A picrate of the reaction product was made with a saturated solution of picric acid in ethanol and recrystallized three times from methanol, m.p. 175–178° dec.

*Anal.* Calcd. for $C_{22}H_{30}N_2O \cdot 2C_6H_6N_3O_7$: C, 51.25; H, 4.57; N, 14.06. Found: C, 51.70; H, 4.80; N, 14.06.

Apparently only the picrate of the imine IV was formed; the picrate of the ketone V, isolated below, is soluble in methanol.

1,1-Diphenyl-1-(β-diethylaminoethoxy)-2-butanone (V).—The mixed product from the above reaction (8.0 g.) was dissolved in 720 ml. of 0.1 *N* hydrochloric acid and allowed to stand at room temperature for one hour. The *p*H of the solution was approximately 3. After extracting the slightly turbid solution once with ether to remove any neutral product formed by hydrolysis, the acid layer was made basic with sodium carbonate and reextracted with ether. This ether extract was dried with sodium sulfate, the ether removed by heating on a steam-bath, and the residue distilled through a Vigreux column; b.p. 171–172° (3 mm.), 6.5 g., $n^{20}D$ 1.5388.

*Anal.* Calcd. for $C_{22}H_{29}NO_2$: C, 77.83; H, 8.61; N, 4.13. Found: C, 78.01; H, 8.35; N, 4.19.

The infrared spectrum shows no absorption in the 2.80–3.20 μ region and shows strong absorption at 5.8 μ characteristic of the carbonyl band. No precipitate with picric acid could be obtained from an alcoholic solution; an oily picrate was formed from aqueous solution. In a preliminary run, similar to the above where the reaction mixture was refluxed in benzene, a 63% yield of a hydrocarbon, identified as unsymmetrical methyldiphenylethylene (VIII),[9] m.p. 50°, was isolated.

The mixed product IV and V, 1.5 g., was dissolved in 6 *N* hydrochloric acid; after standing a few minutes at room temperature the solution became cloudy, and an oil separated. The mixture was warmed on the steam-bath for two hours and the oil which separated was extracted with ether and distilled to give 0.56 g. of a yellow oil, b.p. 110–120° (2 mm.), $n^{20}D$ 1.5850. This is a neutral compound which does not contain nitrogen and shows strong infrared bands at 2.90 and 5.84 μ characteristic of hydroxy and carbonyl groups. It is postulated to be the hydroxy ketone VII, but its identity was not investigated further.

(9) A. Klages, *Ber.*, **35**, 2647 (1902).

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## Studies with N-Halo Reagents. II. New Syntheses of β-Bromo-α-keto Esters, Ethyl Phenylglyoxylate and Phenacyl Bromide Using N-Bromosuccinimide[1]

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The reactions of hydroxy compounds with N-bromosuccinimide were reviewed briefly by Barakat and El-Wahab[2] in their recent account of the degradation of aliphatic α-hydroxy acids with this reagent. The report[3] on the oxidation of alcohols with N-bromosuccinimide led us to investigate reactions of this reagent with α-hydroxy esters as a route to the synthesis of α-keto esters and thence to α-keto acids. Since the α-hydroxy esters were soluble in carbon tetrachloride, we have used it as the reaction medium rather than the aqueous media reported in the studies referred to above.

This study has shown that: (a) the reaction of equimolar amounts of ethyl lactate with N-bromosuccinimide resulted in a mixture of the α-keto ester, ethyl pyruvate and the β-bromo-α-keto ester, ethyl bromopyruvate; this makes the α-hydroxy ester–N-bromosuccinimide reaction generally unattractive for the preparation of unsubstituted α-keto esters (and acids); (b) the 1:2 (or slightly less) mole ratio reactions of ethyl lactate, ethyl DL-α-hydroxybutyrate and ethyl DL-α-hydroxyhydrocinnamate with N-bromosuccinimide gave 64, 66 and 71% yields of the respective β-bromo-α-keto esters; and (c) the reaction of equimolar amounts of ethyl mandelate with N-bromosuccinimide gave ethyl phenylglyoxylate in 79% yield.

Result (b) constitutes a new method of preparing β-bromo-α-keto esters. These esters hydrolyze easily in the cold and thereby are converted to the corresponding β-bromo-α-keto acids. The method is a useful one since α-hydroxy esters are quite readily obtainable in contrast to α-keto esters and acids, which have been employed as starting materials for the preparation of β-bromo-α-keto esters[4] and acids.[5] These results with α-hydroxy esters suggest a number of possibilities of converting hydroxy compounds to α-bromocarbonyl compounds in one easy step.

Result (c) represents a new synthesis of the α-keto ester, ethyl phenylglyoxylate. For cases such as this, where β-bromination cannot occur, the equimolar reaction would be satisfactory for the preparation of α-keto esters, and respectively, acids. The synthesis of ethyl phenylglyoxylate from ethyl mandelate and N-bromosuccinimide appears simpler than by the permanganate oxidation method,[6] the selenium dioxide oxidation of ethyl phenylacetate,[7] the ethyl chloroglyoxylate–benzene condensation[8] or the lead tetraacetate oxidation of methyl mandelate.[9]

An additional study of the one-step hydroxy to α-bromocarbonyl synthesis comprised treating DL-phenylmethylcarbinol with two moles of N-bromosuccinimide. Phenacyl bromide was obtained in 44% yield. Improvements in the synthesis were not investigated.

### Experimental[10]

**Ethyl Bromopyruvate (I).**—To a solution of 5.00 g. (0.042 mole) of freshly distilled ethyl lactate in 75 ml. of C.P. carbon tetrachloride there was added 14.24 g. (0.080 mole) of N-bromosuccinimide. The mixture was refluxed for six hours, during which time a deep red bromine color was dissipated and hydrogen bromide was evolved. The mixture was cooled and filtered with suction to yield 8.1 g. (*ca.* 102%) of crude succinimide. The filtrate was concentrated on a steam-bath to 15 ml., dried over anhydrous sodium sulfate and distilled *in vacuo* from a small modified Claisen flask to yield 5.25 g. (64%) of I, b.p. 83–88° (8 mm.),[11] $n^{24}D$ 1.469, $d^{24}_{20}$ 1.561; $MR_D$ calcd. 34.7, found 34.8.

(1) Presented in part at the Southwest-Southeast Regional Meeting, American Chemical Society, New Orleans, La., December 10, 1953.

(2) M. Z. Barakat and M. F. A. El-Wahab, THIS JOURNAL, **75**, 5731 (1953).

(3) M. Z. Barakat and G. M. Mousa, *J. Pharm. and Pharmacol.*, **4**, 115 (1952).

(4) P. Siefert, E. Vogel, A. Rossi and H. Schinz, *Helv. Chim. Acta*, **33**, 725 (1950).

(5) D. B. Sprinson and E. Chargaff, *J. Biol. Chem.*, **164**, 417 (1946).

(6) H. Gilman and A. H. Blatt (Editors), "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., Coll. Vol. I, 2nd ed., 1946, p. 241.

(7) J. Vene, *Bull. soc. chim.*, **12**, 506 (1945); *C. A.*, **40**, 4661 (1946).

(8) K. Kinder, W. Metzendorf and Dschi-yin-Kwok, *Ber.*, **76B**, 308 (1943); *C. A.*, **37**, 5710 (1943).

(9) E. Baer and M. Kates, THIS JOURNAL, **67**, 1482 (1945).

(10) All m.p.'s and b.p.'s reported herein are uncorrected.

(11) S. Archer and M. G. Pratt, THIS JOURNAL, **66**, 1657 (1944); b.p. 116–121° (27 mm.) and redistilled for analysis, b.p. 92.5–94.0° (10 mm.).

**Ethyl DL-β-Bromo-α-ketobutyrate (II).**—α-Bromo-*n*-butyric acid was prepared in 80% yield in the manner given for α-bromoisocaproic acid.[12] Hydrolysis to α-hydroxy-*n*-butyric acid using potassium carbonate[13] and esterification with absolute alcohol and anhydrous copper sulfate[14] gave ethyl α-hydroxy-*n*-butyrate, b.p. 88–89° (51 mm.), $n^{29}D$ 1.414.[15]

To a solution of 4.63 g. (0.035 mole) of the hydroxy ester in 100 ml. of C.P. carbon tetrachloride there was added 12.59 g. (0.070 mole) of N-bromosuccinimide. The mixture was refluxed for five hours and treated as described for I to yield 4.86 g. (66%) of II, b.p. 79–81° (9 mm.), reported[4] 80–81° (12 mm.), $n^{20}D$ 1.462, $d^{20}_{20}$ 1.455; $MR_D$ calcd. 39.3, found 39.5.

**Ethyl DL-β-Bromophenylpyruvate (III).**—Ethyl DL-α-hydroxyhydrocinnamate was prepared by the action of silver nitrite on phenylalanine[16] followed by esterification. The hydroxy ester showed b.p. 108.0–110.5° (4 mm.),[17] $n^{20}D$ 1.507, $d^{20}_{20}$ 1.099; $MR_D$ calcd. 52.6, found 52.6.

A solution of 7.76 g. (0.040 mole) of the hydroxy ester in 100 ml. of C.P. carbon tetrachloride was treated with 13.68 g. (0.077 mole) of N-bromosuccinimide in the manner described above to give 7.70 g. (71%) of III, b.p. 137–139° (4 mm.), $n^{20}D$ 1.543, $d^{20}_{20}$ 1.408; $MR_D$ calcd. 58.8, found 59.9.

**Ethyl Phenylglyoxylate (IV).**—The reaction of 10.81 g. (0.060 mole) of ethyl mandelate from the esterification of mandelic acid, with 10.68 g. (0.060 mole) of N-bromosuccinimide in 100 ml. of C.P. carbon tetrachloride refluxing for eight hours gave 8.39 g. (78.5%) of IV, b.p. 101.5–102.0° (3.5 mm.); reported[5] 118° (5 mm.), $n^{25.5}D$ 1.513. The behavior of the 2,4-dinitrophenylhydrazone on heating was the same as that described by Brewer and Herbst.[18]

A portion of the keto ester was saponified according to the procedure of Baer and Kates[9] for methyl phenylglyoxylate; the crude oily phenylglyoxylic acid was not distilled but was recrystallized directly twice from carbon tetrachloride; on heating it moistened at 61° and melted at 65–66°, reported[9] m.p. 64.5–65.5°; neutral equivalent found 150.5, calcd. 150.1.

**Phenacyl Bromide (V).**—A solution of 9.15 g. (0.075 mole) of DL-phenylmethylcarbinol in 250 ml. of C.P. carbon tetrachloride was treated with 26.70 g. (0.150 mole) of N-bromosuccinimide. The mixture was refluxed and shortly acquired a deep red color. After 30 minutes the color changed rapidly (characteristic of the reaction of N-bromosuccinimide with secondary hydroxyl groups) to a mixture of an orange solid and pale yellow solution; much hydrogen bromide was evolved. Upon refluxing for five hours the mixture was cooled and filtered to yield 14.90 g. (*ca.* 100%) of crude succinimide, and the filtrate was dried over anhydrous sodium sulfate. Evaporation of the solvent gave a yellow-brown oil which was distilled (in one smaller scale run this oil crystallized in the refrigerator); the product was collected at 93–98° (3 mm.) and allowed to crystallize overnight in the refrigerator. The crystals were collected on a filter, washed several times with cold petroleum ether and dried on filter paper; 6.60 g. (44.2%), m.p. 45–48°[19]; a mixed melting point with a known sample of phenacyl bromide showed no depression.

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(12) N. L. Drake (Editor), *Org. Syntheses*, **21**, 74 (1941).

(13) C. A. Bischoff and P. Walden, *Ann.*, **279**, 102 (1894).

(14) Esterifications of α-hydroxy acids were carried out using the method described by E. Clemmensen and A. H. C. Heitman, *Am. Chem. J.*, **42**, 331 (1909).

(15) H. R. Henze and W. B. Leslie, *J. Org. Chem.*, **15**, 903 (1950); b.p. 74.5° (25 mm.) and $n^{20}D$ 1.4179.

(16) According to a procedure from L. E. McClure, this Laboratory, and S. Thomas, University of California at Los Angeles; see also C. G. Baker and A. Meister, THIS JOURNAL, **73**, 1336 (1951).

(17) E. H. Charlesworth, J. A. McRae and H. M. MacFarlane, *Can. J. Research*, **21B**, 37 (1943); *C. A.*, **37**, 4057 (1943); b.p. 148–150° (15 mm.).

(18) S. D. Brewer and R. M. Herbst, *J. Org. Chem.*, **6**, 867 (1941); *C. A.*, **36**, 757 (1942).

(19) "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., Coll. *Vol. II*, p. 480; m.p. 45–48°.

## Reaction of Isopropylmagnesium Bromide with Alkyl Aryl Ketone

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This communication is an extension of our studies on the reactions of seventeen alkyl *p*-alkylphenyl ketones.[1,2] We have allowed each ketone to react with the Grignard reagent, prepared from isopropylmagnesium bromide, under as nearly identical conditions as possible. The results of these reactions are recorded in Table I. As has been observed in other studies the isopropylmagnesium bromide shows a pronounced tendency to produce an enolization-type reaction with these ketones.[3]

### Experimental

**The Reaction Procedure.**—The reactions herein reported were done as nearly exactly like those using ethylmagnesium bromide[2] as possible. This includes the preparation of the Grignard reagent, the choice of concentration of each reactant, the temperature of the reaction, the time of the reaction, the collection and analysis of gas evolved,[4] the decomposition of the complex formed, and the distillation of the liquid products. Certain variations in handling the liquid products after distillation were used.

TABLE I

ALKYL 4-R-PHENYL KETONES AND ISOPROPYLMAGNESIUM BROMIDE

| 4-R | E[a] | R[b] | A[c] | Liquid recovery, %[d] | Analyses of alcohols: Carbon, % Calcd. | Carbon, % Found | Hydrogen, % Calcd. | Hydrogen, % Found |
|---|---|---|---|---|---|---|---|---|
| | 4-R-$C_6H_4COCH_3$ | | | | | | | |
| H | 24 | 2 | 74 | 97 | 80.49[e] | 80.66[e] | 9.76[e] | 9.54 |
| Me | 29 | 7 | 64 | 80 | 80.90 | 80.76 | 10.11 | 9.96 |
| Et | 34 | 7 | 59 | 90 | 81.25 | 81.26 | 10.42 | 10.25 |
| *i*-Prop | 31 | 7 | 62 | 88 | 81.55 | 81.00 | 10.68 | 10.29 |
| *t*-Bu | 34 | 9 | 57 | 92 | 81.81 | 81.29 | 10.91 | 10.43 |
| | 4-R-$C_6H_4COC_2H_5$ | | | | | | | |
| H | 5 | 6 | 89 | 96 | 80.90[e] | 80.61[e] | 10.11[e] | 9.88[e] |
| Me | 7 | 7 | 86 | 82 | 81.25 | 81.01 | 10.42 | 10.12 |
| Et | 7 | 10 | 83 | 82 | 81.55 | 81.84 | 10.68 | 10.50 |
| *i*-Prop | 8 | 10 | 82 | 85 | 81.81 | 82.13 | 10.91 | 10.60 |
| *t*-Bu | 7 | 11 | 82 | 93 | 82.05 | 81.78 | 11.11 | 10.76 |
| | 4-R-$C_6H_4COCH(CH_3)_2$ | | | | | | | |
| H | 3 | 29 | 68 | 98 | 80.00[f] | 80.26[f] | 9.33[f] | 9.00[f] |
| | | | | | 81.25 | 80.81 | 10.42 | 10.00 |
| Me | 5 | 35 | 60 | 88 | 80.49 | 80.88 | 9.76 | 10.01 |
| | | | | | 81.55 | 81.80 | 10.68 | 11.01 |
| Et | 5 | 35 | 60 | 85 | 80.90 | 80.64 | 10.11 | 10.51 |
| | | | | | 81.81 | 82.21 | 10.91 | 11.13 |
| *i*-Prop | 5 | 37 | 58 | 85 | 81.25 | 80.96 | 10.42 | 10.72 |
| | | | | | 82.05 | 81.62 | 11.11 | 11.49 |
| *t*-Bu | 3 | 38 | 59 | 83 | 81.55 | 81.15 | 10.68 | 10.29 |
| | | | | | 82.26 | 81.68 | 11.29 | 11.08 |
| | 4-R-$C_6H_4$-$COC(CH_3)_3$ | | | | | | | |
| H | 0 | 97 | 3? | 88 | 80.49[g] | 80.18[g] | 9.76[g] | 9.98[g] |
| Me | 0 | 98 | 2? | 86 | 80.90 | 80.47 | 10.11 | 9.93 |

[a] Enolization, %. [b] Reduction, %. [c] Addition calcd. by difference, %. [d] Assuming correctness of gas analysis, this represents grams obtained/grams predicted × 100. [e] All figures in this column are analyses of tertiary alcohols. [f] The first figure in each pair refers to the analysis of the secondary alcohol; the second figure to the analysis of the tertiary alcohol. [g] All figures in this column are analyses of secondary alcohols.

(1) M. J. Craft, B. F. Landrum, E. C. Suratt and C. T. Lester, THIS JOURNAL, **73**, 4462 (1951).

(2) B. F. Landrum and C. T. Lester, *ibid.*, **74**, 4954 (1952).

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(4) Spot checks indicate a reproducibility of ±100 ml. (±2%) in the gas analyses.