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A NEW TYPE OF AROMATIZATION REACTION. SYNTHESIS OF ARYLACETIC ACIDS FROM 3-CYCLOHEXENE-2-OXO-ACETIC ACIDS.

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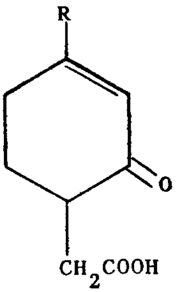
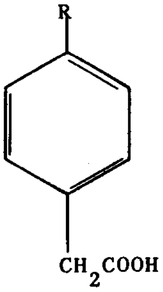
Aromatization reactions of cyclohexenones to the corresponding hydrocarbons have not yet been described in the literature. We now wish to report a new type of aromatization reaction, which allows to convert 3-cyclohexene-2-oxo-acetic acids of general formula (I) to the corresponding arylacetic acids (II), by acid catalysis.



(I)

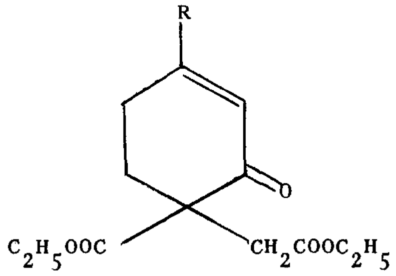


(II)

(Ia) : R = H
(Ib) : R = CH_3
(Ic) : R = C_6H_5
(Id) : R = p-$(OCH_3)C_6H_4$
(Ie) : R = m,p-$(OCH_3)_2C_6H_3$

(IIa) : R = H
(IIb) : R = CH_3
(IIc) : R = C_6H_5
(IId) : R = p-$(OH)C_6H_4$
(IIe) : R = m,p-$(OH)_2C_6H_3$

The above cyclohexene-2-oxo-acetic acids, still unknown, have been synthesized following a general method previously devised for the preparation of analogous substances (1). Acrolein or the proper dialkylaminoethylketone were condensed with ethyl acetosuccinate to give the corresponding ethyl 1-carbethoxy-3-cyclohexene-2-oxo-acetates (III)



(III)

which have been directly hydrolysed in alkaline medium to give the expected acetic acid derivatives (I). The new compounds are summarized in Table I with some of their physical properties.

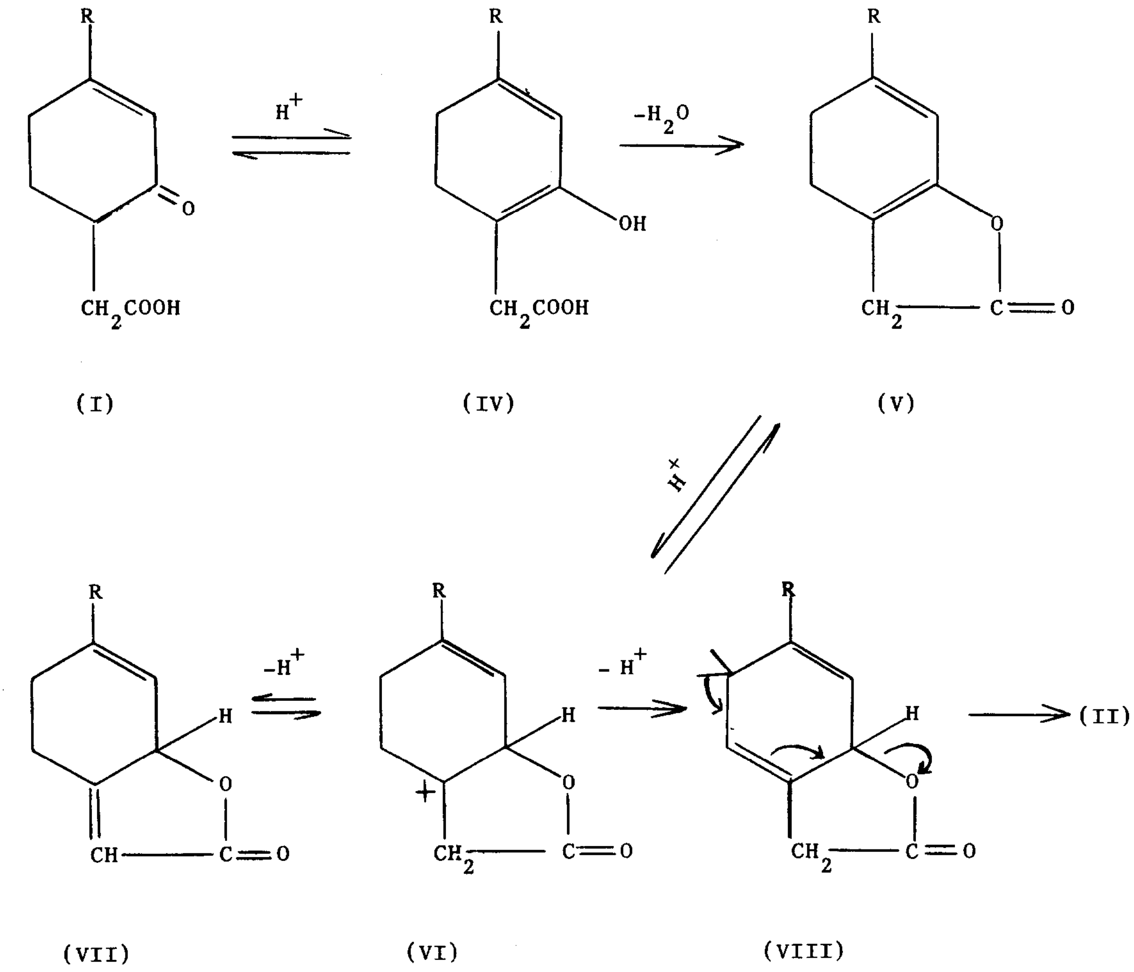
TABLE I.

	m.p.	λ max (mμ)	log ε
Ia	65° (a)	225	4,01
Ib	71° (b)	233	4,12
Ic	144-6° (c)	281	4,24
Id	170-1° (c)	312	4,33
Ie	142-3° (c)	324	4,23
		237	4,00
IIe	213-5° (d)	286	3,99
		267	4,16
IXa	183-5° (d)	312	4,32
		230	4,00
IXb	221° (d)	316	4,26
		231	3,95

(a) from hexane-benzene (b) from ether-petroleum ether

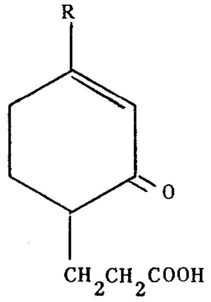
(c) from ethanol (d) from ethanol-water

Aromatization of acids (I) was most effectively performed by heating them at 200° with an equal amount of dry pyridine hydrochloride for about one hour. Yields were normally higher than 85-90%. However lower yields of the same acids (II) could be obtained by the action of dry hydrochlorides of different amines (triethylamine, piperidine, etc.): also effective were HCl and HBr in glacial acetic acid solution or even in concentrated aqueous solution by prolonged heating at about 200-220°. The above outlined aromatizations have been tentatively interpreted on the basis of the reaction mechanism summarized in the following scheme:



The critical point of this mechanism is the possibility that the postulated intermediate carbonium ion (VI) could originate both the tautomeric forms (VII) and (VIII), the latter being the sole form capable of easy aromatization.

An evidence in favor of the above reaction mechanism seems to derive from the reaction of pyridine hydrochloride with 4-p-methoxyphenyl-3-cyclohexene-2-oxo-propionic acid (IXa): this acid did not aromatize, the only reaction being the cleavage of the ether linkage to give (IXb).



(IXa) : R = (p-OCH$_3$)C$_6$H$_4$

(IXb) : R = (p-OH)C$_6$H$_4$

(IX)

In fact, although the formation of a six-membered lactone is possible, such a lactone could not have any tendency to tautomerize to a species in which the exocyclic double bond would be conjugated with the carbonyl group.

Satisfactory elemental analytical data were obtained for all the new compounds reported.

References.

1) F.C. Novello, M.E. Christy, and J.M. Sprague, J. Am. Chem. Soc., **75**, 1330 (1953).