7-(3,4-Methylenedioxyphenyl)-3,5-dioxo-6-heptenoic Acid (IIc).—The dianion of 0.348 g (0.0015 mol) of diketone Ic was carboxylated to give 0.208 g (50% yield) of diketo acid IIc, mp 118–120°. Recrystallization from chloroform gave mp 122–123° dec; ν_{max} 1730, 1630, 1610, 1540–1580, and 1130 cm^{-1}; $\delta_{acetone\text{-}d_6}$ 3.48 (2-CH_2), 5.93 (4-CH), 6.10 (-OCH_2O-), 6.48 and 6.75 (6-CH), and 7.45 and 7.72 ppm (7-CH).

Anal. Calcd for $C_{14}H_{12}O_6$: C, 60.87; H, 4.38. Found: C, 60.63; H, 4.19.

5-(3-Pyridyl)-3,5-dioxopentanoic Acid (IId).—Treatment of the disodium salt of diketone Id with Dry Ice gave an ether-insoluble, tan salt. Acidification afforded only unaltered diketone. Moreover, addition of the salt directly to anhydrous, liquid hydrogen fluoride gave no apparent formation of pyrone.

6-Substituted 4-Hydroxy-2-pyrones III. 4-Hydroxy-6-(3,4-methylenedioxyphenyl)-2-pyrone (IIIa).—Treatment of diketo acid IIa with anhydrous, liquid hydrogen fluoride apparently affected adversely the piperonyl ring system. As an alternative, the diketo acid (0.100 g, 0.00040 mol) was added to 10 ml of acetic anhydride. Initially the mixture was homogeneous; however, after 1 hr white crystals began to appear. After 16 hr the mixture was cooled and the crystals were separated by filtration, washed with water, and dried. Recrystallization from 95% ethanol gave 0.068 g (73% yield) of pyrone IIIa, mp 257–258° (lit.[22] mp 255–257°).

4-Hydroxy-6-(*p*-methoxystyryl)-2-pyrone (IIIb).—Treatment of 0.262 g (0.0010 mol) of diketo acid IIb with acetic anhydride afforded after recrystallization from methanol 0.155 g (63% yield) of pyrone IIIb, mp 235–237° (lit.[11] mp 238°).

4-Hydroxy-6-(3,4-methylenedioxystyryl)-2-pyrone (IIIc).—Diketo acid IIc (0.097 g, 0.00035 mol) and acetic anhydride gave 0.077 g (79% yield) of the monohydrate of pyrone IIIc: mp 230–234°, mp 233–236° after recrystallization from ethanol; ν_{max} 1620–1670 and 3300–3500 cm^{-1}.

Anal. Calcd for $C_{14}H_{10}O_6 \cdot H_2O$: C, 60.87; H, 4.38. Found: C, 60.68; H, 4.50.

6-Substituted 4-Methoxy-2-pyrones IV. 4-Methoxyparacotoin (IVa).—A mixture of 0.0348 g (0.00015 mol) of pyrone IIIa, 2 g of potassium carbonate, and 1 ml of methyl sulfate in acetone was refluxed for 1.5 hr and allowed to stand at ambient temperature for 18 hr. Salts were removed by filtration and the solution was concentrated to give a partially crystalline mixture. The crystals were washed with ether, with 5% sodium hydroxide solution, and with water to give 0.0255 g (69% yield) of pyrone IVa, mp 221–222°. Recrystallization from methanol gave mp 223–224° (lit.[30] mp 222–224°).

Yangonin (IVb).—Methylation of 0.122 g (0.00050 mol) of pyrone IIIb afforded 0.115 g (89% yield) of yangonin, mp 152.5–154°. Recrystallization from methanol gave mp 154–155° (lit.[11] mp 153–154°).

Registry No.—Ic, 16526-73-1; IIc, 16526-74-2; IIIc, 16526-75-3; IVa, 6969-80-8; IVb, 500-62-9.

(22) A. Resplandy, *Bull. Soc. Chim. Fr.*, 1332 (1962).

The Reaction of Some Keto Acids with Anthranilic Acid Anthranilamides, Orthanilamides, and Salicylamide[1]

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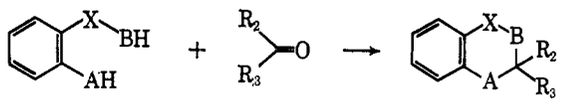
The reaction of 2-acyl- and 2-aroylbenzoic acids and 3- and 4-oxoalkanoic acids with anthranilic acid, anthranilamides, salicylamide, and orthanilamides has been demonstrated to be a useful technique for preparing heterocyclic systems containing nitrogen, oxygen, and sulfur heteroatoms.

The reaction of an aldehyde or ketone (**2**) with an anthranilic acid (**1a**), anthranilamide (**1b**), salicylamide (**1c**), or orthanilamide (**1d**) has found general synthetic application in the synthesis of a variety of 1,2-dihydro-4H-3,1-benzoxazin-4-ones[2] (**3a**), 1,2,3,4-tetrahydroquinazolin-4-ones[3] (**3b**), 2,3-dihydro-4H-1,3-benzoxazin-4-ones[2,4] (**3c**), and 3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides[5] (**3d**).



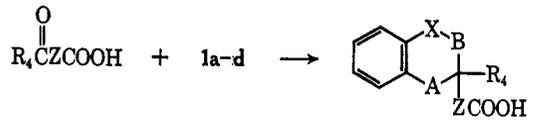
1a, X = CO; A = NH; B = O
b, X = CO; A = NR; B = NR_1
c, X = CO; A = O; B = NH
d, X = SO_2; A = NH; B = NR_1

R, R_1 = H, alkyl, etc.

2, R_2, R_3 = H, alkyl, etc.

3a, X = CO; A = NH; B = O
b, X = CO; A = NR; B = NR_1
c, X = CO; A = O; B = NH
d, X = SO_2; A = NH; B = NR_1

Extension of the carbonyl component (**2**) of this reaction to include ω-acylcarboxylic acids (**4a**) and *o*-acylbenzoic acids (**4b**) suggests that intermediates such as **5** could be formed. Further cyclization of the free carboxy group in **5** with an available nitrogen atom (A or B) could then lead to a variety of tricyclic or tetracyclic systems.



4a, Z = $(CH_2)_{2,3}$
b, Z = *o*-C_6H_4

5

R_4 = alkyl, aryl

Selleri and Caldini[6] and more recently Kratzl and Weinstock[7a] have reported that the reaction of phthaldehydic acids (**6**) with 2-aminobenzenesulfonamides (**7**) gave 6,6a-dihydro-11H-isoindolo[1,2-*c*][1,2,4]benzo-

(1) Portions of this paper were presented at the American Chemical Society Metropolitan Regional Meeting, Stevens Institute of Technology, Hoboken, N. J., Feb 1965.

(2) R. L. McKee in "The Chemistry of Heterocyclic Compounds, Five- and Six-Membered Compounds with Nitrogen and Oxygen," A. Weissberger, Ed., Interscience Publishers, New York, N. Y., 1962, Chapter XIV, pp 341–375.

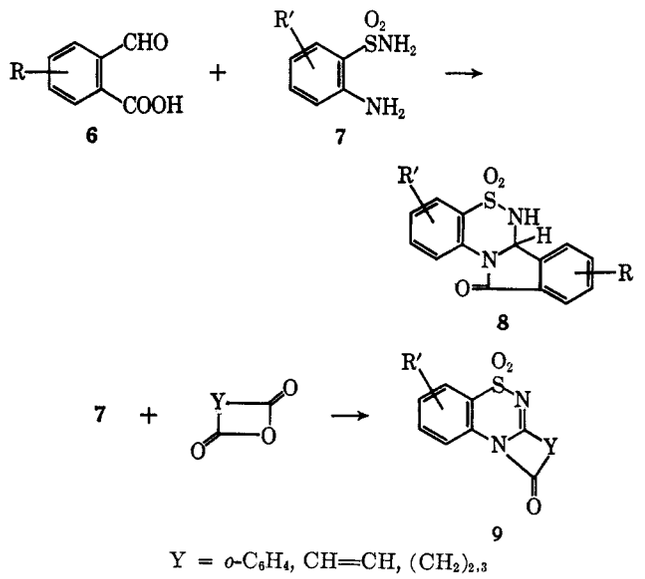
(3) F. Russo and M. Ghelardoni, *Ann. Chim.* (Rome), **56**, 839 (1966); K. H. Hauptmann, *Arzneim.-Forsch.*, **15**, 610 (1965); C. H. Boehringer Sohn, Netherlands Patent Appl. 302,479 (Oct 25, 1966) [*Chem. Abstr.*, **64**, 9743 (1966)]; J. W. Bolger, U. S. Patent 3,257,397 (June 21, 1966) [*Chem. Abstr.*, **65**, 8933 (1966)]; E. S. Schipper, U. S. Patent 3,265,697 (Aug 9, 1966) [*Chem. Abstr.*, **65**, 15399 (1966)].

(4) J. Maillard, M. Vincent, P. Delaunay, V.-V. Tri, and R. Jolly, *Bull. Soc. Chim. Fr.*, 2525 (1966); U. M. Teotino, L. P. Friz, A. Gandini, and D. Della Bella, *J. Med. Chem.*, **6**, 248 (1966).

(5) Numerous examples of this system are reported in "Diuretics," G. De-Stevens, Academic Press Inc., New York, N. Y., 1963.

(6) R. Selleri and O. Caldini, *Boll. Chim. Farm.*, **100**, 323 (1961).

(7) (a) K. Kratzl, R. Weinstock, and H. Ruis, *Oesterr. Chem.-Ztg.* **66**, 315 (1965); (b) R. Weinstock and K. Kratzl, *Monatsh. Chem.*, **96**, 1586 (1965); K. Kratzl, R. Weinstock, and H. Ruis, *ibid.*, **96**, 1592 (1965); (c) K. Kratzl and H. Ruis, *ibid.*, **96**, 1596, 1603 (1965).

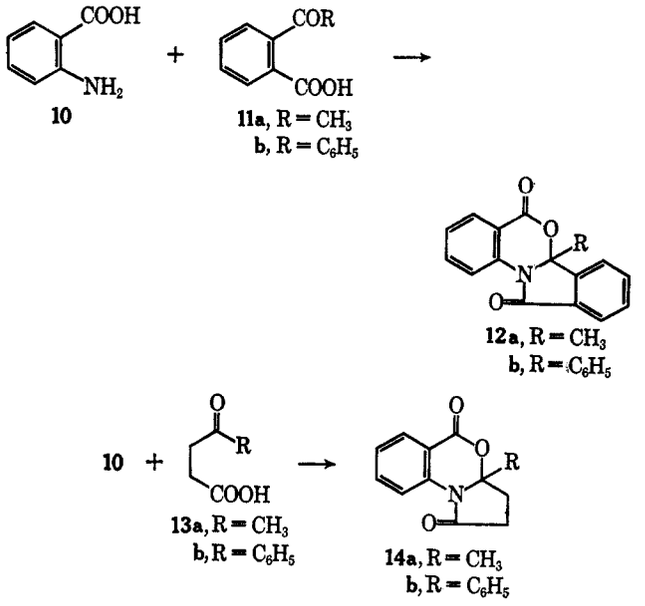


Y = o-C_6H_4, CH=CH, $(CH_2)_{2,3}$

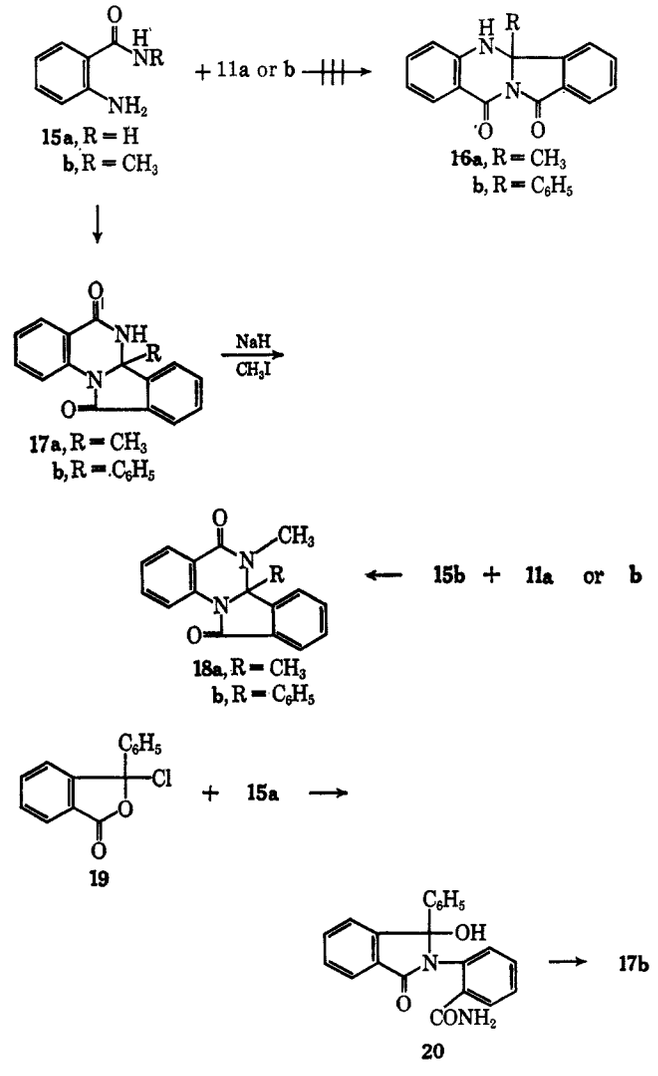
thiadiazin-11-one 5,5-dioxides (**8**). The same ring system has also been obtained by condensing **7** with phthalic acid[7a-c] or phthalic anhydride to form **9** (Y = o-C_6H_4). Borohydride reduction of **9** (Y = o-C_6H_4) gave **8**. From **7** and maleic,[7c,8] succinic,[8] and glutaric[7c,8] anhydride the closely related ring systems **9** [Y = CH=CH, $(CH_2)_{2,3}$] were also prepared.

In the present work the authors wish to report that the reaction of an anthranilic acid, anthranilamide, salicylamide, or orthanilamide with an aromatic or aliphatic keto acid offers a convenient synthetic route for obtaining a variety of heterocyclic systems.

When anthranilic acid (**10**) was allowed to react with 2-acetylbenzoic acid[9] (**11a**) in refluxing dichlorobenzene, compound **12a** was obtained. This substance was shown to be 6a-methyl-6a,11-dihydro-5H-isoindolo-[2,1-a][3,1]benzoxazine-5,11-dione by comparing it with an authentic sample[10] obtained by treating anthranilic acid with 3-oxo-$\Delta^{1,2}$-phthalanacetic acid in refluxing acetic acid. The corresponding 6a-phenyl analog[11] (**12b**) was obtained by reaction of anthranilic acid and 2-benzoylbenzoic acid. Extension of this reaction to 4-oxopentanoic (**13a**) and 3-benzoylpropionic acid (**13b**) gave the related 3a-methyl- and 3a-phenyl-1,2,3,3a-tetrahydro-5H-pyrrolo[1,2-a][3,1]-benzoxazine-1,5-dione (**14a** and **b**). The supporting infrared, ultraviolet, and nmr data are given in Table I.

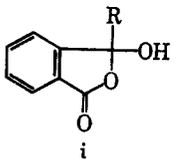


The reaction of anthranilamide (**15a**) with 2-acetylbenzoic acid in refluxing dichlorobenzene resulted in the formation of a compound analyzing for the combination of **11a** and **15a** less 2 mol of water. From a consideration of the cyclization pathway this compound could have either of the tetracyclic structures **16a** or **17a**. To distinguish these structures a dimethylformamide solution of the sodium salt of **16a** or **17a** was



(8) S. C. Bell, P. H. L. Wei, and S. J. Childress, *J. Org. Chem.*, **29**, 3206 (1964).

(9) It is known that 2-acyl- or 2-aroylbenzoic acids can exist in a tautomeric mixture of the open form (**11a** or **b**) or a cyclic form i. The 4- and



i

5-oxoalkonaic acids (**13a**, **b**; **22a**, **b**) exist only in the open structure. (a) W. Graf, E. Girod, E. Schmid, and W. G. Stoll, *Helv. Chim. Acta*, **42**, 1085 (1959); (b) I. S. Trubnikov, R. B. Teplinskaya, Yu. A. Pentin, N. P. Shusherina, and R. Ya. Levina, *J. Gen. Chem. USSR* (Eng. Transl.), **33**, 1186 (1963); (c) M. V. Bhatt and K. M. Kamath, *Tetrahedron Lett.*, 3885 (1966).

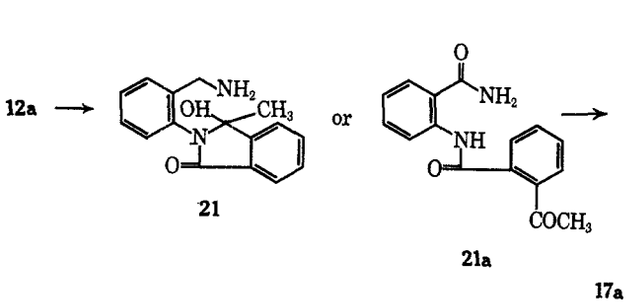
(10) J. Honzl, *Chem. Listy.*, **49**, 1671 (1955); J. Honzl, *Collect. Czech. Chem. Commun.*, **21**, 725 (1965).

(11) After our work had been completed, it was reported that a mixture of methyl anthranilate and 2-benzoylbenzoic acid when heated to 250° gave **12b**: E. Abramowitz and M. Lachen, *J. Chem. Soc.*, 2165 (1965).

treated with methyl iodide to give a monomethyl derivative. The same methyl compound was obtained when N-methylanthranilamide (**15b**) was treated with 2-acetylbenzoic acid. This then established the methyl group on the amide nitrogen, and therefore the monomethyl derivative is 6,6a-dimethyl-5,6,6a,11-tetrahydroisoindolo[2,1-*a*]quinazoline-5,11-dione (**18a**) and 6a-methyl-5,6,6a,11-tetrahydroisoindolo[2,1-*a*]quinazoline-5,11-dione (**17a**) rather than **16a** is the product from anthranilamide and 2-acetylbenzoic acid. When anthranilamide was treated with 2-benzoylbenzoic acid, the corresponding 6-phenyl analog **17b** was obtained. The ring system in **17b** was also established by forming the monomethyl derivative (**18b**) and then forming the same compound from N-methylanthranilamide and 2-benzoylbenzoic acid. Spectral and analytical data (Table I) were in agreement with the structural assignments.

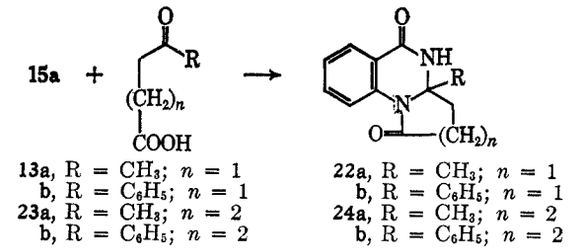
The structure of 9a-phenyl-5,6,6a,11-tetrahydroisoindolo[2,1-*a*]quinazoline-5,11-dione (**17b**) was additionally established by its synthesis from the acid chloride of 2-benzoylbenzoic acid (**19**)[12] and anthranilamide (**15a**) in dimethylformamide. Several unsuccessful attempts were made to isolate **20**, the probable intermediate in this reaction.

Honzl[10] had reported that 6a-methyl-6a,11-dihydro-5H-isoindolo[2.1-*a*][3,1]benzoxazine-5,11-dione (**12a**) on treatment with alcoholic ammonia at room temperature gave an amide which he postulated as being either 2-(*o*-carbamoylphenyl)-3-hydroxy-3-methylphthalimidine (**21**) or 2-(2-acetylbenzamido)benzamide (**21a**). Subsequent treatment of this amide in refluxing acetic acid gave a compound that Honzl postulated as being identical with **17a** prepared in the present work. This work has been repeated here and it was found that the structure (**17a**) postulated by Honzl is correct.



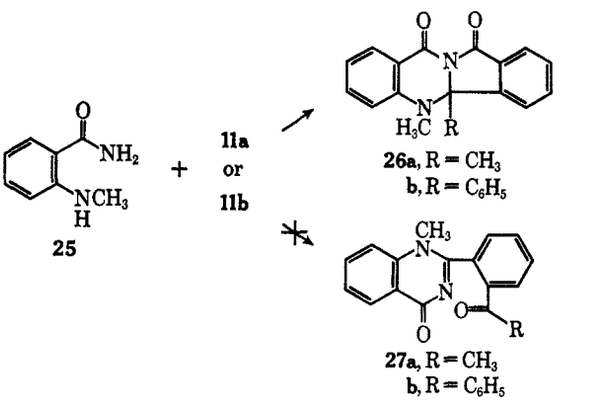
When anthranilamide (**15a**) was treated with the aliphatic acids, 4-oxopentanoic (**13a**), or 3-benzoylpropionic (**13b**), in refluxing dichlorobenzene, condensation occurred to give 3a-methyl- and 3a-phenyl-1,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*]quinazoline-1,5-dione (**22a** and **b**). The homologous 4a-methyl- and 4a-phenyl-1,2,3,4,5,6-hexahydro-4aH-pyrido[1,2-*a*]quinazoline-1,6-diones (**24a** and **b**) were obtained from anthranilamide and 5-oxohexanoic (**23a**) or 4-benzoylbutyric acids (**23b**), respectively. The structural assignment of these compounds is based on spectral data (Table I) and the cyclization pathway established above for anthranilamide with 2-acylbenzoic acids.

(12) Physical measurements have shown that this compound exists mainly in the ring tautomer or pseudo-form **19** but can give rise to products which come from either **19** or the open-chain form 2-benzoylbenzoyl chloride. See ref 9a for some examples.



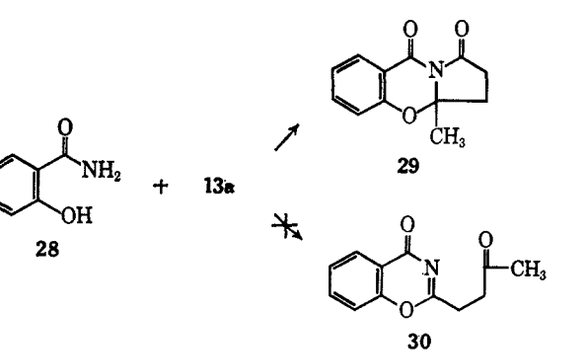
13a, R = CH_3; n = 1 — **22a**, R = CH_3; n = 1
b, R = C_6H_5; n = 1 — **b**, R = C_6H_5; n = 1
23a, R = CH_3; n = 2 — **24a**, R = CH_3; n = 2
b, R = C_6H_5; n = 2 — **b**, R = C_6H_5; n = 2

The reaction of 2-methylaminobenzamide (**25**) with 2-acetyl- or 2-benzoylbenzoic acid gave condensation products analyzing for the expected cyclization products **26a** and **b** or the quinazolones **27a** and **b**. The



latter ring system could form by the condensation of the methylamino and amide nitrogen of 2-methylaminobenzamide with the carboxy group of the starting acids. The spectral evidence is in agreement with assigning these compounds as 5,5a-dimethyl- and 5-methyl-5a-phenyl-5,5a,10-12-tetrahydroisoindolo[1,2-*b*]quinazoline-10,12-dione (**26a** and **b**). The ultraviolet spectrum (Table I) of both compounds are almost identical and quite dissimilar from that reported for a quinazolone system.[13] The similarity of the spectra is in accord with a common chromophoric system being present in both compounds. In the quinazolone structures **27a** and **b** this does not occur since **27a** contains a 2-acetylphenyl chromophore while **27b** contains a 2-benzoylphenyl system. In addition lack of a characteristic C=N infrared band[13,14] rules out the quinazolone system.

From the reaction of salicylamide (**28**) with 4-oxopentanoic acid (**13a**) there was obtained a compound that agreed with the expected product **29** or the benz-



(13) The ultraviolet spectrum of 2-hydroxymethyl- and 2-(1-hydroxethyl)-1-methyl-4(1H)quinazolinone are reported to have maxima at 230, 267–269, 276–277, 306–307, and 314–317 mμ. The carbonyl frequencies are 6.04–6.05 μ, and the C=N bands are 6.23–6.24 μ. M. Uskoković, J. Iacobelli, V. Toome, and W. Wenner, *J. Org. Chem.*, **29**, 582 (1964).

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

TABLE I

PHYSICAL PROPERTIES AND ANALYTICAL DATA[17]

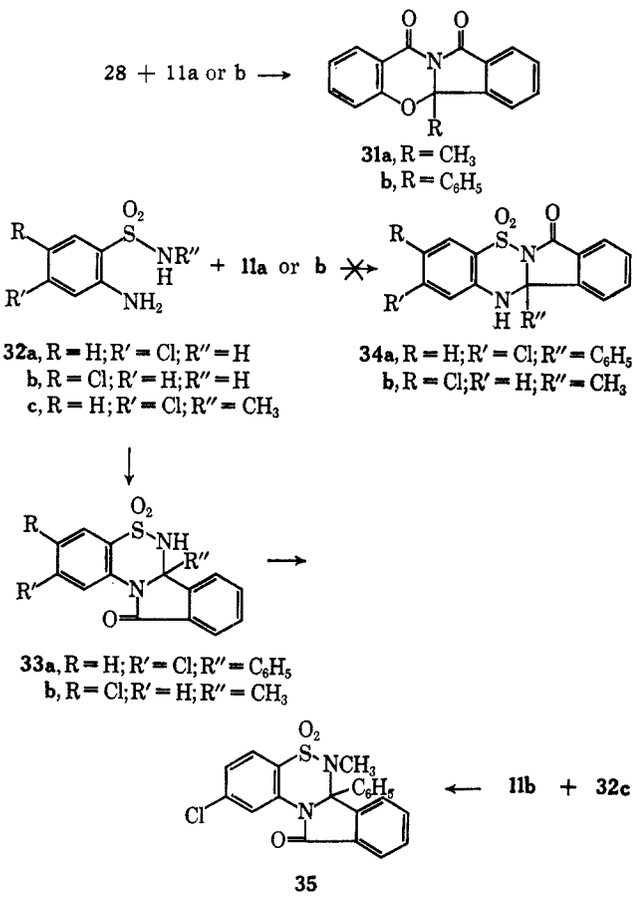
Compd no.	Yield, %	Mp, °C (crystn solvent)[a]	Infrared[b] μ	Infrared[b] Band	Ultraviolet[c] mμ	Ultraviolet[c] ε	Emperical formula	Elemental analysis Calcd., % C	H	N	O	Found, % C	H	N	O
12a	50	149–151[d] (A)	5.77	COO	222	28,270	$C_{16}H_{11}NO_3$[e]	...	...	...	...	...	...	...	...
				CON	243	16,600		...	...	...	...	...	...	...	...
					267	6,860		...	...	...	...	...	...	...	...
					314	5,415		...	...	...	...	...	...	...	...
12b	37	184–184.5[f] (B)	5.77	COO	225	35,330	$C_{21}H_{13}NO_3$	77.1	4.0	4.3	14.7	77.3	4.2	4.4	14.7
				CON	316	5,450									
14a	53	118–120 (B)	5.69	COO	221	24,550	$C_{12}H_{11}NO_3$[g]	66.4	5.1	6.4	22.2	66.8	5.3	6.4	22.1
			5.78	CON	250	8,915									
					306	3,165									
14b	16	136–138 (B)	5.73	COO	224	22,885	$C_{17}H_{13}NO_3$[h]	73.0	4.9	5.0	17.1	72.9	5.0		17.0
			5.83	CON	251	8,070									
					308	2,935									
17a	75	214–215[i] (A)	3.16	NH	221	26,840	$C_{16}H_{12}N_2O_2$[j]	72.7	4.6	10.6	12.1	72.5	4.5	10.7	
			5.82	CON	274	8,800									
			5.98	CONH	316	4,400									
17b	91	>300 (C)	3.17	NH	211	36,080	$C_{21}H_{14}N_2O_2$	77.6	4.0	8.6	9.8	77.3	4.2	8.4	10.0
			5.82	CON	276	7,105									
			5.98	CONH	311	4,950									
18a	54	185–186 (D)	5.84	CON	225	20,745	$C_{17}H_{14}N_2O_2$[k]	73.4	5.1	10.1	11.5	73.6	5.3	10.1	11.4
			6.05	$CONCH_3$	303	5,395									
18b	73	226–227 (E)	5.82	CON	221	34,000	$C_{22}H_{16}N_2O_2$[l]	77.6	4.7	8.2	9.4	77.8	5.1	8.3	9.3
			6.05	$CONCH_3$	306	4,705									
22a	47	179–180 (A)	3.14	NH	232	26,920	$C_{12}H_{12}N_2O_2$[m]	66.7	5.6	13.0	14.8	66.6	5.8	13.3	14.9
			5.79	CON	301	2,755									
			5.94	CONH											
22b	73	>290 (E)	3.14	NH	275	6,490	$C_{17}H_{14}N_2O_2$	73.4	5.1	10.0	11.5	74.0	4.9		11.3
			5.78	CON	310	4,635									
			5.96	CONH											
24a	27	205–206 (A)	3.12	NH	221	22,910	$C_{13}H_{14}N_2O_2$[n]	67.8	6.1	12.2	13.9	68.0	6.4	11.9	13.9
			5.91	CON	245	9,775									
			6.03	CONH	294	2,140									
24b	49	242–243 (A)	3.05	NH	215	24,975	$C_{18}H_{16}N_2O_2$[o]	74.0	5.5	9.6	10.9	73.8	5.8	9.5	11.0
			5.90	CON	245	10,370									
			6.02	CONH	295	2,190									
26a	59	194–195 (E)	5.70	CON (5)	236	32,900	$C_{17}H_{14}N_2O_2$[p]	73.4	5.1	10.1	11.5	73.2	5.4	9.8	11.8
			5.99	CON (6)	253	21,315									
					370	2,415									
26b	40	228–229 (E)	5.70	CON (5)	232	30,220	$C_{22}H_{16}N_2O_2$[q]	77.6	4.7	8.2	9.4	77.4	5.1	8.1	9.9
			6.01	CON (6)	254	20,020									
					369	1,310									
29	52	121 (A)	5.64	CON (5)	250	12,600	$C_{12}H_{11}NO_3$[r]	66.4	5.1	6.4	22.1	66.4	5.3	6.5	22.0
			5.94	CON (6)	310	3,005									
31a	49	169–170 (A)	5.63	CON (5)	255	20,140	$C_{16}H_{11}NO_3$	72.4	4.2	5.3	18.0	72.5	4.2	5.1	17.8
			5.83	CON (6)	311	2,650									
31b	45	214–215 (F)	5.65	CON (5)	254	18,700	$C_{21}H_{13}NO_3$	76.9	4.2	4.3	14.6	76.9	4.0	4.7	14.7
			5.95	CON (6)	308	2,430									
33a	68	>325 (E)	3.13	NH	225	28,450	$C_{20}H_{13}ClN_2O_3S$[s]	60.5	3.3	7.1	12.0	60.1	3.0		
			5.88	CON	277	10,500									
			7.45, 8.48	SO_2											
33b	23	280–283 (E)	3.13	NH	228	26,015	$C_{15}H_{11}ClN_2O_3S$	53.8	3.3	8.4	14.3	54.1	3.6	8.2	14.5
			5.88	CON	274	11,880									
			7.45, 8.48	SO_2											
35	30	247–248 (E)	5.80	CON	226	29,770	$C_{21}H_{15}ClN_2O_3S$	60.5	3.3	7.1	12.1	60.8	3.5	6.8	
			7.47, 8.52	SO_2	280	9,550									

[a] Recrystallization from the following solvents: A, isopropyl alcohol; B, ethanol; C, methanol–water; D, methanol; E, isopropyl alcohol–dimethylformamide; F, ethanol–dimethylformamide. [b] The numbers 5 and 6 found next to the assignment refer to the ring size containing the C=O group. The assignments were based on values reported in ref 9a–c and L. J. Bellamy, "The infrared Spectra of Complex Organic Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958. [c] All spectra were determined in 95% ethanol. [d] Lit.[10] mp 150°. [e] Nmr analysis showed δ 1.91 (s, C–CH_3). [f] Lit.[11] mp 181–182°. [g] Nmr analysis showed 0.77 (s, C–CH_3), 1.81 (A_2B_2, 4 H, CH_2CH_2). [h] Nmr analysis showed a complex multiplet at 2.20–3.00. [i] Lit.[10] mp 215°. [j] Nmr analysis showed 1.81 (s, CH_3). [k] Nmr analysis showed 0.67 (s, C–CH_3), 2.22 (s, N–CH_3). [l] Nmr analysis showed 3.12 (s, N–CH_3). [m] Nmr analysis showed 0.73 (s, C–CH_3), 1.69 (A_2B_2, 4 H, CH_2CH_2). [n] Nmr analysis showed 0.71 (s, C–CH_3), 0.83–1.53 (m, 4 H, 1.81 [t, J = 12.0 cps, 2 H]. [o] Nmr analysis showed 1.88 (m, 2 H), 2.38 (m, 2 H), 2.78 (m, 2 H). [p] Nmr analysis showed 0.85 (s, C–CH_3), 2.12 (s, N–CH_3). [q] Nmr analysis showed 2.17 (s, N–CH_3). [r] Nmr analysis showed 0.75 (s, C–CH_3), 1.68 (m, 4 H, CH_2CH_2). [s] Calcd: Cl, 8.9; S, 8.1. Found: Cl, 8.6; S, 8.0.

oxazinone **30**. The benzoxazine system could form by the condensation of the amino and hydroxyl groups in salicylamide with the carboxyl group of 4-oxopentanoic acid. The nmr of the product gave a methyl singlet at 0.75 ppm and a four-proton complex centered at 1.68 ppm. The high-field position of the methyl signal[15] and the complex signals for the CH_2CH_2 grouping agree with structure **29**. The methyl[16] signal in **30** would be expected in the 2.1–2.4-ppm region. The absence of a C=N[14] band in the infrared spectrum is also in agreement with **29**.

The condensation of salicylamide (**28**) with 2-acetyl- or 2-benzoylbenzoic acid proceeded by the same pathway as 4-oxopentanoic acid to give the related ring derivatives 5a-methyl- and 5a-phenyl-11,12-dihydro-5H-isoindolo[1,2-*b*][1,3]benzoxazine-10,12-dione (**31a** and **b**). Supporting spectral data are listed in Table I.

The reaction of 2-amino-4-chlorobenzenesulfonamide (**32a**) with 2-benzoylbenzoic acid gave 2-chloro-6a-phenyl-6,6a-dihydro-11H-isoindolo[1,2-*c*][1,2,4]benzothiadiazin-11-one 5,5-dioxide (**33a**). By analogy with the cyclization of anthranilamide and 2-benzoylbenzoic



acid the tetracyclic system **34a** has to be considered as an alternate structure for this compound. To distinguish these structures the sodium salt of the condensation product was treated with methyl iodide to give a monomethyl derivative. The same monomethyl derivative was obtained from the condensation of 2-amino-4-chloro-N-methylbenzenesulfonamide (**32c**) with 2-benzoylbenzoic acid. This interconversion establishes the methyl derivative as 2-chloro-6-methyl-6a-phenyl-6,6a-dihydro-11H-isoindolo[1,2-*c*][1,2,4]benzothiadiazin-11-one 5,5-dioxide (**35**) and rules out structure **34a**. Reaction of 2-acetylbenzoic acid with 2-amino-5-chlorobenzenesulfonamide (**32b**) gave 3-chloro-6a-methyl-6,6a-dihydro-11H-isoindolo[1,2-*c*][1,2,4]benzothiadiazin-11-one 5,5-dioxide (**33b**) rather than the tetracyclic system **34b**. Supporting spectral data are given in Table I.

(15) The C–CH_3 group in the closely related compounds **14a**, **22a**, and **24a** also exhibit high-field signals at 0.77, 0.71, and 0.73 ppm, respectively (Table I).

(16) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day Inc., San Francisco, Calif., 1964, p 33.

Experimental Section[17]

General Conditions for Cyclization.—To a flask equipped with a magnetic stirring and heating mantle there was added 0.05–0.10 mol of the anthranilic acid, anthranilamide, salicylamide, or orthanilamide, 0.10–0.05 mol of the oxo acid, 100–250 ml of technical (85%) *o*-dichlorobenzene, and 0.5 mol of *p*-toluenesulfonic acid monohydrate. The flask was fitted with an extractor packed with beryl saddles or glass chips and a reflux condenser. The mixture was then stirred and refluxed until water ceased (6–24 hr) to separate in the condensate. The solvent was removed *in vacuo* on a rotary evaporator, and the residue was crystallized from an appropriate solvent system. If necessary the compound was treated with charcoal during the crystallization procedure.

The compounds prepared by the above procedure together with infrared, ultraviolet, and nuclear magnetic resonance data are given in Table I.

6a-Methyl-5,6,6a,11-tetrahydroisoindolo[2,1-*a*]quinazoline-5,-11-dione (17a).—A mixture of **12a** (1.0 g) and 25 ml of isopropyl alcohol saturated with anhydrous ammonia was stirred at room temperature for 72 hr. The resultant solid was filtered off and recrystallized from isopropyl alcohol to give 0.92 g of **20** as a solid: mp 209–210° (lit.[10] mp 205°); infrared (KBr, μ) 2.98 and 3.13 (NH_2; OH), 5.91 and 6.03 (C=O for CONH, $CONH_2$, and $COCH_3$); ultraviolet, λ_{EtOH}^{inf} 257 mμ (ϵ 5950) and 286 (2820).

Anal. Calcd for $C_{16}H_{14}N_2O_3$: C, 68.1; H, 5.0; N, 9.9; O, 17.0. Found: N, 9.8; O, 17.1.

A solution of **20** (0.60 g) and 10 ml of acetic acid was stirred and refluxed for 6 hr. The solvent was removed *in vacuo* and the residue crystallized from isopropyl alcohol–dimethylformamide gave 0.42 g of solid, mp 213–214°. Comparison of the R_f value and infrared and ultraviolet spectra of this compound with those of **17a** showed them to be identical.

6a-Phenyl-5,6,6a-tetrahydroisoindolo[2,1-*a*]quinazoline-5,11-dione (17b).—A solution of 2-benzoylbenzoic acid chloride[12] (15.0 g, 0.06 mol), anthranilamide (10 g, 0.07 mol), pyridine (5.0 ml), and anhydrous dimethylformamide (100 ml) was maintained at 60° for 48 hr. The solvent was removed *in vacuo* on a rotary evaporator and the residue crystallized from methanol–water. There was obtained 16.3 g (84%) of **17b**, mp >300°. Comparison of the R_f value and the infrared and ultraviolet spectrum of this substance with **17b** prepared from anthranilamide and 2-benzoylbenzoic acid showed them to be identical.

6,6a-Dimethyl-5,6,6a,11-tetrahydroisoindolo[2,1-*a*]quinazoline-5,11-dione (18a).—To a stirred solution of **17a** (5.4 g, 0.02 mol) in anhydrous dimethylformamide (200 ml) there was added 50% sodium hydride–mineral oil dispersion (1.06 g, 0.02 mol as NaH). The solution was maintained at 40° until hydrogen evolution had ceased. After cooling to room temperature the solution was treated with methyl iodide (2.15 g, 0.035 mol) and allowed to stir for about 20 hr at room temperature. The solvent was removed *in vacuo*, and the residue was crystallized from methanol–methylene chloride to give 4.5 g (81%) of solid material, mp 184–186°. Comparison of the mixture melting point, R_f value, and infrared and ultraviolet spectrum with those of **18a** showed them to be identical.

(17) Melting points were determined on a Thomas–Hoover capillary melting point apparatus and have not been corrected. Proton nmr spectra were determined as pyridine solutions on a Varian Associates A-60 spectrometer and are recorded in parts per million (δ) downfield from an internal tetramethylsilane standard. Infrared spectra were determined as potassium bromide pellets using a Perkin-Elmer Model 421 spectrometer or an Infracord. The ultraviolet spectra were obtained on a Beckman Model DB spectrophotometer attached to a Sargent SRL recorder or on a Cary Model 15 spectrophotometer.

2-Chloro-6-methyl-6,6a-dihydro-11H-isoindolo[1,2-c][1,2,4]-benzothiadiazin-11-one 5,5-Dioxide (35).—A mixture of **33a** (3.97 g, 0.01 mol), 50% sodium hydride–mineral oil dispersion (0.72 g, 0.015 mol as NaH), anhydrous dimethylformamide (100 ml), and methyl iodide (2.85 g, 0.02 mol) was allowed to react as in the preparation of **18a**. There was obtained 3.8 g of solid, mp 246–247°. Comparison of the infrared and ultraviolet spectra of this compound with those of **35** showed them to be identical.

Registry No.—**1c**, 65-45-2; **10**, 118-92-3; **12a**, 16240-89-4; **12b**, 801-48-9; **14a**, 16240-91-8; **14b**, 16240-92-9; **17a**, 16240-93-0; **17b**, 16214-87-2; **18a**, 16240-77-0; **18b**, 16214-88-3; **22a**, 16240-78-1; **22b**, 16240-79-2; **24a**, 16240-80-5; **24b**, 16240-94-1; **26a**, 16240-95-2; **26b**, 16240-96-3; **29**, 16240-97-4; **31a**, 16240-98-5; **31b**, 16240-99-6; **33a**, 16214-90-7; **33b**, 16241-00-2; **35**, 16241-01-3.

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Oxidation with Metal Oxides. III. Oxidation of Diamines and Hydrazines with Manganese Dioxide

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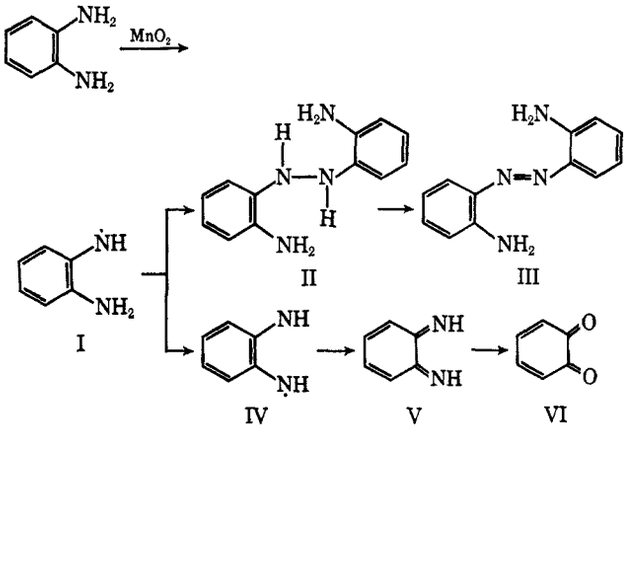
o-Phenylenediamine and *p*-phenylenediamine, on oxidation with manganese dioxide, gave the corresponding diaminoazo compounds. Under similar conditions, 2,2′-diaminobiphenyl gave dibenzopyridazine, whereas *o,o*′-diaminobiphenyl sulfide gave a linear azo compound. The oxidation of N-phenyl-*p*-phenylenediamine and N,N′-diphenyl-*p*-phenylenediamine gave N-phenyl-*p*-benzoquinone monoimine and N,N′-diphenyl-*p*-phenylenediimine, respectively. N,N′-Dibenzenesulfonyl-*p*-benzoquinone imine, benzenesulfonamide, and *p*-benzoquinone were formed from N,N′-dibenzenesulfonyl-*p*-phenylenediamine, whereas, both benzophenone and azobenzene were formed from the oxidation of benzophenone anil. Manganese dioxide oxidation of phenylhydrazine gave biphenyl and azobenzene. *p*-Nitrophenylhydrazine and 2,4,6-trichlorophenylhydrazine gave the corresponding substituted biphenyls, under similar conditions. Oxidation of N-aminopiperidine, N-aminohomopiperidine, N-aminomorpholine, and N,N-diphenylhydrazine gave the corresponding tetrazenes, whereas N,N-dibenzylhydrazine gave mainly bibenzyl.

In previous communications[2,3] we have reported the oxidation of several aldehyde and ketone phenylhydrazones, chalcone phenylhydrazones, pyrazolines, *o*-aminobenzylidine anils, and *o*-hydroxybenzylidine anils, with manganese dioxide. Chalcone phenylhydrazones, for example, give rise to pyrazoles, when oxidized with manganese dioxide in a neutral solvent like benzene. Under similar conditions, *o*-aminobenzylidine anils and *o*-hydroxybenzylidene anils give the corresponding benzimidazoles and benzoxazoles, respectively. The oxidation of aldehyde phenylhydrazones, on the other hand, give a mixture of several oxidative dimers, triazoles and biphenyl, depending on the reaction conditions. During the course of the present investigation, we have examined the oxidation of several aromatic diamines and hydrazines, employing active manganese dioxide.

The oxidation of *o*-phenylenediamine has been reported to give rise to different products, depending on the nature of the oxidizing agent and the reaction conditions. Thus, the oxidation of *o*-phenylenediamine with nickel peroxide[4] or lead tetraacetate[5] gives *cis,cis*-1,4-dicyano-1,3-butadiene, whereas the oxidation with lead peroxide[6] or silver oxide[6] gives a mixture of *o,o*′-diaminoazobenzene and 3,4-diaminophenazine. The formation of these products has been explained in terms of an *o*-quinone imine intermediate. We have examined the oxidation of *o*-phenylenediamine, employing manganese dioxide. When the reaction was carried out in benzene at room temperature, we were able to isolate a 13% yield of *o,o*′-diaminoazobenzene. No other product, including 1,4-dicyano-1,3-butadiene could be obtained from this run. The same reaction has been tried both in refluxing benzene, and also in the absence of any solvent by heating the mixture to around 110°, with a view to detecting the presence of other products which might be formed under these conditions. Considerable amount of ammonia was evolved during these reactions and, from both cases, only *o,o*′-diaminoazobenzene was isolated, but the yields were somewhat higher, compared with that of the room temperature reaction. In a typical run, involving the reaction of *o*-phenylenediamine with manganese dioxide in refluxing benzene, the amount of ammonia liberated was found to be around 21%. A probable mechanism for the formation of *o,o*′-diminoazobenzene is indicated in Scheme I. In this scheme, we assume that manganese dioxide effects the cleavage of one of the N–H bond of the amine

SCHEME I



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