[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF SASKATCHEWAN]

Isomerism in the Diels–Alder Reaction

BY H. L. HOLMES, R. M. HUSBAND[1] AND IN PART BY C. C. LEE[1] AND P. KAWULKA[1]

Several cases of isomerism, the nature of which is not yet apparent, have been encountered in the addition of certain dienophiles to conjugated diene systems (diacetylethylene + 1-vinyl-6-methoxy 3,4-dihydronaphthalene,[2] cinnamic acid + dicyclohexenyl,[6] benzalacetophenone + dicyclohexenyl,[6] β-benzoylacrylic acid (and its 2,4-dimethyl derivative) + 2,3-dimethylbutadiene-1,3[3]). The reaction of an ethanol solution of β-benzoylacrylic with 2,3-dimethylbutadiene-1,3[3] gave a good yield of an acid adduct (m. p. 143°) as well as some ester resulting from interaction with the solvent. Saponification of the ester adduct with alcoholic alkali gave not only the above adduct but 1% of a high-melting (189°) isomer. A similar pair of isomers were obtained when the dienophile in the above reaction was β-[2′,4′-dimethylbenzoyl]-acrylic acid.

If the isomerism of the β-benzoylacrylic acid-2,3-dimethylbutadiene adduct is of a steric nature then the normal adduct (m. p. 143°) must have the *cis* configuration, for alcoholic alkali is known to promote the conversion of *cis* esters, bearing an alpha hydrogen, to the *trans* acid.[4] This is not in accord with experimental fact for saponification of the ethyl ester of the normal acid adduct with ethanolic potassium hydroxide regenerated only the normal acid (no trace of an isomeric acid could be detected). Furthermore, the high melting (m. p. 189°) acid adduct has been prepared directly, if in small yield, by heating a toluene solution of β-benzoylacrylic acid with 2,3-dimethylbutadiene (the analogous product was not obtained when β-[2,4-dimethylbenzoyl]-acrylic acid was the dienophile). Finally, *cis*-2-benzoyl-4,5-dimethyl-Δ^4-tetrahydrobenzoic acid, which differed from both of the above isomeric adducts, was prepared by condensing (*cis*) 4,5-dimethyl-Δ^4-tetrahydrophthalic anhydride with benzene. The failure of the *cis* acid to react with an ethereal solution of diazomethane is suggestive of a lactol structure for this adduct, an observation lending further support to the configuration assigned to this adduct. Dimethyl sulfate and alkali were required to effect this esterification. Saponification of the methyl ester of the *cis* acid with ethanolic sodium ethylate gave the normal acid adduct.

From these observations it must be concluded that the normal adduct has the *trans* configuration and that the high melting isomer probably results from the migration of the double bond from the normal position in the adduct to one of conjugation with either the ketone or carboxyl group or with both of these functional groups.

This work combined with the generalization of Bergmann and Eschinazi[5] that in Diels–Alder reactions "the relative position of the substituents in the olefinic component is retained in the adduct" adds further confirmation to Lutz's[6] characterization of the yellow β-benzoylacrylic acid as the *trans* form.

Experimental Part[7]

β-Benzoylacrylic Acid and its 4-Methoxy- and 2,4-Dimethyl Derivatives.—The β-benzoylacrylic acid (m. p. 95–96°) was prepared by the method of Fieser and Fieser[3]; however, a modification[8] of this reaction improved the yield of the 4-methoxy- and 2,4-dimethyl- derivatives to 80 and 75%, respectively. The β-anisoylacrylic acid melted at 133–134°,[9] while the β-[2,4-dimethylbenzoyl]-acrylic acid, previously prepared by Kozniewski and Marchlewski,[10] melted at 112–113°. Ethyl β-anisoylacrylate boiled at 184–187° (3 mm.).

The Diels–Alder Reactions.—The conditions for the addition of β-benzoylacrylic acid, its 4-methoxy- and 2,4-dimethyl derivatives to 2,3-dimethylbutadiene were the same.

A suspension of 12.00 g. of β-benzoylacrylic acid in 10 cc. of sodium-dry toluene was heated in a sealed tube with 6.2 g. of 2,3-dimethylbutadiene-1,3 for one hundred and twenty hours at 125°. A yield of 15.31 g. of the crude adduct (m. p. 120–140°) was recovered. Recrystallization from ether and petroleum ether raised the melting point to 141–142°. No depression of the melting point was observed when mixed with that prepared by Fieser and Fieser. After removal of the last traces of the product, melting at 141–142°, from the mother liquors, a second product (0.12 g.) crystallized which showed a somewhat indefinite melting point. When the sample, alone or mixed with the high melting isomer of Fieser and Fieser, was introduced into the melting point apparatus at 160° and the bath temperature increased at a rapid rate, it melted at 189° with some previous softening. This high melting isomer is unsaturated toward aqueous permanganate solution and bromine in carbon tetrachloride.

In contrast to the results of the previous workers only the product melting at 150–150.5° was recovered (80%) from the addition of β-[2,4-dimethylbenzoyl]-acrylic acid to 2,3-dimethylbutadiene. The addition product (80%), melting at 149–149.5°, was isolated from the analogous reaction with β-anisoylacrylic acid.

These dienophiles were not affected by these conditions, for, when they were heated in toluene under conditions obtaining in the above reactions, they were quantitatively recovered except in the case of β-benzoylacrylic acid. In the latter case 5% of a white crystalline solid melting at 176–177° was formed. The same product resulted from crystallization of β-benzoylacrylic acid from benzene.

Esterification of the Diene Adducts.—The ester adducts were obtained by boiling the acid adducts for four hours

---

(1) Senior students in the College of Engineering. This work is based on theses submitted to the College of Engineering in partial fulfilment of the requirements for the degree of Bachelor of Science in Chemical Engineering.

(2) Goldberg and Müller, *Helv. Chim. Acta*, **23**, 831 (1940).

(3) Fieser and Fieser, THIS JOURNAL, **57**, 1679 (1935).

(4) Bickel, *ibid.*, **60**, 927 (1938).

(5) Bergmann and Eschinazi, *ibid.*, **65**, 1405 (1943).

(6) Lutz, *ibid.*, **52**, 3405, 3423 (1930).

(7) All melting points are corrected. The analyses were done in the analytical laboratory of Dr. Léo Marion, National Research Council, Ottawa, Canada.

(8) Holmes and Trevoy, *Can. J. Research*, **22**, 109 (1944).

(9) Bougault, *Compt. rend.*, **146**, 411 (1908).

(10) Kozniewski and Marchlewski, *Chem. Zentr.*, **77**, 1190 (1906).

TABLE I

THE COMPOSITION AND PHYSICAL CONSTANTS OF THE ETHYL ESTERS

R =	Yield, %	Boiling point, °C.	Mm.	n^{25}_D	Formula	Composition, % Theoretical Carbon	Hydrogen	Found Carbon	Hydrogen
2-Benzoyl-	73.5[a]	180–181	3	1.5330	$C_{18}H_{22}O_3$	75.49	7.74	75.73 75.48	7.50 7.34
2-[2′,4′-Dimethylbenzoyl]-	85	193–193.5	3	1.5305	$C_{20}H_{26}O_3$	76.40	8.33	76.37 76.23	8.45 8.45
2-[4′-Methoxybenzoyl]-	80	211–212	3	1.5430	$C_{19}H_{24}O_4$	72.12	7.65	72.06 71.99	7.64 7.44

[a] In every case there was a small fraction which boiled slightly higher but on saponification only the starting acid was recovered.

with four times their weight of a solution of absolute ethanol containing sulfuric acid (15% by weight). The reaction mixtures were poured into water, extracted in ether and after washing the ether extracts with water were dried over anhydrous sodium sulfate. After removal of the solvent the esters were distilled under reduced pressure. The analyses and physical constants for these esters are listed in Table I.

Saponification of the ester adducts with ethanolic potassium hydroxide (10% by weight) gave almost quantitative yields of the original acid adducts and no isomeric products could be detected.

***cis*-2-Benzoyl-4,5-dimethyl-Δ⁴-tetrahydrobenzoic Acid.**—A solution of 14.0 g. of 4,5-dimethyl-Δ⁴-tetrahydrophthalic anhydride (m. p. 78–78.5°) in 300 cc. of sodium-dry benzene was added dropwise over a period of 3 hours to a well-stirred and cooled (7–8°) suspension of 23.0 g. of aluminum chloride in 200 cc. of dry benzene. The reaction mixture was allowed to stand seven days at 10–12° and then decomposed in ice and water containing 50 cc. of concentrated hydrochloric acid. The organic layer was separated, the benzene removed by steam distillation and the residual oil dissolved in sodium bicarbonate solution, decolorized (Norit) and acidified. The resulting solid (m. p. 70–80°) was predominantly 4,5-dimethyl-Δ⁴-tetrahydrophthalic anhydride. The major portion of this unchanged starting material was removed in boiling petroleum ether. Several crystallizations of the residual oil from ether and petroleum ether gave 1.0 g. of the acid, melting at 147–148°. When mixed with the low melting adduct (m. p. 141–142°) it melted at 126–127° with previous softening.

Anal. Calcd. for $C_{16}H_{18}O_3$: C, 74.40; H, 7.02. Found: C, 74.61, 74.42; H, 7.17, 6.99.

The above solid was recovered unchanged from the action of a 100% excess of an ethereal solution of diazomethane. The methyl ester (m. p. 108–110°) was obtained by the portionwise addition of methyl sulfate and sodium hydroxide to this product at 80°.

Conversion of the *cis* Ester to the *trans* Acid (m. p. 141–142°).—The methyl ester (0.5 g.) was refluxed with ethanolic sodium ethylate (0.1 g. of sodium and 2.0 cc. of absolute ethanol) for four hours. The reaction mixture, when cold, was diluted with water and acidified. The resulting solid when crystallized from ether–petroleum ether mixture gave 0.1 g. of cubic crystals, which melted alone or on admixture with *trans*-2-benzoyl-4,5-dimethyl-Δ⁴-tetrahydrobenzoic acid at 139–141°.

Acknowledgments.—We wish to acknowledge our indebtedness to Professor L. F. Fieser for the use of his analytical samples which made a direct comparison with our products possible.

Summary

An examination of the isomeric adducts resulting from the reaction of β-benzoylacrylic acid with 2,3-dimethylbutadiene has revealed that the isomer melting at 141–142° is *trans*-2-benzoyl-4,5-dimethyl-Δ⁴-tetrahydrobenzoic acid. The *cis* isomer (m. p. 147–148°) has been prepared and isomerized, through its methyl ester, to the *trans* form (m. p. 141–142°). The isomer, melting at 189°, probably results from the migration of the double bond from the normal position in the adduct to one of conjugation with some other center of unsaturation.

SASKATOON, SASKATCHEWAN RECEIVED MARCH 21, 1947

2-Hydroxyacetylfuran

BY FRANK KIPNIS, HAROLD SOLOWAY AND JOHN ORNFELT

The preparation of 5-nitro-2-hydroxyacetylfuran has been reported by Stillman and Scott.[1] During work in progress at this Laboratory, we have been interested in the preparation of furan ketols, and, in view of the appearance of the above patent, we wish to announce the synthesis of 2-hydroxyacetylfuran and the furoic acid ester thereof.

Diazoacetylfuran has been prepared[2] by the interaction of furoyl chloride with diazomethane. On treatment of the diazoketone with 2 *N* sulfuric acid, nitrogen was evolved, and, by working up the mixture in the usual manner, hydroxyacetylfuran was obtained in good yield. When the diazoketone was heated with furoic acid in benzene, 2-furoyloxyacetylfuran was produced.

Experimental

2-Hydroxyacetylfuran.—Ten and one-half grams (0.077 mole) of diazoacetylfuran[3] was mixed with 150 ml. of 2 *N* sulfuric acid and 60 ml. of dioxane. A vigorous evolution of nitrogen occurred, and the temperature rose spontaneously to 45°. The mixture was stirred and maintained at that temperature (water-bath) for four hours, at the end of which time the temperature was allowed to drop to 25°. After neutralization with solid potassium carbonate, the solution was filtered and distilled from the steam-bath at reduced pressure, removing all of the dioxane and some of the water. The residue was cooled, salted with sodium chloride and extracted six times with 30 ml. of ether. The solvent layer was dried with calcium sulfate, filtered and stripped, finally under reduced pressure, leaving a crystalline residue. This material was recrystallized three times

---

[1] Stillman and Scott, U. S. Patent 2,416,235 (February 18, 1947).

[2] Burger and Harnest, THIS JOURNAL, 65, 2382 (1943); Burger, U. S. Patent 2,400,913 (May 28, 1946).