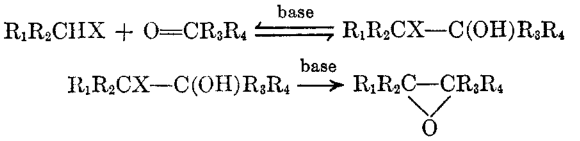
Mechanism of the Darzens Condensation. Isolation of Two Aldol Intermediates

Sir:

It is generally believed[1,2] that a Darzens condensation, *i. e.*, the oxirane-yielding base-catalyzed reaction of a carbonyl compound and a halogenomethylene substance, occurs *via* aldol addition intermediates.

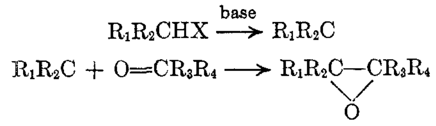


$$R_1R_2CHX + O{=}CR_3R_4 \overset{\text{base}}{\rightleftharpoons} R_1R_2CX{-}C(OH)R_3R_4$$

$$R_1R_2CX{-}C(OH)R_3R_4 \xrightarrow{\text{base}} R_1R_2\underset{\diagdown\, O\, \diagup}{C{-}C}R_3R_4$$

Some features of certain Darzens condensations have been recently reasoned from this assumption.[2] However, no such intermediates have ever been isolated under the condensation conditions.

A mechanism involving bivalent radicals formed by 1,1-elimination of hydrogen chloride at the halogenomethylene component has been favored by some authors.[3]



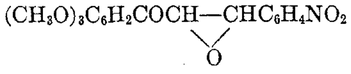
$$R_1R_2CHX \xrightarrow{\text{base}} R_1R_2C$$

$$R_1R_2C + O{=}CR_3R_4 \longrightarrow R_1R_2\underset{\diagdown\, O\, \diagup}{C{-}C}R_3R_4$$

Furthermore, recent kinetic[4a] as well as structural[4b] evidence for bivalent radical formation from certain halogenomethylene substances upon attack by base has given to this mechanism some circumstantial support.

In this connection the authors wish to report that the hydroxyl ion–catalyzed condensation of *m*-nitrobenzaldehyde and 2,4,6-trimethoxyphenacyl chloride at 0°, in aqueous dioxane, gives 98.8% yield of *m*-nitrophenyl-2,4,6-trimethoxybenzoyloxirane, I, m.p. 170–171°. *Anal.* Calcd. for $C_{18}H_{17}NO_7$: C, 60.2; H, 4.8; N, 3.9. Found: C, 60.1; H, 4.8; N, 4.1. When the reaction is run so that only a small fraction of the starting materials are converted into condensation product it is possible to isolate two intermediate chlorohydrins, II, melting at 163.0–164.5° and 111–112°. *Anal.* Calcd. for $C_{18}H_{18}ClNO_7$: C, 54.6; H, 4.6; Cl, 9.0; N, 3.5. Found (m.p. 163–164.5°); C, 54.9; H, 4.7; Cl, 9.0; N, 3.5. Found (m.p. 111–112°): C, 54.7; H, 4.5, Cl, 9.2; N, 3.6. They give almost quantitative yields of I when treated with the base under the usual conditions. The trimethoxyphenacyl chloride is perfectly stable towards hydroxyl ion.

These results are therefore the first compelling evidence ruling out the "bivalent radical" mechanism and showing that *the Darzens condensation is essentially of aldol-addition type.*



$$(CH_3O)_3C_6H_2CO\underset{\diagdown\, O\, \diagup}{CH{-}CH}C_6H_4NO_2$$

(I)

$(CH_3O)_3C_6H_2COCHCl{-}CH(OH)C_6H_4NO_2$

(II)

The details and full discussion of the above-mentioned and other related experimental results will be reported in a forthcoming publication.

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[1] M. Ballester and P. D. Bartlett, *J. Am. Chem. Soc.*, **75**, 2042 (1953); M. Ballester, *Chem. Revs.*, **55**, 283 (1955).

[2] N. H. Cromwell and R. A. Setterquist, *J. Am. Chem. Soc.*, **76**, 5752 (1954); H. Dahn and L. Loewe, *Chimia*, **11**, 98 (1957); H. Kwart and L. G. Kirk, *J. Org. Chem.*, **22**, 116 (1957). See also Kwart's correction to his paper, *J. Org. Chem.*, **22**, 1755 (1957). This correction which concerns one of our previous papers contains an important error: "diastereomerically related intermediates" should be substituted for "diastereomerically related transition states."

[3] S. Bodforss, *Ber.*, **51**, 192 (1918); E. Bergmann and J. Hervey, *Ber.*, **62**, 893 (1929).

[4] (a) J. Hine, *J. Am. Chem. Soc.*, **72**, 2438 (1950); (b) W. von Doering and A. K. Hoffmann, *J. Am. Chem. Soc.*, **76**, 6162 (1954). See also E. D. Hughes, *Quart. Revs.* (*London*), **5**, 245 (1951).