ethanol containing 80 g. of picric acid (10% water); the precipitate of decahydroquinoxaline dipicrate was left standing at 10° for 12 hrs., filtered, rinsed with alcohol, and dried to give 56 g. (62%) of light yellow granular microcrystals of decahydroquinoxaline dipicrate m.p. 280° dec. The above filtrate was diluted with 2 volumes of water. After 12 hrs. at 10°, the precipitate of N-cyclohexylethylenediamine dipicrate was filtered, rinsed, and dried to give 24 g. (27%) of yellow needles m.p. 183–187°.

The crude dipicrate was recrystallized from 1200 ml. of water, using charcoal and filter-aid. Three such recrystallizations gave 12 g. of long yellow needles m.p. 192–194°.

Into a 1 l. conical flask were placed 12 g. of purified N-cyclohexylethylenediamine dipicrate, 100 ml. of 95% ethanol, and 10 ml. of hydrochloric acid (*sp. gr.* 1.19). The mixture was heated to boiling, cooled to 60°, and 300 ml. of acetone was added to the reaction mixture. After 12 hrs. at 10°, 3.5 g. of dihydrochloride salt m.p. 178–180° was obtained. This material was recrystallized from 175 ml. of absolute ethanol to give 3.0 g. of N-cyclohexylethylenediamine dihydrochloride m.p. 210–215°.

When the *free amine* was liberated from the dihydrochloride salt in the same way as was decahydroquinoxaline, 4.7 g. of amine b.p. 103°/10 mm. was obtained from 10 g. of salt. This product was dried over sodium and redistilled, giving 4 g. of colorless, very hygroscopic distillate b.p. 93°/5 mm. A micro b.p. determination gave b.p. 188–189°/761.5 mm.; d_4^{25} 0.9190; n_D^{25} 1.4800.

Anal. Calc'd for $C_8H_{18}N_2$: C, 67.58; H, 12.73; N, 19.69; N.E. 71.1. Found: C, 67.63; H, 13.00; N, 19.03; N.E. 70.9.

Pearson, Jones, and Cope[9] reported b.p. 101–102°/14 mm.; n_D^{25} 1.4800; n_4^{25} 0.9153 for N-cyclohexylethylenediamine.

N-Cyclohexylethylenediamine dihydrochloride was prepared from the pure amine and was recrystallized from absolute ethanol to give white crystals m.p. 211–213°.

Anal. Calc'd for $C_8H_{20}Cl_2N_2$: Cl, 32.95. Found: Cl, 32.94, 33.08.

N-Cyclohexylethylenediamine dipicrate was prepared from the pure amine; recrystallized from boiling water, m.p. 192–194°.

Anal. Calc'd for $C_{20}H_{24}N_8O_{14}$: N, 18.67. Found: N, 18.84, 18.70.

Using the same method as was used to prepare the nitroso derivative of decahydroquinoxaline, no nitroso derivative of N-cyclohexylethylenediamine could be prepared.

A sample of N-cyclohexylethylenediamine was prepared by the method of Pearson, *et al.*[9] This material gave a dihydrochloride and a dipicrate of the same m.p. and mixture m.p. as were obtained from the N-cyclohexylethyleneamine prepared in this laboratory.

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[9] Pearson, Jones, and Cope, *J. Am. Chem. Soc.*, **68**, 1227 (1946).

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Alkylation of α-Substituted Acetoacetic Esters

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Many α,α-disubstituted acetoacetic esters have been prepared by a variety of methods.[1] In view of this, when it was desired to have ethyl α-methyl-α-phenylacetoacetate it was surprising to find that no such aryl derivatives have been reported in the literature. Initial attempts at the alkylation of ethyl α-phenylacetoacetate, using the commonly employed sodium ethoxide with ethanol as solvent, produced cleavage of the ester to give ethyl phenylacetate. This methylation was carried out successfully when sodium sand in dioxane was employed as the metalating agent and the product was obtained in 51% yield. Further investigation, however, showed the use of sodium hydride in a (1:1) mixture of benzene and dimethylformamide to be the method of choice.[2] This procedure led to yields of 51–80% (Table I). The utility of this method extends also to the preparation of dialkylacetoacetic esters and gives improvements over previously reported yields (Table I).

Unexpected difficulty was encountered in the unsuccessful attempts at the preparation of ethyl α-(*p*-chlorophenyl)acetoacetate. This was particularly surprising in view of the ease with which the *ortho* isomer was prepared. When ethanolysis of α-(*p*-chlorophenyl)acetoacetonitrile was tried using gaseous hydrogen chloride and ethanol, the O-ethyl derivative of the nitrile was obtained. Treatment of this derivative or the original nitrile with sulfuric acid and ethanol at reflux temperature gave an unidentified product whose properties are described in the Experimental Part.

When, in view of the above difficulties, some of the other esters were subjected to infrared and ultraviolet examination for purposes of reference, it was found that the α-ethyl-α-phenyl and α-(*o*-chlorophenyl)-α-methyl derivatives contained perhaps 5–10% of the O-alkyl derivative. This would appear to depend on both the aryl group present and the entering alkyl group since the methylation of ethyl α-phenylacetoacetate produced no enol ether.

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EXPERIMENTAL

Ethyl α-phenylacetoacetate. This material was prepared by ethanolysis of α-phenylacetoacetonitrile[3] according to the method of Kimball, Jefferson, and Pike.[4]

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[1] For a general reference see Renfrow and Renfrow, *J. Am. Chem. Soc.*, **68**, 1801 (1946).

[2] Burgstahler, personal communication. See also Stork and Burgstahler, *J. Am. Chem. Soc.*, **73**, 3544 (1951).

[3] Julian, *et al.*, *Org. Syntheses*, Coll. Vol. II, 487 (1943). This nitrile is now available from Benzol Products Co., 237 South Street, Newark 5, New Jersey.

[4] Kimball, Jefferson, and Pike, *Org. Syntheses*, Coll. Vol. II, 284 (1943).

[5] Russell and Hitchings, *J. Am. Chem. Soc.*, **73**, 3763 (1951). These authors reported the compound as an "uncrystallizable oil" and gave no physical constants.

TABLE I

DISUBSTITUTED ACETOACETIC ESTERS
$CH_3COC(R,R')CO_2C_2H_5$

R	R′	Method	Yield, %	B.P., °C.	Mm.	n_D^{25}	Formula	Analyses, Percent Carbon Calc'd	Analyses, Percent Carbon Found	Analyses, Percent Hydrogen Calc'd	Analyses, Percent Hydrogen Found
CH_3	C_6H_5	A	51	112	1.7	1.5024	$C_{13}H_{16}O_3$	70.88	70.73	7.32	7.53
CH_3	C_6H_5	B	77	125–129	3–5	1.5028					
C_2H_5	C_6H_5	B	69	124–126	2.5	1.5115	$C_{14}H_{18}O_3$	71.50	71.27	7.72	7.87
$C_6H_5CH_2$	C_6H_5	B	80	141	0.5	1.5483	$C_{19}H_{20}O_3$	77.00	77.15	6.80	6.58
CH_3	o-ClC_6H_4	B	57	146–147	3.5	1.5218	$C_{13}H_{15}ClO_3$	61.29	61.11	5.94	5.74
C_2H_5	o-ClC_6H_4	B	55	142–146	3	1.5263	$C_{14}H_{17}ClO_3$	62.57	62.31	6.38	6.14
C_6H_{11}	C_6H_5	B	0[a]								
CH_3	CH_3	B	75[b]	180–184	atm.	1.4162					
C_2H_5	C_2H_5	B	70[c]	210–213	atm.	1.4300					
CH_3	C_2H_5	B	72[d]	196–199	atm.	1.4229					
C_2H_5	$CH_2{=}CHCH_2$	B	93[e]	116–118	23	1.4438					

[a] Recovery of 73.2% of the ethyl α-phenylacetoacetate and 86.5% of the cyclohexyl iodide. [b] Folkers and Adkins, *J. Am. Chem. Soc.*, **53,** 1416 (1931), report a 54% yield. [c] Frankland and Duppa, *Ann.*, **138,** 211 (1866). Wislicenus, *Ann.*, **186,** 190 (1877). [d] Saur, *Ann.*, **188,** 257 (1877). [e] Cope, Hoyle, and Heyl, *J. Am. Chem. Soc.*, **63,** 1843 (1941), obtained a 75% yield.

α-(o-Chlorophenyl)acetoacetonitrile. This was prepared in 32% yield in essential accordance with the procedure of Russell and Hitchings.[5] The product was, however, found to be distillable at 120–126° (1 mm.), n_D^{25} 1.5560.

Anal. Calc'd for $C_{10}H_8ClNO$: N, 7.23. Found: N, 7.32.

Ethyl α-(o-chlorophenyl)acetoacetate. Ethanolysis of 0.3 mole of the nitrile was carried out as with α-phenylacetoacetonitrile except that the saturation with hydrogen chloride was carried out at 0–10° and during the succeeding 2 hours of passing in the gas the temperature was held at 18°. After standing overnight, the mixture was chilled and the crystalline imino ether hydrochloride was isolated by filtration. Hydrolysis was effected in a solution of 18 ml. of conc'd sulfuric acid in 600 ml. water at 50–60° according to the previously employed procedure. In this initial heating one hour was required for all the solid to dissolve. Workup and distillation gave 28 g. (49%) of product boiling at 105–107° (1.5 mm.), n_D^{25} 1.5305.

Anal. Calc'd for $C_{12}H_{13}ClO_3$: C, 59.90; H, 5.44; O, 19.93. Found: C, 59.90; H, 5.72; O, 19.68.

Ethyl α-methyl-α-phenylacetoacetate. Method A. To the sodium sand prepared from 6.8 g. (0.296 g.-atom) of sodium in 240 ml. of purified dioxane was added, dropwise with stirring at 40–50°, 61.4 g. (0.296 mole) of ethyl α-phenylacetoacetate. The mixture then was refluxed until all the sodium had disappeared. After cooling, there was added 46 g. (0.32 mole) of methyl iodide, followed by warming at 35-40° overnight. An additional 5 g. of methyl iodide was added and the mixture was heated 36 hours longer. The mixture was neutral at this time. Most of the solvents were removed under reduced pressure; water was added and the product was extracted with ether. Subsequent to drying over magnesium sulfate and removal of the ether by distillation, the material was distilled to give 33 g. (51%) which boiled at 112° (1.7 mm.), n_D^{25} 1.5024.

Anal. Calc'd for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 70.73; H, 7.53.

Method B. A slurry of 26.7 g. (1.1 moles) of sodium hydride was prepared in a mixture of 375 ml. of dimethylformamide (azeotropically distilled from benzene to a boiling point of 150–151°) and 375 ml. of benzene. There then was added, dropwise with cooling to 5–10°, 230.3 g. (1.1 moles) of ethyl α-phenylacetoacetate. The mixture foamed during this time. It then was stirred for 20 minutes before the dropwise addition of 132.5 g. (1.2 moles) of methyl iodide. After coming to room temperature, the mixture was heated at 50° until neutrality was reached (about 3 hours). There was added 20 ml. of ethanol and then 300 ml. of water. The separated benzene[6] layer was washed with water. After drying over magnesium sulfate, the benzene was removed under slightly reduced pressure. Distillation gave 186.2 g. (77%) of product boiling at 125–129° (3–5 mm.), n_D^{25} 1.5028.

Attempted ethanolysis of α-(p-chlorophenyl)acetoacetonitrile. A. Hydrogen chloride method. With gentle warming, 193.5 g. (1.0 mole) of α-(*p*-chlorophenyl)acetoacetonitrile was dissolved in 400 ml. of anhydrous ethanol. The stirred solution was saturated with anhydrous hydrogen chloride at 0° to 10°. This required approximately 8.5 hours. After the mixture was saturated, it was stirred for an additional hour at 10°, cooled to 0°, and filtered to remove the white, crystalline precipitate. After washing with diethyl ether, this material weighed 145 g. It was added to a solution of 100 g. of conc'd sulfuric acid in 3,000 ml. of water. This mixture was heated, with stirring, on the steam-bath for 7 hours. During this time there was no noticeable change in the suspended material. The mixture was cooled to room temperature and was filtered to remove the white solid; m.p. 114–116°. After two recrystallizations from methanol, the material weighed 102.5 g., m.p. 116.5–117.0°. Mixture m.p. with the starting nitrile was 90–92°. Infrared examination showed the presence of an enol ether structure. Ultraviolet absorption indicated that the compound was the enol ether of the starting nitrile.

Anal. Calc'd for $C_{12}H_{12}ClNO$: C, 65.02; H, 5.45; N, 6.31. Found: C, 64.95; H, 5.64; N, 6.11.

B. Sulfuric acid method.[7] To 46 ml. of absolute ethanol, 2.5 ml. of water, and 49 g. (26.5 ml.) of conc'd sulfuric acid was added 48.4 g. (0.25 mole) of the nitrile. The mixture was refluxed for 6 hours and then was poured into 700 ml. of water. Subsequent to ether extraction the ether extracts were washed with water and sodium bicarbonate solution and were dried over magnesium sulfate. Removal of the ether and distillation gave two fractions totaling 18.8 g. of a yellow liquid which boiled at 92–95° (0.75 mm.), n_D^{25} 1.5207.

Anal. Calc'd for $C_{12}H_{13}ClO_3$: C, 59.90; H, 5.44; Cl, 14.73; O, 19.93. Found: C, 61.81; H, 5.43; Cl, 19.16; O, 13.17.

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(6) Only benzene should be used since it was found that if any ether were present it became impossible to eliminate iodine in the product even after washing with sodium bisulfite.

(7) Patterned after the procedure for the ethanolysis of benzyl cyanide, Adams and Thal, *Org. Syntheses*, Coll. Vol. I, 2nd Ed., 270 (1941).

When crystals separated on long standing, they were isolated by filtration and were identified by melting point and infrared data as *p*-chlorobenzoic acid. The filtrate was taken up in ether, washed with sodium bicarbonate solution, dried, and redistilled. The boiling point, index of refraction, and analysis for carbon and hydrogen were essentially unchanged. Infrared and ultraviolet absorption studies indicated the presence of an ester and an α,β-unsaturated carbonyl but no styrene-like configuration. An empirical formula of $C_{19}H_{20}Cl_2O_3$ was calculated from the analytical data.

Application of this same method to 22.16 g. (0.1 mole) of the O-ethyl derivative obtained in (*A*) above gave 7 g. of a yellow liquid which boiled at 86–90° (0.5 mm.), n_D^{25} 1.5203.

Anal. Calc'd for $C_{12}H_{13}ClO_3$: C, 59.90; H, 5.44. Found: C, 61.93; H, 5.58.

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A Comparison of the Electrophilic Reactivity of Styrene and Phenylacetylene

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It has been suggested that the relative reactivity of a comparable alkene-alkyne pair varies: with electrophilic reagents the alkene is more reactive; with nucleophilic reagents the alkyne is more reactive.[1] In order to provide a clear-cut example in the latter category, a qualitative comparison of the reactivity of phenylacetylene and styrene towards a nucleophilic reagent, methoxide ion, was made in the reactions

$$C_6H_5C{\equiv}CH + CH_3OH \xrightarrow{NaOCH_3} C_6H_5CH{=}CHOCH_3$$

$$C_6H_5CH{=}CH_2 + CH_3OH \xrightarrow{NaOCH_3} C_6H_5CH_2CH_2OCH_3 \quad (I)$$

In a recent study[2] it was established that the rate-limiting step in the first reaction was the addition of methoxide ion to phenylacetylene and that its half-life at 149° was about six hours for concentrations of 0.1 mole liter^{-}.[1]

The preparation of I from styrene appears not to have been reported. When styrene was heated with sodium methoxide in methanol at 146–149° in sealed ampules it was found that after two days only traces of I had formed. After 10 or 20 days, however, the presence of this ether could be clearly demonstrated.

In order to eliminate $C_6H_5CH(OCH_3)CH_3$ (II) as a possible product from styrene, I and II were prepared by known procedures.[3,4] Infrared spectra of the products of the methoxide-catalyzed addition of methanol to styrene showed that the ether I, not II, had formed. In this connection it is interesting to note that the charge distribution in styrene must be remarkably sensitive to the nature of the attacking species, for styrene does give the ether II in methanol-sulfuric acid. Apparently the phenyl group can distribute charge best when the attack of either a free radical or a positive or negative species is on the β-carbon. Similar results obtain with phenylacetylene.[5,6]

By direct comparison, it is clear that phenylacetylene is more electrophilic than styrene in its reactivity toward the nucleophilic reagent sodium methoxide. This is in contrast to the greater nucleophilic reactivity of styrene toward free radicals[5] or bromine.[7]

EXPERIMENTAL

Boiling points are uncorrected. Infrared spectra were determined on a Perkin-Elmer Model 21 double beam spectrophotometer with sodium chloride optics: the liquid samples were measured as films between sodium chloride plates or in *ca.* 0.025 mm. sodium chloride cells; a reference sample of polystyrene was measured as a 0.007 mm. sheet.

1-Methoxy-2-phenylethane (I). This ether, prepared by the method of Deshapande,[3] was redistilled from sodium. The distillate had b.p. 81–82° (22 mm.), n_D^{22} 1.4971 [lit.[3] b.p. 68–70° (12 mm.), n_D^{24} 1.4970].

1-Methoxy-1-phenylethane (II). II was prepared by a procedure outlined in a patent.[4] A solution of 30 ml. of styrene, 3 ml. of 95% sulfuric acid, 100 ml. of methanol, and a few crystals of hydroquinone was made up in a flask with a long narrow neck. The flask was cooled in ice, its air space was blown out with nitrogen, and the flask neck was sealed. After 18 hours in a steam-bath, the solution was neutralized with ethanolamine, then treated with water and ether. The crude II obtained from the ether extract was distilled from sodium giving a practically quantitative yield of a liquid, n_D^{25} 1.4888–1.4920. For a middle fraction b.p. 71–76° (32 mm.), n_D^{25} 1.4911 [lit.[8] b.p. 88° (47 mm.), n_D^{25} 1.4905].

Anal. Calc'd for $C_9H_{10}O$: C, 79.36; H, 8.89. Found: C, 79.71; H, 9.01.

Methoxide-catalyzed addition of methanol to styrene. The reaction was carried out in 16 ml. of methanolic solution in Pyrex ampules at 146–150°. In a typical experiment the concentrations of styrene and sodium methoxide in the solution were 3 and 0.6 mole/liter^{-1} respectively. Before each ampule was sealed, it was cooled in Dry Ice and its vapor space was blown out with nitrogen. At the end of a fixed period the ampule was chilled and opened. The solution was poured off from the white solid, presumably polystyrene, washed with water, and then was dried over calcium chloride and potassium hydroxide. A reference sample of styrene was washed and dried by the same procedure. As the reaction progressed, more and more white solid was deposited and correspondingly less liquid product was recovered. Some of the results follow.

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(1) Raphael, *Acetylenic Compounds in Organic Synthesis*, Butterworth's Scientific Publications, London, 1955, p. 21.

(2) Miller and Shkapenko, *J. Am. Chem. Soc.*, **77**, 5038 (1955).

(3) Deshapande, *J. Indian Chem. Soc.*, **15**, 509 (1938).

(4) Stanley, Minkoff, and Youell, U. S. Patent 2,248,518 [*Chem. Abstr.*, **35**, 6598 (1941)].

(5) Kharasch, Jerome, and Urry, *J. Org. Chem.*, **15**, 966 (1950).

(6) Nef, *Ann.*, **308**, 264 (1899).

(7) Robertson, Dasent, Milburn, and Oliver, *J. Chem. Soc.*, 1628 (1950).

(8) Mislow, *J. Am. Chem. Soc.*, **73**, 4043 (1951).