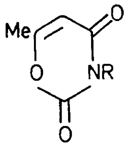
New Syntheses of Some 1,3-Oxazine Derivatives

By SHAMSHAD AHMED, ROY LOFTHOUSE, and GORDON SHAW*
(*School of Chemistry, University of Bradford, Bradford* BD7 1DP)

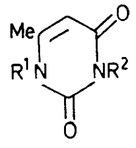
Summary 2,3-Dihydro-6-methyl-1,3-oxazine-2,4-dione has been prepared from *NN*-dimethylurea with either diketen or ethyl acetoacetate and the analogous 6-phenyl oxazine derivative from *NN*-dimethylurea and ethyl benzoyl acetate in acetic acid–acetic anhydride solution; structures of the oxazines were confirmed by ^{13}C n.m.r. spectra and by subsequent conversion with ammonia or amines into substituted uracils.

WHEN a mixture of diketen, and *NN*-dimethylurea in acetic acid solution is warmed to 90° an exothermic reaction occurs, and the cooled solution deposits crystals (>60% of the 1,3-oxazine (Ia) m.p. 243°. The structure of this compound followed from elemental analysis, i.r., m.s. (M^+ 127), ^{1}H n.m.r. δ (ref Me_4Si) 2·19 (Me), 2·44 (NH), and 5·92 (=CH) p.p.m., and ^{13}C n.m.r. The ^{13}C n.m.r. Fourier transform decoupled spectrum of (Ia) in Me_2SO showed five well separated singlets which confirm the presence of five different carbon atoms [chemical shifts 18·59, 100·86, 148·25, 162·54 and 166·44 p.p.m. downfield from Me_4Si of relative intensities 1000 (largest peak), 248, 199, 403 and 145 respectively, assigned to Me,–CH, C·CO·N Me·*C*·O and O·CO·N] whereas a four-membered ring would have C-2 and C-4 identical. The methylated derivative (Ib) (in which tautomerism is not possible) also still shows five singlets plus an extra methyl singlet. The structure assigned to the methyl derivative was confirmed by its conversion into the known 3,6-dimethyluracil (IIa) with ammonia or to 1,3,6-trimethyluracil (IIb) with methylamine. In addition the oxazine (Ia) with hydroxylamine produced 1-hydroxy-6-methyluracil (IIc) m.p. > 300° and in sodium hydroxide solution it underwent self condensation to give a good yield of 6-carboxymethyl-2-hydroxy-4-methyl pyridine (III) identical with an authentic sample.[1] A similar oxazine synthesis does not lead to the unsubstituted oxazine (Ia).[2]

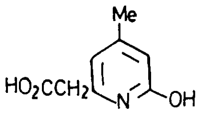
The usefulness of this synthesis is limited by the fact that substituted diketens are not readily available. We now report that the reaction of ethyl acetoacetate with *NN*-dimethylurea or *NN*-diethylurea in acetic acid–acetic anhydride solution produces a good yield of the oxazine (Ia) identical with material produced above. The generality of the reaction was confirmed by the similar reaction of ethyl benzoylacetate and *NN*-dimethylurea in the same solvent to produce the 6-phenyloxazine derivative (IVa) m.p. 240°. The structure of this compound was confirmed by elemental analysis, m.s. (M^+ 189) and by its conversion with ammonia into 6-phenyluracil (IVb).



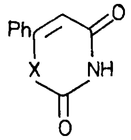
(Ia); R = H
(Ib); R = Me



(IIa); $R^1 = H$, $R^2 = Me$
(IIb); $R^1 = R^2 = Me$
(IIc); $R^1 = OH$, $R^2 = H$



(III)



(IVa); X = O
(IVb); X = NH

(*Received*, 30*th July* 1974; *Com.* 969.)

---

[1] J. N. Collie, *J. Chem. Soc.*, 1897, **71**, (1), 299.
[2] R. N. Lacey, *J. Chem. Soc.*, 1954, 845.