

TABLE I
 PRODUCTS OF THE CONDENSATION OF ACTIVE METHYLENE COMPOUNDS WITH *o*-NITROSTYRENE

| Addendum | Type of adduct | M.p. or b.p., °C. | n_D^{20} | Yield, % | Analyses, % | | | |
|-----------------------------------|-------------------|-------------------|------------|----------|-------------|-------|----------|-------|
| | | | | | Carbon | | Hydrogen | |
| | | | | | Calcd. | Found | Calcd. | Found |
| Ethyl malonate | Mono ^a | 205–210 (1 mm.) | 1.5053 | 72 | 58.24 | 58.14 | 6.16 | 6.29 |
| Methyl malonate | Mono | 200–205 (1 mm.) | 1.5200 | 49 | 55.51 | 55.45 | 5.38 | 5.56 |
| | Di | 117–118 | | 2 | 58.60 | 58.30 | 5.15 | 5.37 |
| Ethyl acetoacetate | Mono ^a | 195–200 (1 mm.) | 1.5221 | 42 | 60.20 | 60.41 | 6.14 | 6.35 |
| Methyl acetoacetate | Mono ^a | 200–205 (1 mm.) | 1.5325 | 32 | 58.86 | 59.19 | 5.70 | 5.97 |
| Ethyl cyanoacetate | Mono ^a | (Hickman still) | | 78 | 59.53 | 58.96 | 5.38 | 5.53 |
| Methyl cyanoacetate | Mono ^a | (Hickman still) | | 69 | 58.06 | 59.12 | 4.87 | 5.18 |
| Cyanoacetamide | Di ^b | 157–158 | | 42 | 59.68 | 59.40 | 4.75 | 4.74 |
| Ethyl ethylmalonate | Mono | 190–194 (1 mm.) | 1.5020 | 44 | 60.52 | 60.66 | 6.87 | 7.07 |
| Ethyl <i>n</i> -butylacetoacetate | Mono | 190–195 (1 mm.) | 1.5108 | 61 | 64.46 | 64.50 | 7.51 | 7.70 |

^a No di product could be isolated. ^b No mono product could be isolated.

 TABLE II
 PRODUCTS OF THE CONDENSATION OF ACTIVE METHYLENE COMPOUNDS WITH *p*-NITROSTYRENE

| Addendum | Type of adduct | M.p. or b.p., °C. | n_D^{20} | Yield, % | Analyses, % | | | |
|-----------------------------------|-----------------|-------------------|------------|----------|-------------|-------|----------|-------|
| | | | | | Carbon | | Hydrogen | |
| | | | | | Calcd. | Found | Calcd. | Found |
| Ethyl malonate | Mono | 180–184 (1 mm.) | 1.5092 | 45 | 58.24 | 57.95 | 6.16 | 6.21 |
| | Di | 135–135.5 | | 34 | 60.25 | 60.09 | 5.72 | 6.03 |
| Methyl malonate | Mono | 200–204 (1 mm.) | 1.5244 | 43 | 55.51 | 55.33 | 5.38 | 5.57 |
| | Di | 136.5–137 | | 32 | 58.60 | 58.62 | 5.15 | 5.36 |
| Ethyl acetoacetate | Mono | 190–195 (1 mm.) | 1.5244 | 47 | 60.20 | 60.29 | 6.14 | 6.29 |
| | Di | 107–108 | | 19 | 61.67 | 61.69 | 5.65 | 5.63 |
| Methyl acetoacetate | Mono | 195–199 (1 mm.) | 1.5333 | 38 | 58.86 | 58.69 | 5.70 | 5.98 |
| | Di | 142–143 | | 24 | 60.86 | 60.60 | 5.35 | 5.13 |
| Ethyl cyanoacetate | Di ^a | 101.5–102 | | 80 | 61.37 | 61.37 | 5.15 | 5.28 |
| Methyl cyanoacetate | Di ^a | 146–147 | | 79 | 60.45 | 60.80 | 4.82 | 5.08 |
| Cyanoacetamide | Di ^a | 160–160.5 | | 73 | 59.68 | 59.45 | 4.75 | 4.56 |
| Ethyl ethylmalonate | Mono | 168–169 | | 56 | 60.52 | 60.78 | 6.87 | 7.03 |
| Ethyl <i>n</i> -butylacetoacetate | Mono | 195–200 (1 mm.) | 1.5082 | 57 | 64.46 | 64.91 | 7.51 | 7.67 |
| Malononitrile | Di ^a | 173–174 | | 36 | 62.63 | 63.02 | 4.43 | 4.82 |

^a No mono product could be isolated.

condensation of acetophenone with *p*-nitrostyrene. Since the attempted reaction of acetophenone with *p*-nitrostyrene under the conditions of these Michael reactions gave no definite products, it was concluded that the 4-(*p*-nitrophenyl)-1-phenyl-1-butanone resulted from a Michael addition of the parent addendum to the *p*-nitrostyrene, followed by favorable cleavages of the primary adducts to give the monoketone.

Other studies are in process on the effect of nuclear substituents on the course of the ionic reactions of a variety of substituted styrenes, using reagents of both electrophilic and nucleophilic character.

Experimental

All melting points and boiling points are uncorrected.

Preparation of β -(*p*-Nitrophenyl)-ethyl Bromide and β -(*o*-Nitrophenyl)-ethyl Bromide.— β -(*p*-Nitrophenyl)-ethyl bromide was obtained in 56% yield by the method of Foreman and McElvain.⁶ After separation of the crystalline *para* isomer, the mother liquors yielded 35% of β -(*o*-nitrophenyl)-ethyl bromide, b.p. 138–142° (2 mm.). These isomeric nitrobromides were used without further purification for the preparation of *o*- and *p*-nitrostyrene. It was found that the reaction time for the nitration of β -phenylethyl bromide could be reduced to 45 minutes by the addition of small pieces of Dry Ice to the reaction mixture during the addition of both nitric acid and β -phenylethyl bromide. The yields of the nitration products and of the related nitro-

styrenes were comparable to those obtained with the slower method of nitration.

Great care was observed in the distillation of these nitrophenylethyl bromides and the nitrostyrenes derived from them. On several occasions, prolonged heating during slow fractionation, localized heating with a hot coil, or distillation to small residues resulted in explosions.

Preparation of *p*-Nitrostyrene.—*p*-Nitrostyrene was prepared in 81% yield by the method of Strassburg, Gregg and Walling⁷ and was used without further purification for the reactions of *p*-nitrostyrene described below.

Preparation of *o*-Nitrostyrene.—Using a method similar to the above preparation of *p*-nitrostyrene, *o*-nitrostyrene was prepared in 65% yield from β -(*o*-nitrophenyl)-ethyl bromide, b.p. 90–93° (1 mm.). Since the crude product was contaminated only with *p*-nitrostyrene, the composition of the mixture was calculated from ultraviolet absorption spectra at the peak of the *para* curve, 290 μ . The crude *o*-nitrostyrene proved to contain 8.8% of the *para* isomer. *o*-Nitrostyrene of this purity was used generally for the experiments described below. Attempts to purify the *ortho* isomer further by careful fractionation resulted in explosive decomposition.

Preparation of *m*-Nitrostyrene.—The procedure of Wiley and Smith⁸ was used with modification. Into a 500-ml., three-necked, round-bottomed flask, equipped with a reflux condenser and stirrer, were placed 150 ml. of quinoline, 40 g. (0.235 mole) of *m*-nitrocinnamic acid and 1 g. of hydroquinone. The mixture was heated until solution of the acid was complete. Six grams of copper powder was then added and the solution was heated for five hours at 215–220° with vigorous stirring. The reaction solution was

(6) E. L. Foreman and S. M. McElvain, THIS JOURNAL, **62**, 1435 (1940).

(7) R. W. Strassburg, R. A. Gregg and C. Walling, *ibid.*, **69**, 2141 (1947).

(8) R. H. Wiley and N. R. Smith, *ibid.*, **70**, 2295 (1948).

acidified with 580 ml. of 3 *N* hydrochloric acid and the *m*-nitrostyrene was removed by steam distillation. A total of 15.5 g. (51%) of *m*-nitrostyrene was obtained, b.p., 85–90° (1 mm.).

Reaction of Enolates with Nitrostyrenes.—The reactions of the active methylene compounds with the nitrostyrenes were all performed in a similar manner. The following example is typical of the whole series.

Reaction of *p*-Nitrostyrene with Ethyl Malonate.—To 100 ml. of absolute ethanol, 0.75 g. (0.033 mole) of clean sodium metal was added. When solution was complete, 25.0 g. (0.15 mole) of ethyl malonate was added, followed by 14.9 g. (0.10 mole) of *p*-nitrostyrene, containing 0.5% hydroquinone. The resulting solution was refluxed for six hours and then allowed to remain overnight at room temperature. The solution was poured into a beaker containing 4 ml. of concentrated hydrochloric acid in 1-l. of water. The product was extracted with ether and the ether extract was washed with water. The extracts were dried over anhydrous sodium sulfate and the solvent removed by distillation. The last traces were removed under vacuum, which caused a small amount of crystalline solid to separate. With the addition of ethanol (50 ml.) and cooling, more of the solid separated. A total of 7.8 g. (34%) of solid (di-addition product) was obtained, m.p., 135–135.5°.

The oil obtained from the above filtrate was distilled. There was obtained 14.1 g. (45%) of a light yellow oil (mono-addition product); b.p. 180–184° (1 mm.).

Reaction of β -(*p*-Nitrophenyl)-ethyl Bromide with Ethyl Malonate.—Ethyl malonate was alkylated with β -(*p*-nitrophenyl)-ethyl bromide using equivalent amounts of reactants and sodium ethoxide in ethanol. A white solid was obtained in 13% yield which was identical with the di-addition product obtained from the above reaction of *p*-nitrostyrene with ethyl malonate.

Reaction of *o*-Nitrostyrene with Ethyl β -(*o*-Nitrophenyl)-ethylmalonate.—To 38 ml. of absolute ethanol was added 0.25 g. (0.011 mole) of sodium metal. After reaction was complete, 15.5 g. (0.05 mole) of ethyl β -(*o*-nitrophenyl)-ethylmalonate and 7.5 g. (0.05 mole) of *p*-nitrostyrene were added. The resulting solution was refluxed for 13 hours. The reaction yielded 9.0 g. (39%) of the di-addition product, m.p. 100–101°.

Anal. Calcd. for C₂₃H₂₆O₃N: C, 60.25; H, 5.72. Found: C, 59.96; H, 5.86.

Reaction of *p*-Nitrostyrene with Acetylacetone.—To 75 ml. of ethanol was added 0.75 g. (0.033 mole) of sodium.

After the reaction was complete 15.0 g. (0.15 mole) of acetylacetone and 14.9 g. (0.10 mole) of *p*-nitrostyrene were added. The resulting solution was refluxed for 12 hours and then allowed to remain overnight at room temperature. The reaction product, isolated as described above, was fractionated under reduced pressure. Five grams of the original *p*-nitrostyrene was recovered together with 7.0 g. (34%) of an orange oil, 5-(*p*-nitrophenyl)-2-pentanone, b.p. 180–184° (1 mm.), *n*_D²⁰ 1.5391.

Anal. Calcd. for C₁₁H₁₃O₃N: C, 63.75; H, 6.32. Found: C, 63.49; H, 6.31.

The semicarbazone of the above compound was prepared and recrystallized from ethanol, m.p. 175–176°.

Anal. Calcd. for C₁₂H₁₅O₃N₄: C, 54.55; H, 6.10. Found: C, 54.31; H, 6.27.

Reaction of *p*-Nitrostyrene with Ethyl Benzoylacetate, Benzoylacetone and Dibenzoylmethane.—To 75 ml. of absolute ethanol was added 0.75 g. (0.033 mole) of sodium. When the reaction was complete 28.8 g. (0.15 mole) of ethyl benzoylacetate and 14.9 g. (0.10 mole) of *p*-nitrostyrene were added and the resulting solution was refluxed for nine hours. The reaction product yielded 8.0 g. of an unidentified oil, b.p. 150–160° (1 mm.), and 5.0 g. (19%) of a white solid, 4-(*p*-nitrophenyl)-1-phenyl-1-butanone, m.p. 109–110°.

Anal. Calcd. for C₁₆H₁₅O₃N: C, 71.36; H, 5.61. Found: C, 71.48; H, 5.70.

The semicarbazone of the 4-(*p*-nitrophenyl)-1-phenyl-1-butanone was prepared and recrystallized from ethanol, m.p. 205–205.5°.

Anal. Calcd. for C₁₆H₁₅O₃N₄: C, 62.56; H, 5.66. Found: C, 62.44; H, 5.66.

When the above reaction was performed using 24.3 g. (0.15 mole) of benzoylacetone instead of ethyl benzoylacetate, there was obtained 5.5 g. (21%) of 4-(*p*-nitrophenyl)-1-phenyl-1-butanone, 6.0 g. of the original *p*-nitrostyrene and 3.5 g. of an unidentified oil, b.p. 155–160° (1 mm.). However, when dibenzoylmethane (33.6 g., 0.15 mole) was used under the same reaction conditions, 5.6 g. (21%) of 4-(*p*-nitrophenyl)-1-phenyl-1-butanone was isolated together with 6.0 g. of unchanged *p*-nitrostyrene and 13.5 g. (75%) of acetophenone (b.p. 65–70° (1 mm.); semicarbazone, m.p. 197–198°; phenylhydrazone, m.p. 104–105°).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MARYLAND]

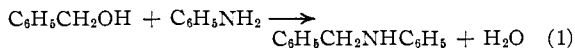
Disproportionative Condensations. II. The *N*-Alkylation of Anilines with Primary Alcohols

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Benzyl alcohol has been found to condense readily with aniline in the presence of potassium benzylate and U.O.P. nickel² to give *N*-benzylaniline. With *para*-substituted benzyl alcohols the reaction rate decreased with decreasing ability of the substituent to release electrons in the order (CH₃)₂N, CH₃O, CH₃, H, Cl. The reverse order was obtained when *para*-substituted anilines were condensed with benzyl alcohol. The products were isolated as the pure hydrochlorides in 80 to 90% yields. *p*-Nitroaniline with benzyl alcohol gave *p,p'*-dibenzalaminoazobenzene in 50% yield while cyclohexylamine gave a 49% yield of *N*-benzalcyclohexylamine. Primary aliphatic alcohols react satisfactorily as exemplified by the 70 to 80% yields of *N-n*-alkylanilines obtained from *n*-hexyl and *n*-decyl alcohols. A reaction course is proposed and evaluated.

Exploratory experiments on the attempted extension of the Guerbet condensation, the subject of the first paper of this series,³ to the condensation of an alcohol with an amine showed that benzyl alcohol readily condensed with aniline in the presence of potassium benzylate and U.O.P. nickel² to give high yields of *N*-benzylaniline.



In Table I are shown the effects of varying the amount of benzyl alcohol. A xylene solution of the specified amount of benzyl alcohol was treated with 0.04 mole of potassium; 0.125 mole of aniline and 1.0 g. of U.O.P. nickel were then added and the mixture was heated under reflux in an apparatus equipped with a Dean-Stark trap until water evolution was complete. Extraction of an ether solu-

(1) From the Ph.D. thesis of E. J. Frazza, Feb., 1954.

(2) National Institutes of Health Fellow, 1952–1954.

(3) E. F. Pratt and D. G. Kubler, *THIS JOURNAL*, **76**, 52 (1954).