Synthesis of 2-Alkylnaphth[2,1-*d*]oxazole-4,5-diones

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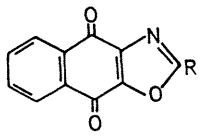
Summary Reaction of 3-acylamino-1,2-naphthoquinones with piperidine gives 4-piperidino-3-acylamino-1,2-naphthoquinones which on treatment with aluminum oxide undergo an internal addition–elimination reaction to yield 2-alkylnaphth[2,1-*d*]oxazole-4,5-diones.

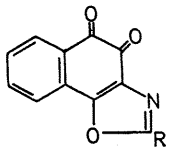
THE preparation of the linear 2-alkylnaphth[2,3-*d*]oxazole-4,5-diones (I) has been reported, and their use as antituberculosis agents and fungicides has been patented.[1–5] However the synthesis of the angular 2-alkylnaphth[2,1-*d*]oxazole-4,5-diones (II) has not been reported.

We report that 2-alkylnaphth[2,1-*d*]oxazole-4,5-diones are conveniently prepared from the corresponding 3-acylamino-1,2-naphthoquinones (III) by a two step procedure. For example, the addition of piperidine to 3-acetamino-1,2-naphthoquinone (IIIa)[6] followed by air oxidation gave 4-piperidino-3-acetamino-1,2-naphthoquinone (IVa). Subjection of (IVa) to chromatography on Woelm neutral aluminium oxide effected an internal addition of the amide carbonyl, probably in the enol form, to the 3,4-double bond of the 1,2-naphthoquinone along with the elimination of piperidine to give 47%† of 2-methylnaphth[2,1-*d*]oxazole-4,5-dione (IIa), m.p. 269—271°. The structural assignment

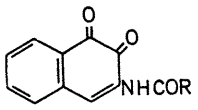
† Overall yield of pure 2-alkylnaphth[2,1-*d*]oxazole-4,5-dione (II) obtained from the corresponding 3-acylamino-1,2-naphthoquinone (III).



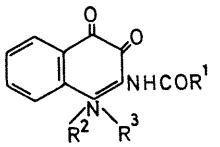
(I)



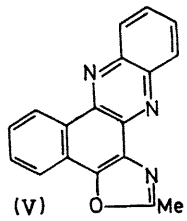
(IIa) R=Me
(IIb) R=$C_6H_{11}[CH_2]_3$-



(IIIa) R=Me
(IIIb) R=$C_6H_{11}[CH_2]_3$-



(IVa) R^1=Me, R^2R^3=$[CH_2]_5$
(IVb) R^1=$C_6H_{11}[CH_2]_3$-, R^2R^3=$[CH_2]_5$
(IVc) R^1=Me, R^2=C_5H_9-, R_3=H



(V)

was based on the elemental analysis, the i.r. spectrum which showed quinone carbonyl absorption at 1685 cm.$^{-1}$ and showed the absence of NH and amide carbonyl absorption, and the u.v. spectrum which showed λ_{max} (MeOH) 207 ($\epsilon \times 10^{-3}$ 21·5), 257 (31·6), 264 (32·2), 33 (1·7) and 417 (1·8)nm. The latter absorption is typical of 4-alkoxy- or 4-aryloxy-1,2-naphthoquinones. Additional evidence for the presence of the 1,2-quinone structure was obtained by conversion of (IIa) into the benz[*a*]phenazine derivative (V), m.p. 226—228° 2-(3′-cyclohexylpropyl)naphth[2,1-*d*]oxazole-4,5-dione (IIb), m.p. 158·5—160° was prepared from (IIIb) in 41% yield† by a procedure similar to that described for the synthesis of (IIa).

The conversion of (IV) into (II) is a reversible reaction. When (IIa) was treated with a chloroform solution of piperidine (IVa) was reformed in good yield. In contrast to (IVa) and (IVb), the adduct (IVc) obtained from 3-acetamino-1,4-naphthoquinone and cyclopentylamine is stable to aluminium oxide.

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