several times from alcohol (Darco) afforded pure XIII, m.p. 205.2–206.2°.

Anal. Calcd. for $C_{16}H_8O_2S$: C, 72.6; H, 3.0. Found: C, 72.6; H, 2.9.

The mixture of quinones XII and XIII formed by cyclization of X and XI was analyzed by infrared spectroscopy in carbon disulfide solution using bands for XII at 7.55, 7.95, 10.95 and 12.2 μ and bands for XIII at 7.7 and 10.5 μ, and by comparison of melting range with a melting point curve diagram. Analysis by each method indicated that the same mixture of quinones formed on cyclization of X or XI consisted of about 60 ± 5% of XII and 40 ± 5% XIII.

Preparation of Normal and Pseudo Methyl Esters.—All normal methyl esters were prepared by treatment of ethereal solutions with diazomethane. The esters so obtained in almost quantitative yield were recrystallized from methanol to constant melting points. The pseudo-esters were prepared[25] by shaking about 1 g. of acid chloride with 40 ml. of methanol saturated with urea at room temperature for 4 hours. The reaction mixture was then poured into water and the ester extracted with ether–benzene. These extracts were immediately washed with 10% potassium carbonate solution and dried by passing over magnesium sulfate. The solvents were removed under vacuum and the crystalline residues recrystallized from pure methanol in flasks which had been steamed out for several minutes to remove possible traces of absorbed acid. The acid chlorides were prepared by heating the pure acids and an excess of pure thionyl chloride for 3 hours at reflux. The reagent was removed under reduced pressure and the acid chlorides were recrystallized from benzene–petroleum ether, b.p. 35–50°. In each case the infrared spectrum had a strong band between 5.6 and 5.7 μ which indicated that all of the acid chlorides had the pseudo (cyclic) structure. The acid chlorides were sensitive compounds and proved difficult to crystallize. The melting points are listed (but none was analyzed): III, 127.5–129.5°; IV, 117–119°; VI, 130.5–133.5°; VII, 129–130°; X, 114.5–116.5°; and XI, 147–150°. The melting points of normal and pseudo esters of III, IV, VI, VII, X and XI are listed in Table I.

Esterification with 100% Sulfuric Acid.—In each experiment 0.50 g. of finely ground keto acid was dissolved in 5 ml. of 100% sulfuric acid at room temperature. Shortly after the last solid had dissolved the solution, usually red, was stirred into 50 ml. of cold methanol. This solution was then poured into 150 ml. of water and the products were extracted thoroughly with ether. These extracts were well extracted with 10% potassium carbonate to remove acid. The ether solution was then dried by filtration through magnesium sulfate and solvent removed by evaporation in an apparatus arranged so that the residue could be collected quantitatively by sublimation under reduced pressure onto a cold finger. The esters thus obtained were analyzed by taking the infrared spectra of the mixtures in chloroform solutions of known concentration and matching the absorption of the ketone carbonyl (near 6.0 μ) with solutions of known concentration of pure normal ester.

TABLE I

NORMAL AND PSEUDO METHYL ESTERS

Acid	Ester	M.p., °C.	Analyses, found,[21] %[a] C	H	S
III	*n*	130.5–131.5	53.4	2.8	
	ψ	143.5–144.5	53.5	3.1	11.1
IV	*n*	118.0–119.0	53.6	3.2	
	ψ	96.0– 96.5	53.7	3.4	11.2
VI	*n*	134.7–135.5	53.5	3.3	
	ψ	91.2– 92.0	53.5	2.9	10.9
VII	*n*	160.0–161.0	53.7	3.4	
	ψ	87.0– 88.5	53.3	2.9	
			Found[21b]		
X	*n*	139.8–140.4	68.8	4.2	
	ψ	113.6–114.2	69.2	3.9	
XI	*n*	138.8–139.8	69.0	4.0	
	ψ	117.5–118.6	68.8	4.3	

[a] Calcd.: C, 53.6; H, 3.2; S, 11.0. [b] Calcd.: C, 68.9; H, 4.1.

TABLE II

ESTERIFICATION IN 100% SULFURIC ACID[14,18]

Acid	Acid recovd., %	Ester, % Formed	Ester, % Normal	Pseudo
III	77	10	4	96
IV	42	47.5	12	88
VI	30	65.5	5.5	94.5
VII	36	56	5	95
X	Trace	94	6	94
XI	1	88	6	94

The results of these esterifications are listed in Table II. It is likely that pure pseudo-ester formed initially in every case as blank experiments, in which 100% sulfuric acid was added to solutions of pure pseudo-ester dissolved in methanol, showed that about 7–10% of pseudo-ester was isomerized into normal ester in times which approximated the times required to work up the experiments cited above.

COLUMBUS 10, OHIO

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[25] Compare M. S. Newman and C. D. McCleary, THIS JOURNAL, **63**, 1537 (1941).

[CONTRIBUTION FROM THE WILLIAM H. NICHOLS LABORATORY, NEW YORK UNIVERSITY]

Alkylation and Cyclization of Benzoylacetanilides[1]

BY A. LANGLEY SEARLES[2a] AND DANIEL RESSLER[2b]

RECEIVED JANUARY 28, 1958

Benzoylacetanilide and *p*-nitrobenzoylacetanilide have been mono- and di-α-alkylated with alkyl halides, using ethanolic sodium ethoxide or sodium hydride in dimethylformamide. O-Alkylation often accompanied C-alkylation, and the enol ethers thus produced occasionally comprised the chief products of the reaction. All types of alkylated products were convertible into 3-alkyl-4-arylcarbostyrils by the action of sulfuric acid; in the case of the dialkylated compounds this reaction involved elimination of the α-alkyl group capable of forming the more stable carbonium ion. Electronic factors were shown to play a more important role than steric factors in the cyclization process.

It has been reported that the action of acidic reagents upon certain compounds containing a $-NHCOCR_2CO-$ moiety may bring about their dealkylation.[3–6] For two of these reactions, mechanisms have been proposed which correlate

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[1] Presented in part before the 132nd National Meeting of the American Chemical Society, New York, N. Y., September 9, 1957.

[2] (a) Chemistry Department, College of Mount St. Vincent, New York 71, N. Y.; (b) deceased, February 8, 1958.

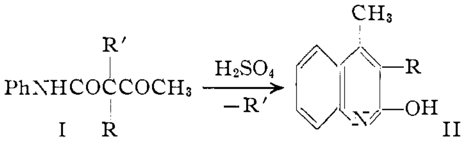
[3] D. Heyl and A. C. Cope, THIS JOURNAL, **65**, 669 (1943).

[4] R. M. Warren, Ph.D. thesis, New York University, 1951, p. 19.

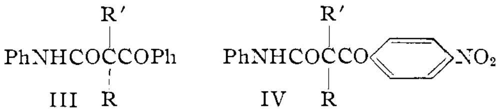
[5] E. W. Maynert and E. Washburn, THIS JOURNAL, **75**, 700 (1953).

[6] A. L. Searles and R. J. Kelly, *ibid.*, **78**, 2242 (1956).

dealkylation with the creation of aromatic conjugation and the stabilities of the carbonium ions derived from the ejected alkyl groups.[5,6] Dealkylation has been shown to occur most readily with the α,α-dialkylacetoacetanilide system (I),[6] and consequently other β-ketoanilides seemed appropriate for further study.



The fact that α-benzyl-α-acetyl-β-phenylpropionanilide (I, R = R′ = benzyl) gave only a very low yield of 3-benzyl-4-methylcarbostyril (II, R = benzyl) in this reaction[6] suggested that steric factors play an important role in cyclization and/or dealkylation. To test this hypothesis, a series of compounds believed to offer greater steric barriers (IIIb and IIIc) to these processes was therefore formulated, as well as, for purposes of comparison, one offering the same barriers and also electronic enhancement (IVb and IVc).



IIIa and IVa, R = R′ = H
IIIb and IVb, R = alkyl, R′ = H
IIIc and IVc, R and R′ = alkyl

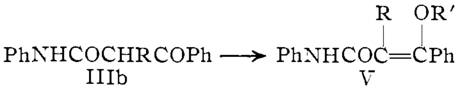
Benzoylacetanilide (IIIa) was prepared from ethyl benzoylacetate and aniline in the manner previously reported,[7] and converted to IIIb by alkylation in ethanolic sodium ethoxide according to methods that have been used for the synthesis of α-alkyl-β-ketoanilides.[8–10] The structures of these compounds were authenticated by deacylating[11] two of them to anilides of known structures. Contrary to reported experiences,[6,9] the second alkylation usually failed or proceeded poorly when sodium ethoxide was the base employed[12]; but sodium hydride, which has been used successfully to prepare the analogous α,α-dialkylacetoacetic esters,[13] gave satisfactory results. The structures of IIIc were verified by reversing the order of alkylation as described earlier[6] and comparing the reaction products by mixed melting points and infrared absorption. Table I summarizes these preparations. Only one compound listed there (which was prepared by other methods) has been previously reported.[14,15]

Duplication of the known method for preparing ethyl p-nitrobenzoylacetate,[16] from which substances of type IV were to be made, proved troublesome; however, useful modifications were devised. The reaction of this compound with aniline[17] gave the desired p-nitrobenzoylacetanilide (IVa). Contrary to what might have been anticipated, the presence of the nitro group did not facilitate alkylation of IVa by sodium ethoxide. The products were occasionally mixtures from which the desired substances could not be isolated conveniently, and even when the more effective sodium hydride was used as a base the times of reaction were generally greater than those required to prepare the comparably substituted IIIb and IIIc. Relevant data on the synthesis of IVb and IVc are summarized in Table II.

The preparation of α-methyl-α-benzoylvaleranilide (IIIc, R = methyl, R′ = n-propyl), successful or merely attempted, is illustrative of the behavior encountered frequently during the second alkylation part of this investigation. As can be seen from Table I, no desired product was obtained by the n-propylation of α-benzoylpropionanilide (IIIb, R = methyl) using ethanolic sodium ethoxide. Instead, considerable starting compound was recovered, together with two other substances. One of these, a liquid identified as ethyl benzoate, suggested that a reaction competitive with C-alkylation was taking place. (The similarity to a reverse Claisen condensation is notable.)

$$\mathrm{PhCOCH(CH_3)CONHPh} + \mathrm{C_2H_5O^{\ominus}} \longrightarrow \mathrm{PhCOOC_2H_5} + \mathrm{CH_3CHCONHPh^{\ominus}}$$

The second was a solid whose empirical formula proved to be identical with that of the desired product, but whose chemical properties were not those expected of IIIc. This solid absorbed bromine with no evolution of HBr, showed an absence of ketonic properties by failing to give a 2,4-dinitrophenylhydrazone, and could be cleaved to the starting compound by ethanolic sulfuric acid (*i. e.*, it lost an n-propyl group). These observations, together with spectral data on analogous compounds,[18] and conversion of the substance to a carbostyril of unequivocal identity (*vide infra*), established its structure as an enol ether, *viz.*, α-methyl-β-n-propoxy-β-phenylacrylanilide (Vc, R = methyl, R′ = n-propyl), and showed that O-alkylation is also a competing reaction under these conditions.



$$\underset{\text{IIIb}}{\mathrm{PhNHCOCHRCOPh}} \longrightarrow \underset{\text{V}}{\mathrm{PhNHCO}\overset{\mathrm{R}}{\mathrm{C}}=\overset{\mathrm{OR'}}{\mathrm{C}}\mathrm{Ph}}$$

When α-benzoylpropionanilide (IIIb, R = methyl) was n-propylated using sodium hydride, however, both the enol ether (Vc, R = methyl, R′ = n-propyl) and the desired C,C-dialkylated anilide were obtained. These O-alkylations are described in Table III.

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[7] E. C. Horning, ed., "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 108.

[8] D. J. Cook and W. C. Lawall, THIS JOURNAL, **70**, 1918 (1948).

[9] R. A. Laforge, C. E. Cosgrave, R. B. Keller and V. E. Johnson, *J. Am. Pharm. Assn.*, **41**, 303 (1952).

[10] A. L. Searles and R. J. Kelly, THIS JOURNAL, **77**, 6075 (1955).

[11] A. L. Searles, A. M. Mascherin and R. J. Kelly, method to be reported.

[12] A similar failure ascribed to reasons apparently inapplicable here is noted by B. M. Dubinin and G. V. Chelintsev, *Zhur. Obshchei Khim.*, **7**, 2365 (1937) (*C. A.*, **32**, 2123 [1938]).

[13] F. J. Marshall and W. N. Cannon, *J. Org. Chem.*, **21**, 245 (1956).

[14] L. Wolff and R. Greulich, *Ann.*, **394**, 47 (1912).

[15] L. Horner and E. Spietschka, *Ber.*, **85**, 225 (1952).

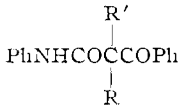
[16] C. Bulow and E. Hailer, *ibid.*, **35**, 915 (1902).

[17] B. Eistert, *Ann.*, **556**, 91 (1944).

[18] Comparison of the infrared absorption of α-benzoyl-β-methylbutyranilide (IIIb, R = i-propyl) and α-n-propyl-β-i-propoxy-β-phenylacrylanilide (Va, R = n-propyl, R′ = i-propyl) showed a strong absorption peak at 1690 cm.$^{-1}$ (aryl ketone stretching frequency) present in the former spectrum and absent from the latter, while peaks at 1090 and 1070 cm.$^{-1}$ (aliphatic ether moiety) were absent from the former and present in the latter; see Fig. 1.

Table I

Alkylation of Benzoylacetanilides[a]



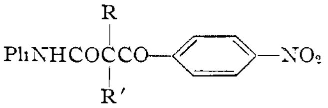
$$\mathrm{PhNHCO}\overset{\displaystyle R'}{\underset{\displaystyle R}{C}}\mathrm{COPh}$$

Group present (R)	Group intrd. (R′)	Base used[b]	Reacn. time, hr.	Yield, %[c]	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
H	Me	NaOEt	0.5	82	137.0–138.3[d]	75.9	76.1	5.98	5.98
H	Et	NaOEt	3.0	96[e]	151.0–151.8	76.4	76.6	6.41	6.37
H	*n*-Pr	NaOEt	6.5	71[f]	160.0–161.0	76.9	77.1	6.81	6.60
H	*i*-Pr	NaOEt	15.0	33[g]	156.6–157.6	76.9	76.8	6.81	6.77
H	*i*-Pr	NaH[h]	18.0	32[g,p]					
H	CH_2Ph	NaOEt	1.5	86[i]	158.5–159.8	80.2	80.5	5.82	5.57
Me	Et	NaH	1.2	51	107.5–108.2	76.9	76.6	6.81	6.87
n-Pr	Me	NaH[j]	0.3	100[k]	141.0–141.7	77.3	77.5	7.16	7.14
Me	*n*-Pr	NaH	3.0[l]	20[k,m]					
Me	*n*-Pr	NaOEt	5.0	0[n]					
n-Pr	Et	NaH	2.0	33	130.0–133.0	77.6	77.4	7.49	7.48
Me	CH_2Ph	NaOEt	2.0	60[o]	129.0–130.3	80.5	80.4	6.17	6.37

[a] Unless otherwise indicated, all products characterized here were purified by crystallization from ethanol or aqueous ethanol, whence they separated as white or transparent needles. [b] With NaOEt reactions were carried out at refluxing temperatures; with NaH, at 50° unless otherwise noted. [c] A product, the lower limit of whose m.p. range was no more than 15° below that of the analytical sample, was arbitrarily chosen for the calculation of yields. [d] The literature reports 137–138° (ref. 14) and 137° (ref. 15). [e] Deacylation to butyranilide was effected in 32% yield; the 2,4-dinitrophenylhydrazone melts at 157–160°. [f] The 2,4-dinitrophenylhydrazone melts at 165–168°. [g] The 2,4-dinitrophenylhydrazone melts at 183–186°. [h] At 80–90°. [i] Deacylation to β-phenylpropionanilide was effected in 74% yield. [j] At 40°. [k] The 2,4-dinitrophenylhydrazone melts at 215–219°. [l] Plus overnight standing at room temperature. [m] 11% of the O-alkylation product also was isolated. [n] See compound Vc, Table III, for the nature of the products obtained in this reaction. [o] Platelets. [p] The infrared absorption spectrum is given in Fig. 1.

Table II

Alkylation of *p*-Nitrobenzoylacetanilides[a]

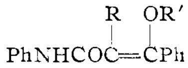


Group present (R)	Group intrd. (R′)	Base used[b]	Reacn. time, hr.	Yield, %[c]	M.p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found	Crystln. solvent[d]
H	Me	NaOEt	1.0	74	170.8–171.8	9.39	9.39[e]	A
H	Et	NaOEt	8.0[f]	31	155.0–156.3			A
H	Et	NaH	6.0	47	155.2–156.5	8.98	9.18	A
H	*n*-Pr	NaH[g]	4.5	20	162.0–163.6	8.59	8.61	B[h]
H	CH_2Ph	NaOEt	2.0	56	158.7–159.4	7.48	7.68[i]	A, B
Et	Me	NaH	0.33	74[j]	122.0–124.0	8.59	8.29	B
Et	*n*-Pr	NaH[k]	4.0[f]	60[j]	146.3–147.3	7.91	7.89	B
CH_2Ph	Me	NaH[k]	0.75	76[j,l]	198.3–199.6	7.21	7.34	A[m]

[a] Unless otherwise noted, all products characterized here were in the form of yellow needles. [b] With NaOEt reactions were carried out at refluxing temperatures; with NaH, at 50° unless otherwise noted. [c] See note *c*, Table I. [d] A = absolute ethanol + benzene; B = absolute ethanol. [e] Also: carbon 64.4% calcd., 64.3% found; hydrogen 4.73% calcd., 4.58% found. [f] Plus overnight standing at room temperature. [g] At 90°. [h] Preceded by trituration with ethyl ether at room temperature. [i] Also: carbon 70.6% calcd., 70.5% found; hydrogen 4.85% calcd., 4.85% found. [j] The compound was colorless. [k] At 60°. [l] Granules. [m] Followed by ethanol–benzene–nitrobenzene and ethanol–nitrobenzene mixtures.

Table III

O-Alkylation of Benzoylacetanilides



$$\mathrm{PhNHCO}\overset{\displaystyle R}{C}=\overset{\displaystyle OR'}{C}\mathrm{Ph}$$

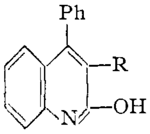
Cpd.[a]	Group present (R)	Group intrd. (R′)	Base used	Yield, %	Time, hr.	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Va	*i*-Pr	*n*-Pr	NaH	47[f]	5.5[b]	110.2–111.2	78.0	77.8	7.79	7.61
Vb	*n*-Pr	*i*-Pr	NaH	61	1.5[c]	72.6–73.7	78.0	77.9	7.79	7.68
Vc	Me	*n*-Pr	NaOEt	20[d]	5.0[e]	114–115	77.3	77.6	7.16	7.18

[a] These were purified by successive crystallization from aqueous and absolute ethanol, whence they separated as white needles. [b] At 85°; in another experiment, after 10 hours at 50°, the reaction was still incomplete ($pH > 7$) and 34% of the starting compound was recovered. [c] At 90°. [d] Plus 23% starting compound and 37% $PhCOOC_2H_5$. [e] At refluxing temperature. [f] The infrared absorption spectrum is given in Fig. 1.

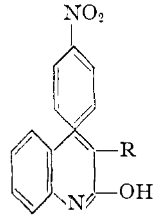
Steric factors operated markedly in the alkylations of IIIb and IVb. C-Alkylation (to give IIIc and IVc) was favored when the entering group was small or activated (as methyl or benzyl), while O-alkylation (to give V) gradually predominated when the bulk of the entering group increased (as *n*- or *i*-propyl).

Because mixtures were frequently encountered, simple diagnostic tests for determining their nature were essential. IIIa and IVa could easily be distinguished from their alkylated derivatives, since the latter gave negative ferric chloride[10,19a] and mercuric chloride in sodium ethoxide[19b] tests, while for the former these tests were positive. Reaction with bromine in carbon tetrachloride[19c] proved the most convenient method for distinguishing among the three kinds of alkylated products. Monoalkylated compounds (IIIb and IVb) rapidly decolorized the bromine with evolution of hydrogen bromide[20]; di-C-alkylated compounds (IIIc and IVc) did not react; and enol ethers (V) produced decolorization without hydrogen bromide evolution. Furthermore, V could be distinguished from IIIc by treatment with ethanolic sulfuric acid, which cleaved the ether linkage in V to give IIIb.

Cyclization of benzoylacetanilide (IIIa) by concentrated sulfuric acid has been shown to give 4-phenylcarbostyril.[21] We have found that with a single exception compounds of type IIIb, IVa and IVb were also smoothly converted into 4-arylcarbostyrils (VI and VII, respectively); 76% sulfuric acid was employed in order to minimize the sulfonation of free phenyl groups which has been shown to occur[22] with the concentrated acid. The exceptional compound was α-benzoyl-β-phenylpropionanilide (IIIb, R = benzyl). (Although other α-benzyl-β-ketoanilides have been reported to behave similarly,[8,12,23] this is the first instance of such difficulty not being overcome by avoiding the use of concentrated sulfuric acid.[10,24]).



VI



VII

During most cyclizations of IIIb a pleasant odor emanated from the reaction mixture. In two instances the source of this odor was identified as a phenyl ketone, thus pointing to hydrolysis competing with cyclodehydration.[25] In one instance (α-benzoyl-β-methylbutyranilide (IIIb), R = *i*-propyl), indeed, the ketone was the chief product isolated.

$$\underset{\text{IIIb}}{\text{PhNHCOCHRCOPh}} + H_2O + H^{\oplus} \longrightarrow PhNH_3^{\oplus} + CO_2 + PhCOCH_2R$$

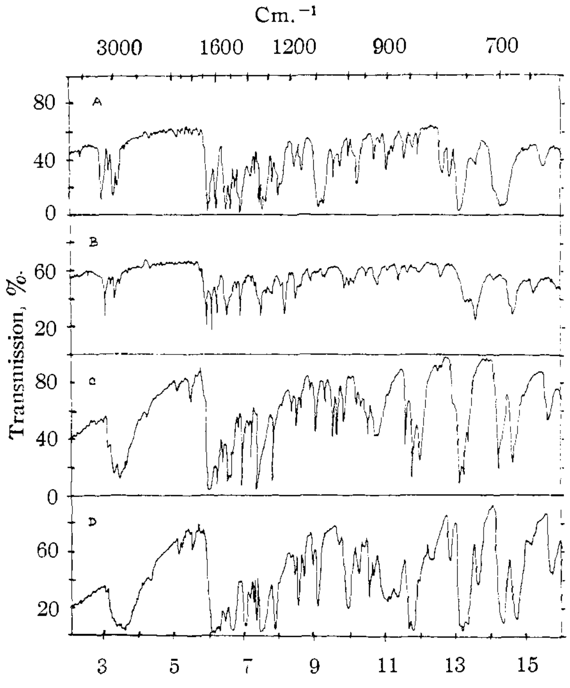


Fig. 1.—Infrared spectra of: A, α-*n*-propyl-β-isopropoxy-β-phenylacrylanilide (Va); B, α-benzoyl-β-methylbutyranilide (IIIb, R = *i*-propyl); C, 3-ethyl-4-(*p*-nitrophenyl)-carbostyril (VII, R = ethyl); D, 3-methyl-4-(*p*-nitrophenyl)-carbostyril (VII, R = methyl).

The yields of the carbostyrils VI and VII diminished as R became bulkier. The fact that yields of VII from IVb were both consistently higher and more rapidly attained than were those of VI and from IIIb showed, however, that any opposing steric factors present could be offset by the enhancing electronic effect of the *p*-nitro group. Table IV summarizes these results.

Cyclization of IIIc and IVc to give VI and VII occurred with concomitant loss of one of the two α-alkyl groups. As anticipated from previous work[5,6] the departing group was that capable of forming the more stable carbonium ion. As one or both alkyl group(s) in IIIc grew larger, however, the anilides became inert to cyclization. Starting compounds only were recovered when α-ethyl-α-benzoylvaleranilide (IIIc, R = ethyl, R′ = *n*-propyl) and α-methyl-α-benzoyl-β-phenylpropionanilide (IIIc, R = methyl, R′ = benzyl) were treated with 76% sulfuric acid. While the inertness of the latter was not unexpected in view of the experience with α-benzoyl-β-phenylpropionanilide (IIIb, R = benzyl; *vide supra*), it should be noted that in previous investigations no difficulty was encountered in cyclizing identically substituted acetoacetanilides.[6,10]

In comparable *p*-nitrobenzoylacetanilides (IVc) the presence of an electron-withdrawing group overcame much of this resistance to cyclization. The only difficulty experienced was with α-methyl-α-(*p*-nitrobenzoyl)-β-phenylpropionanilide (IVc, R = methyl, R′ = benzyl). This substance proved al-

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(19) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," third edition, John Wiley and Sons, Inc., New York, N. Y., 1948; (a) p. 98, (b) p. 109, (c) p. 93.

(20) With the exception of α-benzoyl-β-methylbutyranilide (IIIb, R = *i*-propyl), which did not react; also, α-benzoyl-β-phenylpropionanilide (IIIb, R = benzyl) reacted rather slowly.

(21) C. R. Hauser and G. A. Reynolds, THIS JOURNAL, **70**, 2402 (1948).

(22) E. Ritchie, *J. Proc. Roy. Soc. N. S. Wales*, **78**, 147 (1945)

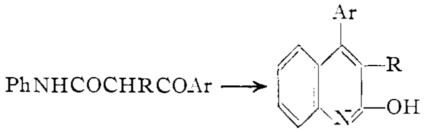
(23) A. L. Searles and H. G. Lindwall, THIS JOURNAL, **68**, 988 (1946).

(24) When treated with 70% H_2SO_4 up to six hours at 110° only starting compound was recovered, and refluxing for two hours resulted in charring, evolution of SO_2 and no isolable carbostyril; using 81%, 86% or concentrated acid gave no water-insoluble product. Polyphosphoric acid at 140° likewise proved ineffective.

(25) Hydrolysis also has been noted when α-acetyl-α-benzylpropionanilide was refluxed with 30% H_2SO_4 (ref. 6).

TABLE IV

CYCLIZATION OF MONO-α-ALKYL-BENZOYLACETANILIDES



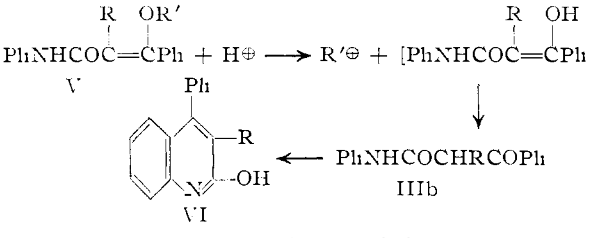
R	Ar	Reacn. time, hr.[a]	Yield, %[b]	Crystln. solvent[c]	M.p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
Me	Ph	1	89	A	238.0–238.7	5.95	6.00
Et	Ph	3	70[e]	A	234.3–235.7	5.40	5.67
n-Pr	Ph	2	55	B	205.0–206.0	5.32	5.11
i-Pr	Ph	6[f]	7[g]	B, A[h]	277.0–281.0	5.32	5.48
CH_2Ph	Ph	1–6	0				
H	*p*-NO_2Ph	1	95	C[i]	305–307[d]	10.52	10.52
Me	*p*-NO_2Ph	1	97[j]	C[h]	341–343[d]	10.00	9.93
Et	*p*-NO_2Ph	1	72[j]	C[h]	340–344[d]	9.52	9.34
n-Pr	*p*-NO_2Ph	1	65	E[h]	295–299[d]	9.09	9.16
CH_2Ph	*p*-NO_2Ph	2	53	D[h]	260.5–261.7	7.86	7.50

[a] All reactions were run in excess 76% H_2SO_4 at steam-bath temperature; unless otherwise noted, the products were colorless or white, and crystallized as needles. [b] See note *c*, Table I. [c] A = 50% aq. ethanol; B = absolute ethanol; C = benzene + nitrobenzene; D = benzene + ethanol (2:1); E = ethanol + nitrobenzene (3:1). [d] Decomposition occurred slowly when these compounds were heated, so that determinations conducted in the usual manner were unreliable; however, when the sample was immersed in the bath fluid at a temperature about 10° below the expected m.p. (as estimated by preliminary determinations) and the temperature increased by 2° per minute, the reproducible values given here were attained with a minimum of heat-induced decomposition. [e] 20% of *n*-butyrophenone also was isolated. [f] No reaction in one hour. [g] 43% of isovalerophenone was also isolated. [h] Prisms. [i] Yellow prisms. [j] The infrared absorption spectrum is given in Fig. 1.

most completely insoluble in 76% sulfuric acid at 95°, and when acid of greater concentration was used (alone or in conjunction with such solvents as nitrobenzene and dimethylformamide) either starting compound was recovered or no water-insoluble product was formed. The technique finally employed with success involved dissolving the compound in concentrated sulfuric acid, rapidly diluting the latter with water to 76%, and then proceeding in the usual manner. When solutions were kept dilute the reaction then proceeded in good yield.

These dealkylative cyclizations are described in Table V.

The action of 76% sulfuric acid on the enol ethers is of interest. When Vc was treated with this acid, 3-methyl-4-phenylcarbostyril (VI, R = methyl) was obtained. When Vb was similarly treated, a mixture of 3-*n*-propyl-4-phenylcarbostyril (VI, R = *n*-propyl) and α-benzoylvaleranilide (IIIb, R = *n*-propyl) apparently was produced. However, Va gave only α-benzoyl-β-methylbutyranilide (IIIb, R = *i*-propyl). These apparent anomalies can be explained by the reaction sequence



V

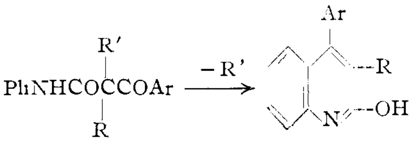
VI

IIIb

Whether IIIb, VI or a mixture of the two is formed from V under these conditions depends on the ease of conversion of IIIb to VI, which already has been discussed.

TABLE V

DEALKYLATIVE CYCLIZATION OF DI-α-ALKYLBENZOYLACETANILIDES



R	R'	Ar	Reacn. time, min.[a]	Yield, %[b]
Me	Et	Ph	120	91
Me	*n*-Pr	Ph	120	63[c]
Et	*n*-Pr	Ph	150	0[d]
Me	CH_2Ph	Ph	180[e]	0[f]
Me	Et	*p*-NO_2Ph	60	78[g]
Et	*n*-Pr	*p*-NO_2Ph	60	72
Me	CH_2Ph	*p*-NO_2Ph	60	82

[a] All reactions were run in excess 76% H_2SO_4 at steam-bath temperature. The products (described in Table IV) were identified by mixed m.p.'s (see note *d*, Table IV) with authentic samples unless otherwise indicated. [b] See note *c*, Table I. [c] Plus 14% recovered starting compound. [d] 80% of the starting compound was recovered. [e] No reaction occurred in 8 hours heating. [f] 93% of the starting compound was recovered. [g] The product here was identified by comparison of the infrared absorption spectra; see Fig. 1 and the Experimental section of this paper.

Acknowledgment.—The authors are indebted to Messrs. H. Adelman, H. J. Brodie and L. V. Dvorken for determination of absorption spectra. Those cited were taken in KBr with a Baird double beam spectrophotometer using a NaCl prism.

Experimental[26]

The following procedures typify the variations applied in the course of preparing, isolating and purifying the compounds described in this paper.

Ethyl *p*-Nitrobenzoylacetate.—Ethyl acetoacetate (124.7 g., 0.96 mole) was cooled to −10°, and a solution of sodium

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[26] Melting points cited here and in the preceding tables are uncorrected. All microanalyses were performed by the Schwarzkopf Microanalytical Laboratory.

(22.1 g., 0.96 gram-atom) in commercial absolute ethanol (300 ml.), which had been kept at a temperature above 60° to prevent solidification, was introduced. The temperature of the reaction mixture was now maintained at 0–10° by external cooling during the dropwise addition of a solution of *p*-nitrobenzoyl chloride (89.0 g., 0.48 mole) in anhydrous ether (1850 ml.); this addition required 30 minutes. The yellow slurry thus obtained was stirred for an additional hour, and then additions of sodium ethoxide and *p*-nitrobenzoyl chloride in the same amounts repeated, keeping the temperature below 10°. Finally the reaction mixture was stirred at 10° for two hours. It was then filtered, and the collected solid washed with anhydrous ether until the washings were colorless. After vacuum-drying to constant weight the yellow solid product weighed 290.5 g.; assuming this to be an equimolecular mixture of sodium chloride and the sodium salt of ethyl α-(*p*-nitrobenzoyl)-acetoacetate[27] the yield was 84.2%.

The salt mixture was dissolved in water (6.5 l.). Ammonium chloride (42.5 g.) and concentrated ammonia solution (47.2 g.) were added with stirring and the solution allowed to stand 24 hours at room temperature. At the end of this time the mixture consisted of a yellow solid suspended in a yellow liquid. The solid was collected by filtration, washed with water until the washings were colorless, and dried in a vacuum oven at 50°. The crude ethyl *p*-nitrobenzoylacetate melted at 68–190°. Upon crystallization from absolute alcohol (190 ml.) the recovery of product melting at 68–75° was 79.0 g. (46.2% of theory). Further crystallization changed the melting point to 68–71°.

The high-melting contaminant was isolated by refrigerating the combined mother liquors from which the crude product had been filtered. The additional solid which precipitated was crystallized, first from absolute ethanol and then twice from 50% aqueous ethanol. In this way there were obtained thick, pale tan needles, m.p. 200.5–202.0°. A mixed m.p. of this substance with an authentic sample of *p*-nitrobenzamide showed no depression.[28]

α-(*p*-Nitrobenzoyl)-propionanilide.—*p*-Nitrobenzoylacetanilide (40.1 g., 0.140 mole) was dissolved in a solution of sodium (3.41 g., 0.148 gram-atom) in commercial absolute ethanol (300 ml.). To the deep red-brown solution thus produced methyl iodide (21.1 g., 0.149 mole) was added, and the reaction mixture refluxed for one hour with mechanical stirring. During this period additional methyl iodide (10.5 g., 0.075 mole) was added portionwise. At the end of the heating period the solution was yellow and neutral to Hydrion paper. It was poured into water (1.5 l.), stirred briefly, and the resulting mixture of yellow solid and colorless liquid filtered after standing for 15 minutes at room temperature. The solid was washed well with water and dried in air at 80°; in this manner 40.8 g. of crude product, m.p. 142–162°, was obtained. This was crystallized from a mixture of absolute ethanol (200 ml.) and benzene (50 ml.) to give 30.9 g. (74% yield) of pale yellow needles melting at 169–171°. Two further recrystallizations from the same solvent pair raised the melting point to 170.8–171.8°.

α-Methyl-α-benzoylvaleranilide (Method A).—A mixture of anhydrous benzene (40 ml.), dimethylformamide (20 ml., dried by distillation, discarding that portion boiling below 150°) and sodium hydride (1.16 g., 0.046 mole based on a 95% assay) was cooled to 10°, α-benzoylvaleranilide (12.3 g., 0.044 mole) was added, and the mixture was stirred for 30 minutes, by the end of which a clear solution was present. Upon the addition of methyl iodide (12.0 g., 0.085 mole) there took place an immediate exothermal reaction which necessitated external cooling. A white solid precipitated during this time. When the initial vigor of the reaction had subsided the mixture was stirred for an additional 10 minutes at 40°. It was then neutral to Hydrion paper. Water (100 ml.) was added, and after stirring for 10 minutes the two phases which resulted were separated. The benzene layer was washed twice with 10-ml. portions of saturated aqueous sodium chloride, then dried over anhydrous sodium sulfate. The resulting liquid was evaporated under reduced pressure until no further loss of weight occurred. In this manner there was obtained 13.2 g. of white solid, m.p. 132–138°, which corresponded to a quantitative yield. When this crude product was crystallized from aqueous ethanol (1:3, 80 ml.) there was recovered 9.9 g. (75%) of short white needles, m.p. 138–140°. Further recrystallization from absolute ethanol raised the melting point to 141.0–141.7°.

Method B.—Anhydrous benzene (40 ml.), dried dimethylformamide (20 ml.) and sodium hydride (1.46 g., 0.058 mole based on a 95% assay) were cooled to 10°. α-Benzoylpropionanilide (14.7 g., 0.058 mole) was added, and the mixture stirred for 30 minutes, by the end of which a clear solution was present. *n*-Propyl bromide (10.0 g., 0.081 mole) was added, the mixture stirred for 3 hours at 50°, then allowed to stand overnight at room temperature. After this the mixture of colorless liquid and white solid was neutral to Hydrion paper. Water (100 ml.) was added, and after stirring for 10 minutes the two phases which resulted were separated. The benzene layer was washed twice with 10-ml. portions of saturated aqueous sodium chloride and dried with anhydrous magnesium sulfate. The resulting liquid was then evaporated under reduced pressure until the weight of the residue remained constant. The 16.5 g. of white solid thus obtained was crystallized from absolute ethanol (60 ml.), the mixture being refrigerated overnight before filtration. The recovery was 11.8 g. of material melting at 100–133°. An additional crystallization from absolute ethanol (45 ml.) in the same manner gave 9.5 g. of solid melting at 100–127°. When this was recrystallized from absolute alcohol (40 ml.), with the mixture being allowed to stand at room temperature 24 hours before filtration, there was recovered white needles (3.5 g., 20% yield) melting at 140.0–141.3°. The mixed m.p. between this compound and that produced by method A showed no depression.

When the mother liquor from the second crystallization above had stood for 4 days at room temperature, an additional 2.0 g. (11% yield) of solid had been deposited. After crystallization from absolute ethanol (10 ml.) it melted at 113.3–114.5°. This compound proved to be identical (mixed m.p.) with α-methyl-β-*n*-propoxy-β-phenylacrylanilide (Vc, see below).

The Sodium Ethoxide Alkylation of α-Benzoylpropionanilide.—α-Benzoylpropionanilide (15.3 g., 0.060 mole) was dissolved in a solution of sodium (1.55 g., 0.067 gram-atom) in commercial absolute ethanol (200 ml.). *n*-Propyl bromide (8.2 g., 0.067 mole) was added, and the solution refluxed with mechanical stirring for 5 hours. During this time additional *n*-propyl bromide (5.0 g., 0.040 mole) was added portionwise. The mixture, consisting of a white solid and a colorless liquid, was filtered, and the filtrate evaporated to a volume of approximately 100 ml. Water (1 l.) was added with stirring, and the resulting mixture of liquids refrigerated overnight. The addition of a few drops of hydrochloric acid followed by vigorous agitation served to solidify the organic phase. However, since it remelted on warming to room temperature, the entire mixture was steam distilled, and the distillate (750 ml.) extracted with ether (five 50-ml. portions). The combined extracts were dried with anhydrous magnesium sulfate, the ether evaporated under reduced pressure, and the residue distilled through a 24-inch Vigreux column. The product distilled at 86–88° (3 mm.). Redistillation gave a liquid boiling at 94–95° (14 mm.). Elemental analysis corresponded to $C_9H_{10}O_2$; its density was 1.054^{25}_{25}, and its $n^{25}D$ 1.5035. On the basis of these facts, the compound was identified as ethyl benzoate.[29]

The yield of redistilled product was 3.3 g. (37%).

The residue from the steam distillation, consisting of a semi-solid material suspended in water, was extracted with ether (six 50-ml. portions). The combined extracts were dried with Drierite and the ether removed by evaporation. The residue, a wet solid, was triturated with low-boiling petroleum ether (40 ml.) and the mixture filtered. The

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[27] This assumption was verified by conversion with aqueous H_2SO_4 to the known ethyl α-(*p*-nitrobenzoyl)-acetoacetate, m.p. 52.5–55.5° (reported[16] 53–55°).

[28] Previous workers have erroneously claimed that this substance was the ammonium salt of ethyl *p*-nitrobenzoylacetate, and that it formed only when an excess of ammonia was used in the deacylation (ref. 16); we find that it is formed whether or not an excess of ammonia is used, which indicates competition between the two existing paths whereby deacylation may occur. A similar experience has been reported (J. Buchi, P. Schneeburger and R. Liebenherr, *Helv. Chim. Acta*, **36**, 1402 (1953)).

[29] E. H. Huntress and S. P. Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1941, p. 324.

white solid remaining was crystallized twice from aqueous ethanol (1:2, 20 ml.), giving 3.5 g. (23% recovery) of white needles whose m.p. (134–137°) was undepressed upon admixture with the starting compound.

When the petroleum ether extract mentioned above was evaporated to dryness and the solid tan residue crystallized from aqueous ethanol (1:10, 22 ml.), 2.6 g. of white solid melting at 80–112° was obtained. Two further crystallizations from absolute ethanol (10-ml. portions) yielded short white needles melting at 114–115°. Elementary analyses were consistent with the formula $C_{19}H_{21}NO_2$. A mixed m.p. between this compound and α-methyl-α-benzoylvaleranilide showed marked depression. The substance readily absorbed bromine with no evolution of hydrogen bromide, and gave 3-methyl-4-phenylcarbostyril when treated with 76% sulfuric acid. It was dealkylated in the following manner: To 0.34 g. dissolved in ethanol (10 ml.) concentrated sulfuric acid (10 ml.) was added, and the resulting solution refluxed for 30 minutes. Water (35 ml.) was added with stirring, and the white solid which precipitated was separated from the liquid by filtration after the solid had been refrigerated for one hour. The solid was washed well with water, then air-dried to yield 0.27 g. of crude product melting at 129–137°. Crystallization from absolute ethanol (5 ml.) resulted in the recovery of white needles melting at 136.2–138.2°; this proved identical (mixed m.p.) with authentic α-benzoylpropionanilide. These facts, in conjunction with spectrographic evidence (see Fig. 1), support the belief that the compound recovered from the petroleum ether extract above was the enol ether of the starting substance, *viz.*, α-methyl-β-*n*-propoxy-β-phenylacrylanilide (Vc). The yield of purified product was 20%.

4-(*p*-Nitrophenyl)-carbostyril.—*p*-Nitrobenzoylacetanilide (1.13 g., 0.0040 mole) and 76% sulfuric acid (10 ml.) were heated on a steam-bath for an hour with occasional stirring. The original slurry became a clear yellow solution within several minutes, and underwent no further change in appearance during the heating period. The solution was poured with stirring into crushed ice and water (100 g.) while still hot, and the light yellow solid which precipitated was collected by filtration after the ice had melted. It was then washed successively with water, 2% aqueous sodium carbonate and water. After air-drying, the crude product weighed 1.01 g. (95% yield) and melted at 292–305°. Crystallization from a mixture of benzene (20 ml.) and nitrobenzene (22 ml.) gave 0.87 g. (86% recovery) of pale yellow prisms melting at 304–307°. After another crystallization from the same solvent pair the m.p. was 305–307° (see note *d*, Table IV).

The Action of 76% Sulfuric Acid on α-Benzoylbutyranilide.—α-Benzoylbutyranilide (1.06 g., 0.0040 mole) and 76% sulfuric acid (5 ml.) were heated on a steam-bath for 3 hours. After 30 minutes the mixture became homogeneous. At the end of the heating period it possessed a strong ketonic odor and was dark red in color. It was poured into crushed ice and water (100 g.) while still hot, and the mixture filtered, the filtrate being set aside. The tan solid thus collected was washed successively with water, 2% aqueous sodium carbonate and water, then air-dried to constant weight. It was triturated with low-boiling petroleum ether (five 10-ml. portions) and again air-dried, the combined washings being set aside. The yield of crude product melting at 198–225° was 0.70 g. (70%). Recrystallization from 50% aqueous ethanol (60 ml.) gave 0.51 g. (73% recovery) of long, white needles, m.p. 234.3–235.7°. Further recrystallization from the same solvent did not alter this m.p.

The acidic mother liquor remaining after filtration of the crude product was extracted with low-boiling petroleum ether (five 25-ml. portions). These were combined with the petroleum ether washings set aside, and evaporated. From the liquid residue 0.26 g. (20%) of crude 2,4-dinitrophenylhydrazone was prepared. After two crystallizations from an ethanol–ethyl acetate mixture (2:1, 45 ml. each) the compound consisted of long, flat, scarlet needles, m.p. 193.8–194.8°. (The m.p. of *n*-butyrophenone 2,4-dinitrophenylhydrazone has been reported as 188°[30] and 190°.[31])

3-Benzyl-4-(*p*-nitrophenyl)-carbostyril.—α-(*p*-Nitrobenzoyl)-β-phenylpropionanilide (1.07 g., 0.0029 mole) and 76% sulfuric acid (10 ml.) were heated on a steam-bath for two hours with frequent stirring. Complete solution did not occur; two phases remained until the end of the heating period. The reaction mixture was poured into crushed ice and water (100 g.) while still hot. The mixture was filtered, and the solid washed successively with water, 2% aqueous sodium bicarbonate and water. After drying in a vacuum oven at 60° the crude product weighed 0.99 g. and melted at 241–243°. When it was crystallized from a mixture of benzene and absolute ethanol (2:1, 30 ml.), white prisms (0.55 g., 53% yield) melting at 254–261° were recovered. Three further recrystallizations from the same solvent pair raised the m.p. to 260.5–261.7°.

The Action of 76% Sulfuric Acid on α-Methyl-α-benzoylvaleranilide.—α-Methyl-α-benzoylvaleranilide (2.18 g., 0.0074 mole) and 76% sulfuric acid (20 ml.) were heated on a steam-bath for 2 hours with occasional stirring. The initial two-phased slurry became a cherry-colored solution within 20 minutes. At the end of the heating period the color had changed to orange-brown. The solution was poured with stirring into crushed ice and water (100 g.) while still hot, and filtered after the ice had melted. The white solid thus collected was washed successively with water, 2% aqueous sodium bicarbonate and water. No ketonic odor was noted at any time. The air-dried solid was triturated with low-boiling petroleum ether (20 ml.), and the resulting slurry allowed to stand at room temperature for 16 hours before filtering. In this manner 1.18 g. of white solid was obtained, m.p. 214–236°. Repetition of the trituration process gave 1.09 g. (63%) of product melting at 231–236°. Crystallization of this from 50% aqueous ethanol raised the m.p. to 233.0–236.5°, which was not depressed upon admixture with an authentic sample of 3-methyl-4-phenylcarbostyril.

The Action of 76% Sulfuric Acid on α-Methyl-α-(*p*-nitrobenzoyl)-butyranilide.—α-Methyl-α-(*p*-nitrobenzoyl)-butyranilide (1.01 g., 0.031 mole) and 76% sulfuric acid (10 ml.) were heated on a steam-bath for an hour with occasional stirring. Within 15 minutes the slurry had become homogeneous and dark red in color. During the heating period this color became progressively less intense. The solution was poured with stirring into crushed ice and water (100 g.) while still hot. Filtration yielded a white solid which was washed successively with water, 2% aqueous sodium bicarbonate and water. The air-dried crude product weighed 0.84 g. and melted at 270–330° with decomposition. Crystallization from a mixture of benzene (20 ml.) and nitrobenzene (45 ml.) gave white prisms (0.65 g.) melting at 338–343°.

Mixed melting points of this product with authentic 3-methyl-4-(*p*-nitrophenyl)-carbostyril and with authentic 3-ethyl-4-(*p*-nitrophenyl)-carbostyril showed no depression. A mixed melting point of the two authentic compounds themselves likewise showed no depression. Identification was therefore made by means of infrared absorption spectra. While the spectra of the two authentic compounds were quite similar (see Fig. 1), those of the product and 3-methyl-4-(*p*-nitrophenyl)-carbostyril proved virtually identical. The yield in this dealkylative cyclization was 78%.

The Action of 76% Sulfuric Acid on α-Methyl-β-*n*-propoxy-β-phenylacrylanilide (Vc).—α-Methyl-β-*n*-propoxy-β-phenylacrylanilide (0.49 g., 0.0017 mole) and 76% sulfuric acid (5.0 ml.) were heated for 2 hours on a steam-bath with occasional stirring. The slurry became homogeneous within several minutes, and the pale yellow color deepened to dark yellow-brown as the heating progressed. The solution was poured into crushed ice and water (50 g.) while still hot. The white solid which precipitated was collected by filtration, washed successively with water, 5% aqueous sodium bicarbonate and water, and then dried in a vacuum oven at 60°. In this manner there was obtained 0.31 g. of product melting at 168–208°. This was crystallized from 83% ethanol (12 ml.), giving 0.15 g. of white needles melting at 227–235°. Two further recrystallizations from 72% ethanol raised the m.p. to 234–237°, which was not depressed upon admixture with an authentic sample of 3-methyl-4-phenylcarbostyril. The yield of product melting at 227–235° was 38%.

The Action of Sulfuric Acid on α-Isopropyl-β-*n*-propoxy-β-phenylacrylanilide (Va).—α-Isopropyl-β-*n*-propoxy-β-phenylacrylanilide (1.01 g., 0.0031 mole) and 76% sulfuric acid (10 ml.) were heated on a steam-bath for an hour with occasional stirring. The reaction mixture became homogeneous within a few minutes, and turned yellowish-pink during the course of the heating. Shortly before

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[30] J. Ferrante and A. Bloom, *Am. J. Pharm.*, **105**, 383 (1933).

[31] D. P. Evans, *J. Chem. Soc.*, 788 (1930).

the heating was terminated, the solution turned cloudy. It was poured with stirring into crushed ice and water (100 g.) while still hot. A white, gummy material separated, but this hardened to a solid after several days of refrigeration. At this time the mixture was filtered, and the solid thus collected washed successively with water, 5% aqueous sodium bicarbonate and water. The air-dried crude product (0.71 g.) melted at 143–151°, a value that was not improved significantly by trituration with low-boiling petroleum ether. Crystallization from 83% ethanol, then twice from 55% ethanol gave a product of m.p. 154.5–156.3°. The mixed m.p. between this substance and authentic α-benzoyl-β-methylbutyranilide (m.p. 156.6–157.6°) was 153.5–157.2°, thus confirming its identity. The yield of crude product was 82%.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY, CORNELL UNIVERSITY]

Polynuclear Aromatic Hydrocarbons. VIII.[1] The Reaction between Allylsuccinic Anhydride and Benzene

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The Friedel–Crafts reaction between allylsuccinic anhydride (I) and benzene afforded a complex mixture of acids from which, after esterification, it has been possible to isolate and characterize methyl α-phenacyl-γ-phenylvalerate (IV, R = CH_3), methyl 3-phenylcyclohexanone-5-carboxylate (III, R = CH_3) and a small amount of methyl 4-methyltetralone-2-acetate (II, R = CH_3). One of these (IV) has been converted to the carcinogenic hydrocarbon 5-methylbenzo[c]phenanthrene (VI). The contrasting results obtained with β-methallylsuccinic anhydride are discussed and a tentative explanation for the difference in behavior is suggested.

In a recent communication[4] we reported the use of β-methallylsuccinic anhydride as a convenient starting material for the preparation of substituted benzo[c]phenanthrenes. Although the synthetic scheme described in the earlier paper was particularly useful for the preparation of the *gem*-dimethyl derivatives of 5,6-dihydrobenzo[c]phenanthrene, the difficulties encountered in the final dehydrogenation step prompted us to investigate the use of allylsuccinic anhydride (I) in the original Friedel–Crafts condensation with benzene. Although some of the results paralleled those previously reported,[4] the principal product (III) of the reaction was of an entirely different structure than we had anticipated. Moreover, only trace amounts of the tetralone ester (II, R′ = H) could be isolated whereas the corresponding dimethyl compound (II, R′ = CH_3) was the *major* product when β-methallylsuccinic anhydride was employed as starting material.[4]

The condensation between allylsuccinic anhydride (I) and benzene resulted in the formation of a complex mixture of acids that was best separated by fractional distillation of the corresponding methyl esters. In this way it was possible to isolate from the highest boiling fractions about 14% of the acylated-alkylated product (IV) whose structure was established by its ultimate conversion to 5-methylbenzo[c]phenanthrene (VI). This was accomplished by saponification of IV (R = CH_3) followed by reduction of the carbonyl group to the corresponding methylenic derivative. This reduced acid then was cyclized to the tetralone (V, only one of two possible isomers) which was in turn reduced to the alcohol, cyclodehydrated with sulfuric acid and the resulting hexahydrobenzo[c]phenanthrene dehydrogenated to VI. Although the yield of IV was rather low, this sequence of reactions nevertheless provided a convenient synthesis of 5-methylbenzo[c]phenanthrene (VI), a hydrocarbon of interest because of its carcinogenic activity.[5]

From the fractions of intermediate boiling point there was isolated about 18% of a crystalline solid which initially was assumed to be the tetralone ester (II, R′ = H, R = CH_3) because some of its properties were similar to those of the corresponding compound (II, R = R′ = CH_3) isolated in the previous work.[4] The spectroscopic evidence[6] was not in favor of structure II, however, and it soon became evident that the compound contained an isolated carbonyl function. Moreover, permanganate oxidation afforded benzoic acid, an experimental fact that was incompatible with its formulation as II, R′ = H. The correct structure (III, R = CH_3) for this substance was deduced from several pieces of chemical and physical evidence. When the carbonyl group was removed by the Huang-Minlon modification of the Wolff–Kishner reduction and the product subsequently dehydrogenated, there was obtained a mixture of biphenyl and biphenyl-3-carboxylic acid, thus establishing the skeletal structure and the 1,3-relationship of the phenyl and carboxyl groups in III. Moreover, the reduction product was shown to be 3-phenylcyclohexanecarboxylic acid (Va, probably *cis*) by an independent synthesis. The important intermediates in this synthesis (VIa → VII → VIII (X = OH) → VIII (X = Br) → Va) are shown in Chart I but, because of the straightforward nature of these interconversions, the chemistry is discussed only in the Experimental section.

The position of the ketone group in III was readily established by catalytic and sodium borohydride reduction to the corresponding hydroxy ester

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(1) Paper VII, THIS JOURNAL, **78**, 5438 (1956).

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(3) From the thesis submitted by T. B. H. to Cornell University in partial fulfillment of the requirements for the Ph.D. degree, February, 1958.

(4) D. D. Phillips and A. W. Johnson, THIS JOURNAL, **77**, 5977 (1955).

(5) W. E. Bachmann, *et al.*, *Proc. Roy. Soc.* (*London*), **B123**, 343 (1937); I. Berenblum, *Cancer Research*, **5**, 561 (1945).

(6) The Experimental section should be consulted for pertinent data in this respect.