d_{21} 0.9269; hence $MR = 58.82$, while (X) requires $MR = 59.15$. We were unable to obtain this substance absolutely free from an impurity of diketonic character, which gave a positive response to the pyrrole test.

Butyrolactone[9] (VIII, 7.5 g.), in ethereal solution was treated with **phenylmagnesium bromide** (prepared from 2.1 g. of magnesium and 13.7 g. of bromobenzene); violent reaction took place. The reaction product, isolated as usual, crystallized spontaneously. By recrystallization from benzene, the needles of 1,1-diphenylbutane-1,4-diol (XII), m. p. 108°, were obtained; yield 2 g. *Anal.* Calcd. for $C_{16}H_{18}O_2$: C, 79.3; H, 7.4; active H, 0.827. Found: C, 78.9; H, 7.5; active H, 0.728.

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[9] Johansson and Sebelius, *Ber.*, **51**, 4820 (1918), b. p. 104° at 19 mm.

Summary

The reaction between dimethyl maleate and maleic anhydride and Grignard compounds (benzylmagnesium chloride, butylmagnesium bromide, ethylmagnesium bromide) has been studied. Dimethyl maleate gives, by interaction with 3 mols of the organometallic compound, 1,4-diketones of the general formula $RCOCH_2CH(R)COR$, while from maleic anhydride γ,γ-dialkyl-γ-hydroxycrotonic acids and a variety of neutral products are obtained.

The reaction mechanism is discussed.

Rehovoth, Palestine Received July 12, 1938

[Contribution from the Chemical Laboratory of Harvard University]

The Influence of α-Halogen Substitution on the Enolization of Ketones

By E. P. Kohler[1] and H. M. Sonnichsen

Halogen substitution in the α-position is known to promote the enolization of ketones in acid media,[2] but the effect of α-halogen substitution on the enolization of ketones in basic solution has been investigated less extensively. Bartlett's measurements of the rate of bromination and chlorination of acetone in basic solution[3] have indicated that enolization is the rate-controlling step in the reaction of ketones with halogens in the presence of bases, and if this mechanism is correct there can be no doubt that α-halogen substitution promotes enolization in basic media, for in practically every case[4] the only product which can be isolated from the alkaline halogenation of a methyl ketone is a trihalo methyl ketone or its cleavage products. Furthermore, if mono- and dihalomethyl ketones are prepared, they are found to react with halogens in the presence of bases more rapidly than the corresponding unsubstituted ketones.[5]

Direct chemical evidence for the theory that α-halogen substitution promotes enolization of carbonyl compounds is not plentiful. Watson observed that brominated acetones and acetophenones are acidic, but later proved that this acidity was to be ascribed to hydrolysis rather than enolization.[6] Fisher[7] found that several substituted dibromo acetophenones were markedly acidic, but like Watson did not attribute this acidity to enolization.

Thus, all discussion of the influence of α-halogen substitution on the enolization of carbonyl compounds in basic solution has been based on assumptions concerning the mechanism of bromination of ketones. In the experiments with α-bromo-β,β-diphenyl propionyl mesitylene described below, we have found direct chemical evidence in support of the theory that α-halogen substitution promotes the enolization of ketones in basic media, independent of any assumptions concerning the mechanism of the reactions of carbonyl compounds.

Investigations in this Laboratory and elsewhere[8] have indicated that the mesityl radical has a marked influence on the stability of enols; therefore it might be expected that α-bromo-β,β-diphenyl propionyl mesitylene would be a rather easily enolized ketone. One would not expect the influence of the mesityl radical to be strong enough, however, to produce any marked peculiarities in the behavior of a monoketone, so it

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[1] The investigations described in this paper were completed under the direction of Professor Kohler, but the manuscript was prepared for publication by the junior author after Professor Kohler's death.

[2] Watson and Yates, *J. Chem. Soc.*, 3318 (1931); 1207 (1932).

[3] Bartlett, This Journal, **56**, 967 (1934).

[4] Fuson has been able to obtain stepwise halogenation in only one case [Bull, Ross and Fuson, *ibid.*, **57**, 764 (1935)].

[5] Fuson, Lewis and DuPuis, *ibid.*, **54**, 1114 (1932).

[6] Watson, Nathan and Laurie, *J. Chem. Phys.*, **3**, 170 (1935); Edwards, Evans and Watson, *J. Chem. Soc.*, 1942 (1937).

[7] Fisher and Walling, This Journal, **57**, 1562 (1935).

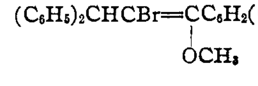
[8] (a) Kohler and Thompson, *ibid.*, **59**, 886 (1937); (b) Kohler, Tishler and Potter, *ibid.*, **57**, 2517 (1935); (c) Barnes and Green, *ibid.*, **60**, 1549 (1938); (d) Lutz and Wood, *ibid.*, **60**, 705 (1938); (e) Barnes, *ibid.*, **57**, 937 (1935); **60**, 1168 (1938).

was with considerable astonishment that we first observed that the above-mentioned bromoketone was extremely soluble in cold methyl alcoholic potassium hydroxide, so soluble in fact that it is extracted easily from benzene by alcoholic alkali.

The solubility of the bromide in ethanol is 0.214 g. per 100 cc. at 25°. In saturated ethyl or methyl alcoholic potassium hydroxide the solubility is at least 50 g. per 100 cc. The bromide could be recovered quantitatively from these solutions by acidification or dilution with water, but if they were allowed to remain for any length of time at room temperature, enough unsaturated ketone, $(C_6H_5)_2C{=}CHCOC_6H_2(CH_3)_3$, was formed to color the product yellow. The corresponding saturated ketone, $(C_6H_5)_2CHCH_2COC_6H_2(CH_3)_3$, although it is quite soluble in alcohol, shows no evidence of solubility in methyl alcoholic potassium hydroxide. The corresponding α-bromoketone in the phenyl series, $(C_6H_5)_2CHCHBrCOC_6H_5$, was soluble in methyl alcoholic potassium hydroxide, but to a much smaller extent, and the original compound could not be recovered by acidification. Instead, a new substance melting at 230–240° was obtained, which was not investigated further.

The presence of the enolic modification of α-bromo-β,β-diphenyl propionyl mesitylene in solutions in alcoholic potassium hydroxide was demonstrated by the formation of the enol methyl ether in alkaline solution. Dimethyl sulfate gave a 30% yield of $(C_6H_5)_2CHCBr{=}\underset{OCH_3}{C}C_6H_2(CH_3)_3$, and 65% of the bromide was recovered unchanged, along with traces of β-phenyl benzalacetomesitylene. Traces of the same ether were produced by methyl iodide.

α-Bromo-β,β-diphenyl propionyl mesitylene prepared by bromination of the Grignard addition product of phenylmagnesium bromide and benzalacetomesitylene often contains more bromine than the theoretical percentage. A large batch of crude bromide was methylated with dimethyl sulfate, yielding 20% of the ether and about 75% of unchanged starting material. The recovered bromoketone was then recrystallized and analyzed. Methylation of the analyzed sample gave the methoxyl derivative in 30% yield, leaving little doubt that only the bromoketone in the crude bromide underwent reaction as follows



$$(C_6H_5)_2CHCHBrCOC_6H_2(CH_3)_3 + (CH_3)_2SO_4 \longrightarrow (C_6H_5)_2CHCBr{=}\underset{OCH_3}{C}C_6H_2(CH_3)_3$$

Proof of the position of the bromine atom in α-bromo-β,β-diphenyl propionyl mesitylene was hardly necessary, since the same substance has been prepared by direct bromination of the saturated ketone, and the reactions of the Grignard reagent formed by treating the bromoketone with C_2H_5MgBr[8b] leave little doubt as to its structure. Further evidence of the position of the bromine atom was furnished by the bromination of benzhydrylacetomesitylene in alkaline solution according to Fuson's method for brominating acetomesitylene.[9] The dibromide obtained, $(C_6H_5)_2CHCBr_2COC_6H_2(CH_3)_3$, was identical with that formed by the alkaline bromination of α-bromo-β,β-diphenyl propionyl mesitylene.

To prove that the methoxyl compound did not have an indene structure, it was heated for forty-eight hours on the steam-bath with methyl alcoholic potassium hydroxide. The insoluble crystals gradually changed to a clear colorless oil, and potassium bromide was deposited. On acidification of the solution, the oil became bright yellow, and from the ether extract crystals of pure β-phenyl benzalacetomesitylene were obtained. Their identity was proved by hydrogenation to the corresponding saturated ketone and by their failure to depress the melting point of an authentic sample.

Experimental

α-Bromo-β,β-diphenyl Propionyl Mesitylene.—Twenty-five grams of benzalacetomesitylene in ether was added to a solution of phenylmagnesium bromide prepared from 5 g. of magnesium and 34 g. of bromobenzene. The solution was boiled for one hour, then cooled to −10° and stirred vigorously while 11 cc. of dry bromine was added dropwise, keeping the temperature below −5°. The magnesium derivative was decomposed immediately with ice and sulfuric acid and the precipitated bromoketone filtered off. The ether solution was washed with water, dried over calcium chloride and evaporated to recover the remainder of the bromoketone. The crude solid was recrystallized from benzene: yield of purified material, 80 to 90%, m. p. 172–173°.

Preparation of $(C_6H_5)_2CHC(Br){=}C(OCH_3)C_6H_2(CH_3)_3$.—α-Bromo-β,β-diphenyl propionyl mesitylene was dissolved in saturated methyl alcoholic potassium hydroxide by adding to the dry solid a number of cubic centimeters of the basic solution equal to twice the number of grams of solid. To prevent formation of unsaturated ketone, the bromide was ground finely and dissolved as rapidly as possible. Addition of 1 cc. of ether per 10 cc. of alcoholic alkali facilitated solution of the bromide, but if more than this was added the yield of methoxyl compound was reduced. After the solution became clear it was cooled in an ice-bath

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(9) Fuson and Walker, THIS JOURNAL, 52, 3269 (1930).

and a number of cubic centimeters of dimethyl sulfate equal to the number of grams of bromide used was added with vigorous stirring and efficient cooling. The dimethyl sulfate was added as rapidly as possible without allowing the solution to boil. The maximum rate was three or four drops per second in runs on more than 25 g. of material and less in smaller runs. When about two-thirds of the dimethyl sulfate had been added, evolution of gas became noticeable, and the mixture became semi-solid. The gas evolved was the same as that produced when methyl alcoholic potassium hydroxide was treated with dimethyl sulfate; it was identified as dimethyl ether by its boiling point. The reaction mixture was allowed to stand at ice-bath temperatures for several hours, usually overnight, then thoroughly washed with water to remove sodium sulfate and filtered to remove the rather insoluble starting material. This recovered bromide was washed with ether to remove all traces of methoxyl compound. The ether filtrate contained the methoxyl compound, quite large amounts of bromide and barely enough unsaturated ketone to color the solution yellow. The ether solution, dried and evaporated to a small volume, deposited crystals of the bromide. The methoxyl compound separated from the filtrate, but, following this, a mixture of the reaction product and starting material was obtained, the bromide in fine needles and the methoxyl compound in large hexagonal plates. Separation of the mixture was effected by extracting the diluted ether solution with methyl alcoholic potassium hydroxide, thus removing the bromide completely. The crystals could also be separated mechanically.

The methoxyl compound, m. p. 115–116°, separates as hexagonal plates from ether, is slightly soluble in petroleum ether and quite soluble in acetone and benzene.

Anal. Calcd. for $C_{25}H_{25}OBr$: C, 71.3; H, 6.0; Br, 18.97; CH_3O, 7.36; mol. wt., 421. Found: C, 71.1; H, 6.2; Br, 19.1, 19.4; CH_3O, 7.0; molecular weight in boiling acetone, 410, 409, 403.[10]

The bromine determinations were carried out by the Carius method, but in order to decompose the sample completely it was necessary to heat the tubes for six hours at 250°, open them and boil out the spent acid, then add fresh fuming acid and heat above 300° for eighteen hours. Analyses by the Parr bomb method failed to decompose the sample.

α,α-Dibromo-β,β-diphenyl Propionyl Mesitylene.—β,β-Diphenyl propionyl mesitylene and α-bromo-β,β-diphenyl propionyl mesitylene both gave nearly quantitatively the same dibromide, $(C_6H_5)_2CHC(Br)_2COC_6H_2(CH_3)_3$, when shaken for one week with a solution of bromine in aqueous alkali.[9]

Anal. Calcd. for $C_{24}H_{22}OBr_2$: Br, 32.86. Found: Br, 33.0, 33.0.

The ether solutions of α,α-dibromo-β,β-diphenyl propionyl mesitylene rapidly became colored on standing and liberated bromine. The pure white solid dibromide, m. p. 135–136°, is stable at ordinary temperatures, but turns red on heating. When the dibromide was heated on the steam-bath for thirty hours with 20% aqueous potassium hydroxide, about 75% of the dibromide was recovered unchanged. The remainder was a yellow oil, which deposited crystals of β-phenyl benzalacetomesitylene. When 2 g. of the dibromide was boiled with 25 cc. of saturated methyl alcoholic potassium hydroxide for five hours, all of the bromine was removed, since the resulting oil, after it had been taken up in benzene and washed with water, no longer gave a Beilstein test. When the solvent was evaporated, crystals of β-phenyl benzalacetomesitylene were deposited.

Summary

α-Bromo-β,β-diphenyl propionyl mesitylene was shown to exist as the enolic modification in solutions in alcoholic potassium hydroxide by the preparation of the enol methyl ether in alcoholic alkali.

The ease with which α-bromo-β,β-diphenyl propionyl mesitylene is enolized by bases is attributed to the influence of the halogen atom in the α-position. This supports the theory that α-halogen substitution favors enolization in alkaline media.

CAMBRIDGE, MASS. RECEIVED AUGUST 23, 1938

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(10) These determinations were made by Mr. D. M. Bowen.