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SOME TRANSFORMATIONS OF 4-CHLOROMETHYL-3,5-DIACETYL-1,4-DIHYDRO-2,6-LUTIDINE AND DERIVED PRODUCTS

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Rearrangements of the dihydropyridines (I; R = OMe and OEt) have recently been described[1-4]. We now report some reactions of the diacetyl analogue (I; R = Me)[5].

By analogy with the esters (I; R = OMe and OEt), treatment of (I; R = Me) with aqueous alcoholic potassium cyanide afforded the expected cyanodihydroazepine (II; R = Me, X = CN), m.p. 151°.

Brief treatment of (I; R = Me) with water containing a small amount of an organic solvent at 100° afforded a compound, $C_{12}H_{16}O_4$*, m.p. 76° (50%). The mother liquors slowly deposited yellow needles, $C_{17}H_{22}O_4N$, m.p. 189° (10%). The latter substance was clearly a dihydropyridine as shown by its U.V. spectrum which strongly resembled that of the starting material. The I.R. and n.m.r. spectra indicated its structure to be (III; R = COMe), further confirmed by the formation of metal chelates, colouration with ferric chloride, conversion into an oxime, and alkaline hydrolysis to the triketone (III; R = H).

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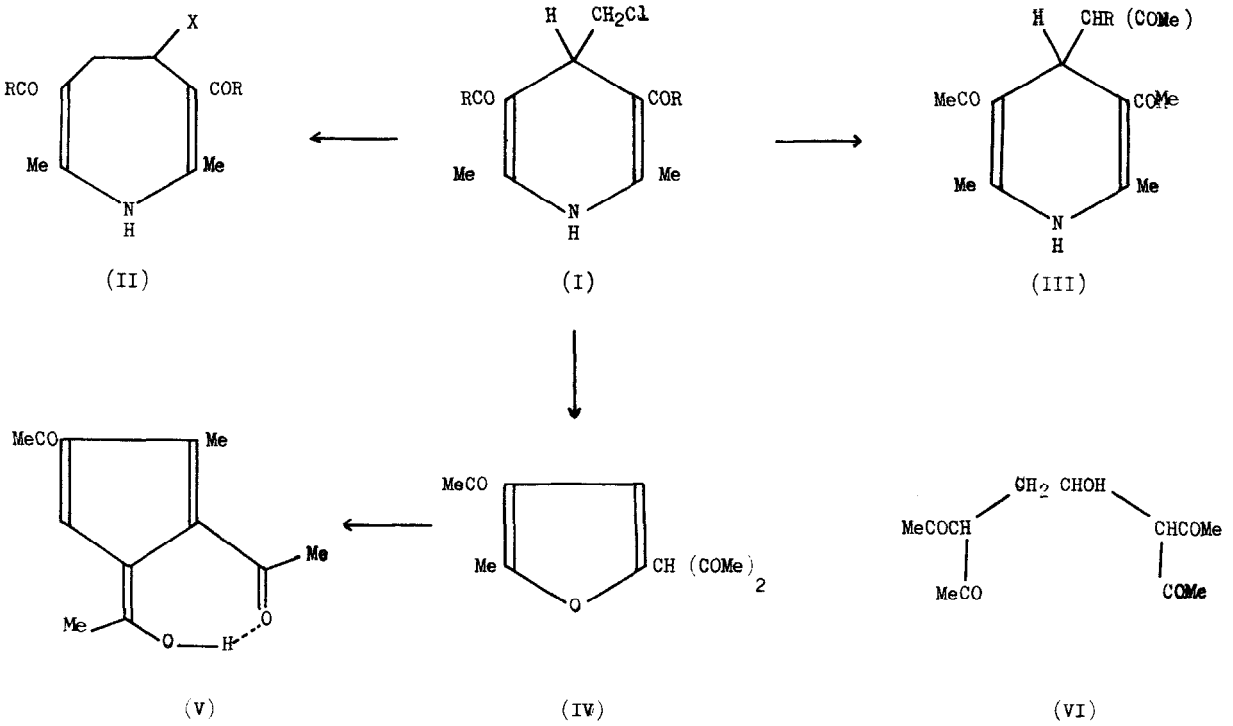
* Satisfactory elemental analyses were obtained for all new compounds.


X
RCO
COR
Me
Me
N
H
H
CH2Cl
CHR (COMe)
MeCO
COMe
MeCOCH
CH2 CHOH
CHCOMe
CH (COMe)2
O
(II)
(I)
(III)
(IV)
(V)
(VI)

The other product, $C_{12}H_{16}O_4$, also formed metal chelates and gave a colouration with ferric chloride. It had λ max. 275 mμ (ε 12,300), and $\nu_{max.}$ 1720, 1700, 1625, and 1615 cm^{-1}, indicating the presence of unsaturated and saturated (β-diketone) carbonyl groups. The n.m.r. spectrum, details of which will appear elsewhere, was wholly consistent with the dihydrofuran structure (IV). One of the interesting features of this spectrum is the presence of two separate singlets at τ 7.03 and 7.25 for the two methyl groups of the β-diketone side chain due to restricted rotation. Further confirmation of structure was obtained from the mass spectrum, which will be discussed in detail in a future publication.

The dihydrofuran (IV) slowly reacted with water containing 10% isopropanol at 100°, giving, among other products which are currently under investigation, acetylacetone and yellow needles, $C_{12}H_{14}O_3$, m.p. 125° (7%). The latter substance could be readily sublimed and was strongly acidic (soluble in aqueous alkali). It formed metal chelates and gave a derivative with phenylhydrazine. It had λ max. 282, 338, and 360 mμ (ε 34,600; 6,900; 8,600), ν max. 1655, 1620, 1560 cm^{-1}. The n.m.r. spectrum showed singlets at τ 7.21, 7.37, 7.42, 7.52 (three protons each) 2.28 and -8.77 (one proton each), the latter peak diminishing on deuteration. The physical and chemical properties are consistent with the fulvene structure (V). Johnson et al.[6] have recently described the rearrangement of dihydropyridines and azepines to fulvenes and have synthesed (V) by two independent routes, without, however, reporting any physical constants. The above authors postulate that the fulvenes are formed by rearrangement of an intermediate azepine. In our case it is possible for the dihydrofuran (IV) to rearrange to an oxepine which is then converted into the fulvene (V). However, this mechanism is highly speculative and the course of the reaction is being studied further.

The formation of (IV) from (I; R = Me) is postulated to proceed via

an intermediate dihydroazepine (II; R = Me, X = OH), by analogy with related ring expansions[1,2]. This undergoes hydrolytic fission to (VI) followed by cyclisation.

Available evidence suggests that the dihydropyridine (III; R = COMe) is not formed from (I; R = Me) by direct replacement of the halogen by acetylactone (produced by hydrolysis). Further structural and mechanistic studies will be published in full elsewhere.

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