Tetrahedron Letters No.8, pp. 719-722, 1967. Pergamon Press Ltd. Printed in Great Britain.

ENAMINE ACYLATION OF METHYLACETOACETATE

R. Balaji Rao, U.P. Singh* & G.V. Bhide

Biology Division

Atomic Energy Establishment Trombay

Bombay - 8, India.

(Received 3 November 1966)

Although enamine acylation and alkylation of carbonyl compounds are well known, relatively little has been done on the alkylation of enamines derived from β-ketoesters[1]. As the acylation of these enamines has not been studied, we now report the acylation of the pyrrolidine enamine of methyl acetoacetate with benzoyl chloride.

The pyrrolidine enamine, I, (3.38 g; 0.2 m. mole) of methyl acetoacetate m.p. 69° (white needles, hexane) $\tau^{CDCl_3}_{T.M.S.}$ 7.54 (Singlet, CH_3-C(N)=C, three protons), 6.7 (Triplet, methylenes $\alpha\alpha'$ to nitrogen, four protons), 8.08 (multiplet, methylenes $\beta\beta'$ to nitrogen, four protons), 5.54 (singlet, = CH, one proton), 6.35 (singlet, $-COOCH_3$, three protons) when treated with benzoyl chloride (2.8 g; 0.2 m. mole) in boiling benzene (100 ml.) under nitrogen, yielded a solid product with evolution of CO_2. Heating under reflux was continued for 5 hr, and the product was then filtered off and washed with benzene (yield 2 g.) m.p. 321-24°C (dec) (inserted at 300°C).

This product, dissolved in water, was treated with cold 40% NaOH aq yielding a solid which was treated with phosphate buffer at pH 6.5. The resulting mixture when crystallized from ethanol yielded a compound II m.p. 150 (0.74 g, white needles). From the mother liquor two compounds,

* Present address: Department of Chemistry, University of Adelaide, Adelaide, South Australia.

III m.p. 140° (white needles, hexane) and IV m.p. 108° (yellow plates, ethanol) were separated by column chromatography (silica gel-celite; benzene-chloroform).

The Compound II $C_{21}H_{21}NO_2$ was soluble in dil HCl and could be reprecipitated with $NaHCO_3$ aq. It has λ_{max}^{EtOH} (in mμ) 244, 348 (ε, 22,300; 21,700); λ_{max}^{KBr} (in μ) 5.95 (S) Ph-CO; 6.5 (S) -C(N)=C-C=O; $\tau_{T.M.S.}^{CDCl_3}$ 1.8-2.21; 2.51 - 2.59 (ten benzoyl protons) 6.57 (triplet, methylenes α,α' to nitrogen, four protons) 8.03 (multiplet, methylenes ββ' to nitrogen, four protons) 4.95 (singlet, Ph-CO-CH_2-C(N)=C- two protons) 4.24 (singlet, Ph-COCH=C(N)- one proton). On the basis of this evidence it is probably the pyrrolidine enamine of 1:3-dibenzoylacetone. This was confirmed by its preparation from 1:3-dibenzoylacetone and pyrrolidine, when other products (not identified) were also formed.

The compound III, m.p. 140°, $C_{17}H_{12}O_2$ together with pyrrolidine is obtained from II by the action of boiling alcoholic HCl in over 95% yield, based on the recovery of II. It has λ_{max}^{EtOH} (in mμ) 257,,284 (ε, 15,400; 17,600), λ_{max}^{KBr} (in μ) 6.02 (C=O conj.), 6.19 (C=C). $\tau_{T.M.S.}^{CCl_4}$ 2.05- 2.21; 2.4 - 2.59 (ten phenyl protons) and the signal at 3.31 (singlet, two protons) can be attributed to Ph-C=CH-C=O protons. Hence it can be assigned the structure as 2:6-diphenyl-1:4-pyrone.

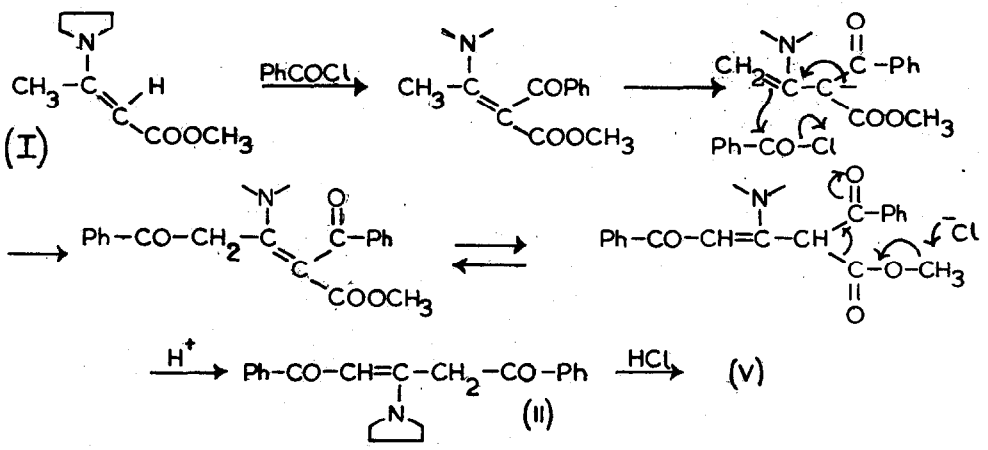
The compound IV m.p. 108°, $C_{17}H_{14}O_3$ is soluble in dil NaOH aq. and gives positive $FeCl_3$ test. It is also formed from III by the action of strong alkali and may be dehydrated to III by treatment with strong mineral acids. It has λ_{max}^{EtOH} (in mμ) 240, 395 (ε, 6,400; 22,000), $\lambda_{max}^{CH_2Cl_2}$ (in μ) 6.0 (S) Ph-C=O, 6.25 (V.S) C=C, 6.5 (V.S) chelated enolised 1:3 diketone. Hence it was assigned the structure as 1:3-dibenzoylacetone. The NMR shows that both the methylenes are enolised, one completely and the other to a lesser extent. The residual amount of Ph-$COCH_2$-C-(OH)=CH-CO-Ph is

small. $\tau^{CCl_4}_{T.M.S.}$ 6.02 (singlet, residual methylene protons), 3.99, 3.67 (singlets, vinyl protons), 2.1 - 2.3; 2.5 - 2.7 (multiplet, phenyl protons), -4.7 (singlet, enolic hydroxyls).

Reference to the literature revealed that compounds III and IV are known[2] and have been shown to undergo similar interconversions. Hence these were prepared by the known procedure for comparison.

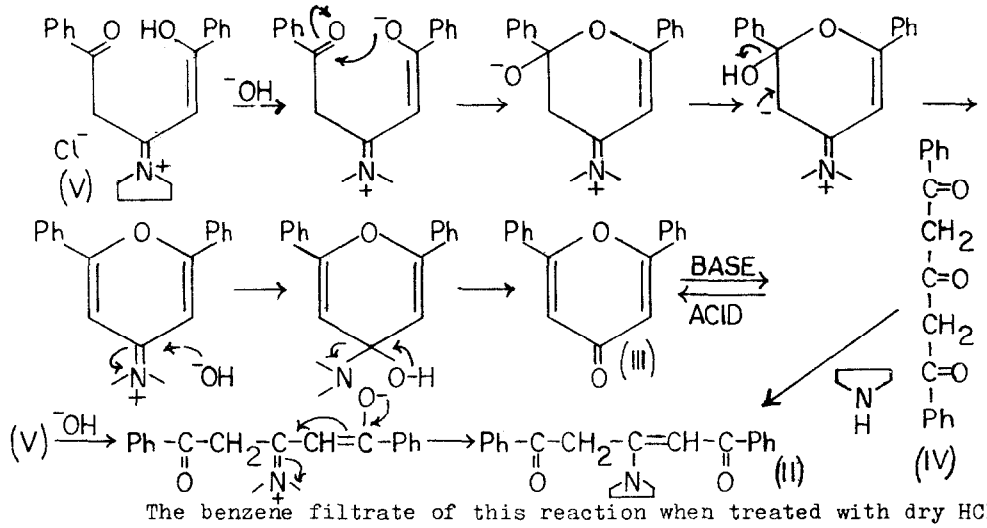
The benzene insoluble product V m.p. 321-24° (dec) (inserted at 300°) (amorphous solid; ethanol-ethyl acetate) $C_{21}H_{22}NO_2Cl$ has λ^{EtOH}_{max} (in mμ) 260, 320 (ε, 15,000; 32,300) λ^{KBr}_{max} (inμ) 5.72 (w), 6.09 (V.S) $\overset{+}{N}=C$. It was also obtained by passing dry HCl gas into a boiling benzene solution of II. Hence it is probably the imminium chloride of II[3].

The possible mechanism for the formation of V in the reaction is as shown below:*



If the structure V is assumed for the compound m.p. 321-24°, the formation of compounds II, III and IV can readily be rationalised.

* We are thankful to Professor G. Stork, Columbia University, New York for suggesting this mechanism.



The benzene filtrate of this reaction when treated with dry HCl gas and methanol yielded the enamine I.

A similar reaction takes place with two moles of I per mole of benzoyl chloride.

We are thankful to Dr. T.M. Spotswood of the University of Adelaide, Adelaide, South Australia and Dr. P.M. Nair of National Chemical Laboratory, Poona, India for the N.M.R. spectra.

REFERENCES

1. J. Szmuszkovicz in Advances in Organic Chemistry, Methods and Results. Vol. IV, page 4, 1963 (edited by Ralph A. Raphael, Edward C. Taylor and Hans Wynberg). Interscience Publishers, Inc., New York.
2. Charles R. Hause and Thomas M. Harris. J. Am. Chem. Soc. 80, 6360 (1958)
3. G.H. Alt and A.J. Speziale. J.O.C. 30, 1407 (1965) and references cited therein.