Bülow, Ber., 1902, 35, 4311.
  - <sup>8</sup> C. Bülow and E. Klemann, Ber., 1907, 40, 4749.

<sup>&</sup>lt;sup>4</sup> A. I. Vogel, "Practical Organic Chemistry," 3rd edn., Longmans, London, 1956, (a) p. 347; (b) p. 638. Z

<sup>&</sup>lt;sup>5</sup> F. Nerdel, E. Henkel, R. Kayser, and G. Kannelbley, J. prakt. Chem., 1956, (4), **3**, 153. <sup>6</sup> L. Jones, C. K. Hancock, and R. B. Seligman, J. Org. Chem.,

the compound obtained by the reduction of the product of nitrosation of *cis*-2,5-dimethylpyrrolidine.<sup>9</sup> Its n.m.r. spectrum shows a single peak due to the two ringmethyl groups, which supports its formulation as the symmetrical N-aminopyrrole (IV;  $R = CO_2Et$ ). A second, isomeric product from the reaction of diethyl aa'-diacetylsuccinate and hydrazine had been provisionally formulated <sup>10</sup> as diethyl 1,4-dihydro-3,6-dimethylpyridazine-4,5-dicarboxylate (V) on the basis of its infrared spectrum, which shows absorption at 3275 (NH) and at 1690 and 1725 cm.<sup>-1</sup> (two different ester groups). We have now examined the n.m.r. spectrum of this product, which confirms that it is the 1,4-dihydropyridazine (V). The n.m.r. spectrum shows absorption due to the two different ring-methyl groups (singlets, three protons each;  $\tau$  7.68 and 7.88), which must both be attached to carbon atoms not bearing hydrogen atoms since the signals are in each case unsplit, the NH group (broad singlet,  $\tau 2.13$ ), and the single proton at C-4, which has a similar chemical shift to the protons in the ester-methylene groups (unsymmetrical quartet, 5 protons, centred on  $\tau$  5.83; the proton at C-4 has  $\tau$ ca. 5.65). The absorptions due to the two ester-ethyl groups are indistinguishable, as are those due to the two ester-methyl groups in the related compound dimethyl 1,4-dihydropyridazine-3,6-dicarboxylate.<sup>11</sup> A minor, extremely insoluble product from the reaction of Brady's reagent with diethyl  $\alpha \alpha'$ -diacetylsuccinate appears to be the corresponding bis-2,4-dinitrophenylhydrazone.

In view of these results we prepared the compound obtained previously<sup>3</sup> from diethyl aa'-diacetylsuccinate and 4-nitrophenylhydrazine, and formulated as an N-aryl-1,4-dihydropyridazine.<sup>3</sup> Its n.m.r. spectrum shows the equivalence of the two ring-methyl groups and of the two ester-ethyl groups, so this compound is diethyl 2,5-dimethyl-1-(4-nitroanilino)pyrrole-3,4-dicarboxylate (II;  $R = R' = CO_2Et$ ; no *o*-nitro-group in the anilino-group).

The compound, m. p. 110-111°, obtained 6 from the reaction of acetonylacetone (I; R = R' = H) with 2,4-dinitrophenylhydrazine in pyridine, was confirmed as the mono-2,4-dinitrophenylhydrazone of acetonylacetone. It gave correct analytical values, showed absorption at 1700 cm.<sup>-1</sup> (CO), and had an n.m.r. spectrum in agreement with this structure. However, the minor product from the reaction of acetonylacetone with Brady's reagent, m. p. 174-177°, was shown to be 1-(2,4-dinitroanilino)-2,5-dimethylpyrrole (II;  $\mathbf{R} =$ R' = H) and not a mono-2,4-dinitrophenylhydrazone as previously formulated.<sup>5</sup> The analytical results pointed to the cyclic structure, which was also supported by the ultraviolet spectrum, which was different from that of the mono-2,4-dinitrophenylhydrazone of acetonylacetone. The n.m.r. spectrum showed only a single peak due to the two methyl groups, thus ruling out an

*N*-aryldihydropyridazine structure. The structural assignment was confirmed by a synthesis of (II; R =R' = H) by the reaction of (IV; R = H) with 1-fluoro-2,4-dinitrobenzene. The N-aminopyrrole (IV; R = H) was prepared by using benzyloxycarbonylhydrazine and acetonylacetone as intermediates.<sup>9</sup>

Since the major product from diethyl aa'-diacetylsuccinate and Brady's reagent is the 1-(2,4-dinitroanilino)pyrrole (II;  $R = R' = CO_2Et$ ) but the major product from acetonylacetone is the bis-2,4-dinitrophenylhydrazone, it was of interest to study the reaction of the monoester diketone (I; R = H,  $R' = CO_2Et$ ) with Brady's reagent. In this case two major products resulted; with either a 1:1 or 1:2 ratio of diketone to 2,4-dinitrophenylhydrazine, they were obtained in roughly equal amounts. One product was rapidly precipitated at  $0^{\circ}$ , but the other remained in the supernatant solution. The insoluble product, which was the bis-2,4-dinitrophenylhydrazone of the diketone (I;  $R = H, R' = CO_2Et$ ), was unstable in contact with acid, and gave a mixture containing the second product and 2,4-dinitrophenylhydrazine. This product was shown to be ethyl 1-(2,4-dinitroanilino)-2,5-dimethylpyrrole-3-carboxylate (II; R = H,  $R' = CO_2Et$ ) by its i.r., u.v., and n.m.r. spectra. The bisphenylhydrazone of acetonylacetone eliminates phenylhydrazine in acidic conditions, and gives a compound formulated as the N-aminopyrrole (II; R = R' = H; no NO<sub>2</sub> groups in the anilino-group).<sup>12</sup> It is of interest that the bis-2,4dinitrophenylhydrazone of (II; R = H,  $R' = CO_{0}Et$ ) behaves similarly. It seems probable that the N-(2,4dinitroanilino) pyrroles (II; R = R' = H and R = R' =CO<sub>2</sub>Et) from the other two 1,4-diketones (I; R = R' =H and  $R = R' = CO_2Et$ ) arise in a similar way through the bis-2,4-dinitrophenylhydrazones, and that the presence of the ester groups facilitates the reaction. thus accounting for the increasing amounts of the N-(2,4-dinitroanilino) pyrroles as the number of ester groups in the 1,4-diketone structure (I) is increased.

## EXPERIMENTAL

For general directions see the preceding Paper.<sup>1</sup> A few n.m.r. spectra were measured on an A.E.I. RS-2 instrument in CDCl<sub>3</sub> or CCl<sub>4</sub> using tetramethylsilane as internal standard.

Reaction of Diethyl aa'-Diacetylsuccinate with Hydrazine.---Diethyl 1-amino-2,5-dimethylpyrrole-3,4-dicarboxylate (IV;  $\mathrm{R}=\mathrm{R}^{\prime}=\mathrm{CO_{2}Et}$  ), m. p. 102° (lit., 7 102–103°), and diethyl 1,4-dihydro-3,6-dimethylpyridazine-4,5-dicarboxylate (V), m. p.  $66-67^{\circ}$  (lit.,  $^{7}68-69^{\circ}$ ), were both obtained from the reaction of diethyl aa'-diacetylsuccinate with hydrazine hydrate, using the method of Bülow.<sup>7</sup> The n.m.r. spectrum of (IV;  $R = R' = CO_2Et$ ) showed a peak at  $\tau$  7.7 (2 CH<sub>3</sub>).

Diethyl 1-(2,4-Dinitroanilino)2,5-dimethylpyrrole-3,4-dicarboxylate (II;  $R = R' = CO_2Et$ ).—(a) A warm solution of diethyl  $\alpha \alpha'$ -diacetylsuccinate <sup>13</sup> (12.9 g., 1 mol.) in ethanol

<sup>9</sup> C. G. Overberger, L. C. Palmer, B. S. Marks, and N. R. Byrd, J. Amer. Chem. Soc., 1955, 77, 4100. <sup>10</sup> W. L. Mosby, J. Chem. Soc., 1957, 3997.

<sup>&</sup>lt;sup>11</sup> M. Avram, G. R. Bedford, and A. R. Katritzky, Rec. Trav. chim., 1963, 82, 1053.

<sup>&</sup>lt;sup>12</sup> A. Smith, Annalen, 1896, 289, 310, footnote 4 (p. 311); A. Smith and H. N. McCoy, Ber., 1902, 35, 2169.
<sup>13</sup> J. A. Bilton and R. P. Linstead, J. Chem. Soc., 1937, 922.

(50 ml.) was added to a solution of 2,4-dinitrophenylhydrazine (9.9 g., 1 mol.) in ethanol (200 ml.) containing sulphuric acid (7.5 ml.). The precipitate which had formed after 1 hr. at room temperature was collected, and on recrystallisation from ethanol gave the N-(2,4-dinitroanilino)pyrrole (11.0 g.), m. p. 162—164°,  $\lambda_{max}$ . 235, 258, and 320 mµ ( $\epsilon$  22,220, 17,850, and 15,330) (Found: C, 51.5; H, 4.8; N, 13.5. C<sub>18</sub>H<sub>20</sub>N<sub>4</sub>O<sub>8</sub> requires C, 51.5; H, 4.8; N, 13.3%). The n.m.r. spectrum showed bands at ( $\tau$ -values): 7.7 (ring CH<sub>3</sub>; singlet, 6 protons); 8.64 (ester CH<sub>3</sub>: triplet, 6 protons); 5.65 (ester CH<sub>2</sub>; quartet, 4 protons). The Nacetyl-derivative, obtained with acetic anhydride in pyridine, had m. p. 131—133° after recrystallisation (charcoal) from ethanol (Found: C, 52.3; H, 4.5; N, 12.0. C<sub>20</sub>H<sub>22</sub>N<sub>4</sub>O<sub>9</sub> requires C, 51.9; H, 4.8; N, 12.1%).

(b) Diethyl 1-amino-2,5-dimethylpyrrole-3,4-dicarboxylate (2.54 g., 1 mol.) and 1-fluoro-2,4-dinitrobenzene (1.0 g., 0.5 mol.) were heated under nitrogen at 100° for 20 hr. The mixture was then cooled and extracted with chloroform. The extract was washed with 10N-hydrochloric acid, 2Nsodium hydroxide, and water, dried, treated with charcoal, and the chloroform distilled. Recrystallisation of the residue from ethanol gave the N-(2,4-dinitroanilino)pyrrole (0.34 g.), m. p. and mixed m. p. 162—163°.

Diethyl 2,5-Dimethyl-1-(4-nitroanilino)pyrrole-3,4-dicarboxylate.—Diethyl  $\alpha\alpha'$ -diacetylsuccinate <sup>13</sup> (1·7 g., 1 mol.) was dissolved, by warming, in a mixture of acetic acid (14 ml.) and water (6 ml.), and the solution added to 4-nitrophenylhydrazine (0·7 g., 0·7 mol.) in a mixture of acetic acid (17 ml.) and water (8 ml.). The solution was kept at room temperature for 1 hr. and at 0° for 12 hr. and then diluted with water. The resultant precipitate (1·4 g.) was collected, and after recrystallisation from ethanol (charcoal) gave the N-(4-nitroanilino)pyrrole, m. p. 120— 122° (lit.,<sup>3</sup> 122—123°),  $v_{max}$  1690 cm.<sup>-1</sup>,  $\lambda_{max}$  335 m $\mu$  ( $\varepsilon$ 14,210) (Found: C, 57·8; H, 5·6; N, 11·3. C<sub>18</sub>H<sub>21</sub>N<sub>3</sub>O<sub>6</sub> requires C, 57·6; H, 5·6; N, 11·2%). The n.m.r. spectrum showed bands at ( $\tau$ -values): 7·7 (ring CH<sub>3</sub>; singlet, 6 protons); 8·6 (ester CH<sub>3</sub>; triplet, 6 protons); 5·6 (ester CH<sub>2</sub>; quartet, 4 protons).

*Acetonylacetone* Mono-2,4-dinitrophenylhydrazone.—The mono-2,4-dinitrophenylhydrazone of acetonylacetone, m. p. 110—111° (from carbon tetrachloride), was prepared from acetonylacetone and 2,4-dinitrophenylhydrazine in pyridine (lit.,<sup>6</sup> m. p. 116—117°),  $\nu_{max}$ . 1700 cm.<sup>-1</sup> (C=O),  $\lambda_{max}$ . 362 mµ ( $\epsilon$  20,250) [acetone 2,4-dinitrophenylhydrazone has  $\lambda_{max}$ . 360 mµ ( $\epsilon$  20,890) <sup>14</sup>]. The n.m.r. spectrum showed bands at ( $\tau$ -values): 7.88 and 7.73 (2 CH<sub>3</sub>; singlets, each 3 protons); 7.16 (2 CH<sub>2</sub>; triplet, 4 protons).

1-Amino-2,5-dimethylpyrrole.—1-Amino-2,5-dimethylpyrrole, m. p. 49—50° (lit.,<sup>9</sup> 51·5—52°), was prepared by the method of Overberger, Palmer, Marks, and Byrd.<sup>9</sup>

1-(2,4-Dinitroanilino)-2,5-dimethylpyrrole (II; R = R' = H).—(a) Acetonylacetone (2.0 g., 1 mol.) was added to a solution of 2,4-dinitrophenylhydrazine (3.3 g., 1 mol.) in methanol (155 ml.) containing 10N-hydrochloric acid (3.5 ml.). The precipitate which had formed after 1 hr. at room temperature was collected on a filter, and washed with cold methanol, and the residual solid was then extracted with hot methanol (2 × 100 ml.). Distillation of the methanol from the extract gave a solid (120 mg.), which on recrystal-

<sup>14</sup> J. D. Roberts and C. Green, J. Amer. Chem. Soc., 1946, **68**, 214.

lisation from methanol (charcoal) gave l-(2,4-dinitroanilino)-2,5-dimethylpyrrole, m. p. 174—177° (lit.,<sup>5</sup> 175°),  $\lambda_{max}$  220 and 328 mµ ( $\epsilon$  13,360 and 11,310) (Found: C, 52·3; H, 4·8; N, 20·2. C<sub>12</sub>H<sub>12</sub>N<sub>4</sub>O<sub>4</sub> requires C, 52·2; H, 5·2; N, 20·3%). The n.m.r. spectrum showed a peak at  $\tau$  7·9 (2 CH<sub>3</sub>).

(b) 1-Amino-2,5-dimethylpyrrole (1·1 g., 1 mol.) and 1-fluoro-2,4-dinitrobenzene (1·0 g., 0·54 mol.) were heated under nitrogen at 100° for 20 hr. The mixture was then cooled and extracted with chloroform. The combined extracts were washed with 10n-hydrochloric acid, 2nsodium hydroxide, and water, dried, treated with charcoal, and the chloroform distilled. Recrystallisation of the residue alternately from methanol and chloroform eventually gave the N-(2,4-dinitroanilino)pyrrole (0·21 g., 15%), m. p. and mixed m. p. 175—177°.

Reaction of Ethyl  $\alpha$ -Acetonylacetoacetate (I; R = H,  $R' = CO_2Et$ ) with Brady's Reagent.—Ethyl  $\alpha$ -acetonylacetoacetate <sup>15</sup> (0.93 g., 1 mol.) in ethanol (10 ml.) was added rapidly to a cold solution of 2,4-dinitrophenylhydrazine (1.98 g., 2 mol.) in ethanol (40 ml.) containing sulphuric acid (2 ml.). The bis-2,4-dinitrophenylhydrazone (1.15 g.) was precipitated during 0.5 hr. at  $0^{\circ}$  and was collected on a filter and washed with ethanol and water. After drying at 100°/10 mm. it had m. p. 183—189° (softens 178°),  $\nu_{\rm max}$ 1735 cm.<sup>-1</sup> (ester C=O),  $\lambda_{max}$  (CHCl<sub>3</sub>) 359 mµ ( $\epsilon$  42,700) (Found: C, 46.4; H, 4.15; N, 20.6. C<sub>21</sub>H<sub>22</sub>N<sub>8</sub>O<sub>10</sub> requires C, 46.1; H, 4.1; N, 20.5%). The filtrate was diluted with water (100 ml.), and a second precipitate (0.98 g.) formed. This was collected, washed with water until the washings were neutral, and recrystallised (charcoal) from ethanol, to give ethyl 1-(2,4-dinitroanilino)-2,5-dimethylpyrrole-3carboxylate (II; R = H,  $R' = CO_2Et$ ), m. p. 132-133°,  $\nu_{\rm max}$  3310 (NH) and 1700 cm.  $^{-1}$  (ester C=O),  $\lambda_{\rm max}$  258 and 323 mµ (z 13,740 and 12,970) (Found: C, 51.8; H, 4.8; N, 16.0.  $C_{15}H_{16}N_4O_6$  requires C, 51.7; H, 4.6; N, 16.1%). The n.m.r. spectrum showed bands at (7-values): 7.89  $(5-CH_3; \text{ singlet, } 3 \text{ protons}); 7.6 (2-methyl; \text{ singlet, } 3$ protons); 8.64 (ester CH<sub>3</sub>; triplet, 3 protons); 7.6 (2methyl; singlet, 3 protons); 8.64 (ester CH<sub>3</sub>; triplet, 3 protons); 5.7 (ester CH<sub>2</sub>; quartet, 2 protons).

Reaction of Ethyl a-Acetonylacetoacetate Bis-2,4-dinitrophenylhydrazone with Acid.-The bishydrazone (300 mg.), suspended in ethanol (50 ml.) containing sulphuric acid (0.5 ml.), was stirred at room temperature overnight. Chloroform (50 ml.) was then added and the mixture poured into ice-water. The aqueous layer was separated and extracted with chloroform  $(4 \times 10 \text{ ml.})$ . The combined chloroform solutions were dried, and the chloroform was distilled. The residual solid was extracted with chloroform (5 ml.), leaving 2,4-dinitrophenylhydrazine (50 mg.), m. p. 198-200° (lit.,4b 200°). The chloroform-soluble portion was purified by thin-layer chromatography on silica gel G, using 25 imes 25-cm. glass plates with 10% etherbenzene as the developing solvent, and gave the N-(2,4-dinitroanilino)pyrrole (II; R = H,  $R' = CO_2Et$ ) (30 mg.), m. p. and mixed m. p. 132-133°.

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THE UNIVERSITY,

SHEFFIELD 10. [5/1010 Received, September 20th, 1965]

<sup>15</sup> H. B. Stevenson and J. R. Johnson, J. Amer. Chem. Soc., 1937, **59**, 2525.