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An efficient, base-induced rearrangement of 2-[(1,2-dioxo-2-(methylamino)ethyl)phenylamino]benzoic acid methyl ester (7a) to the isomeric 2-[(1,2-dioxo-2-(phenylamino)ethyl)methylamino]benzoic acid methyl ester (27a) is described. This novel rearrangement must proceed through a spiro intermediate wherein benzoate is acting as a Michael receptor. When 2-[(1,2-dioxo-2-(methylamino)ethyl)methylamino]benzoic acid methyl ester (28)-an oxamide which would produce a degenerate spiro intermediate - was subjected to rearrangement conditions, the product obtained was 1,3-dimethyl-2,4-(1H,3H)quinazolinedione (29). This latter transformation may have proceeded *via* a benzodiazepinetrione intermediate.

The benzo-1,4-diazepine-2,3,5-trione ring system (general structure **1**) is unknown. This report describes several attempts to prepare representative compounds of this unknown class. Although all of our attempts to generate **1** were unsuccessful, we did encounter a novel rearrangement of oxamides which is of interest from a mechanistic and a preparative standpoint.
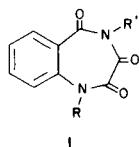
Benzo-1,4-diazepine-2,3,5-trione

Our most staightforward attempt to prepare a compound of general structure **1** is shown in Scheme I. N-Methyl-2-(phenylamino)benzamide (**3**) was prepared from 2-(phenylamino)benzoyl chloride (**2**) and methylamine. Treatment of **2** with oxalyl chloride in toluene afforded 3-methyl-1-phenyl-2,4-(1H,3H)quinazolinedione (**4**), rather than **1** (R = C₆H₅,R' = CH₃). An authentic sample of **4** for comparison was prepared from methyl 2-(phenylamino)benzoate (**5**) and methyl isocyanate.
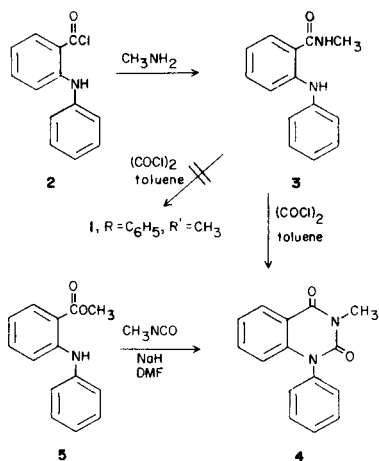
Our next attempts employed methyl 2-[(2-chloro-1,2-dioxoethyl)phenylamino]benzoate (**6**), whose synthesis we have earlier described (1), as a starting material (Scheme II). Treatment of **6** with methylamine and ethylamine cleanly afforded oxamides **7a** and **b**, respectively. Compound **7a**, when treated with polyphosphoric acid (PPA), afforded anthrone (**8**). This cyclization-hydrolysis reaction was not too surprising, however, in view of the facile conversion of N-phenylanthranilic acid to **8** with sulfuric acid (2). Oxamides **7a** and **b** were next treated with sodium hydride in dimethylformamide. These reactions resulted in clean conversions to different materials (Compounds A and B, respectively) which were isomeric with the starting oxamides.

Our initial assessment of these results is shown in Scheme III, where we envisioned benzodiazepinediones **9a** and **b** as intermediates. Subsequent cleavage of these intermediates by sodium methoxide might then produce unknown Compounds A and B. While attack by methoxide at the 5-position would only regenerate **7a** and **b**, attack at the 3-position would lead to oxamates **10a** and **b**. Attack at the 2-position would produce oxamates **11a** and **b**. The
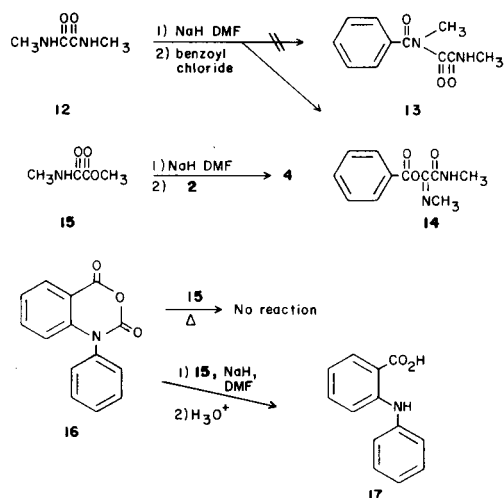
SCHEME I
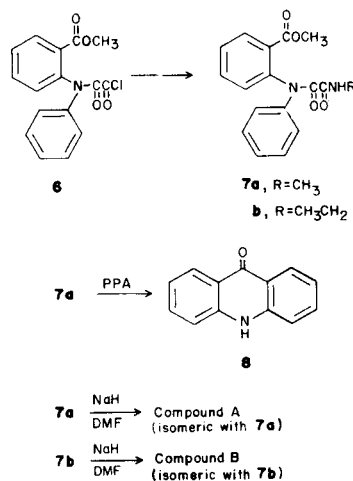
SCHEME II

SCHEME III
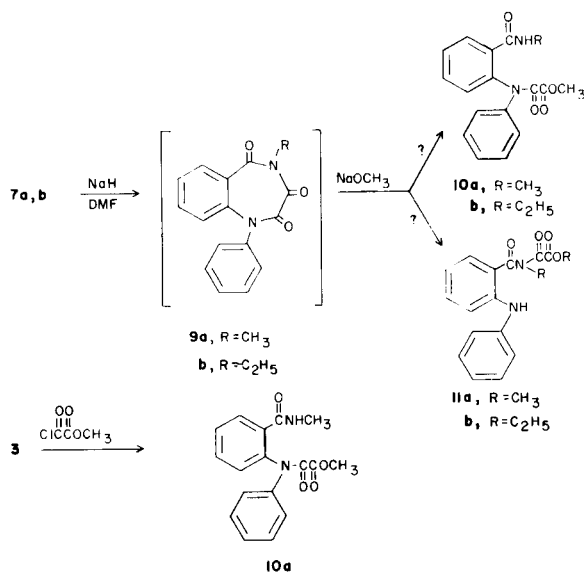
first of these hypotheses, *i.e.*, whether **10a** was produced from **7a**, was relatively simple to test. Treatment of **3** with methyl chlorooxalate afforded N-[2-((methylamino)carbonyl)phenyl]-2-oxo-N-phenylglycine methyl ester (**10a**). Compound **10a**, however, was *not* the same as Compound A.

The second hypothesis, that oxamates **11a** and **b** had resulted when **7a** and **b** were transformed by sodium hydride, was not easily tested. Prior to attempting the synthesis of **11**, we treated a solution of N,N'-dimethyloxamide (**12**) in dimethylformamide with sodium hydride, followed by benzoyl chloride. Rather than the desired N-benzoylated product **13**, we isolated the O-benzoylated product **14**. Notwithstanding this result, we prepared oxamate **15** (tediously, from dimethyl oxalate and methylamine) and treated it, in similar fashion, with acid chloride **2**. A product of this reaction, which we isolated in low yield, was quinazolinedione **4**. (It is interesting to speculate on the mechanism of this reaction; it is possible that **9a** is an intermediate in this transformation). We also treated N-phenylisatoic anhydride (**16**) with **15**, in dimethylformamide for two hours at 130°, which resulted only in the recovery of **16**. Treatment of **16** with the sodium salt of **15** in dimethylformamide, followed by work-up with aqueous acid, led only to N-phenylanthranilic acid. Thus, our efforts to produce **11**, which are summarized in Scheme IV, were not successful.

At this point, we took a new approach to ascertaining the structures of Compounds A and B. We had earlier observed a facile thermal conversion of **6** to methyl 2-(2,3-dihydro-2,3-dioxo-1H-indol-1-yl)benzoate (**18**), upon attempted distillation of **6** or upon heating **6** in decahydronaphthalene (Scheme V). Hoping to effect a similar annelation of Compound A (be it structure **11a** on something else) to aid in its characterization, we treated Compound A

with polyphosphoric acid (PPA). An expected product of this reaction was N-phenylanthranilic acid (**17**). 2-Methylaminobenzoic acid (**19**) and its methyl ester (**20**) were surprises, as was oxindole **21**. We readily prepared an authentic sample of **21** for comparison from isatin (**22**) and aniline (**23**).
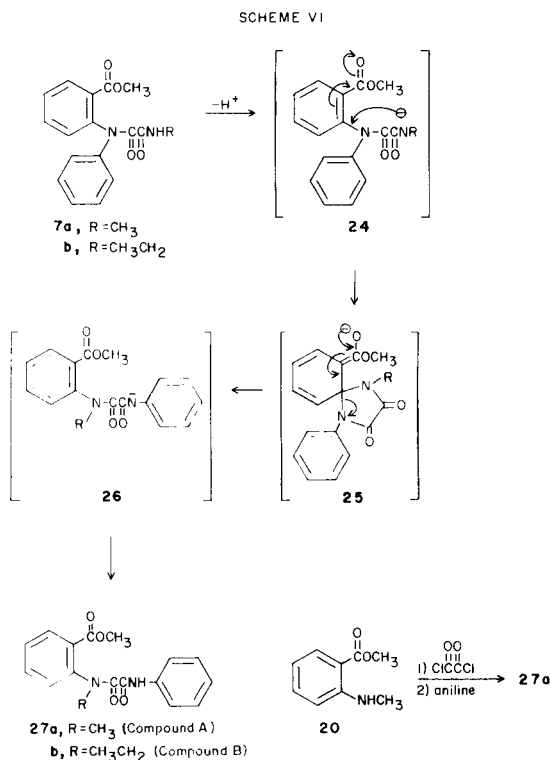
SCHEME IV

SCHEME V
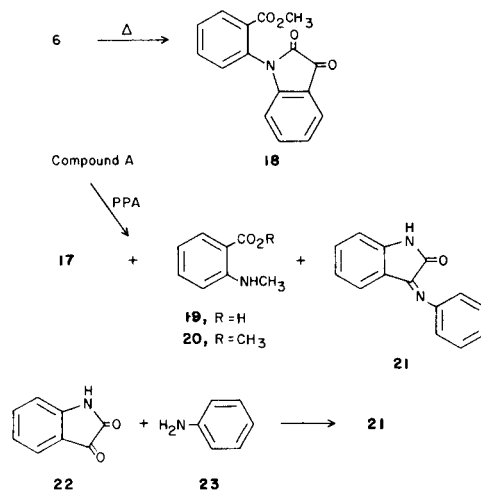
In view of the production of **19** and **20** from Compound A and PPA, we proposed structures for Compounds A and B (**27a** and **b**, respectively) as indicated in Scheme VI. We felt that the initially formed **24** was undergoing an internal Michael addition to produce spiro intermediate **25**. A reverse Michael reaction would then produce **26**, which is a protonation step away from the rearranged products **27a** and **b**. A driving force for the complete rearrangement of **7a** and **b** to **27a** and **b** would be the formation of a lower energy anionic species in the basic medium. Intermediate **26** is of lower energy than initially formed intermediate **24**, because charge delocalization is more extensive in in-

termediate **26**. The lower-energy intermediate **26** is efficiently produced from spiro intermediate **25**, wherein the arylamino anion is a better leaving group than the alkylamino anion. The mechanism presented in Scheme VI was substantiated by the preparation of an authentic sample of **27a**. Treatment of methyl 2-(methylamino)benzoate (**20**) with oxalyl chloride and treating the resulting acid chloride with aniline gave **27a**, which was identical to compound A.

The formation of 1,3-dihydro-3-(phenylimino)-2*H*-indol-2-one (**21**) from **27a** and PPA is easily rationalized. Hydrolysis of **27a** at the tertiary amide linkage would produce *N*-phenyloxamic acid, which could then cyclize under the reaction conditions to yield isatin (**22**). Hydrolysis at the other amide linkage would yield aniline (**23**) which could condense (readily, with acid-catalysis and dehydrative conditions) with **22** to yield **21**. Interestingly, the formation of *N*-phenylanthranilic acid (**17**) from **27a** and PPA clearly indicates that a spiro intermediate similar to (protonated) **25** is produced, which eventuates in **17**.

SCHEME VI

7a, R = CH₃
b, R = CH₃CH₂

24

26

25

27a, R = CH₃ (Compound A)
b, R = CH₃CH₂ (Compound B)

20

1) ClCCCl
2) aniline → 27a

It seemed imperative to prepare an oxamide related to **7a** and **b** which could only give rise to a degenerate spiro intermediate when treated with base. To this end we prepared oxamide **28**, from **20** and oxalyl chloride, followed by treatment of the resulting acid chloride with methylamine (Scheme VII). Interestingly, treatment of **28** with sodium hydride in dimethylformamide afforded a 70% yield of 1,3-dimethyl-2,4-(1*H*,3*H*)quinazolinedione (**29**).

We feel that this transformation may have involved an initially formed benzo-1,4-diazepine-2,3,5-trione intermediate (**30**), from which quinazolinedione **29** was formed by the loss of carbon monoxide in one of two ways. Intermediates **31** and **32** are the potential precursors to **29**, which we envision would result from ring-contraction of **30** through the interaction of nucleophilic nitrogen and electrophilic carbonyl centers. Loss of a carbon monoxide unit from either **31** or **32** would then yield quinazolinedione **29**. We have previously postulated similar mechanistic pathways for the ring contraction of 1,3,4-benzotriazepine-2,5-diones (3).

SCHEME VII

20

28

29

30

31

32
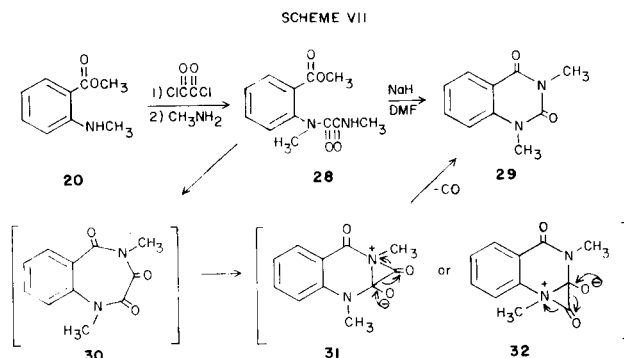
Although benzoic acid derivatives are not commonly thought of as Michael receptors, they are α,β-unsaturated carbonyl compounds and certain reactions of substituted benzoic acids can be viewed as Michael reactions. For instance, the preparation of *N*-arylanthranilic acids from 2-halobenzoic acids and anilines (with copper catalysis) (4) can be viewed as a Michael-retro-Michael process. The novel rearrangement described in Scheme VI is unique in that the Michael-retro-Michael process is intramolecular. The low-entropy nature of the intramolecular addition-elimination rearrangement, perhaps, allows a relatively inactive Michael receptor to function.

EXPERIMENTAL

Materials.

2-(Phenylamino)benzoyl chloride (**2**), m.p. 45-48° [lit. m.p. 50° (5)] was prepared from *N*-phenylanthranilic acid (**17**) and phosphorus pentachloride using the procedure of Drozdov (5). Methyl 2-(phenylamino)benzoate (**5**), b.p. 155° (0.9-1.0 mm), m.p. 55-57° [lit. (6a) m.p. 57-58°; lit. (6b) m.p. 58-59°] was prepared from *N*-phenylanthranilic acid (**17**) using a standard esterification procedure. Methyl 2-[(2-chloro-1,2-dioxoethyl)-phenylamino]benzoate (**6**) [lit. (1) m.p. 64-67°] was prepared as previously described (1). Methyl *N*-methyl-2-oxoglycinate (**15**), m.p. 80.5-82.5° [lit. (7) m.p. 84°] was prepared using the general procedure of Sah and Chien (8). *N*-Phenylisatoic anhydride (**16**), m.p. 174-175° [lit. (9) m.p. 177-179°] was prepared from **17** and ethyl chloroformate as described by Santilli (9). Methyl 2-(methylamino)benzoate (**20**), b.p. 95° (0.40 mm), [lit. (10a)

b.p. 134-155° (16 mm); lit. (10b) b.p. 130-131° (15 mm)] was prepared from N-methylanthranilic acid using a standard esterification procedure. 1,3-Dihydro-3-(phenylimino)-2H-indol-2-one (21), m.p. 219.5-220° [lit. (11) m.p. 221°] was prepared using the general procedure of Popp (12).

N-Methyl-2-(phenylamino)benzamide (3).

To a solution of 11.6 g. (50.0 mmoles) of 2 in 50 ml. of ether was carefully added 30 ml. of 40% aqueous methylamine. After stirring overnight, the mixture was treated with water and the separated ether layer was dried (sodium sulfate) and concentrated to leave 11.1 g. (98%) of 3 as an oil, which upon trituration with ether gave a white solid, m.p. 86-87° (ether-hexane) [lit. (13) m.p. 75-78°]; ir (Nujol): 3360 (amino NH), 3190 (amide NH) cm^{-1}.

1-Phenyl-3-methyl-2,4-(1H,3H)quinazolinedione (4). A. From 3.

To a stirring solution of 5.66 g. (25.0 mmoles) of 3 in 40 ml. of toluene was added a solution of 3.17 g. (25.0 mmoles) of oxalyl chloride in 10 ml. of toluene. The resulting mixture was heated at reflux for 2 hours. Water was added and the toluene layer was separated, dried (sodium sulfate) and concentrated. The resulting solid was triturated with ether and collected to yield 1.90 g. (30%) of 4, mp. 234-236° [lit. (14) m.p. 234°]; ir (Nujol): 1705 (C=O), 1655 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d$_6$): δ 8.17-8.02 (m, 1H, aromatic), 7.70-7.15 (m, 7H, aromatic), 6.43 (d, J = 8 Hz, 1H, aromatic), 3.30 (s, 3H, CH$_3$); ms: (70 eV, electron impact) m/e 252 (molecular ion).

B. From 5.

To a mixture of 2.00 g. (83.3 mmoles) of dry sodium hydride in 30 ml. of dimethylformamide was added 11.4 g. (50.0 mmoles) of 5. The addition was accompanied by gas evolution. A 3.99-g. (70.0 mmoles) quantity of methylisocyanate was added dropwise (exothermic). After two hours of stirring, the mixture was diluted with water and the solid was collected and air-dried to yield 8.10 g. (64%) of 4, m.p. 230-231°; m.p. 234-235° (dimethylformamide-water) [lit. (14) m.p. 234°]. This material was spectrally identical to that prepared in Part A.

C. From 15 and 2.

To a mixture of 750 mg. (31.2 mmoles) of dry sodium hydride and 10 ml. of dimethylformamide was added 2.93 g. (25.0 mmoles) of 15. After 10 minutes of stirring, 5.79 g. (25.0 mmoles) of 2 was added. After stirring for one hour, the mixture was poured into water and extracted with methylene chloride. The organic extracts were dried (sodium sulfate) and concentrated to leave 2.30 g. of a yellow, oily solid. Trituration with ether and collection gave 0.230 g. (4%) of 4, m.p. 238-239° (ethanol) [lit. (14) m.p. 234°]. This material was identical in all respects to that prepared in Part A.

2-[(2-(Methylamino)-1,2-dioxoethyl)phenylamino]benzoic Acid Methyl Ester (7a).

A solution of 28.0 g. (88.1 mmoles) of 6 in 75 ml. of ether was carefully treated with 20 ml. of 40% aqueous methylamine. The addition was highly exothermic. An oil separated, which solidified upon scratching. The solid was collected, washed with ether and water and air-dried to yield 20.1 g. (73%) of 7a, m.p. 120-121°; m.p. 120-121° (ethanol); ir (Nujol): 3400 (NH), 1715 (ester C=O), 1690 (C=O), 1665 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 8.12-7.93 (m, 1H, aromatic), 7.67-6.80 (m, 9H, aromatic and NH), 3.86 (s, 3H, CO$_2$CH$_3$), 2.69 (d, J = 6 Hz, 3H, NCH$_3$).

Anal. Calcd. for C$_{17}$H$_{16}$N$_2$O$_4$: C, 65.37; H, 5.16; N, 8.97. Found: C, 65.29; H, 5.05; N, 9.02.

2-[(2-(Ethylamino)-1,2-dioxoethyl)phenylamino]benzoic Acid Methyl Ester (7b).

A solution of 25.0 g. (78.7 mmoles) of 6 in 75 ml. of ether was carefully treated with 20 ml. of 70% aqueous ethylamine. The addition was highly exothermic. The resulting oil which separated quickly solidified. The solid was collected, washed with ether and water and air-dried to yield 17.8 g. (69%) of 7b, m.p. 122-124°, m.p. 122-124° (ethanol); ir (Nujol): 3295 and 3280 (NH), 1710 (ester C=O); nmr (deuteriochloroform): δ

8.10-7.93 (m, 1H, aromatic), 7.67-6.90 (m, 10H, aromatic and NH), 3.87 (s, 3H, CO$_2$CH$_3$), 3.16 (q, J = 7.5 Hz, 2H, CH$_2$), 1.13-0.80 (m, 3H, CH$_2$CH$_3$).

Anal. Calcd. for C$_{18}$H$_{18}$N$_2$O$_4$: C, 66.24; H, 5.56; N, 8.58. Found: C, 66.29; H, 5.71; N, 8.73.

Treatment of 7a with PPA.

A mixture of 4.00 g. (12.8 mmoles) of 27a and 60 g. of polyphosphoric acid (PPA) was stirred at 80-90° for 5 hours. The reaction mixture was cooled and poured into sodium bicarbonate solution. The resulting solid was collected and recrystallized (ethanol) to yield 2.40 g. (96%) of acridone (8), m.p. > 300° [lit. (15) m.p. 354-355°]. This material was spectrally identical to an authentic sample of acridone.

N-[2-((Methylamino)carbonyl)phenyl]-2-oxo-N-phenylglycine Methyl Ester (10a).

To solution of 2.26 g. (10.0 mmoles) of 3 in 50 ml. of toluene was added 1.23 g. (10.0 mmoles) of methyl oxalyl chloride in 10 ml. of toluene. The solution was heated for two hours at reflux, and the resulting mixture was concentrated and partitioned between methylene chloride and water. The organic layer was dried (sodium sulfate) and concentrated, and the resulting solid was recrystallized from benzene-hexane to yield 1.20 g. (38%) of 10a, m.p. 124-126°; ir (Nujol): 3370 (NH), 1745 (ester C=O), 1660 (C=O) cm^{-1}; ms: (70 eV, chemical ionization, methane) m/e 313 (M$^+$+1), 341 (M$^+$+29), 353 (M$^+$+41).

Anal. Calcd. for C$_{17}$H$_{16}$N$_2$O$_4$: C, 65.37; H, 5.16; N, 8.97. Found: C, 65.60; H, 5.22; N, 8.90.

Benzoic Acid Anhydride with N-Methyl-2-(methylamino)-2-oxoethanimidic Acid (14).

To a solution of 11.6 g. (0.100 mole) of N,N'-dimethyloxamide (12) in 50 ml. of dimethylformamide was added 2.40 g. (0.100 mole) of dry sodium hydride. After 10 minutes of stirring, 14.1 g. (0.100 mole) of benzoyl chloride was added dropwise (exothermic). The resulting mixture was stirred for 30 minutes and partitioned between methylene chloride and water. The organic layer was concentrated and triturated with water to produce a solid which was collected and air-dried to yield 9.00 g. (41%) of 14, m.p. 225-227° (ethanol); ir (Nujol): 3200 (NH), 1770 (C=O), 1705 (C=O) cm^{-1}; nmr (dimethylsulfoxide-d$_6$): δ 7.78 (s, 1H, NH), 7.48 (s, 5H, aromatic), 2.68 (s, 6H, both CH$_3$ groups); ms: (70 eV, elecron impact) m/e 220 (molecular ion).

Anal. Calcd. for C$_{11}$H$_{12}$N$_2$O$_3$: C, 59.99; H, 5.49; N, 12.72. Found: C, 60.10; H, 5.54; N, 12.64.

Treatment of 15 with N-Phenylisatoic Anhydride (16).

When equimolar amounts of 15 and 16 in dimethylformamide were heated at 125-135° for two hours, dilution with water and collection of the resulting precipitate led to a quantitative recovery of 16.

To a mixture of 0.760 g. (31.7 mmoles) of dry sodium hydride in 15 ml. of dimethylformamide was added 2.93 g. (25.0 mmoles) of 15. To the resulting thick paste was added 5.98 g. (25.0 mmoles) of 16. The mixture was diluted with 25 ml. of dimethylformamide, stirred for 30 minutes and poured into cold water. A small amount (500 mg.) of precipitate was removed by filtration, and the filtrate was neutralized with hydrochloric acid. The resulting white precipitate was collected and air-dried to yield 3.46 g. (65%) of N-phenylanthranilic acid (17). The ir of this material was identical to that of an authentic sample of 17.

2-(2,3-Dihydro-2,3-dioxo-1H-indol-1-yl)benzoic Acid Methyl Ester (18).

A mixture of 7.00 g. (22.0 mmoles) of 6 and 25 ml. of decalin was heated on a hot plate. At ca. 80°, a solution resulted, and at reflux, a golden-brown color developed. After 15 minutes at reflux, the solution was cooled, which caused an oil to separate. A solution was regenerated by the addition of 50 ml. of ether. Orange crystals then separated from the solution, which were collected, washed with ether and air-dried to yield 2.62 g. (42%) of 18, m.p. 147-151°; ir (Nujol): 1760 (ketone C=O), 1735 (ester C=O), 1720 (amide C=O) cm^{-1}; nmr (deuteriochloroform): δ 8.40-8.13 (m, 1H, aromatic), 7.94-7.03 (m, 6H, aromatic), 6.63 (d, J = 7.5 Hz, 1H, aromatic), 3.80 (s, 3H, CH$_3$); ms: (70 eV, chemical ionization,

methane) 282 (M⁺ + 1), 310 (M⁺ + 29), 322 (M⁺ + 41).

Anal. Calcd. for $C_{16}H_{11}NO_4$: C, 68.32; H, 3.94; N, 4.98. Found: C, 68.55; H, 4.14; N, 5.23.

Treatment of Compound A (27a) with PPA.

A mixture of 2.30 g. (7.36 mmoles) and *ca.* 40 g. of PPA was heated at 80-90° for 2 hours. The dark, foamy mixture was poured into aqueous sodium carbonate and the resulting mixture was extracted with methylene chloride. The organic layer was dried (sodium sulfate) and concentrated to leave a red oil. Trituration with ether caused an orange solid to separate, which was collected to yield 0.68 g. This solid was dissolved in a minimal volume of chloroform and applied to a 100-g. column of silica gel 60 (EM Reagents, 70-230 mesh) and eluted with chloroform to afford 25 100-ml. fractions. Fractions 10-21 were combined and concentrated to leave 0.210 g. of 1,3-dihydro-3-(phenylimino)-2*H*-indol-2-one (21), m.p. 216-218° (ethanol-water) [lit. (11) m.p. 221°]. This material was spectrally identical to an authentic sample of 21 which we prepared from isatin (22) and aniline (23), using the general procedure of Popp (12).

The filtrate from the 0.68 g. of orange solid was concentrated to leave 1.20 g. of an orange semi-solid. When slurried with chloroform an orange precipitate remained which was collected to yield an additional 0.120 g. of 21. The filtrate was then applied to a 150-g. column of silica gel 60 and eluted with chloroform to afford 30 100-ml. fractions. Fractions 1 and 2 were combined and concentrated to leave 0.180 g. of methyl 2-(methylamino)benzoate (20), which was spectrally identical to an authentic sample of 20 which we prepared for comparison (16). Fractions 8-11 afforded 0.340 g. of recovered 27a. Fractions 15-20 gave 70.0 mg. of *N*-phenylanthranilic acid (17), m.p. 171-174° [lit. (18) m.p. 184°], whose infrared spectrum was identical to that reported (19) for 17. Finally, fractions 25-30 gave 0.170 g. of additional 21.

2-[(1,2-Dioxo-2-(methylamino)ethyl)phenylamino]benzoic Acid Methyl Ester (27a). A. From 7a.

To a mixture of 0.264 g. (11.0 mmoles) of sodium hydride in 25 ml. of dimethylformamide was added 3.12 g. (10.0 mmoles) of 7a. After 1 hour, the solution was poured into water and the mixture was acidified with dilute hydrochloric acid. The mixture was extracted with methylene chloride and the extracts were dried (sodium sulfate) and concentrated to leave 2.80 g. (90%) of 27a as an oil, which on trituration with ether afforded a white solid, m.p. 96-97°; m.p. 98-99° (benzene-hexane); ir (Nujol): 3310 (NH), 1720 (ester C=O), 1695, 1640 cm⁻¹; nmr (deuteriochloroform): δ 9.57 (broad s, 1H, NH), 8.25-8.02 (m, 1H, aromatic H ortho to ester), 7.87-6.80 (m, 8H, remaining aromatic), 3.85 (s, 3H, OCH₃), 3.36 (s, 3H, NCH₃); ms: (70 eV, electron impact) m/e 312 (molecular ion).

Anal. Calcd. for $C_{17}H_{16}N_2O_4$: C, 65.37; H, 5.16; N, 8.97. Found: C, 65.50; H, 5.29; N, 9.11.

B. From 20.

To a solution of 50.0 g. (0.394 mole) of oxalyl chloride in 150 ml. of toluene was added, dropwise with ice bath cooling, a solution of 16.5 g. (0.100 mole) of 20 in 50 ml. of toluene. After standing overnight the solution was concentrated, and twice treated with carbon tetrachloride and reconcentrated to yield 24.3 g. of brown oil. To a solution of this acid chloride in 100 ml. of toluene was added, dropwise with icebath cooling, a solution of 17.7 g. (0.190 mole) of aniline in 40 ml. of toluene. A precipitate formed during the addition. After standing overnight, the mixture was washed with water and the clear toluene layer was dried (sodium sulfate) and concentrated. The resulting oil was triturated with ether to produce a white solid, which was collected to afford 18.8 g. (60% from 20) of 17a, m.p. 105-106°. This material was spectrally identical to that prepared in Part A.

2-[(1,2-Dioxo-2-(phenylamino)ethyl)ethylamino]benzoic Acid Methyl Ester (27b).

To a mixture of 0.264 g. (11.0 mmoles) of dry sodium hydride in 30 ml. of dimethylformamide was added 3.26 g. (10.0 mmoles) of 7b. After 1

hour, the solution was poured into water and the mixture was acidified with dilute hydrochloric acid, and extracted with methylene chloride. The dried (sodium sulfate) organic phase was concentrated to leave 2.90 g. (89%) of 27b as an oil, which upon trituration with ether, afforded a white, crystalline solid, m.p. 102-103°; ir (Nujol): 3330 (NH), 1725 (ester C=O), 1705, 1645 cm⁻¹; nmr (deuteriochloroform): δ 9.43 (broad s, 1H, NH), 8.20-7.97 (m, 1H, aromatic), 7.77-8.03 (m, 8H, remaining aromatic), 4.20-3.47 (m, 5H, NCH₂ and OCH₃, with OCH₃ s at 3.84), 1.15 (t, J = 7.2 Hz, 3H, NCH₂C*H₃*); ms: (70 eV, chemical ionization, methane) m/e 327 (M⁺ + 1), 355 (M⁺ + 29), 367 (M⁺ + 41). The mass spectrum also displayed a molecular ion for a species corresponding to M-32. This could have been the corresponding benzotriazepinedione, being formed in the mass spectrometer by methanol extrusion. The same phenomenon was observed with 27a when we recorded its mass spectrum in the chemical ionization mode.

Anal. Calcd. for $C_{18}H_{18}N_2O_4$: C, 66.24; H, 5.56; N, 8.58. Found: C, 65.90; H, 5.59; N, 8.55.

2-[(1,2-Dioxo-2-(methylamino)ethyl)methylamino]benzoic Acid Methyl Ester (28).

To a solution of 171 g. (1.35 moles) of oxalyl chloride in 400 ml. of toluene was added, with icebath cooling over a 40-minute period, a solution of 56.0 g. (0.339 mole) of 20 in 100 ml. of toluene. After stirring for 2 hours, the solution was thoroughly concentrated to leave 83.2 g. (96%) of 2-[(2-chloro-1,2-dioxoethyl)methylamino]benzoic acid methyl ester, which was used as such in the preparation of 28.

A solution of 81.2 g. (0.317 mole) of the acid chloride in 200 ml. of ether was carefully added to 70 ml. of a 40% aqueous methylamine solution. After standing overnight, a white solid was collected, washed with water and ether and air-dried to yield 43.4 g. (55%) of 28, m.p. 100-102°; ir (Nujol): 3320 (NH), 1715 (ester C=O), 1685 (C=O), 1640 (C=O) cm⁻¹; nmr (deuteriochloroform): δ 8.15-7.93 (m, 1H, aromatic), 7.75-7.20 (m, 3H, aromatic), 3.83 (s, 3H, OCH₃), 3.27 (s, 3H, NCH₃ adjacent to aromatic ring), 2.67 (d, J = 6 Hz, 3H, NHC*H₃*; collapses to s at 2.67 when deuterium oxide is added); ms: (70 eV, electron impact) m/e 250 (molecular ion).

Anal. Calcd. for $C_{12}H_{14}N_2O_4$: C, 57.59; H, 5.64; N, 11.20. Found: C, 57.50; H, 5.62; N, 11.27.

1,3-Dimethyl-2,4-(1*H*,3*H*)quinazolinedione (29).

To a mixture of 1.50 g. (62.5 mmoles) of dry sodium hydride in 40 ml. of dimethylformamide was added 12.5 g. (50.0 mmoles) of 28 in portions. After the addition was complete the mixture was stirred for 2 hours, poured into cold water, and acidified with dilute hydrochloric acid. The mixture was extracted with methylene chloride and the organic extract was dried (sodium sulfate) and concentrated to leave 6.65 g. (70%) of 29, m.p. 167° (ethanol) [lit. (20a) m.p. 170°; lit (20b) m.p. 166-167°]; ir (Nujol): 1700 (C=O), 1655 (C=O) cm⁻¹; nmr (deuteriochloroform): δ 8.30-8.10 (m, 1H, aromatic), 7.80-7.55 (m, 1H, aromatic), 7.38-7.11 (m, 2H, aromatic), 3.57 (s, 3H, CH₃), 3.43 (s, 3H, CH₃); ms: (70 eV, electron impact) m/e 190 (molecular ion).

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(16) In another experiment where we similarly treated **27a** with PPA but did not employ column chromatography in the isolation of reaction products, we did isolate the carboxylic acid corresponding to **20** (19), m.p. 176-178° [lit. (17); m.p. 178-179°].

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