Nickel has been considered to be inferior to platinum as a catalyst for hydrogenation because, in general, nickel is not active as a catalyst at room temperature. This characteristic has its advantages, however, as it permits selective reduction between two reducible groups through control of temperature of hydrogenation. Such selective reduction was achieved at 125° with acetylbenzoylmethane, phenyl ethyl ketone, benzoin, benzil, benzophenone, isonitrosopropiophenone, benzyl cyanide and *o*-methyl phenyl cyanide when the carbonyl, oxime or cyanide group was reduced without affecting the benzenoid ring. At 175 to 200° complete reduction of these compounds occurred. By a similar temperature control it was found possible to reduce the pyridinoid ring in quinoline, α-pyridylphenylethylene, γ-pyridylphenylethylene and α-benzylpyridine without reducing the benzenoid ring.

Summary

The preparation of a reasonably active nickel catalyst has been described and experimental details are given for the satisfactory reduction of forty-five representative organic compounds. The results have been summarized and need not be repeated here. In general, it may be said that an apparatus and technique have been used which have made it possible to determine rather accurately the amount of hydrogen absorbed and the rate of the reduction. This has made it feasible readily to carry on selective reduction of one of two reducible structures through the control of the temperature or time interval of the reduction. The merits of methylcyclohexane, alcohol and ether as solvents during reduction have been discussed.

MADISON, WISCONSIN

[CONTRIBUTION FROM THE LABORATORY OF THE UNIVERSITY OF BUFFALO]

THE KETO-ENOL EQUILIBRIUM OF ETHYL ALPHA-PHENYL ACETOACETATE

BY HOWARD W. POST AND GLADYS A. MICHALEK[1]

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The keto–enol equilibrium of ethyl acetoacetate and its derivatives has already received considerable attention, most of the data published being concerned with the unsubstituted ester or its alkyl derivatives. The effect of substituents in the α-position, especially phenyl, has not been extensively investigated as far as the keto–enol equilibrium of the compounds is concerned. It was our purpose to prepare ethyl α-phenyl acetoacetate and to study its keto–enol equilibrium by means of bromine titration as well as its index of refraction.

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[1] Presented to the Committee on Graduate Study of the University of Buffalo by the second author in partial fulfilment of the requirements for the degree of Master of Arts.

At ordinary temperatures pure ethyl acetoacetate exists in the enol form to the extent of about 7.7% while α-methyl acetoacetic ester contains about 4.1% enol (at 18°). α,γ-diphenyl acetoacetic ester contains about 18.5% enol at 100°.[2]

Ethyl thiolacetoacetate shows 30.8% enol.[3]

The enol form may be titrated against standard bromine solution[4] or we may depend on some physical property such as refractive index.[5]

The n_D^{20} of ethyl acetoacetate has been found to be 32.000, corresponding to 59.2% enol at 20°. Obviously this is at wide variance with the value 7.7% obtained by bromine titration and it was our intention to investigate the composition of equilibrium mixtures of ethyl α-phenyl acetoacetate as evidenced by the figures on enol content obtained both by bromine titration and by the determination of the refractive index.

We prepared ethyl α-phenyl acetoacetate by the method of Beckh, modifying the procedure, however, to increase the yield, which was none too great even then. Enol content was determined by bromine titration (indirect method) and by the determination of the molecular refraction.

Preparation of the Ester.—α-Phenyl substitution products of acetoacetic ester may be made by treating the sodium derivative of ethyl acetoacetate with the proper aryl halide providing there are substituents in the ring to give the halogen the necessary negativity. The indirect method of Beckh,[6] however, had to be resorted to in the preparation of the phenyl derivative, modified as follows.

Benzyl cyanide and ethyl acetate were condensed in the presence of sodium ethylate to give the sodium derivative of acetobenzyl cyanide. This nitrile was then hydrolyzed to the ester by means of hydrochloric acid and ethyl alcohol, through the stage of the imide of the ester.

Our procedure differed from that of Beckh in several particulars. In the first place, instead of dissolving the sodium in absolute alcohol, it was suspended in dry ether and the alcohol added. This was merely for the sake of convenience. Second, after condensation of the ethyl acetate and benzyl cyanide, Beckh removed unchanged benzyl cyanide by dissolving the salt in water and extracting with ether. We found it somewhat more effective and considerably more convenient to wash the salt with ether before dissolving in water. After freeing the acetobenzyl cyanide with carbon dioxide, Beckh extracted it with ether. At the comparatively low temperature which was obtained by using a strong stream of carbon dioxide from a tank, the acetobenzyl cyanide came down as crystals which could be removed by filtration. This gave a somewhat purer product than would have been obtained by extraction. Our greatest deviation, however, from the method of Beckh lay in the decomposition of the imido ester. We poured the alcohol solution directly into ice water, extracted with ether, washed the ether solution directly into ice water, and washed the ether solution with sodium carbonate solution, while Beckh allowed the alcoholic solution to stand over potassium hydroxide or soda lime for several days.

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[2] Dieckmann, *Ber.*, **55B**, 2470 (1923).

[3] Baker and Reid, This Journal, **51**, 1567 (1929).

[4] Meyer, *Ann.*, **380**, 212; Grossmann, *Z. physik. Chem.*, **109**, 305 (1924).

[5] Auwers, *Ber.*, **44**, 2523 (1911).

[6] Beckh, *ibid.*, **31**, 3160 (1898).

Allowing the mixture to stand over soda lime or potassium hydroxide did not remove all the hydrochloric acid even when a considerably longer time than directed was allowed. In one run we attempted to remove it by blowing dry air through the solution held at about 40°. Before all the acid was removed the solution began to precipitate and on completing the hydrolysis we recovered the acetobenzyl cyanide almost quantitatively.

The yields were never high. In the condensation between ethyl acetate and benzyl cyanide the yield was between 25 and 30% of the theoretical. About 25% of the benzyl cyanide could be recovered. In the hydrolysis of the acetobenzyl cyanide the purified ester never represented more than 10% of the theoretical amount and often as low as five.

Acetobenzyl cyanide crystallized in glistening white crystals melting at 90°; insoluble in water, easily soluble in alcohol, ether and ethyl acetate. The alcoholic solution gave a weak green color with ferric chloride. It is also soluble in sodium carbonate solution and other alkaline media, from which it can be precipitated by acidification. It absorbs bromine readily.

Ethyl α-phenyl acetoacetate is a colorless, slightly viscous oil boiling at 145–147° at 11-mm. pressure. Its alcoholic solution gives a strong violet color with ferric chloride solution.

Anal. Calcd.: C, 68.86; H, 6.84. Found: C, 68.66, 68.56; H, 6.66, 6.50.

The phenylhydrazone of ethyl α-phenylacetoacetate was prepared by heating the ester with phenylhydrazine. It crystallizes in white needles turning yellow on exposure to the air; melting point, 103.9 to 104.2°, Beckh reporting 104°.

1,4-Diphenyl-3-methyl-5-pyrazolone was prepared by heating the hydrazone to 170°, whereupon it melted and then solidified, forming crystals which when recrystallized from acetic acid melted at 193–195°. Beckh reported this melting point as 196°.

Bromine Titration

In titrating the enol form of ethyl α-phenyl acetoacetate against standard bromine solution, we first compared what are known as the direct and the indirect methods. By the direct method[7] the alcohol was cooled to −7°, the ester dissolved therein quickly and titrated against freshly prepared bromine ($N/5$). Since the alcoholic bromine solution is not stable for any great length of time, it must be standardized at the time of use. By the indirect method[8] the sample is dissolved in alcohol as before and alcoholic bromine added. The bromine is here approximately of $N/5$ strength and is added until a faint yellow color persists. The excess is then removed by the addition of 2 cc. of alcoholic β-naphthol solution. Potassium iodide solution is then added and the solution heated generally for twenty minutes on the water-bath in the dark, the liberated iodine being titrated against sodium thiosulfate solution. Trying both methods we found the volumes of thiosulfate and bromine to check.

Number	1	2	3
Bromine, cc.	4.60	5.05	5.45
Direct. $Na_2S_2O_3$ equiv., cc.	7.2	8.45	8.45
Indirect, $Na_2S_2O_3$, cc.	7.15	8.3	8.45

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[7] Auwers and Eisenlohr, *Z. physik. Chem.*, **83**, 429 (1913).

[8] Meyer, *Ber.*, **44**, 2718 (1911).

Using the indirect method of Meyer we obtained the following values for ethyl α-phenyl acetoacetate

Sample, g.	0.4223	0.3317	0.3012	
$Na_2S_2O_3$, cc.	10.8	8.7	7.9	
Enol, %	27.9	28.9	28.9	Av.. 28.6

The literature seems to agree that the amount of thiosulfate used is directly proportional to the amount of bromine absorbed. We suggest, as a mechanism, the splitting off of positive bromine, its reaction with potassium iodide to liberate 2I and the reaction of the 2I with sodium thiosulfate. Obviously it would be rather difficult to prove this—isolation of bromo ester undoubtedly would not give us positive bromine united to carbon for very long—a shift to negative bromine would be expected to take place almost immediately when isolated.

Molecular Refraction

Using the additive values found in the literature for the various elements in ethyl acetoacetate and applying these values to the α-phenyl ester, including modifications for various constructions, we calculated the molecular refraction for the equilibrium mixture as follows

$$n_D^{20} = 1.5130 \text{ and } d_4^{20} = 1.0850$$

Then using the formula

$$\frac{n^2 - 1}{n^2 + 2} \times \frac{M}{d} = 57.10$$

The data for ethyl acetoacetate compared with those for ethyl α-phenylacetoacetate can be plotted as follows

	100% keto calcd.	Found	100% enol
$CH_3COCH_2COOC_2H_5$	31.57	32.00	32.62
$CH_3COCH(C_6H_5)COOC_2H_5$	55.66	57.10	56.71

using Brühl refraction equivalents.[9]

From these figures it will be seen that ethyl acetoacetate shows an enol content of 59.2% by the method of the refractive index and ethyl α-phenyl acetoacetate, 137.13%. These results are nowhere near the values obtained by bromine titration, 7.7 and 28.6%, respectively, and under the circumstances we prefer to place more reliance on the latter pair of figures, as indeed do all those who have preceded us in this sort of work.

We explain our "abnormal" results by assuming an effect due to the presence of the phenyl group in the α-position. We have here at least one pair of conjugate double bonds and if we do not wish to pin ourselves down to any structure of benzene, at least we have the anomalous structure of the phenyl radical, whatever its actual configuration, to use as a reason for this increase in molecular refraction over the value calculated additively. Other investigators have met with the same obstacles.

[9] Brühl, *Ber.*, **27**, 2478 (1894).

Discussion of Results

Ethyl α-phenyl acetoacetate has been found to contain 28.6% of the enol form at room temperatures (20°) in pyrex glass. This is higher than that of the unsubstituted ester and the methyl derivative. These and other values mostly taken from the literature are as follows

$(CH_3CO)_2CHCOOC_2H_5$	100% enol
$CH_3COCH(C_6H_5)COOC_2H_5$	28.6% enol
$CH_3COCH_2COOC_2H_5$	7.7% enol
$CH_3COCH(CH_3)COOC_2H_5$	4.1% enol
$CH_3COCH(CH_2C_6H_5)COOC_2H_5$	3.4% enol
$CH_3COCH(C_2H_5)COOC_2H_5$	Mostly ketonic
$CH_3COCH(CH_2\text{—}CHCH_2)COOC_2H_5$	Mostly ketonic

From data at hand, then, it would appear that electropositive substituents repress enolization or at least are accompanied by such repression and electronegative groups facilitate this process.

Conclusions

Lowry and Burgess propose the chelate ring formula for acetoacetic ester.[10] If we modify this conception to admit of oscillation of affinity to account for keto and enol shift, the effect of an electronegative group, substituted in the α-position is more apparent. This group facilitates ionization of the α-hydrogen in much the same manner that chlorine is said to facilitate ionization of the substituted acetic acids.

Materials.—Benzyl cyanide was obtained from the Eastman Kodak Co., and used as received. That recovered from the acetobenzyl cyanide synthesis was washed with water, dried over calcium chloride and distilled under reduced pressure.

Ethyl acetate was washed with dilute alkali, then several times with water and dried over calcium chloride or anhydrous copper sulfate. It was then separated and distilled.

Hydrochloric acid gas was generated by dropping concentrated sulfuric acid on dry sodium chloride.

Summary

1. A method for the preparation of α-phenyl acetoacetic ester is outlined. This method is a modification of one already in the literature.

2. Reliable data from bromine titration of this ester show that it has an enol content at equilibrium, room temperature, in pyrex glass, of 28.6%. A mechanism is suggested for this series of reactions.

3. Data on the enol content obtained from a determination of the molecular refraction show 137.13%, obviously unreliable.

4. The increase in enol content of the α-phenyl ester over that of the unsubstituted ester is ascribed to the greater electronegativity of the phenyl over hydrogen, and the abnormally large value obtained by the refractive index method, to the presence of the anomalous benzene ring.

BUFFALO, NEW YORK

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[10] Lowry and Burgess, *J. Chem. Soc.*, 123, 2111 (1923).