

Condensations at the 6-Methyl Position of Dehydracetic Acid. A Novel Site of Reactivity

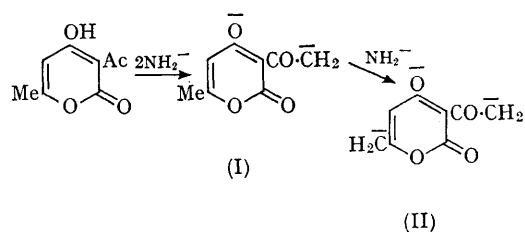
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EXTENSIVE study has been made of the chemistry of dehydracetic acid, the structure of which was finally established by Rassweiler and Adams after much controversy.¹ Condensations of dehydracetic acid with aldehydes have been effected at the acetyl methyl position by means of piperidine catalysis.² No condensations at the 6-methyl position have been described.

We report the first such condensation. Treatment of dehydracetic acid with two equivalents of sodium amide in liquid ammonia gave a clear green solution, whereas the use of three equivalents of this base gave considerable precipitation of a yellow salt. It was concluded that in the first case a dianion [probably (I)] was formed, and in the second case trianion (II). Although the dianion

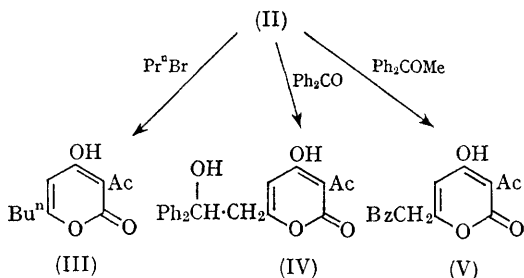
did not show appreciable reactivity toward electrophilic reagents in liquid ammonia, trianion (II) reacted rapidly at the 6-methyl position.



Treatment of trianion (II) with n-propyl bromide in liquid ammonia afforded after neutralization and

isolation a good yield of 6-alkylation product (III), m.p. 75.5–77° (Lit.³ m.p. 77°). The structural assignment of the product was confirmed by comparison of it with authentic (III) prepared by acetylation of 6-butyl-4-hydroxy-2-pyrone.

The condensation of benzophenone with (II) gave carbinol (IV), m.p. 182.5–183.5°, in 62% yield.* The anionic adduct of (II) and the ketone was neutralized by addition to a solution of ammonium chloride in liquid ammonia.⁴ The structure of carbinol (IV) was supported by the n.m.r. spectrum in which the acetyl methyl signal (2.68 p.p.m.) of dehydracetic acid remained



(2.57 p.p.m.) but the 6-methyl signal (2.27 p.p.m.) had been replaced by a methylene signal at 3.47 p.p.m.†

Treatment of (II) (2 equiv.) with methyl benzoate (1 equiv.) gave an excellent yield of benzoylation product (V), m.p. 137–138°.* The n.m.r. spectrum indicated that the site of reaction had been the same as in the two previous reactions.†

An attempted condensation with carbon dioxide in ether was unsuccessful but other condensations in ammonia including a conjugate addition of chalcone have been effected satisfactorily. It appears likely that the condensations of this intermediate (II) are fairly general.

The formation of ketone (V) is particularly noteworthy, since this compound and related acylation products are potential sources of 1,3,5,7-tetraketones^{5,6} and 3,5,7-triketo-acids.^{6,7} There is currently much interest in the conversion of pyrones into aromatic derivatives *via* polycarbonyl compounds⁸ because of the possible relationship of these aromatizations to biogenetic processes.⁹

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* New compounds gave satisfactory elemental analyses and single spots on thin-layer chromatography.

† N.m.r. spectra were determined with deuteriochloroform solutions using a Varian A-60 spectrometer and are reported in p.p.m. downfield from internal tetramethylsilane.

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