Reactions of Anthranilamide and *o*-Aminoacetophenone with Benzil and Benzoin[1]

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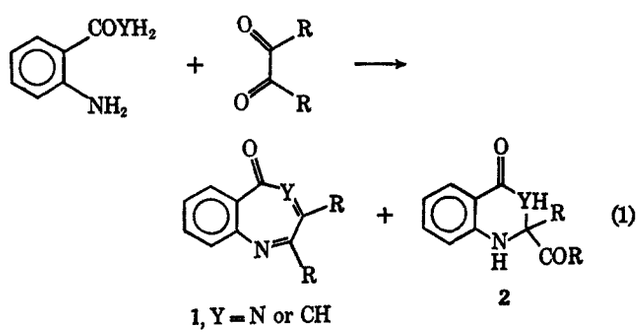
Received August 29, 1968

Attempts to obtain seven-membered cyclic products from the title reactions failed. Dihydroquinazolinone **5** was obtained from anthranilamide and benzil; **5** rearranged to α,α-diphenyl-2-quinazolinonemethanol (**8**) in acid or base. Cyclodehydration of **8** gave indoloquinazolinone **12**. The only product characterized from the reaction of *o*-aminoacetophenone and benzil in base was indogenide **17**. Ketone **18** from anthranilamide and benzoin underwent cleavage with base to *o*-benzylaminobenzamide and related products.

A long-standing point of interest in the chemistry of seven-membered heterocycles lies in completely unsaturated compounds analogous to tropone. Simple derivatives such as **1** are not known, however, despite a great deal of synthetic effort, particularly in the benzo-1,4-diazepine series,[2] and the potentially simple access provided by condensation of the type shown in eq 1. An obvious and common pitfall in this approach



1, Y = N or CH

to any highly unsaturated seven-membered heterocyclic system is the incursion of competing reactions leading to smaller rings, *e.g.*, **2**. On the other hand, a number of successful syntheses of fused seven-membered ring compounds have been realized in which alternative cyclizations of polyfunctional components could occur, notably in the formation of benzo-1,5-diazepines from *o*-phenylenediamines and 1,3-dicarbonyl derivatives.[2] We were therefore led to examine the possibility of obtaining compounds of type **1** in this way. The results are described in this paper.

The condensation of anthranilamide (**3**) and benzil (**4**) was first examined, using zinc chloride, an effective catalyst for the formation of anils of **3**[3] in refluxing acetic acid. In the absence of air, an insoluble zinc chloride complex rapidly precipitated; liberation of the base with ammonia gave a compound corresponding to a 1:1 adduct of **3** and **4** with loss of 1 mol of water. This compound was shown to be the 2,2-disubstituted dihydroquinazolinone **5** by mild permanganate oxidation in 90% yield to 2-phenylquinazolinone (**9**) and benzoic acid. On refluxing **3** and **4** in the presence of air with a catalytic amount of zinc chloride, **9** and another product (A), isomeric with **5**, were obtained in low yields. The latter compound was found to arise from **5** by further treatment in hot acetic acid–zinc chloride.

Compound A contained a hydroxyl group, as shown by infrared (ir) and formation of an acetate; a dehydration product was obtained under forcing conditions (polyphosphoric acid or *p*-toluenesulfonic acid). These findings suggested the possibility that A was the hydroxydiazepinone **7**, and the anhydro compound was the desired diazatroprone **1** (Y = N). Several other facts, however, including the complete inertness of A to base or catalytic hydrogenolysis,[4] and the formation of a brilliant red lake in concentrated sulfuric acid from A but *not* from its dehydration product, contraindicated this structure.

The red sulfuric acid color and the finding that A was also formed very readily from **5** with alcoholic sodium ethoxide led to the conclusion that A was the product of a rearrangement of **5** and is in fact α,α-diphenylquinazolinonemethanol (**8**). This structure was confirmed by reduction of the compound with hydriodic acid, under conditions appropriate for triarylcarbinols,[5] to 2-benzhydrylquinazolinone (**11**) (Scheme I), identical with a sample prepared from anthranilamide and diphenylacetaldehyde by standard procedures.[6]

The conversion of **5** into the tertiary alcohol **8** bears a a resemblance to the benzilic acid rearrangement. The mechanistic details must differ from those involved in the rearrangement of benzils, since the base-catalyzed rearrangement leading to **8** requires strictly anhydrous conditions. In aqueous ethanolic hydroxide, the dihydroquinazolinone **5** was cleaved in high yield to 2-phenyldihydroquinazolinone (**6**) and benzoic acid.

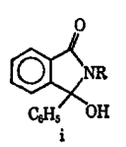
Two reactions of the quinazolinonemethanol **8** deserve mention and lend support to the structure. Thermal cleavage of **8** (and also **5**) occurred when the compound was held above the melting point, and 4-quinazolinone (**10**) and benzophenone were isolated in nearly quantitative yields. The dehydration of **8**,

(1) Supported by Grant GP-5219 from the National Science Foundation.

(2) For a recent review, see J. A. Moore and E. Mitchell, "Heterocyclic Compounds," Vol. 9, R. C. Elderfield, Ed., John Wiley & Sons, Inc., New York, N. Y., 1967, p 332.

(3) J. A. Moore and L. D. Kornreich, *Tetrahedron Lett.*, 1277 (1963).

(4) Hydrogenolysis of compound i, which contains the same functional system, occurs very readily [W. Metlesics, T. Anton and L. H. Sternbach, *J. Org. Chem.*, **32**, 2185 (1967)].

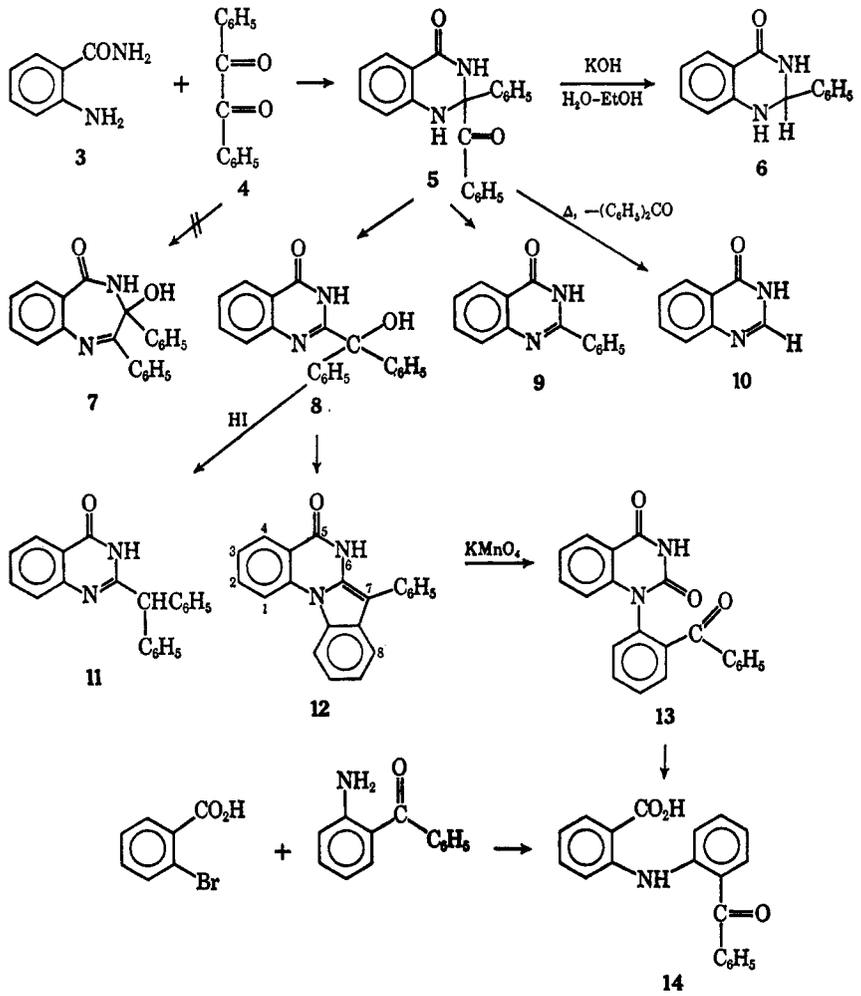


i

(5) L. F. Fieser, "Organic Experiments," D. C. Heath and Co., Boston Mass., 1964, p 93.

(6) T. A. K. Smith and H. Stephen, *Tetrahedron*, **1**, 38 (1957).

SCHEME I



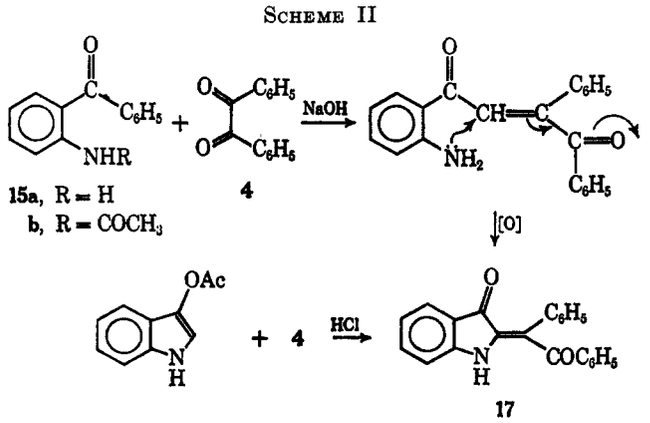
mentioned above, led to a yellow, weakly acidic anhydro compound; a more convenient preparation was effected by fusion of the dihydroquinazolinone **5** with zinc chloride. The anhydro compound was readily methylated in alkaline solution. A plausible structure for this product was the indoloquinazolinone **12** or the linearly fused isomer, which would arise by cyclization analogous to the well-known cyclialkylation of triarylcarbinols to 9-arylfluorenes.[7,8]

The anhydro compound was rapidly oxidized by cold alkaline permanganate, in keeping with the 2-aminoindole grouping, and the acidic product isolated was formulated as the 1-arylquinazolinedione **13**. Hydrolysis of **13** gave ammonia and the yellow acid **14** which was identical with a sample prepared by Ullmann coupling of *o*-bromobenzoic acid and *o*-aminobenzophenone. This degradation defines structure **14** as opposed to the linear isomer, which would have given aminobenzophenone and anthranilic acid as fragments.

Rather thorough study of the anthranilamide–benzil reaction leads us to conclude that no significant amounts of benzodiazepine derivatives are available by this approach. The reaction of anthranilamide and phenylglyoxal was explored briefly with wholly unpromising results; no products were isolated.

Another attempt to effect condensation according to eq 1 was made with *o*-aminoacetophenone (**15a**). The reaction of equimolar quantities of **15a** or the acetamide **15b** and benzil in the presence of zinc chloride gave significant amounts of unreacted benzil and presumably self-condensation products of the amino ketone.[9] Condensation in ethanolic base led to very complex mixtures, but a brilliant red 1:1 product was consistently obtained in low yield. The composition of this product, $C_{22}H_{15}NO_2$, corresponded to the elimination of water and hydrogen, ruling out quinoline structures, and suggested the indogenide structure **17** (Scheme II),

SCHEME II



(7) F. Bergmann and S. Israelashwili, *J. Amer. Chem. Soc.*, **68**, 1, 354 (1946).

(8) L. R. C. Barclay in "Friedel-Crafts and Related Reactions," Vol. II, part 2, G. Olab, Ed., Interscience Publishers, New York, N. Y., 1964, p 844.

(9) A. Besthorn and E. Fisher, *Ber.*, **16**, 68 (1883); G. Kempter, P. Andratschke, D. Heilmann, H. Krausmann, and M. Mietasch, *Chem. Ber.*, **97**, 16 (1964).

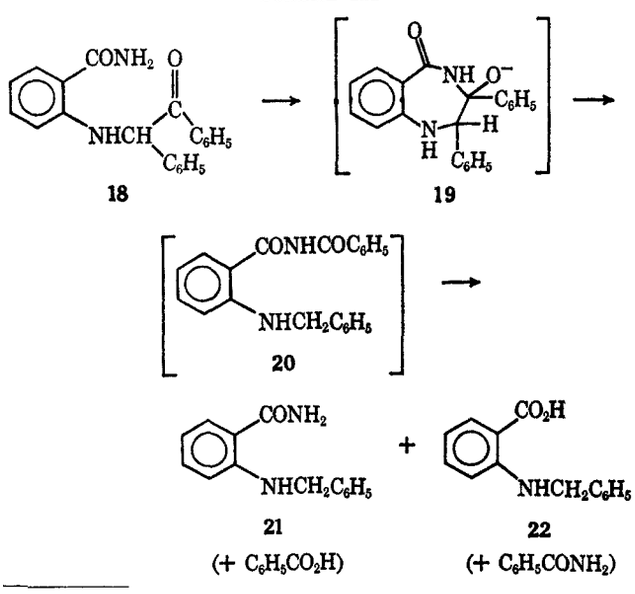
which was confirmed by synthesis of the compound from indoxyl acetate and benzil by the procedure of Abramovitch and Marko.[10]

Formation of the indogenide must occur by initial condensation of **15** and **4** to give the α-benzoylchalcone **16**, 1,4 addition, and final oxidation. Another product obtained in very small amounts corresponded in composition to a dihydro derivative of the azepinone **1** (Y = CH), but characterization data were not sufficent to permit structural conclusions. The oxidation levels of products in these reactions are of little significance because of the low yields and potential oxidizing and/or reducing properties of the starting materials; ethyl benzoate was detected in several reactions regardless of precautions to exclude air.

Thwarted in efforts to obtain seven-numbered products from the reactions with benzil, ketone **18** derived from anthranilamide and benzoin appeared to offer a somewhat better possibility for cyclization to a dihydrobenzodiazepinone. Acid-catalyzed ring closure of the analogous *o*-phenacyloxybenzamide to 3-phenyl-5-oxo-4,5-dihydro-1,4-benzoxazepine has been reported by Schenker.[11] The precursor **18** was readily obtained by the procedure described for desylaniline.[12] Treatment of **18** with zinc chloride–acetic acid gave mixtures containing six to ten components; separation was not attempted. The complexity of the reaction probably reflects in part the occurrence of Bischler-type condensations leading to indoles.

With potassium *t*-butoxide, **18** again gave a complex mixture, but separation appeared feasible, and seven compounds were isolated and characterized. The main products were benzoic acid (60%) and *o*-benzylaminobenzamide (**21**, 48%). Much smaller amounts of the congruent pair, benzamide (5%) and N-benzylanthranilic acid (**22**, 8%) were also obtained. Formation of the latter products requires bonding of the amide nitrogen in **18** to the terminal benzoyl group prior to cleavage of the C–C bond; cyclization as shown in Scheme III, leading *via* a seven-membered carbinolamine to the imide **20** and subsequent hydrolysis, could account for the formation of **22** and benzamide. The quinazolinones **6** and **9** were isolated in very small amounts and probably arose by enolization of the amino ketone **18** prior to cyclization. A final product (10%) isolated after tedious chromatography corresponded in composition to a dehydration product of **18**.

SCHEME III



In summary, we must conclude that condensations of the type explored offer little promise for the preparation of benzazepine or -diazepine derivatives.

Experimental Section

2-Benzoyl-2-phenyl-2,3-dihydro-4(1H)-quinazolinone (5).—A suspension of 10.2 g (0.075 mol) of anthranilamide and 15.8 g (0.075 mol) of benzil in 100 ml of glacial acetic acid containing 3 g of zinc chloride was deaerated by a stream of nitrogen and then refluxed for 3 hr with stirring under a nitrogen stream. An additional 3 g of zinc chloride was then added. After cooling (2 hr), the solid was collected, washed with acetic acid, and air dried, giving 22.7 g (76%) of cream-colored powder, mp 198–202° dec. This material had the approximate composition of a 2:1 quinazolinone–zinc chloride complex; the composition appeared to change on attempted recrystallization and the compound was analyzed and used without purification.

Anal. Calcd for $(C_{21}H_{16}N_2O_2)_2 \cdot ZnCl_2$: C, 63.6; H, 4.1; Cl, 8.9. Found: C, 61.5; H, 4.1; Cl, 8.9.

The free dihydroquinazolinone **5** was prepared by shaking a mixture of 10 g of the above complex with aqueous methanolic ammonia and 100 ml of CH_2Cl_2. The aqueous layer was further extracted with CH_2Cl_2 and the combined organic phase was washed, dried, and evaporated to a glass which was crystallized from ethanol–hexane to give 6.3 g (76%) of **5**, mp 153–154°. Further recrystallization gave pale yellow prisms: mp 158–159°; ν^{Nujol} 3380, 3350, 1660, 1600 cm^{-1}.

Anal. Calcd for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91; N, 8.53. Found: C, 76.52, 76.77; H, 4.74, 5.02; N, 8.30.

Oxidation of **5** (0.50 g) in 20 ml of acetone with 0.40 g of $KMnO_4$ gave, after a standard isolation procedure, 0.27 g of 2-phenylquinazolinone **5**, mp 240–242°.

α,α-Diphenyl-2-[4(3H)-quinazolinone]methanol (8) and 2-Phenyl-4(3H)-quinazolinone (9).—A solution of 3 g of the dihydroquinazolinone **5** and 0.1 g of zinc chloride in 125 ml of acetic acid was refluxed for 12 hr in the presence of air. After the solution was concentrated, 2 g of zinc chloride dissolved in acetic acid was added, and 1.60 g of the complex of unreacted **5** was collected. The filtrate was evaporated and the residue in CH_2Cl_2 was washed with aqueous ammonia and water, dried, and evaporated. Crystallization of the residue gave initially 0.30 g of the quinazolone **9**, mp 239–240°, and then 0.47 g of **8**, mp 190–192°. Further crops gave alternately **9** and **8**. A total of 0.37 g of **9** (32% based on starting **5** not recovered) and 0.61 g of **8** (36%) was obtained. From the aqueous extract, 0.072 g (11%) of benzoic acid was isolated.

Recrystallization of **9** from methanol gave filaments, mp 243–244° (lit.[6] mp 238°), identical (ir) with a sample prepared from anthranilamide and benzaldehyde, followed by oxidation.

The quinazolinonemethanol **8** was recrystallized from methanol to give stout white prisms: mp 192–193°; ν^{KBr} 3390, 1670, 1610 cm^{-1}.

Anal. Calcd for $C_{21}H_{16}O_2N_2$: C, 76.81; H, 4.91; N, 8.53. Found: C, 76.92; H, 5.00; N, 8.50.

After a solution of **5** (3 g) and zinc chloride (0.1 g) in 125 ml of glacial acetic was refluxed under nitrogen for 10 hr, 2.41 g of the zinc chloride complex of **5** was recovered (67% of starting **5**). After treatment as described above, 0.61 g (20% yield, 61% based on **5** consumed) of **8**, mp 192–193°, was isolated.

Under the same conditions but with 0.5 g of zinc chloride, 52% of **5** was recovered as the complex and 0.60 g of **8** (42% based on **5** consumed) was obtained. In addition, 46 mg (3%) of quinazolone **9** was isolated.

The **acetate** of quinazolinonemethanol **8** was prepared by refluxing a solution of 500 mg of **8** in 10 ml of acetic anhydride for 2.7 hr. The green solution was cooled, water and bicarbonate were added, and the oil was extracted. The residue from the dried methylene chloride solution was crystallized to give 425 mg

(10) R. A. Abramovitch and A. M. Marko, *Can. J. Chem.*, **38**, 131 (1960).
(11) K. Schenker, *Chimia* (Aarau), **20**, 157 (1966); *Helv. Chim. Acta*, **51**, 413 (1968).
(12) P. L. Julian, E. W. Meyer, A. Magnani, and W. Cole, *J. Amer. Chem. Soc.*, **67**, 1203 (1945).

of pale green solid, mp 213–227°. Recrystallization from chloroform–ethanol gave colorless crystals: mp 219–222°; ν^{KBr} 1760 cm^{-1}.

Anal. Calcd for $C_{23}H_{18}N_2O_3$: C, 74.58; H, 4.90; N, 7.56. Found: C, 74.31; H, 5.14; N, 7.48.

No spot corresponding to the anhydro compound **12** was present in the thin layer chromatogram of the above reaction mixture.

2-Diphenylmethyl-4(3H)-quinazolinone (11) from 8.—A solution of 200 mg of the quinazolinemethanol **8** in 3 ml of 57% hydriodic acid was heated for 90 min on the steam bath; crystals separated from the deep brown solution. After cooling, the solution was treated with excess bisulfite and then made alkaline. The solid which separated (100 mg) was recrystallized from methanol to give colorless prisms of **11**, mp 232–235°, identical (ir) with the sample described below.

Diphenylacetaldehyde N-(*o*-Carboxamidophenyl)imine (N_2-Diphenylethylideneanthranilamide).—A solution of 2.1 g of anthranilamide and 3.0 g of diphenylacetaldehyde in 70 ml of ethanol was heated for 10 min. The solid which separated from the hot solution was collected and washed with ethanol, giving 4.6 g of yellow solid. Recrystallization from a large volume of ethanol gave the anil as long yellow spears, mp 205–209°.

Anal. Calcd for $C_{21}H_{18}N_2O$: C, 80.23; H, 5.77. Found: C, 80.46; H, 5.83.

2-Diphenylmethyl-2,3-dihydro-4(1H)-quinazolinone.—A solution of 5 g of the above anil and 12 ml of 2 *N* NaOH in 300 ml of ethanol was refluxed for 1 hr under a nitrogen stream, neutralized with acid, and concentrated *in vacuo*. The resulting solid was dissolved in methylene chloride and, after the solution was washed with water and dried, it was evaporated to give 4.35 g of white solid. Recrystallization from methanol gave white prisms of the dihydroquinazolinone, mp 173–175°.

Anal. Calcd for $C_{21}H_{18}N_2O$: C, 80.23; H, 5.77. Found: C, 80.02; H, 5.89.

When this cyclization was carried out in the presence of air, the results were erratic, and the quinazolinone **11** was isolated in one run.

2-Diphenylmethyl-4(3H)-quinazolinone (11).—A solution of 0.37 g of the foregoing dihydroquinazolinone in 30 ml of acetone was treated dropwise at 25° with a solution of 0.23 g of $KMnO_4$ in acetone. After addition of bisulfite and removal of MnO_2, the product was isolated by standard operations as colorless prisms: mp 233–235°; ν^{KBr} 1660, 1610 cm^{-1}.

Anal. Calcd for $C_{21}H_{16}N_2O$: C, 80.75; H, 5.16. Found: C, 80.73; H, 5.10.

Quinazolinone 8 from 5 with Sodium Ethoxide.—To a solution of 2.0 g of the dihydroquinazolinone **5** in boiling absolute ethanol, under a nitrogen stream, was added a solution prepared from 0.5 g of sodium in 25 ml of ethanol. After refluxing for 3 hr the solution was cooled, neutralized with acetic acid, and evaporated. After extraction with methylene chloride, etc., the product was crystallized from methanol to give 950 mg (48%) of the quinazolinonemethanol **8**, mp 192–193°. Further crops of **8** were contaminated with phenylquinazolinone **9**.

In a similar procedure using potassium *t*-butoxide in *t*-butyl alcohol, 581 mg of **8**, mp 193–194° after recrystallization, was obtained from 1.0 g of **5**.

Reaction of 5 with Aqueous Base.—A solution of 0.25 g of NaOH and 0.50 g of **5** in 30 ml of ethanol was stirred at 25°. A solid separated after 10 min; after 1 hr, tlc showed the absence of **5**. After evaporation, extraction, etc., the neutral product was crystallized from methanol, giving 301 mg (88%) of **2-phenyl-2,3-dihydro-4(1H)-quinazolinone (6)**, mp 228–231°, identical (ir) with a sample prepared from anthranilamide and benzaldehyde. Acidification of the bicarbonate layer from the extraction gave 185 mg (98%) of benzoic acid.

Pyrolysis of 5.—One gram of quinazolinonemethanol **5** was melted in a test tube and kept in an oil bath at 260–280° for 10 min. After cooling, the resulting glass was crystallized from ether–hexane to give 217 mg (98%) of 4(3H)-quinazolinone (**10**): mp 218–219° (lit.[13] mp 220°); ir in agreement with literature values.

Anal. Calcd for $C_8H_6N_2O$: C, 66.75; H, 4.14; N, 19.17. Found: C, 66.28; H, 4.00; N, 19.48.

(13) H. Culbertson, J. C. Decius, and B. E. Christensen, *J. Amer. Chem. Soc.*, **74**, 4834 (1952).

Evaporation of the hexane mother liquor from **10** gave 267 mg (96%) of benzophenone, mp 45–47°.

7-Phenylindolo[1,2-*a*]-6H-5-quinazolinone (12).—An intimate mixture of 10 g of the zinc chloride complex of dihydroquinazolinone **5** and 5 g of powdered anhydrous zinc chloride was heated in an oil bath at 210° for 10–15 min (until foaming ceased). The cooled orange melt was removed from the flask by rubbing with a mixture of 60 ml of ammonia and sufficient methylene chloride (about 600 ml) to dissolve all of the solid. After the solution was washed with acid, $NaHCO_3$, and water, the methylene chloride was evaporated to give, in two crops, 2.01 g of a yellow solid (**12**), mp 237–242°. The third crop of solid, 3.48 g, was a mixture by tlc. Chromatography in chloroform on 90 g of silica acid gave in early fractions an additional 0.46 g of **12**: total yield 37%. Recrystallization of **12** from chloroform–ethanol gave yellow needles: mp 250–251°; λ_{max}^{EtOH} 378 mμ (ϵ 1000).

Anal.[14] Calcd for $C_{21}H_{14}N_2O$: C, 81.27; H, 4.55; N, 9.03; mol wt, 310.1106. Found: C, 81.11; H, 4.54; N, 9.17; *m/e* 310.1122.[15]

Later chromatographic fractions gave 0.33 g of a colorless isomeric compound, mp 241–244°, which was not further examined, and 0.43 g of phenylquinazolinone **9**.

The indoloquinazolinone **12** was obtained from quinazolinonemethanol **8** by heating a solution of 1 g of **8** in polyphosphoric acid at 90° for 2 hr. After the usual isolation, 0.54 g of a mixture of yellow needles and white prisms was obtained; mechanical separation gave 0.18 g of **12**, mp 251–252°, and 0.06 g of another colorless isomeric compound, mp 271–273°, which was not further examined.

After a solution of **8** (0.5 g) and *p*-toluenesulfonic acid (0.05 g) in toluene was refluxed for 48 hr, **12** was isolated in 30% yield.

6-Methyl-7-phenylindolo[1,2-*a*]-6H-5-quinazolinone.—Compound **12** (0.5 g) was dissolved by warming in a mixture of 25 ml of methanol and 15 ml of 1 *N* NaOH, and the orange solution was treated with 1 ml of dimethyl sulfate. Some yellow solid separated, this was redissolved by addition of methanol and 2 ml of NaOH, and a further portion of dimethyl sulfate was added. After repeating this procedure twice, the solid was collected: 0.45 g; mp 218–219°. Several recrystallizations from chloroform–methanol gave yellow needles, mp 223–224°.

Anal. Calcd for $C_{22}H_{16}N_2O$: C, 81.46; H, 4.97; N, 8.64. Found: C, 81.46; H, 5.15; N, 8.49.

1-(2-Benzoylphenyl)-1H,3H-2,4-quinazolinedione (13).—To a vigorously stirred suspension of 4.00 g of **12** in 300 ml of 2 *N* NaOH at room temperature was added, in portions, 12.2 g of solid potassium permanganate. The yellow solid dissolved in about 1 hr, and after 20 hr the green solution was treated with bisulfite and filtered to remove MnO_2. Acidification of the yellow filtrate with HCl gave a copious precipitate which was collected and dried to give 3.3 g of pale yellow powder. Repeated recrystallizations from ethyl acetate gave slightly tan crystals of **13**: mp 239–242°; ν^{KBr} 1700, 1670, 1610, 1460 cm^{-1}.

Anal. Calcd for $C_{21}H_{14}N_2O_3$: C, 73.67; H, 4.12; N, 8.18. Found: C, 73.26; H, 3.88; N, 8.04.

A solution of 100 mg of **13** in 20 ml of methanol was treated with excess ethereal diazomethane. After 5 min the solution was evaporated to give a white solid which was recrystallized from ethanol–water to give crystals of the N-methylquinazolinedione, mp 175°.

Anal. Calcd for $C_{22}H_{16}N_2O_3$: C, 74.14; H, 4.53. Found: C, 74.80; H, 4.66.

N-(2-Benzoylphenyl)anthranilic Acid (14).—A solution of 0.5 g of **13** in 150 ml of 2 *N* NaOH was refluxed for 24 hr. The solution became yellow, a basic vapor was evolved, and a yellow precipitate separated. After 24 hr, water was added to dissolve the precipitated salt, the solution was acidified, and the resulting yellow solid was collected and combined with the ether extract of the filtrate. A significant amount of brown ether-insoluble material was removed, the ether solution was treated with charcoal, and the resulting yellow solution was evaporated to give

(14) Considerable difficulty was encountered in obtaining satisfactory analytical data on this and other compounds in this series. Other samples of **12** of ostensibly equivalent purity gave carbon values 1–2% low in different laboratories.

(15) We are indebted to Dr. R. J. Highet, National Heart Institute, for the mass spectral determination.

50 mg of crystals, mp 176–178°. Recrystallization from ether–heptane gave yellow prisms, mp 180–181°, identical (ir) with the Ullmann product described below.

Ullmann Synthesis of 14.—A mixture of 5.45 g of *o*-bromobenzoic acid, 10 g of *o*-aminobenzophenone,[16] 4.1 g of potassium carbonate, 0.10 g of cupric oxide, and 10 ml of nitrobenzene was refluxed with stirring for 2 hr. The resulting brown mixture was steam distilled until solid appeared in the condenser and the aqueous distillation residue was diluted to 1 l. with water and filtered. Acidification of the red filtrate gave a greenish yellow precipitate which was collected and dried, giving 5.2 g of solid. The solid was extracted with ether and the ether solution, after treatment with charcoal, was evaporated to give 1.43 g of yellow crystals: mp 178–180°; ν^{KBr} 1660, 1640, 1570, 1500 cm^{-1}.

Anal. Calcd for $C_{20}H_{15}NO_3$: C, 75.69; H, 4.76; N, 4.41. Found: C, 75.72; H, 4.79; N, 4.21.

In an attempt to resynthesize the quinazolinedione **13,** a mixture of 0.55 g of the acid **14** and 0.1 g of urea was heated to 200°. After cooling, the melt was crystallized from chloroform to give yellowish needles, mp 215–220°. This product was distinctly different from **13** by ir and was not further investigated; tlc of the melt showed no indication of **13.**

Condensation of *o*-Aminoacetophenone and Benzil.—A mixture of 3.0 g of *o*-aminoacetophenone and 4.7 of finely divided benzil in 10 ml of ethanol was treated with 1.1 g of KOH in 10 ml of ethanol and heated for 8 hr. The cooled reaction mixture was dissolved in ether and water, and the washed and dried layer was evaporated to a very dark red oil. Chromatography on silicic acid from chloroform solution gave initial fractions containing unreacted benzil (0.3 g) and ethyl benzoate. From some of the next group of fractions, a solid was obtained by trituration with ether. Recrystallization from ethanol gave pale yellow prisms: mp 246–247°; ν^{KBr} 3300, 1640 cm^{-1}. The structure of this compound is not known.

Anal. Calcd for $C_{22}H_{17}NO$: C, 84.86; H, 5.50; N, 4.50. Found: C, 84.69; H, 5.43; N, 4.53.

The final crystalline fractions were brilliant red. Crystallization from ether gave 910 mg (13%) of beautiful red prisms of **2-(α-phenylphenacylidene)-3-indolinone (17):** mp 172–173°; λ_{max}^{EtOH} 482 mμ (ε 6600); ν^{KBr} 3200, 1660, 1580 cm^{-1}.

Anal. Calcd for $C_{22}H_{15}NO_2$: C, 81.21; H, 4.65; N, 4.31. Found: C, 80.99; H, 4.55; N, 4.42.

To obtain a comparison sample of the indogenide **17,** a deoxygenated solution of 250 mg of indoxyl acetate[17] and 300 mg of benzil in aqueous ethanol was treated with 1 ml of deaerated 8 *N* NaOH. After stirring and refluxing for 2 hr under a nitrogen atmosphere, the reaction mixture was diluted with water and the precipitated indigo (105 mg, 56%) was collected. The filtrate was extracted with methylene chloride and, after washing, drying, and evaporation, crystallization of the residue from ether gave 140 mg of **17** as red needles, mp 172–173°.

***o*-[(α-Phenylphenacyl)amino]benzamide (18).**—A mixture of 6.27 g (0.0296 mol) of benzoin and 4.00 g (0.029 mol) of anthranilamide was moistened with 2 drops of concentrated HCl and heated in a 150° bath for 45 min. The amber melt was poured into ethanol and the solution was crystallized after charcoal treatment, giving 4.16 g (43%) of **18,** mp 185–188°. Several recrystallizations from ethanol gave cream-colored prisms: mp 192–193°; λ_{max}^{EtOH} 255 mμ (ε 21,600), 344 (5800); ν^{KBr} 1680–1560 cm^{-1} (broad band with five peaks, most intense at 1640 cm^{-1}).

Anal. Calcd for $C_{21}H_{18}N_2O_2$: C, 76.36; H, 5.49; N, 8.48. Found: C, 76.40; H, 5.52; N, 8.57.

Acid-Catalyzed Reaction of 18.—A solution of 1 g of **18** in 40 ml of glacial acetic acid containing 0.2 g of zinc chloride was refluxed under nitrogen for 13 hr. After evaporation, the product was isolated in the usual way to give an orange oil. Tlc showed ten components of which six were very minor; one of these appeared to be unreacted **18.**

After similar treatment for 90 min, the product mixture contained three minor and three major components; 25% of the starting material, mp 188–190°, was recovered.

Reaction of 18 with Potassium *t*-Butoxide in *t*-Butyl Alcohol.—*t*-Butyl alcohol (14 ml) containing 13.2 mequiv of potassium *t*-butoxide (prepared from metal and dry alcohol) was added to a refluxing solution of 4.24 g of **18** (12.8 mmol) in 100 ml of dry *t*-butyl alcohol. Both solutions were previously flushed with nitrogen and the mixture was then refluxed for 68 hr under nitrogen. An initial orange color faded gradually during this period and a white precipitate separated.[18] Water was added, causing the solid to dissolve, and the alcohol was evaporated. The residue was brought to neutral pH and extracted with methylene chloride. After extraction with $NaHCO_3$, the methylene chloride layer was evaporated to a dark green solid. Acidification of the bicarbonate solution and extraction gave 723 m of benzoic acid, mp 117–119°.

Crystallization of the methylene chloride residue gave 1.04 g of a yellow solid, mp 170–173°. Recrystallization from methanol gave 0.82 g of a solid, mp 174–176°, and 0.13 g, mp 168–171°, or a total of 0.95 g of ***o*-(benzylamino)benzamide (21,** 33%). The mother liquor contained approximately equal amounts of **21** and the acid **22.** Further recrystallization of **21** gave coarse needles: mp 176–177° (lit.[19] mp 171–172°); ν^{KBr} 3300, 1620, 1570.

Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found: C, 74.44; H, 6.50; N, 12.41.

Hydrolysis of the amide by refluxing in 10% aqueous–methanolic NaOH for 11 hr gave a basic gas; the acidic fraction was identified as N-benzylamino acid **22,** mp 177–178°, identical (ir) with authentic material described below.

The filtrate from the 1.04 g of crude **21** was chromatographed from $CHCl_3$ solution on 200 g of silicic acid; fractions were eluted on the basis of band colors. Fractions 1–5 contained 114 mg of gum which was not examined further.

The sixth fraction consisted of 526 mg of off-white solid. Crystallization from ethyl acetate–hexane furnished 202 mg of crystals, mp 176–177°; a further 44 mg of the same substance, mp 175–177°, was isolated from the mother liquor after $NaHCO_3$ extraction. This compound was recrystallized from methanol and ether acetate–hexane to give needles, mp 177–178°.

Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.14; H, 5.84; N, 6.21.

The compound was identified as N-benzylanthranilic acid (**22**) by comparison with an authentic sample (mp 175–177°) prepared by benzylation of anthranilic acid by the procedure of Heuben and Brassert;[20] 28 peaks in the ir spectrum of each sample coincided in position and relative intensity.

From the mother liquor of **22,** 185 mg of benzoic acid was isolated by bicarbonate extraction.

Fraction 7 (723 mg) crystallized from ethanol to give 440 mg of ***o*-(benzylamino)anthranilamide (21),** mp 174–176°; the third crop gave a further 102 mg of **21.** The second crop from the crystallization, 56 mg, was 2-phenyl-3(H)-4-quinazolinone (**9**), also encountered in fraction 8.

Fraction 8 (182 mg) was recrystallized from ethanol to give 2-phenyl-4-quinazolinone (**9**), mp 244–245°, identical by ir comparison with authentic **9.**

Fraction 9 (60 mg of pale green solid) was recrystallized from ethanol to give 14 mg of 2-phenyl-1,2-dihydroquinazolinone (**6**), mp 229–230°, identical (ir) with authentic **6.**

Fractions 10–12, eluted with chloroform–1–3% methanol (total 790 mg of amber glass) were crystallized from methanol to give a total of 490 mg of colorless solid: mp 191–194°; λ_{max}^{EtOH} 307 mμ (ε 2000), 317 (1850); ν^{KBr} 1650, 1600; ν^{CDCl_3} 5.43 μ (s, 2), 7.2–7.8 (m, 16). The structure of this compound is not known.

Anal. Calcd for $C_{21}H_{16}N_2O$: C, 80.75; H, 5.06; N, 8.97. Found: C, 80.75; H, 5.50; N, 8.98.

Fraction 13, eluted with 3–10% methanol, consisted of 185 mg of gummy yellow solid. Tlc suggested the presence of benzamide, and the gum was therefore extracted with hot water. Extraction of this aqueous phase with ether then gave 69 mg of colorless solid, mp 117–121°. The ir spectrum was identical with that of authentic benzamide in the position and intensities of 20 peaks, with one small extraneous peak. Recrystallization gave 40 mg of benzamide, mp 127–128°.

Registry No.—**3,** 88-68-6; **4,** 134-81-6; **5,** 18963-

(16) We thank Dr. Ian Fryer, Hoffmann-La Roche, Inc., for a generous sample of this compound.

(17) Prepared by Mr. Clifford Stirba, whose help is greatly appreciated, by method of R. D. Arnold, W. M. Nutter, and W. L. Stepp, *J. Org. Chem.*, **24,** 117 (1959).

(18) In a separate reaction, this material was found to be potassium benzoate; we thank Dr. Aiko Nabeya for this result.

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80-9; **5** (zinc chloride complex), 12321-53-8; **6**, 954-91-6; **8**, 18963-82-1; **8** (acetate), 18963-83-2; **11**, 18963-84-3; **12**, 18963-85-4; **13**, 18963-86-5; **13** (N-methyl derivative), 18975-91-2; **14**, 18964-23-3; **15a**, 551-93-9; **17**, 18963-87-6; **18**, 18963-88-7; **21**, 5363-37-1; **22**, 6622-55-5; benzoin, 119-53-9; N_2-diphenylethylideneanthranilamide, 18964-20-0; 2-diphenylmethyl-2,3-dihydro-4(1H)-quinazolinone, 18964-21-1; 6-methyl-7-phenylindolo[1,2-*a*]-6H-5-quinazolinone, 18964-22-2.

The Application of Polarography to the Kinetics of Aromatic Cyclodehydration

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Received August 26, 1968

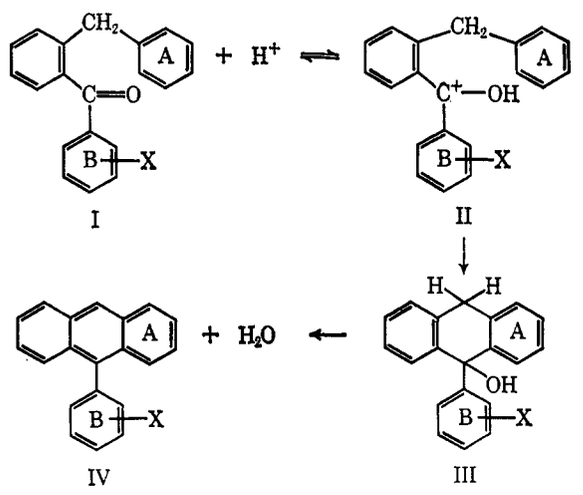
The kinetics of cyclization of *o*-benzylbenzophenones to 9-phenylanthracenes were studied with reference to variations with temperature. The rate of disappearance of the ketones was followed polarographically in strongly basic aqueous alcohol solutions using KCl as supporting electrolyte. Advantages of this method of analysis are indicated and the results further confirm the previously postulated mechanism.

One of the important methods for the preparation of polynuclear aromatic hydrocarbons is the acid-catalyzed cyclodehydration of certain aromatic aldehydes and ketones.[2] Recent applications of the method include the preparation of 7-phenyldibenz[*a*,*h*]anthracene,[3] 7- and 12-thienylbenz[*a*]anthracenes,[4] and 9-(2-benzo[*b*]thienyl)anthracene.[5]

Although other strongly acid media have been used, the most common is a mixture of hydrobromic and acetic acids. Previous kinetic studies, which have all been limited to the simple 9-phenylanthracene series, have led to the proposed mechanism[6-9] outlined in Scheme I which involves a preliminary equilibrium between I and II, the rate-controlling step in which the carbonium ion (II) attacks ring A, followed by a rapid loss of a molecule of water. The reaction is observed to be first order at a given acidity and solvent composition and acid catalyzed and the rate is reported to increase faster than the stoichiometric concentration of the acid catalyst.[10] The rate is very sensitive to the water content of the solution being greatly retarded thereby.[10]

In previous studies, different investigators used different temperature and different HBr–HOAc–H_2O compositions. It seemed desirable to study the temperature dependence of the rates so that this, along with the known changes with changes in solvent composition,[10] would allow comparison of all the data currently available. The kinetic data reported at 150°,[9] while sufficiently accurate to make the conclusions drawn still valid, was obtained without the benefit of a constant-temperature bath and needed to be restudied.

SCHEME I



With these things in mind it was decided to study the kinetics of cyclodehydration of six ketones (I, X = H, 4-Cl, 3-CF_3, 2-F, 2-Cl, and 2-Br) at the two temperatures where most of the previous work was done (100 and 117.5°) and at a higher temperature, 127.5°, so that values for the very slow 2′-chloro- and 2′-bromo-2-benzylbenzophenones could be obtained, all in the same solvent.

Results

Our first attempts, using the method of Brice and Katstra[10] in which the production of 9-phenylanthracene

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