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ACTION OF LEWIS ACIDS ON BENZOYLACETANILIDES AND RELATED COMPOUNDS

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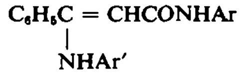
Abstract—Benzoylacetanilides form 2-phenyl-4(1H)-quinolones when acted on by an equimolar proportion of $AlCl_3$, $AlBr_3$ or $SnCl_4$. BF_3 affords the difluoroborane derivative of the anilide. Complexes of the anilides with $AlBr_3$ and $SnCl_4$ were prepared and heated to give the 4(1H)-quinolones. A mechanism for the anilide–quinolone transformation is suggested.

THE effect of anhydrous aluminum chloride on benzoylacetanilides (Ia) at 200° has been reported: equimolar proportions of the reactants give 2-phenyl-4(1H)-quinolones whilst with excess of reagent the products are 4-phenyl-2(1H)-quinolones.[2] Acetoacetanilides (Id) and a 3-molar amount of the chloride at 130–135° readily yielded 4-methyl-2(1H)-quinolones and the reaction occurred also in refluxing xylene; at this temperature the benzoylacetanilides (Ia) were little affected demonstrating the relatively greater ease of cyclization of Id.

$RCOCH_2CONHAr$

Ia, $R = C_6H_5$
b, $R = Ar = C_6H_5$
c, $R = C_6H_5$; $Ar = p\text{-}CH_3C_6H_4$
d, $R = CH_3$


$C_6H_5C(NHAr') = CHCONHAr$

II
a, $Ar = p\text{-}CH_3C_6H_4$; $Ar' = C_6H_5$
b, $Ar = Ar' = p\text{-}CH_3C_6H_4$
c, $Ar = Ar'$

In support of the view[2] that the 4(1H)-quinolones are formed intermolecularly and arise via an intermediate of type IIc were the following observations:

(i) On heating together benzoylacet-*p*-toluidide, *p*-toluoylacetanilide and aluminum chloride in the molar ratio 1:1:2 a number of 4(1H)-quinolones were produced including the "cross-over" products 2-phenyl-4(1H)-quinolone and 2-*p*-tolyl-6-methyl-4(1H)-quinolone.

(ii) *β*-Phenylpropionanilide when acted on by an equimolar amount of aluminum chloride at 200° provided little if any *ω*-(*o*-aminobenzyl)acetophenone[3] and the anilide was recovered in ~50% yield; this made unlikely *ω*-(*o*-aminobenzoyl)acetophenone[4] as intermediate in the 35% conversion of Ib to 2-phenyl-4(1H)-quinolone under similar conditions.[2,5]

That aluminum chloride is capable of condensing aniline with benzoylacet-*p*-toluidide to *β*-phenylaminocinnam-*p*-toluidide (IIa) was revealed indirectly by heating

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* This work is dedicated to the memory of Professor H. Stephen.

[1] To whom any correspondence should be addressed.

[2] B. Staskun, *J. Org. Chem.* **29**, 1153 (1964).

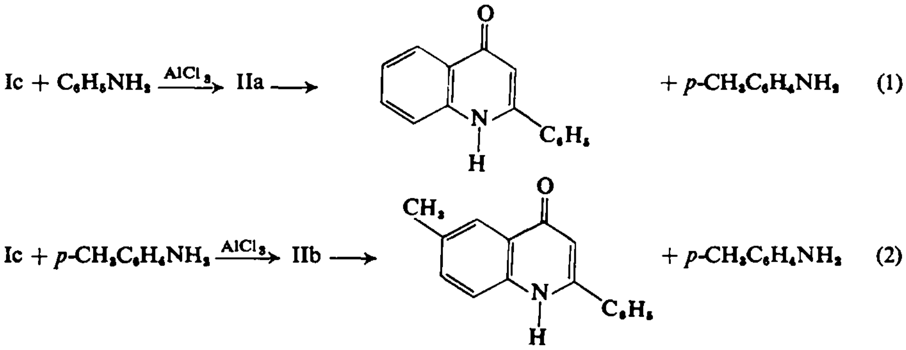
[3] J. F. J. Dippy and J. H. Wood, *J. Chem. Soc.* 2719 (1949).

[4] B. Staskun and S. S. Israelstam, *J. Org. Chem.* **26**, 3191 (1961).

[5] The acylation by benzoylacetylchloride of aniline to *ω*-(*o*-aminobenzoyl)acetophenone in ~35% yield under the above reaction conditions may be discounted; the product would be expected to consist almost entirely of the *p*-amino derivative.[3]

the reactants at 200° to yield 2-phenyl-4(1H)-quinolone together with 2-phenyl-6-methyl-4(1H)-quinolone (Table 1). In the absence of the Lewis acid the product was di-*p*-tolylurea. Since both quinolones were formed also at 130°, at which relatively low temperature Ic is little affected by aluminum chloride, the intervention of intermediates IIa and IIb in the reaction is suggested as shown in Scheme I. A similar mechanism can account also for the same two quinolones being formed, albeit in decreased yields, on passage of hydrogen chloride into a mixture of aniline and Ic at 180°.

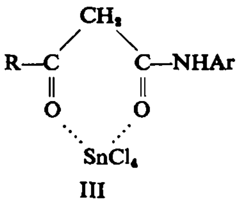
Scheme I



Not unexpectedly, aniline and ethyl benzoylacetate when heated together in the presence of aluminum chloride gave 2-phenyl-4(1H)-quinolone, presumably via ethyl *β*-phenylaminocinnamate as intermediate.[4]

In deciding on the mode of action of aluminum chloride on Ia and Id, the effect of other Lewis acids on the anilides was considered. Anhydrous aluminum bromide gave results similar to and comparable with those obtained with the chloride: an equimolar mixture with Ia at 200° yielded the 2-phenyl-4(1H)-quinolone whilst an excess of reagent (3 moles) caused cyclization of the anilides Ia and Id to the respective 2(1H)-quinolones. In contrast, utilization of a 3-molar as well as an equimolar proportion of anhydrous stannic chloride in the reaction with benzoylacetanilide (Ib) at 210° led to 2-phenyl-4(1H)-quinolone in 30–35% yields; the excess reagent, in the former case, merely refluxed from a relatively stable stannic chloride–anilide adduct produced in an initial reaction and gradually evaporated after which the residual complex decomposed to the 4(1H)-quinolone (see below).

The anilides Ia and Id in benzene solution were respectively treated at room temperature with an equimolar amount of stannic chloride and yielded insoluble 1:1 anilide : reagent addition compounds which are tentatively formulated as III on the basis of their IR spectra. Under similar conditions aluminum bromide afforded benzene-insoluble 2:1 anilide:reagent complexes.

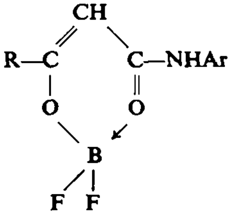


III

The strong keto CO absorption in the anilides Ia and Id was replaced by a weak-medium band at a slightly lower frequency in the Lewis acid adducts. Coordination of the reagent at both O atoms, as shown in III, was suggested by a similar shift of the amide CO absorption band (Table 2).[6] NH absorption was shown in the stannic chloride derivatives by a sharp undisplaced medium peak and in the aluminum bromide complexes by a strong broad band suggestive of hydrogen bonding.

When heated at 220° the 2:1 addition compound of Ib and aluminum bromide gave 2-phenyl-4(1H)-quinolone in 15% yield. The stannic chloride complexes of Ib and Ic afforded the respective 4(1H)-quinolones in appreciably higher yields comparable with those obtained from direct reaction of equimolar amounts of I and stannic chloride at 220°.

Little is known of the action of boron trifluoride on the anilides Ia and Id: acetoacetanilide reacts with loss of hydrogen fluoride to form a compound $C_{10}H_{10}O_2NBF_2$ in which the BF_2 moiety is presumably substituted at the β- O atom.[7] As it was of relevance to confirm this structural assignation, benzoylacetanilides (Ia), including N-ethylbenzoylacetanilide, were treated with boron trifluoride etherate at room temperature and readily furnished similar difluoroborane derivatives. These are formulated as IV in accordance with the analytical data and the IR spectra which exhibited a NH peak and revealed the absence of keto CO absorption. The amide I band in the derivatives was, moreover, at a lower frequency than found in the anilides (Table 2).



IV

a, R = Ar = C_6H_5
b, R = C_6H_5; Ar = p-$CH_3C_6H_4$
c, R = CH_3; Ar = C_6H_5

Since boron trifluoride coordinates at the O atom in amides $RCONHR_1$,[8] structure IV, which is similar to that proposed for the boron difluoride complex of α-acetylphenylacetamide,[9] is preferred to an alternative formulation which shows N → B coordination.

Difluoro[[1-phenyl-2-(*p*-tolylcarbamoyl)vinyl]oxy]borane (IVb)[10] gave no immediate coloration with ferric chloride, dissolved unchanged in dilute alkali, and was hydrolyzed to Ic by hot dilute acid. On heating with excess of either concentrated sulfuric acid,[7] polyphosphoric acid[4] or anhydrous aluminum chloride,[2] it was converted into 4-phenyl-6-methyl-2(1H)-quinolone. Compounds IVa and IVb in the absence of acidic reagents decomposed at 240–250° without however furnishing 4-phenyl-2(1H)-quinolones. Heating acetoacetanilide with excess boron trifluoride etherate gave

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[6] D. Cook, *Canad. J. Chem.* **41**, 515 (1963).

[7] J. R. Killelea, *J. Amer. Chem. Soc.* **70**, 1971 (1948).

[8] E. F. J. Duynstee, W. van Raayen, J. Smidt, and Th. A. Veerkamp, *Rec. Trav. Chim.* **80**, 1323 (1961).

[9] J. F. Wolfe, C. J. Eby, and C. R. Hauser, *J. Org. Chem.* **30**, 55 (1965).

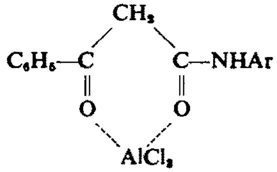
[10] Nomenclature preferred by Chemical Abstracts.

difluoro[[1-methyl-2-(phenylcarbamoyl)vinyl]oxy]borane (IVc);[10] on prolonged refluxing of the mixture the IVc underwent decomposition to yield what appears to be anilinium tetrafluoroborate. Compound IVc was recovered unchanged after keeping at 160° for 1 hr and further demonstrated the reluctance of difluoroborane derivatives IV to cyclize to 2(1H)-quinolones when heated.

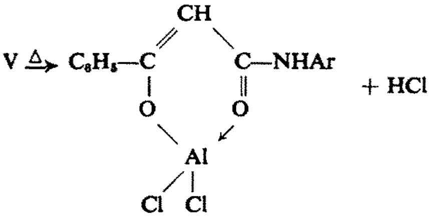
In the light of the above and other[2] observations the conversion of benzoylacetanilides (Ia) into 2-phenyl-4(1H)-quinolones by means of, for example, aluminum chloride at 200° is tentatively assumed to proceed as outlined in Scheme II.[11]

Scheme II

Ia + $AlCl_3$ → complexed anilide, for example, V



V[a] (1)



(2)

VI[b]

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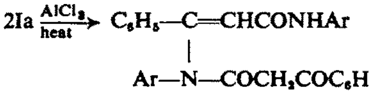
[11] Alternative possibilities for the transformation as indicated in Schemes III and IV were considered and decided against. It is difficult, for example, to reconcile the reactions shown below with the observation that utilization of an increased amount of aluminum chloride leads solely to the isomeric 4-phenyl-2(1H)-quinolone in high yield.[3]

Scheme III



$$2\text{Ia} \xrightarrow[\text{heat}]{AlCl_3} \begin{array}{l} C_6H_5\text{—}C\text{=}CHCONHAr \\ \quad\quad\ | \\ Ar\text{—}N\text{—}COCH_2COC_6H_5 \end{array} \quad (1)$$

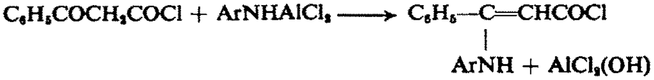
VIII

$$\text{VIII} \xrightarrow{\text{heat}} \text{VII} + ArNH_2 + \text{other products} \quad (2)$$

This route was suggested by the ability of $AlCl_3$ to effect the condensation of amides, $RCONH_2$, with *β*-keto esters to *β*-acylaminocrotonic esters as shown by E. Benary, *Ber. Dtsch. Chem. Ges.* **42**, 3922 (1909).

Scheme IV

$$\text{Ia} \xrightarrow[\text{heat}]{AlCl_3} C_6H_5COCH_2COCl + ArNHAlCl_2 \quad (1)$$



$$C_6H_5COCH_2COCl + ArNHAlCl_2 \longrightarrow \begin{array}{l} C_6H_5\text{—}C\text{=}CHCOCl \\ \quad\quad\ | \\ \quad ArNH + AlCl_2(OH) \end{array} \quad (2)$$

IX

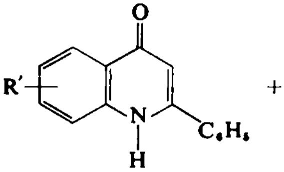
$$\text{IX} \xrightarrow{\text{heat}} \text{VII} \quad (3)$$

This process is a modification of the Dippy and Wood[9] proposal for the rearrangement of anilides $RCONHR_1$ into aminoketones.

V and/or VI + HCl $\longrightarrow$ $ArNH_2$ + other products (3)

V and/or VI + $ArNH_2$ $\longrightarrow$ IIc[c] (4)

IIc $\longrightarrow$



+ $ArNH_2$ (5)

VII

[a] The formation of an anilide-reagent addition compound during the conversion was indicated by the reaction mixture remaining solid even at temps exceeding the m.p. of the anilide (Ia). The 1:1 adduct (V) is, of course, speculative as is also the suggested partial coordination of the reagent with both 0 atoms which would make difficult or prevent electrophilic attack by the polarized keto CO group to give a 4-phenyl-2(1H)-quinoline. [b] The structure VI resembles that of the difluoroborane derivatives (IV) and perhaps again, the suggested coordination would prevent cyclization to the Knorr quinoline. [c] In the presence of a 'foreign' anilide, a mixture of different II could arise and so account for the 'cross-over' products obtained.

The effect of acidic reagents including zinc chloride and sulfuryl chloride on the anilides (Ia and Id) is being further studied.

EXPERIMENTAL[12]

Action of Lewis Acids on Anilides

A. *Anhydrous aluminum chloride*

2-p-*Tolyl-6-methyl-4*(1H)-*quinolone*. *p*-Toluoylacet-*p*-toluidide (1 g) was converted by an equimolar amount of reagent (0·55 g) at 200–220° for 1 hr[3] into alkali-insoluble 2-*p*-tolyl-6-methyl-4(1H)-quinolone (0·53 g, 57% crude yield); colorless tiny crystals from EtOH, m.p. 325–328°, giving no color with alcoholic $FeCl_3$. (Found: N, 5·70. Calc. for $C_{17}H_{15}NO$: N, 5·62%.) The quinolone was very sparingly soluble in EtOH and in hot 2N NaOH and its IR spectrum showed no absorption at 13·9 μ and 14·4 μ which served to distinguish it from 2-phenyl-6-methyl-4(1H)-quinolone. The product proved to be identical with the base resulting from cyclization of methyl β-amino-α-(N-*p*-tolyl-*p*-toluimidoyl)crotonate in liquid paraffin.[13]

β-Phenylpropionanilide (1 g) on similar treatment with $AlCl_3$ (0·6 g) at 200–205° for 1 hr likewise evolved HCl; addition of dil NaOHaq to the reaction mixture afforded insoluble crude unchanged anilide (0·4–0·5 g) identified by its IR spectrum, together with a small amount (ca. 0·05 g) of a colorless base.

'Cross-over' reactions

(i) A mixture of *p*-toluoylacetanilide (0·8 g, 0·0032 mole), benzoylacet-*p*-toluidide (0·8 g, 0·0032 mole) and powdered $AlCl_3$ (0·9 g, 0·0067 mole) was kept at 205–210° for 1 hr and then treated with EtOH and 2N HCl.[3] The acid-insoluble material was removed and separated by means of hot 2N NaOH into alkali-insoluble 2-*p*-tolyl-6-methyl-4(1H)-quinolone (~0·1 g; crude m.p. 295–305°; identified by its IR spectrum) and an alkali-soluble fraction (0·36 g; m.p. 225–232°) which was shown by its IR spectrum to be a mixture of 2-phenyl-4(1H)-quinolone and 2-phenyl-6-methyl-4(1H)-quinolone. The presence in the alkali-soluble fraction of 2-*p*-tolyl-4(1H)-quinolone was not established.

(ii) A similar reaction of *p*-toluoylacet-*p*-toluidide (1 g, 0·0037 mole), N-ethylbenzoylacetanilide (1 g, 0·0037 mole), and $AlCl_3$ (1 g, 0·0074 mole) at 200–220° for 1 hr afforded 2-phenyl-6-methyl-4(1H)-quinolone (0·1 g; crude m.p. 282–292°; somewhat soluble in hot 2N NaOH, insoluble in cold alkali; identified by its IR spectrum) and an alkali-insoluble gum which was not further studied.

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[12] M.ps are uncorrected. IR spectra were taken on a Perkin–Elmer Infracord Model 137 spectrophotometer using 1–2 mg sample per 300 mg KBr.

[13] P. C. Anderson and B. Staskun, *J. Org. Chem.* **30**, 3033 (1965).

TABLE 1

Anilide	Amine	Molar ratio Anilide:AlCl$_3$:Amine	Reaction temp	Yield, % 4(1H)-Quinoline 2-Phenyl-6-methyl	Yield, % 4(1H)-Quinoline 2-Phenyl	Yield, % Other products
Benzoylacet-anilide	Aniline	1:1:3	200°			Diphenylurea, 15
		1:2:1	200°		35	
		1:3:1	200°		20	
		1:3:2	200°		50	
		1:4:1	200°		30	4-Phenyl-2(1H)-quinolone, 10
	p-Toluidine	1:3:2	170°		30	
		1:1:3	200°			Di-*p*-tolylurea, 10
		1:3:2	200°	23	15	
		1:3:2	180°	13	17	
		1:3:2	170°	10	17	
		1:3:2	150°	10	15	
		1:3:2	130°	Trace	Trace	Anilide recovered, 20
Benzoylacet-*p*-toluidide	Aniline	1:3:2	200°	25	20	
		1:3:2	170–180	10	20	
		1:3:2	150°	10	15	
		1:3:2	130°	Trace	Trace	Anilide recovered, 25

TABLE 2. REACTION OF LEWIS ACIDS WITH ANILIDES AT ROOM TEMP

Anilide	Lewis acid	Formula of product	M.p.	Calc. %			Found %			Infrared absorption (μ)[a]		
				Br	Cl	N	Br	Cl	N	NH	Keto CO	Amide CO
Benzoylacet-anilide	—									3·08 (m)	5·92 (s)	6·05 (s)
	AlBr$_3$	$C_{30}H_{26}N_2O_4AlBr_3$		32·2			30·4			3·1 (s)br	6·0 (m)	6·2 (s)
	SnCl$_4$	$C_{15}H_{13}NO_2SnCl_4$			28·4			28·2		3·1 (m)	6·0 (w)	6·2 (s)
	BF$_3$	$C_{15}H_{12}NO_2BF_2$	214–215°			4·88			4·85	3·05 (m)	abs	6·2 (s)
Benzoylacet-*o*-toluidide	—									3·05 (m)	5·92 (s)	6·05 (s)
	AlBr$_3$	$C_{32}H_{30}N_2O_4AlBr_3$		31·0			31·7			3·0 (s)br	6·05 (m)	6·25 (s)
	SnCl$_4$	$C_{16}H_{15}NO_2SnCl_4$			27·6			26·8		3·1 (m)	6·0 (w)	6·25 (s)
Benzoylacet-*p*-toluidide	—									3·1 (m)	5·95 (s)	6·05 (s), 6·12 (s)
	SnCl$_4$	$C_{16}H_{15}NO_2SnCl_4$			27·6			26·0		3·1 (m)	6·0 (w)	6·2 (s)
	BF$_3$	$C_{16}H_{14}NO_2BF_2$	233–235°			4·65			4·58	3·05 (m)	abs	6·15 (s)
N-Methyl-benzoylacet-anilide	—									abs	6·2 (s)	
	BF$_3$	$C_{16}H_{14}NO_2BF_2$	150–151			4·65			4·32	abs	abs	6·22 (s)
N-Ethyl-benzoylacet-anilide	—									abs	6·2 (s)	
	BF$_3$	$C_{17}H_{16}NO_2BF_2$[b]	148–149°			4·45			4·37	abs	abs	6·25 (s)
p-Toluoyl-acetanilide	—	$C_{16}H_{15}NO_2$	112–114°[c]			5·53			5·43	3·1 (m)	5·97 (s)	6·05 (s), 6·1 (s)
p-Toluoylacet-*p*-toluidide	—	$C_{17}H_{17}NO_2$	145–147			5·24			5·28	3·1 (m)	5·99 (s)	6·1 (s), 6·15 (s)
Acetoacet-anilide	—									3·1 (m)	5·84 (s)	6·05 (s)
	AlBr$_3$	$C_{20}H_{22}N_2O_4AlBr_3$		38·6			35·8			3·2 (s)br	5·9 (m)	6·2 (s)
	SnCl$_4$	$C_{10}H_{11}NO_2SnCl_4$			32·4			32·2		3·1 (m)	5·9 (w)	6·1 (s)
	BF$_3$	$C_{10}H_{10}NO_2BF_2$	153–155[d]			6·23			6·20	3·05 (m)	abs	6·2 (s)
Acetoacet-*o*-toluidide	SnCl$_4$	$C_{11}H_{13}NO_2SnCl_4$			31·4			30·9				

[a] w = weak; m = medium; s = strong; abs = absent; br = broad.

[b] Mol. wt.: Calc.: 315. Found: 308,[16] 315 (mass spectrometer).

[c] J. Moszew and A. Inasinki, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.* **9**, 303 (1961); *Chem. Abstr.* **60**, 4055 (1964), give m.p. 114–116°.

[d] Lit.[7] m.p. 154–155°.

Cyclization of acetoacetanilides to 4-methyl-2(1H)-quinolones

Acetoacetanilide (3 g) was mixed with a 3-molar amount of $AlCl_3$ (7·0 g) and heated at ~130° for 1 hr under anhydrous conditions;[3] reaction occurred readily with evolution of HCl. The product was dissolved in warm 2N HCl and the filtered solution was made slightly alkaline with NaOHaq and chilled; the 4-methyl-2(1H)-quinoline which separated in ~65% yield was identified by its m.p.[14] and IR spectrum after recrystallization from dil EtOH. Acetoacet-*o*-toluidide and acetoacet-*p*-toluidide were likewise cyclized to the respective 2(1H)-quinolones[14] in ~70% yield; similar yields were obtained when heating for 15 min.

Reaction in presence of xylene

(i) A mixture of benzoylacet-*p*-toluidide (2·5 g, 0·01 mole) and $AlCl_3$ (4 g, 0·03 mole) in sodium-dried xylene (40 ml) was stirred and warmed; the reactants formed a heavy red oil which, on further heating, eventually dissolved in the xylene to give an opaque brown solution. This was heated under reflux (~133°) for 1 hr (HCl was evolved slowly) and then cooled and treated with water (~10 ml). The insoluble gummy material which precipitated was collected and separated by means of hot 2N NaOH into crude unchanged anilide (1·3 g) and 4-phenyl-6-methyl-2(1H)-quinolone (0·15 g, 7%; crude m.p. 220–235°; very sparingly soluble in cold alkali); the identity of each component was confirmed by its IR spectrum.

(ii) A ready evolution of HCl occurred on similarly reacting acetoacetanilide (1·8 g, 0·01 mole) for 30 min. Water was added to the cooled mixture and the precipitated yellow material was separated from the xylene and dissolved in warm 2N HCl. The filtered (charcoaled) acid solution was chilled and deposited colorless 4-methyl-2(1H)-quinolone in ~30% yield identified by its IR spectrum.

Direct synthesis of 2-phenyl-4(1H)-quinolone from ethyl benzoylacetate and aniline

An equimolar mixture of the ester (2 g), amine (1 g), and $AlCl_3$ (1·4 g) was stirred at 140–150° for 1 hr. The reaction product was extracted with warm 2N NaOH and the alkaline filtrate was acidified with glacial acetic acid to deposit 2-phenyl-4(1H)-quinolone and benzoylacetanilide. The mixture of bases was refluxed with 50% (v/v) H_2SO_4 for 1 hr and the identity of the unaffected quinolone (obtained in ~10% yield) was confirmed by its IR spectrum.

Reaction in the presence of added arylamine

p-Toluidine (2·1 g, 0·02 mole) was added to an intimate mixture of benzoylacetanilide (2·4 g, 0·01 mole) and $AlCl_3$ (4·0 g, 0·03 mole) and the reactants were then kept at 200° for 1 hr under anhydrous conditions.[3] The reaction product was dissolved in EtOH and the solution was treated with 2N HCl and chilled. The acid-insoluble material was removed and was separated by means of 2N NaOH into 2-phenyl-6-methyl-4(1H)-quinolone (0·55 g, 23% crude yield) and alkali-soluble 2-phenyl-4(1H)-quinolone (0·35 g, 15% crude yield); the identity of each component was confirmed after recrystallization by its m.p.[2] and its IR spectrum. Table 1 lists the results obtained at other temps and with various molar proportions of the reactants.

Equimolar amounts of benzoylacetanilide (2.4 g) and *p*-toluidine (1·1 g) were heated together at 200–220° for 1 hr and furnished alkali-insoluble *di-p*-tolylurea, m.p. 263–265°, in about 10% crude yield, identified by comparison with an authentic sample. The same product resulted also from benzoylacet-*p*-toluidide and aniline and from benzoylacet-*p*-toluidide alone. Dry HCl was passed into the two anilide–amine mixtures indicated above at 180° for 1 hr; in each case 2-phenyl-4(1H)-quinolone (~5% yield) together with 2-phenyl-6-methyl-4(1H)-quinolone (~5% yield) was obtained. Benzoylacetanilide hydrochloride (1 g)[15] was kept at 180° for 1 hr and reacted to give ~5% 2-phenyl-4(1H)-quinolone.

B. *Anhydrous aluminum bromide*

Conversion of anilides to quinolones. Powdered $AlBr_3$ (2·7 g, 0·01 mole) and benzoylacetanilide (2·4 g, 0·01 mole) were well mixed together under anhydrous conditions and heated at 200–210° for 1 hr; reaction occurred with evolution of HBr and the sublimation of a yellow oil. 2-Phenyl-4(1H)-quinolone was isolated in the usual manner[3] in ~35% crude yield and little if any isomeric

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[14] A. K. Mallams and S. S. Israelstam, *J. Org. Chem.* **29**, 3548 (1964).

[15] L. Knorr, *Liebigs Ann.* **236**, 83 (1886).

2(1H)-quinolone was formed. Benzoylacet-*p*-toluidide (2·5 g, 0·01 mole) behaved likewise and gave 2-phenyl-6-methyl-4(1H)-quinolone in 40% yield.

With a 3-molar proportion of the reagent under similar conditions, the two anilides (2 g) were cyclized to 4-phenyl-2(1H)-quinolone (50%) and to 4-phenyl-6-methyl-2(1H)-quinolone (70%), respectively; a yellow liquid sublimate was absent and the corresponding isomeric 4(1H)-quinolones were not obtained.

A mixture of acetoacetanilide (1·8 g, 0·01 mole) and excess $AlBr_3$ (8·0 g, 0·03 mole) was heated at 130–135° for 1 hr and afforded 4-methyl-2(1H)-quinolone in over 50% yield. On similar reaction with an equimolar amount (2·7 g, 0·01 mole) of the reagent acetoacetanilide was converted into an acid-insoluble material which was shown by its IR spectrum to be neither 4-methyl-2(1H)-quinolone, 2-methyl-4(1H)-quinolone, nor unchanged anilide.

HBr was evolved also on warming acetanilide (1·3 g, 0·01 mole) with $AlBr_3$ (2·6 g, 0·01 mole) at 130° for 30 min; water was added to the reaction mixture to recover unchanged acetanilide in ~50% yield.

Addition compounds from anilides. A solution of benzoylacetanilide (2·4 g, 0·01 mole) in sodium-dried benzene (100 ml) was stirred at 20–30° and treated over ~15 min with a solution of $AlBr_3$ (~3 g, ~0·01 mole) in dry benzene (70 ml) under anhydrous conditions; a pale yellow addition compound was precipitated immediately. After stirring for an additional 30 min the insoluble product (3·3 g) was filtered off, washed with dry benzene, and dried in a 50° oven.

A convenient wt. (±200 mg) of the compound was dissolved in 70% aqueous MeOH (20 ml), the solution was neutralized with solid $NaHCO_3$, and the bromide determined by titration with 0·1 M $AgNO_3$ using fluorescein as indicator. (Found: Br, 30·4. Calc. for $(C_{15}H_{13}NO_2)_2.AlBr_3$: Br, 32·2%.)

The same 2:1 anilide:reagent complex resulted on employment of a 1·5 molar proportion of $AlBr_3$ in the reaction. The product gave no immediate color with alcoholic $FeCl_3$; a purple color developed gradually on allowing the solution to stand. On contact with water the addition compound was readily hydrolyzed to unchanged benzoylacetanilide. Several other anilides were similarly reacted with an equimolar amount of $AlBr_3$; in each case a 2:1 anilide:reagent complex was precipitated from solution and the relevant details are collected in Table 2. The substances had no definite m.ps. and decomposed when heated at elevated temps.

The complex (2 g) from benzoylacetanilide and $AlBr_3$ was heated at 200–220° for 1 hr; the substance gradually liquified and reacted with liberation of a yellow oil and HBr. The residue was warmed with 2N NaOH and the filtered alkaline extract was acidified with acetic acid to deposit 2-phenyl-4(1H)-quinolone (0·15 g, ~15% crude yield) together with some benzoylacetanilide.

C. *Anhydrous stannic chloride*

Conversion of anilides to 4(1H)-*quinolones.* Stannic chloride (1·5 ml, 3·3 g, 0·013 mole) was added to benzoylacetanilide (2·4 g, 0·01 mole) contained in a 50 ml round-bottom flask fitted with an air-condenser stoppered with cotton wool and the mixture was placed in an oil-bath at 150–160°; the temp was raised over ~10 min to 210–220° and the reaction allowed to proceed for 1 hr. Some $SnCl_4$ refluxed and HCl was evolved. The mixture became molten only when the temp greatly exceeded the m.p. of the anilide owing to the presence of an addition compound which was produced in a preliminary reaction between the anilide and reagent (see below). Work-up in the usual manner[3] furnished 2-phenyl-4(1H)-quinolone (30–35% crude yield), identified by its IR spectrum, and negligible unchanged benzoylacetanilide was recovered. Utilization of a 3-molar proportion of $SnCl_4$ in the reaction gave essentially the same yield of 2-phenyl-4(1H)-quinolone. Benzoylacet-*p*-toluidide (1·5 g, 0·006 mole) was similarly converted by $SnCl_4$ (1·2 ml, 2·68 g, 0·01 mole) to 2-phenyl-6-methyl-4(1H)-quinolone in ~58% crude yield.

Acetoacetanilide (2 g) was heated under reflux with excess of $SnCl_4$ (7 ml) for 45 min under anhydrous conditions. The mixture was cooled and the insoluble pale-yellow product (3·9 g) which had been present throughout the heating was filtered off, washed with benzene, and dried; it was identified by its IR spectrum as the 1:1 anilide: reagent complex (see below). Benzoylacetanilide and excess $SnCl_4$ at 130–135° likewise afforded the corresponding addition compound as the sole product of reaction.

Addition compounds from anilides. A solution of benzoylacetanilide (2·4 g, 0·01 mole) in sodium-dried benzene (70 ml) was treated with $SnCl_4$ (3·3 g, 0·013 mole) dissolved in benzene (20 ml) as for the preparation of the $AlBr_3$ complexes. The pale yellow insoluble adduct (4·0 g) separated immediately and was filtered off, washed with dry benzene, dried at 50° and analyzed volumetrically as above. (Found: Cl, 28·2. Calc. for $C_{16}H_{15}NO_2.SnCl_4$: Cl, 28·4%.)

Utilization of a 2-molar amount of $SnCl_4$ in the reaction afforded the same 1:1 anilide:reagent complex. A purple color developed almost immediately with alcoholic $FeCl_3$ and suggested a rapid hydrolysis of the complex to the anilide. The 1:1 addition compounds obtained by reaction of other anilides with an equimolar proportion of $SnCl_4$ are listed in Table 2. The substances had no definite m.ps and tended to decompose when heated above 150°.

Action of heat on complexes. The addition compound (3·6 g) from benzoylacet-*p*-toluidide and $SnCl_4$ was heated at 220–225° for 1½ hr; the solid gradually was converted to a dark-brown effervescent mass which liberated HCl and a yellow oil. Work-up[3] of the product afforded 2-phenyl-6-methyl-4(1H)-quinolone (1·03 g, 62% crude yield) identified by its IR spectrum. A similar treatment of the benzoylacetanilide-stannic chloride complex gave 2-phenyl-4(1H)-quinolone in ~30% yield; the quinolone was not obtained at 130° however, and benzoylacetanilide only was isolated.

D. *Boron trifluoride etherate*

Difluoro[[1-*phenyl*-2-(*phenylcarbamoyl*)*vinyl*]*oxy*]*borane* (IVa)—*Method A.* An excess of BF_3-etherate (supplied by British Drug Houses; 5 ml, ~0·04 mole) was added over ~10 min to a stirred suspension of benzoylacetanilide (2·4 g, 0·01 mole) in sodium-dried ether (50 ml) at room temp under anhydrous conditions. Stirring was continued for an additional 30 min and the reaction mixture was then poured into an excess of cold 1M $NaHCO_3$aq. The ether was evaporated at room temp after which the solid residue was filtrated off, washed with water, and recrystallized from dil EtOH to give colorless crystals, m.p. 214–215°. (Found: N, 4·85; mol. wt., 308. Calc. for $C_{15}H_{12}NO_2BF_2$: N, 4·88%; mol. wt., 287.)

The mol. wt. was determined by an isopiestic method[16] (acetone solvent) and showed the compound to be monomeric; evaporation of the acetone yielded unchanged IVa.* Compound IVa (0·5 g) readily dissolved in warm (ca. 40°) 2N NaOH (20 ml); the solution was cooled and kept at room temp for 10 min and was then neutralized with glacial acetic acid to deposit unchanged IVa (m.p. 209–213°) as evidenced by its IR spectrum.

Difluoroborane derivatives of other anilides were obtained in a similar manner and are listed in Table 2.

Method B. An excess of BF_3-etherate (10 ml, 0·08 mole) was added in one portion to a suspension of benzoylacetanilide (3·6 g, 0·015 mole) in sodium-dried benzene (40 ml); on swirling the mixture the anilide rapidly dissolved to give a yellow-brown solution and there was a negligible thermal effect. Crystals of the difluoroborane compound (IVa) soon commenced to separate and were filtered off after 30 min, washed with dry benzene, and dried at 50°. The IR spectrum of the product (3·2 g, 74%; m.p. 213–215°) was identical with that of the recrystallized material obtained in method A. *Difluoro*[[1-*phenyl*-2-(p-*tolycarbamoyl*)*vinyl*]*oxy*]*borane* (IVb), m.p. 233–235°, identified by its IR spectrum, likewise separated from solution in almost theoretical yield. In the case of N-ethylbenzoylacetanilide, material was not deposited, and after several hr the reaction solution was poured into excess ice-cold $NaHCO_3$aq; the organic layer was evaporated off and the insoluble difluoroborane derivative was collected (~90% yield), washed with water, and recrystallized from dil EtOH to give colorless tiny needles, m.p. 148–149°, identical with the product obtained in method A.

The above compounds gave no immediate color reaction with alcoholic $FeCl_3$; the respective solutions eventually attained a purple color as a result of the IV hydrolyzing.[7]

Reactions of the difluoroborane derivatives. Compound IVb (0·2 g) was warmed with conc. H_2SO_4 (1 ml) on the water bath for 1 hr and evolved acidic fumes;[7] addition of water to the solution precipitated 4-phenyl-6-methyl-2(1H)-quinolone in ~50% crude yield. The latter quinolone was produced also from IVb and 10 times its wt of PPA at 140° for 20 min.

A mixture of IVa (1·4 g, 0·005 mole) and *p*-toluidine (0·8 g, 0·007 mole) was stirred at 200° for 30 min; the acid- and alkali-insoluble product which was isolated proved to be di-*p*-tolylurea.

Compound IVa (1 g) was added to 20 g of liquid paraffin at 200° and the mixture was stirred at ±250° for 15 min; acidic fumes were evolved and the red insoluble oil present reacted with

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* Mass spectrometry unequivocally established the molecular weight to be 287.

[16] J. E. Morton, A. D. Campbell and T. S. Ma, *Analyst* 78, 722 (1953).

effervescence. The mixture was cooled, treated with ether, and the insoluble product (ca. 0·2 g) was removed, washed with ether and shown by its IR spectrum not to be 4-phenyl-2(1H)-quinolone.

Conversion of IVa (1 g) to alkali-insoluble 4-phenyl-2(1H)-quinolone (25% crude yield) was achieved by heating with a 3-molar proportion of $AlCl_3$ (1·4 g) at ±210° for 1 hr; treatment of the alkaline filtrate with glacial acetic acid deposited benzoylacetanilide (ca. 0·2 g).

Compound IVc (1 g) was kept at 160° for 1 hr. The reaction mixture was cooled and extracted with 2N NaOH; neutralization of the filtrate with acetic acid led to the recovery (~50%) of unchanged IVc identified by its IR spectrum.

Acetoacetanilide (2 g) was heated under reflux (ca. 120°) with excess BF_3-etherate (10 ml) for 1½ hr; the claret-colored solution was chilled and the material which had separated was filtered off, washed with dry ether and dried to yield 1·4 g colorless crystals, m.p. 230–260° and giving no color with alcoholic $FeCl_3$. The IR spectrum showed it to be neither IVc nor 4-methyl-2(1H)-quinolone. The product appeared to be anilinium tetrafluoroborate (lit.[17] m.p. 265°) since it dissolved readily in water and the solution on making alkaline liberated aniline (identified as its benzoyl derivative) and was not further studied. The reactants when refluxed for a shorter period (15 min) furnished the difluoroborane derivative IVc in 20–30% yield together with a small amount of the above aniline salt.

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[17] I. G. Ryss and S. L. Idel's, *Zh. Neorg. Khim.* **4**, 1990 (1959); *Chem. Abstr.* **54**, 11792 (1960).