Tetrahedron Letters No.9, pp. 927-930, 1966. Pergamon Press Ltd.
Printed in Great Britain.

C_1-ALKYLATION OF HAGEMANN'S ESTER

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(Received 14 December 1965; in revised form 11 January 1966)

Uptil now, it is generally accepted that Hagemann's ester (1) (ethyl 2-methyl-4-oxocyclohex-2-enyl-1-carboxylate) (I) is monoalkylated exclusively at C_3 (2), and the reaction has found application in numerous syntheses. During one such alkylation with ethyl β -chloropropionate in presence of ethanolic sodium ethoxide, we obtained in addition to the normal keto-ester (II), previously reported (3), a crystalline acidic product, m.p.172° in 12-15% yield. The yield was subsequently increased to 25-30% using an excess of base (1.5 mole). The molecular weight, 236 and elemental analysis of the compound corresponded to a formula, $C_{13}H_{16}O_4$, derivable from the neutral ester (II) through elimination of one molecule of ethanol. This together with its UV and IR absorption data: $\lambda_{max.}$(EtOH) 325 mμ. (log ϵ 4.37) and 394 mμ. (log ϵ 4.14), $\lambda_{max.}$(NaOEt) 394 mμ. (log ϵ 5.24), ν (KBr) 2600 (OH)*, 1718 (CO_2Et), 1615 (C=O), and 1580 $cm.^{-1}$(C=C), indicated a vinylogous diketo-ester structure (e.g.,III) existing in H-bonded enol form in the solid state. NMR and IR in chloroform solution, on the other hand, were consistent with a mixture of keto- and enol-forms.

The compound on hydrolytic decarboxylation, afforded an acidic diketone, m.p.177°, $\lambda_{max.}$(EtOH) 318 mμ. (log ϵ 4.40) and $\lambda_{max.}$(NaOH) 382 mμ. (log ϵ 4.92),

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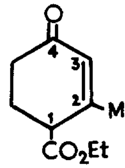
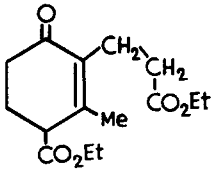
* The usual hydroxyl band at 3400-3200 $cm.^{-1}$ is shifted to about 2600 $cm.^{-1}$ due to formation of strong H-bonds (4).

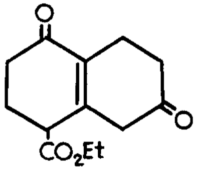
which was different from 1,2,3,4,5,6,7,8-octahydro-1,6-dioxonaphthalene, m.p.44-46° (5), expected from the structure (III), but was identical with the enol form of the isomeric octal-2,7-dione (V), m.p.174-176° (6). The diketone was further characterised by the formation of a monomethyl ether, m.p.98° (2 vinyl H's at 4.28 and 4.58 τ), and a N-methylanilido-derivative, m.p.170°. The original diketo-ester had therefore the alternative structure (IV) with an angular carboethoxyl group. Its formation could be explained by an initial alkylation of Hagemann's ester at C_1 to the keto-ester (VI) which subsequently underwent an internal Claisen condensation in presence of base. The diketo-ester (IV) afforded a monomethyl ether, m.p.107°, $\lambda_{max.}$ (EtOH) 310 mμ. (log ε 4.48); its structure was confirmed by its NMR spectrum: a triplet (3H) at 8.78 τ and a quartet (2H) at 5.82 τ (J=7 c/s) ($CO_2CH_2CH_3$), broad multiplet (8H) at 8.3-7.4 τ, a sharp singlet (3H) at 6.45 τ (OCH_3) and two singlets (1+1 H) at 4.50 and 4.10 τ (vinyl H's).



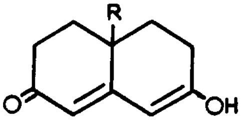
I

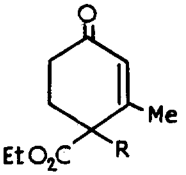


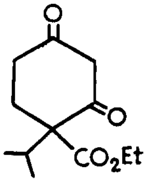
II



III







IV : $R = CO_2Et$

V : $R = H$

VI : $R = CH_2CH_2CO_2Et$

VII : $R = CHMe_2$

VIII

The isolation of the diketo-ester (IV) indicates that the alkylation of Hagemann's ester is not as selective as formerly believed, but it leads, atleast in some cases, to a mixture of C_3- and C_1-alkylated products. The failure to identify the latter in the past may be due to the fact that C_1-substituted product is more resistant to hydrolysis and is therefore left out in the higher-boiling fraction during such operation. It may be noted that all structural determinations were based on the reactions of the hydrolysed products.

We also reinvestigated isopropylation of Hagemann's ester (2a) and found that the alkylated product afforded two semicarbazones, one having m.p.141.5° (major) and the other m.p.210°. Hydrolysis of the mixed keto-esters furnished 2-isopropyl-3-methylcyclohex-2-en-1-one and some residual keto-ester (~15%) as the high-boiling fraction. The latter readily formed a semicarbazone, m.p.210° (identical with the above), and a dinitrophenylhydrazone, m.p.145°(7) and was found to be identical with ethyl 1-isopropyl-2-methyl-4-oxocyclohex-2-enyl-1-carboxylate (VII), an authentic specimen of which was synthesised as follows: Ethyl 2-carboethoxy-2-isopropyl-5-oxohexanoate on internal Claisen condensation afforded ethyl 1-isopropyl-2,4-dioxocyclohexyl-1-carboxylate (VIII). The latter was converted into its 4-isobutyl enol ether and then treated successively with methylmagnesium iodide and dilute acid (8). Identity of the two keto-esters was established by comparison of semicarbazones and phenylhydrazones.

It is interesting to note that the keto-ester (II) does not cyclise with base though the isomeric compound (VI) seems to cyclise very readily. The quaternary carboethoxyl group in the latter has possibly something to do with the ring-closure.

Partial support of this work by donation of E.I.P.W. of Calcutta is gratefully acknowledged.

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