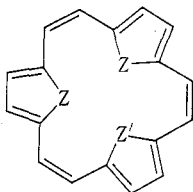


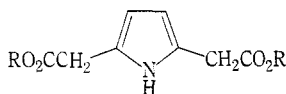
PREPARATION OF PYRROLE-2,5-DIACETIC ACID*

By G. M. BADGER,[†] J. A. ELIX,[†] and G. E. LEWIS[†]

Following the successful syntheses of [18]annulene trisulphide (I; $Z = Z' = S$),¹ [18]annulene trioxide (I; $Z = Z' = O$),² [18]annulene oxide-disulphide (I; $Z = S$, $Z' = O$),³ and [18]annulene dioxide-sulphide (I; $Z = O$, $Z' = S$),⁴ attention has been given in these laboratories to the possible synthesis of analogous compounds in which one or more of the Group VI elements is substituted by an imino grouping. Pyrrole-2,5-diacetic acid (II; $R = H$) was selected as a likely key intermediate for the projected syntheses; and it was obvious that the compound could be obtained by hydrolysis of ethyl pyrrole-2,5-diacetate (II; $R = Et$).



(I)



(II)

Ethyl pyrrole-2,5-diacetate can be prepared from ethyl succinyldiacetate and ammonium acetate,⁵ but this method is suitable only for small-scale preparations. It has been found that ethyl pyrrole-2,5-diacetate may be obtained in much more satisfactory quantities by a method similar to that⁶ used for the synthesis of ethyl *N*-methylpyrrole-2,5-diacetate from *N*-methylpyrrole via ethyl *N*-methylpyrrole-2-acetate, the ethoxycarbonylmethyl side-chains being introduced stepwise by the action of ethyl diazoacetate and copper powder. The diester (II; $R = Et$) then afforded pyrrole-2,5-diacetic acid in reasonable yield when hydrolysed under alkaline conditions.

Although pyrrole-2,5-diacetic acid is an unstable compound, and must accordingly be used as soon as possible after preparation, a satisfactory micro-analysis was obtained. It was further characterized by analysis of its bispiperidinium salt.

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[†] Department of Organic Chemistry, University of Adelaide.

¹ Badger, G. M., Elix, J. A., and Lewis, G. E., *Aust. J. Chem.*, 1965, **18**, 70.

² Badger, G. M., Elix, J. A., and Lewis, G. E., *Aust. J. Chem.*, 1966, **19**, 1221.

³ Badger, G. M., Lewis, G. E., and Singh, U. P., *Aust. J. Chem.*, 1966, **19**, 257.

⁴ Badger, G. M., Lewis, G. E., and Singh, U. P., *Aust. J. Chem.*, 1966, **19**, 1461.

⁵ Willstätter, R., and Bommer, M., *Liebigs Ann.*, 1920, **422**, 15.

⁶ Nenitzescu, C. D., and Solomonica, E., *Ber. dt. chem. Ges.*, 1931, **64**, 1924.

Experimental

Ethyl Pyrrole-2-acetate

This was prepared according to the directions given by Nenitzescu and Solomonica.⁶

Ethyl Pyrrole-2,5-diacetate

Ethyl pyrrole-2-acetate (25 g) was mixed with copper powder (1.0 g) and heated on a boiling water-bath; and during the course of 1 hr ethyl diazoacetate (25 g) was added dropwise to the mixture. The reaction mixture was warmed and stirred for a further 15 min, and the copper powder was then removed by filtration. The filtrate, on being subjected to distillation under reduced pressure, yielded one fraction (6.6 g), b.p. 86–120°/0.6 mm, which consisted mainly of unchanged ethyl pyrrole-2-acetate. From the remaining liquid ethyl pyrrole-2,5-diacetate (8.1 g, 21%) was collected as a pale yellow oil, b.p. 150–155°/0.6 mm. On crystallization from ethanol (charcoal) the compound formed colourless prisms, m.p. 73° (lit.⁵ 74–75°).

Pyrrole-2,5-diacetic Acid

Ethyl pyrrole-2,5-diacetate (5.6 g) was mixed with ethanol (4 ml), water (8 ml), and potassium hydroxide (7 g) and the mixture was heated under reflux for 1 hr. Most of the ethanol was then removed by distillation, and the remaining solution was cooled, acidified, and extracted repeatedly with ether. The ethereal extracts were combined, washed with a small amount of cold water, and dried, and the ether was removed under reduced pressure. The residue was recrystallized from ether/hexane (charcoal) to give *pyrrole-2,5-diacetic acid* (2.3 g, 54%) as colourless needles, m.p. 120.5–121° (dec.) (Found: C, 53.0; H, 5.2; N, 7.6. $C_5H_5NO_4$ requires C, 52.5; H, 4.95; N, 7.65%).

On being allowed to stand, the acid decomposes and the crystals acquire a dark violet colouration. Pyrrole-2,5-diacetic acid was treated with piperidine and thereby formed *bispiperidinium pyrrole-2,5-diacetate* which crystallized from ethanol/ether as pale pink plates, m.p. 156–158° (dec.) (Found: C, 60.9; H, 8.7; N, 11.7; O, 18.5. $C_{18}H_{31}N_3O_4$ requires C, 61.2; H, 8.8; N, 11.9; O, 18.1%).

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