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A NOVEL DECARBOXYLATIVE CONDENSATION OF β-KETO ACIDS WITH 2-CYCLOHEXEN-1-ONE

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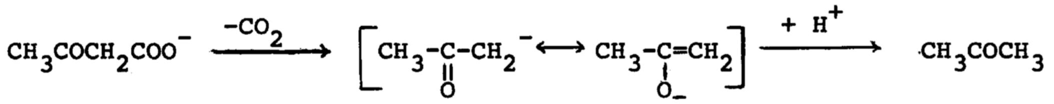
In the presence of aniline catalyst, acetoacetic acid(I) reacted smoothly with 2-cyclohexen-1-one(II) to give 3-acetonylcyclohexan-1-one(III) at room temperature, with evolution of carbon dioxide. Similarly the reaction between 2-oxocyclohexane-1-carboxylic acid(IV) and II gave the analogous decarboxylative condensation product, bicyclohexyl-2,3'-dione(V).

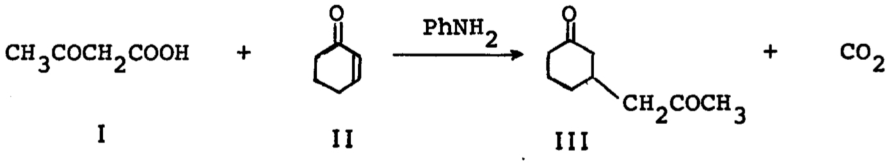
Carbanions enter into a wide variety of condensation reactions as nucleophiles regardless of their mode of formation. It is well known that the mode of decarboxylation of β-keto acids, represented by acetoacetic acid, involves the carbanion or enolate intermediate, as depicted in the following reaction.

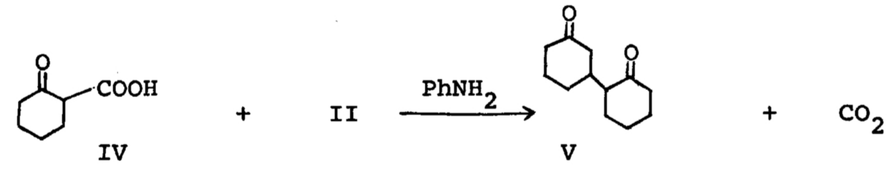


$$CH_3COCH_2COO^- \xrightarrow{-CO_2} \left[CH_3-\underset{\underset{O}{\|}}{C}-CH_2^- \longleftrightarrow CH_3-\underset{\underset{O_-}{|}}{C}=CH_2 \right] \xrightarrow{+\ H^+} CH_3COCH_3$$

It is, therefore, likely that the carbanion intermediate serves as a nucleophile in condensation reactions even in the absence of a strong base or in a neutral medium.

In the present communication, we report some preliminary results of the aniline catalyzed decarboxylative condensation reaction of β-keto acids such as acetoacetic acid(I) or 2-oxocyclohexane-1-carboxylic acid(IV) with 2-cyclohexen-1-one(II) leading to the formation of Michael type adducts, 3-acetonylcyclohexan-1-one(III) or bicyclohexyl-2,3'-dione(V), respectively.





When a mixture of I and II was left to stand at room temperature, the expected condensation reaction hardly occurred and only decarboxylative decomposition of I was predominant. However, the reaction rate was markedly increased by addition of a catalytic amount of aniline. Thus, when a mixture of I[2] (0.77 g. 7.5 mmol) and II (0.48 g, 5.0 mmol) in 8 ml of ether was treated with aniline (80 mg, 0.86 mmol) and stirred at room temperature, the evolution of carbon dioxide ceased after 24 hr. After removal of the ether, the resulting residue was chromatographed on silica gel with chloroform-ethyl acetate (5:1) to give 0.14 g of unreacted II (29.1%) and 0.51 g of III[3] (66.1% yield based on II) as an oily substance. Anal. Found: C, 69.95 ; H, 9.42%. Calcd for $C_9H_{14}O_2$: C, 70.10 ; H, 9.15% : ir max (liq), 1715(sh), 1710, 1430, 1360, and 1268 cm^{-1}: mass 154(M^+), 139(M^+-CH_3), 111(M^+-CH_3CO), 97($M^+-CH_3-COCH_2$) : nmr (60 MHz, CCl_4, TMS) δ2.07(3H, s, CH_3), 1.67-2.50(9H, m, cyclohexane ring), ca. 2.30 ppm (2H, m, $\underline{CH_2}COCH_3$[4]). 2,4-Dinitrophenylhydrazone. M.p. 213-214°C Anal. Found: C, 48.62 ; H, 4.35 ; N, 21.23%. Calcd for $C_{21}H_{22}N_8O_8$: C, 49.03 ; H, 4.31 ; N, 21.78%.

Using a similar procedure as mentioned above, the decarboxylative condensation reaction of IV[5] (1.07 g, 7.5 mmol) with II (0.48 g, 5.0 mmol) gave the product (V) (0.63 g, 64.8%). Anal. Found: C, 74.16 ; H, 9.55%. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34% : ir max (liq), 1707 cm^{-1} ; mass,[6] 194(M^+), 137, 98, 97, 96 : nmr (60 MHz, CCl_4, TMS) 1.2-2.6 ppm (18 H, m, cyclohexane ring). 2,4-Dinitrophenylhydrazone. M.p. 235-236°C. Anal Found: C, 51.89 ; H, 4.68 ; N, 19.97%. Calcd for $C_{24}H_{26}N_8O_8$: C, 51.98 ; H, 4.73 ; N, 20.21%.

To confirm the structures of the reaction products, an authentic sample of V was prepared independently by catalytic hydrogenation of 2-(3-oxocyclohexyl)-2-cyclohexen-1-one obtained by alkaline condensation of 2-cyclohexen-1-one.[7] The ir and nmr spectra of the authentic sample of V thus obtained were completely identical with those of the reaction product derives from II and IV, indicating that the decarboxylative addition of β-keto acids takes place at the 3-position of II.

The present decarboxylative condensation of β-keto acids provides a new route for the synthesis of δ-diketones under mild reaction conditions.

REFERENCES AND NOTES

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