

γ -ALKYLATION OF METHYL 4-BROMOCROTONATE, A VINYLOGOUS DARZENS REACTION

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The utility of a 4-halocrotonic ester as an alkylating agent has been demonstrated by its reaction with enamines.² Such reactions depend upon the electrophilic character of 4-halocrotonic esters. In contrast, the nucleophilic derivatives of 4-halocrotonic esters have not been utilized in synthesis.³

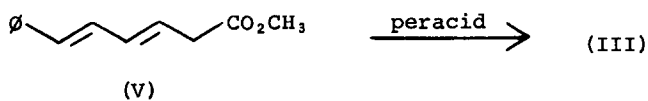
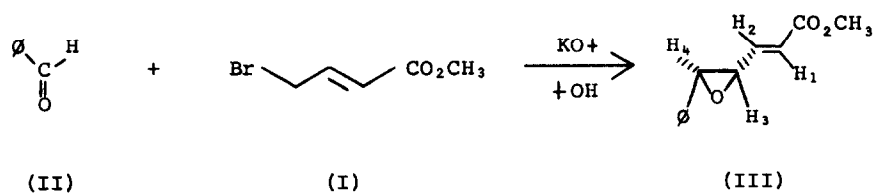
The intriguing possibility of alkylating the anion derived from methyl 4-bromocrotonate (I) with benzaldehyde (II) and the potentiality of finding selectivity in such a reaction stimulated this investigation. An electrophile was selected which would allow the position of alkylation to be elucidated and which would also demonstrate the usefulness of the synthetic method.

Treatment of (I) and (II) with potassium t-butoxide in t-butanol at 0° for 40 min afforded a 70% yield of a mixture of (III) and (IV) (7:3, respectively).⁴ Thick layer chromatography on silica gel eluted with 2:1 petroleum ether:ether separated (III) and (IV) with R_f values of 0.52 and 0.46, respectively.⁵

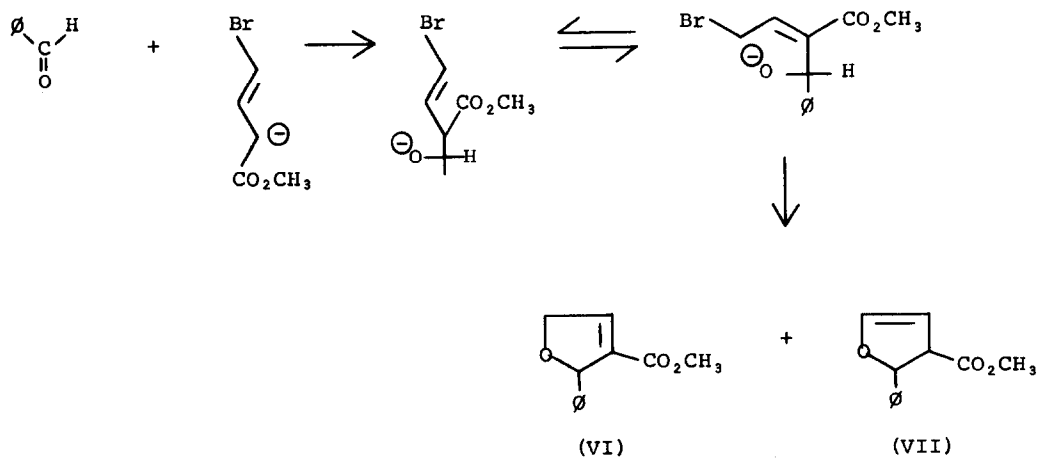
The spectral data, ir [λ_{\max} (CHCl₃) 5.83 and 6.1 μ], nmr τ (CDCl₃) [H₂, 2.15 (doublet of doublets, J_{2,3}=7 Hz, J_{2,1}=15 Hz), H₁, 3.81 (doublet, J_{1,2}=15 Hz), H₄, 6.18 (doublet, J_{4,3}=7 Hz), H₃, 6.53 (doublet of doublets, J_{3,4}=2 Hz, J_{3,2}=7 Hz)] and mass spectrum [m/e 204 (M⁺), 98 (base)] are consistent with structure (III).

The structure assignment was confirmed by treatment of methyl 5-phenyl-2,4-pentadienoate (V) with *m*-chloroperbenzoic acid to give (III).

The assignment of structure (IV) was made on the basis of its nmr: τ (CDCl₃) [H₂, 3.50 (doublet of doublets, J_{2,3}=7 Hz, J_{2,1}=16 Hz), H₁, 3.82 (doublet, J_{1,2}=16 Hz), H₄, 5.66 (doublet, J_{4,3}=4 Hz), H₃, 6.15-6.30 (multiplet)] and mass spectrum [m/e 204 (M⁺) 98 (base)].⁶



Scheme 1



Apriori, (III) and (IV) could have been formed either by γ -alkylation of (I) or by α -alkylation followed by rearrangement. If (I) had undergone initial α attack (Scheme 1), one might have expected the formation of the dihydrofuran derivatives, (VI) and (VII), which were clearly demonstrated not to be in the reaction mixture; in addition, the reports of γ -alkylation of α,β -unsaturated esters indicate that prolonged reaction time and/or elevated temperature are required to effect rearrangement.^{7,8}

The results described here demonstrate the feasibility of γ -alkylation of 4-halocrotonic ester systems and also extend the scope of the Darzens condensation to include vinylogues of α -halo esters. Utilization of this method in the synthesis of heretofore inaccessible natural products is under investigation.

Acknowledgement: The author is grateful to Professor Gilbert Stork for his encouragement.

References

1. A portion of this work was carried out in the laboratories of Professor Gilbert Stork, Columbia University, New York, New York.
2. A. Chatterjee, Tetrahedron Lett., 959 (1965).
3. I am considering the anionic system in which the bromine atom is an integral part as opposed to that in which it has dissociated as in a Reformatsky type reaction.
4. Satisfactory elemental analyses were obtained.
5. Compounds (III) and (IV) resisted all attempts at crystallization.
6. The mass spectra of (III) and (IV) are virtually identical.
7. A. S. Dreiding, R. J. Pratt, J. Amer. Chem. Soc. 75, 3717 (1953).
8. J. F. Bagli, H. Immer, Can. J. Chem. 46, 3115 (1968).