[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Transetherification of Ethyl β-Ethoxycrotonate with Cinnamyl Alcohol

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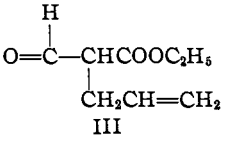
RECEIVED JUNE 29, 1953

Transetherification of ethyl β-ethoxycrotonate with cinnamyl alcohol gives ethyl α-(α-phenylallyl)-acetoacetate. Since inversion of the cinnamyl group takes place, it is assumed that ethyl β-cinnamoxycrotonate is first produced and that it rearranges under the conditions present during transetherification. Earlier attempts to prepare ethyl β-cinnamoxycrotonate apparently yielded its rearrangement product ethyl α-(α-phenylallyl)-acetoacetate.

Transetherification of β-ethoxyacrylates with allyl alcohols yields β-alloxyacrylates, which are capable of undergoing rearrangement. Accordingly, ethyl β-ethoxyacrylate (I) is converted to ethyl β-alloxyacrylate (II) and ethyl α-formylallylacetate (III) upon heating with allyl alcohol in the presence of sodium bisulfate.[2]

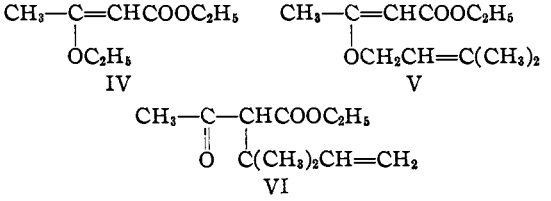
$C_2H_5O-CH=CHCOOC_2H_5$ (I)

$CH_2=CH-CH_2O-CH=CHCOOC_2H_5$ (II)



(III)

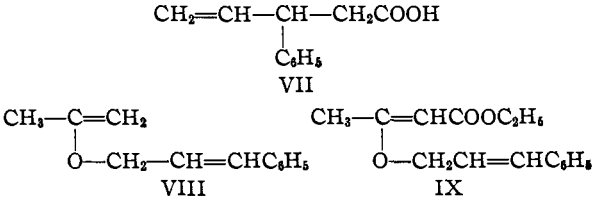
The application of transetherification in the case of ethyl β-ethoxycrotonate (IV) and γ,γ-dimethylallyl alcohol yields the rearrangement product, ethyl α-(α,α-dimethylallyl)-acetoacetate (VI). In this case the intermediate γ,γ-dimethylallyl enol ether (V) could not be isolated, but the fact that formation of the product VI involved inversion of the allyl group points to the occurrence of the γ,γ-dimethylallyl enol ether as an intermediate in the formation of the product.[3]



(IV) (V) (VI)

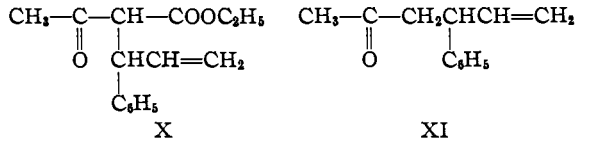
This case is of particular interest since it involves the inversion of a γ,γ-dialkylallyl group without the intervention of abnormal rearrangement.[4]

The interaction between ethyl β-ethoxycrotonate and cinnamyl alcohol was investigated by Bergmann and Corte.[5] The main product, $C_{15}H_{18}O_3$, upon alkaline hydrolysis yielded two products, (1) β-phenyl-β-vinylpropionic acid (VII) and (2) a compound, $C_{12}H_{14}O$, which they designated as cinnamyl isopropenyl ether (VIII). On this basis, the compound $C_{15}H_{18}O_3$ was regarded as ethyl β-cinnamoxycrotonate (IX) and it was believed that, on treatment with alkali, some rearrangement with inversion of the cinnamyl group had occurred. The



(VII) (VIII) (IX)

present study indicates that the compound $C_{15}H_{18}O_3$ is ethyl α-(α-phenylallyl)-acetoacetate (X) and that the enol ether VIII is in reality (α-phenylallyl)-acetone (XI)



(X) (XI)

Ethyl β-cinnamoxycrotonate (IX), like ethyl β-(γ,γ-dimethylallyl)-crotonate (V), apparently rearranges easily, and methods of preparation which would be expected to yield the enol ether actually give its rearrangement product. Another method of preparation of this kind was described by Lauer and Kilburn.[6] The action of sodium cinnamoxide on ethyl β-chlorocrotonate (and β-chloro-isocrotonate) was assumed to give compound IX; it is now evident that its rearrangement product X was obtained. In this case, as in the case involving transetherification, the intermediate formation of IX is very likely since inversion of the cinnamyl group takes place. Ethyl β-alloxycrotonate is more stable; it can be isolated and on rearrangement gives ethyl α-allylacetoacetate.

Ethyl β-ethoxycrotonate (IV) upon treatment with 2,4-dinitrophenylhydrazine yields the 2,4-dinitrophenylhydrazone of ethyl acetoacetate. The same product should result in the case of ethyl β-cinnamoxycrotonate (IX). The compound which results from transetherification of ethyl β-ethoxycrotonate (IV) with cinnamyl alcohol in the presence of a small amount of potassium bisulfate, gives under similar treatment with 2,4-dinitrophenylhydrazine the 2,4-dinitrophenylhydrazone of ethyl α-(α-phenylallyl)-acetoacetate (X). That the transetherification product actually is ethyl α-(α-phenylallyl)-acetoacetate (X) was confirmed by hydrolysis to (α-phenylallyl)-acetone (XI), $CH_3COCH_2CH(C_6H_5)CH=CH_2$, which was in turn converted to its 2,4-dinitrophenylhydrazone and its semicarbazone. Comparable results were obtained from the product resulting from the action of sodium cinnamoxide on ethyl β-chlorocrotonate (and isocrotonate).

(1) This paper is based on part of the Ph.D. Thesis, 1953, of Nicolas Brodoway.

(2) W. J. Croxall and J. O. VanHook, THIS JOURNAL, **72**, 803 (1950).

(3) K. Brack and H. Schinz, *Helv. Chim. Acta*, **34**, 2005 (1951).

(4) W. M. Lauer and O. Moe, THIS JOURNAL, **65**, 289 (1943).

(5) E. Bergmann and H. Corte, *J. Chem. Soc.*, 1363 (1935).

(6) W. M. Lauer and E. I. Kilburn, THIS JOURNAL, **59**, 2586 (1937).

The isomeric derivatives of ethyl α-cinnamylacetoacetate were also prepared for purposes of comparison.

Experimental

Ethyl β-Ethoxycrotonate[7] **(IV).**—A mixture of 203.8 g. (1.57 moles) of ethyl acetoacetate and 240 g. (1.62 moles) of ethyl orthoformate was cooled in an ice-bath and six drops of concd. sulfuric acid was added. The mixture was cooled for one-half hour and then allowed to stand at room temperature for 24 hours. The acid was neutralized with excess potassium carbonate. The excess salt was removed by filtration and the filtrate was concentrated by distillation under reduced pressure at room temperature. The residue was then distilled at atmospheric pressure and the product was collected at 175–196°. The product, after cooling overnight in a refrigerator, solidified almost completely and the solid (171.3 g.) was separated by filtration. The filtrate, after distillation yielded an additional amount (16.2 g.) of solid product. The total yield was 187.5 g. (75%).

Ethyl α-(α-Phenylallyl)-acetoacetate (X).—A mixture of 31.6 g. (0.2 mole) of ethyl β-ethoxycrotonate (IV), 31.6 g. (0.24 mole) of cinnamyl alcohol and 0.2 g. of potassium bisulfate contained in a flask fitted with a short column was heated for 1.5 hours at 140–160°. During this time 6.1 g. of ethyl alcohol was collected at 77–79°. The residue was cooled, filtered and distilled at reduced pressure. The product, 24.6 g. (50%), was collected at 101–115° (0.4 mm.). Redistillation through a short column yielded a product boiling at 100–108° (0.1 mm.), $n^{25}D$ 1.5100. The refractive index of a small portion collected separately at 106° (0.1 mm.), was $n^{25}D$ 1.5074.

The 2,4-dinitrophenylhydrazone of X melted at 140–141°.

Anal. Calcd. for $C_{21}H_{22}O_6N_4$: C, 59.15; H, 5.21; N, 13.14. Found: C, 59.64; H, 5.45; N, 12.97.

The transetherification product X was heated under the following conditions. No change in physical properties was observed in: (1) two hours at 160–165° with the addition of a small amount of β-naphthol; (2) four hours at 105–115° with the addition of a small amount of ammonium chloride; (3) four hours at 210–220°; (4) six hours at 115–120° with potassium bisulfate.

One gram of the above described product (X) resulting from the transetherification of ethyl β-ethoxycrotonate (IV) with cinnamyl alcohol was treated with hydrazine hydrate (1 ml., 80%) and ethanol (4 ml., 65%) at steam-bath temperature for a period of ten minutes and then allowed to stand at 0–5° for one day. There was no immediate separation of pyrazolone crystals. The reaction mixture was allowed to stand for two additional days at room temperature. At the end of this time interval, crystals of the pyrazolone (m.p. 184–188°, Lauer and Kilburn[5] reported 182–184°) appeared.

Ethyl α-(α-Phenylpropyl)-acetoacetate.—The transetherification product, ethyl α-(α-phenylallyl)-acetoacetate (X) (6.0 g. dissolved in 50 ml. of methanol) was hydrogenated at room temperature in the presence of Raney nickel catalyst. The hydrogenation product (4.4 g., 73%, b.p. 167–170° (17 mm.), $n^{25}D$ 1.4934) formed a pyrazolone which melted at 195–196° (Lauer and Kilburn,[5] 193–195°). **The 2,4-dinitrophenylhydrazone** of ethyl α-(α-phenylpropyl)-acetoacetate, which melted at 97.5–98.5°, was analyzed.

Anal. Calcd. for $C_{21}H_{24}O_6N_4$: C, 58.87; H, 5.67; N, 13.08. Found: C, 58.90; H, 5.76; N, 13.25.

The Hydrolysis of Ethyl α-(α-Phenylallyl)-acetoacetate (X).—A solution of the ester X (4.75 g.) in ethanol (30 ml., 85%) containing potassium hydroxide (2.5 g.) was heated under reflux for one hour. The reaction mixture was then added to cold water (175 ml.) and the oil which separated was taken up in ether. The ether extract yielded a product (2.4 g., b.p. 134–136.5° (17 mm.), $n^{25}D$ 1.5188). **The 2,4-dinitrophenylhydrazone** (m.p. 106.5–107°) of the hydrolysis product, α-phenylallylacetone (XI), was prepared. Carroll[8] reported the melting point of this compound to be 101–102°.

Anal. Calcd. for $C_{18}H_{18}O_4N_4$: C, 61.01; H, 5.12; N, 15.81. Found: C, 60.88; H, 5.35; N, 15.81.

The semicarbazone (m.p. 97.5–98.5°) was also prepared.

Anal. Calcd. for $C_{13}H_{17}ON_3$: C, 67.50; H, 7.41; N, 18.17. Found: C, 67.94; H, 7.27; N, 18.59.

The Hydrolysis of Ethyl α-Cinnamylacetoacetate.—This ester (5.0 g., b.p. 150–154° (1 mm.), $n^{25}D$ 1.5273) was dissolved in alcoholic sodium hydroxide (50 ml., 10% solution) and heated under reflux for one hour. The cooled reaction mixture was then added to water (200 ml.) and the oil was extracted with ether. The ether extract (dried over $MgSO_4$) yielded a product (1.25 g., b.p. 165–169° (23 mm.), $n^{25}D$ 1.5452), which, in turn gave the derivatives; (a) **2,4-dinitrophenylhydrazone of cinnamylacetone,** m.p. 147–148° (Carroll reports 145–146.5°)[8]; (b) **cinnamylacetone semicarbazone,** m.p. 129–131° (Fischer, *et al.*, 132°).[9]

The aqueous solution after ether extraction was acidified with hydrochloric acid and cooled in an ice-bath. Cinnamylacetic acid, m.p. 90–92°, separated. (Fichter and Kestenholz report 90–91°.)[10]

The Action of Sodium Cinnamoxide on a Mixture of Ethyl β-Chlorocrotonate and Ethyl β-Chloroisocrotonate.—A suspension of sodium cinnamoxide was prepared by adding portionwise cinnamyl alcohol (28.1 g.) in benzene (30 ml.) to sodium hydride (4.8 g.) and benzene (30 ml.). The above suspension was stirred and heated under reflux for four hours. A solution of a mixture of ethyl β-chlorocrotonate and ethyl β-chloroisocrotonate (27.9 g., b.p. 103–124° (107 mm.)) in benzene (25 ml.) was added dropwise with stirring to the suspension of sodium cinnamoxide. The reaction mixture was then allowed to stand for 18 hours and filtered. A portion of the filtrate was next distilled at reduced pressure. An impure product (b.p. 95–115 (0.2 mm.), $n^{25}D$ 1.5289) was obtained; it yielded a **2,4-dinitrophenylhydrazone** (m.p. 140–141°) which was identical with that obtained from ethyl α-(α-phenylallyl)-acetoacetate (X), the transetherification reaction product described above.

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