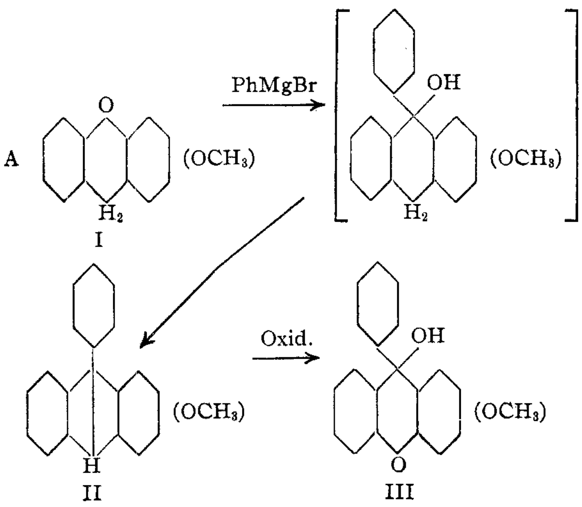
[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF MICHIGAN]

Derivatives of 9-Hydroxy-9-phenylanthrone-10[1]

BY F. F. BLICKE AND R. D. SWISHER[2]

This investigation, the object of which was explained previously,[3] represents a continuation of our study of anthrones.

By the use of reaction scheme A—interaction of 2-, 3- and 4-methoxyanthrone-9,[4] (I), respectively, with phenylmagnesium bromide—the three anthracenes, 2-, 3- and 4-methoxy-9-phenylanthracene (II) and the 2-, 3- and 4-methoxy-9-hydroxy-9-phenylanthrone-10 (III) were prepared.



It was found by Jones and Root[5] that diphenylphthalin and thionyl chloride yield 9-phenyl-9-chloroanthrone-10. Repetition of the experiment by us yielded similar results. In the event that 4′,4″-dimethoxydiphenylphthalin and thionyl chloride behaved in the same manner 3-methoxy-9-chloro-9-(4′-methoxyphenyl)-anthrone-10 should be formed; hydrolysis of the chloro derivative should yield the corresponding 9-hydroxyanthrone. It was found, however, that instead of the anthrone there was formed 2-(4″-methoxybenzoyl)-4′-methoxybenzophenone.[6]

From 4′-methoxydiphenylphthalin and thionyl chloride there was obtained 3-methoxy-9-hydroxy-9-phenylanthrone-10 and 9-hydroxy-9-(4′-methoxyphenyl)-anthrone-10.[7]

It has been shown previously[8] that when 4′,4″-dimethoxy- or 4′,4″-dihydroxydiphenylphthalin is treated with sulfuric acid and the reaction product obtained subjected to oxidation there are produced, respectively, 2-(4″-methoxybenzoyl)-4′-methoxy- and 2-(4″-hydroxybenzoyl)-4′-hydroxybenzophenone. We have discovered that 4′-methoxydiphenylphthalin, when treated with sulfuric acid, is converted into a yellow, amorphous product which yields intense blue-green fluorescent solutions. This material is undoubtedly 2-phenyl-5-(4′-methoxyphenyl)-benzofuran; upon oxidation the latter product was converted into 2-(4″-methoxybenzoyl)-benzophenone. In addition there was obtained from this reaction 9-hydroxy-9-(4′-methoxyphenyl)-anthrone-10.

Experimental Part

Methoxyanthrones.—2-Methoxyanthrone-9 was synthesized by ring closure of 2-(4′-methoxybenzyl)-benzoic acid.[9] Upon oxidation[10] of the anthrone, 2-methoxyanthraquinone was obtained; the latter, when treated with copper and sulfuric acid, yielded 3-methoxyanthrone-9.[11]

In order to obtain 4-methoxyanthrone-9, 900 cc. of sulfuric acid diluted with 300 cc. of water was added to 90 g. of 2-(2′-methoxybenzyl)-benzoic acid.[12] The mixture was heated at 50° for one hour, poured into 8000 cc. of water, the precipitate filtered, washed with sodium bicarbonate solution, then with water and dried; yield 40 g.; m. p. 134–135° after recrystallization from alcohol. *Anal.* Calcd. for $C_{15}H_{12}O_2$: C, 80.32; H, 5.40. Found: C, 80.22; H, 5.43. Upon acidification of the bicarbonate solution 18 g. of unchanged acid was recovered.

1-Methoxyanthraquinone, which was required for another investigation, is obtained readily from 4-methoxyanthrone-9 as shown by the following experiment. To 40 g. of the crude anthrone, dissolved in 300 cc. of acetic

---

[1] This paper represents the third part of a dissertation which has been submitted to the Graduate School by Mr. Swisher in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the University of Michigan.

[2] The Upjohn Company Fellow.

[3] Blicke and Weinkauff, THIS JOURNAL, **54**, 1460 (1932).

[4] 4-Methoxyanthrone-9 may also be called 1-methoxyanthrone-10.

[5] Jones and Root, THIS JOURNAL, **48**, 183 (1926). The initial reaction product, the acid chloride of triphenylmethane-2-carboxylic acid, was also isolated by them.

[6] Ref. 3, p. 1457.

[7] Ref. 3, p. 1461.

[8] Ref. 3, p. 1456.

[9] Barnett, Goodway and Savage, *Ber.*, **64**, 2191 (1931); Ref. 3, p. 1462.

[10] Ref. 3, p. 1463.

[11] Attree and Perkin, *J. Chem. Soc.*, 152 (1931).

[12] This substance was obtained by reduction of 2-(2′-methoxybenzoyl)-benzoic acid with zinc and ammonia water according to the method used by Steyermark and Gardner [THIS JOURNAL, **52**, 4891 (1930)] for the reduction of the corresponding hydroxybenzoylbenzoic acid.

acid, there was added 40 g. of sodium dichromate, dissolved in a small amount of water. The mixture was heated for thirty minutes on a steam-bath, cooled, the precipitate filtered, washed with water and recrystallized from acetic acid; the anthraquinone weighed 32 g. and melted at 165–167°.[13]

2-, 3- and 4-Methoxy-9-phenylanthracene.—To a benzene solution of the required methoxyanthrone there was added three times the calculated amount of phenylmagnesium bromide. The green, fluorescent mixture was heated for one hour, decomposed with ice and hydrochloric acid and subjected to steam distillation.

The crude, oily 2-methoxy compound was treated with ether and the ether solution separated from a small amount of insoluble, crystalline material. Acetic acid was added to the ether solution and after some time 2-methoxy-9-phenylanthracene separated in crystalline form.

The 3-methoxy compound was obtained in crystalline form in the manner described above. The 4-methoxy compound became solid during the steam distillation.

2-, 3- and 4-Methoxy-9-hydroxy-9-phenylanthrone-10.—The preparative procedure is illustrated only in the case of the 3-methoxy compound.

A mixture of 1.5 g. of 3-methoxy-9-phenylanthracene, 1.0 g. of sodium dichromate and 8 cc. of acetic acid was heated for fifteen minutes on a steam-bath. The mixture was cooled, the crystals filtered and washed with water; yield 1.5 g.

2-, 3- and 4-Methoxy-9-methoxy-9-phenylanthrone-10.—Hydrogen chloride was passed into the required methoxy-9-hydroxy-9-phenylanthrone-10, suspended in absolute methyl alcohol. The material soon dissolved. Upon concentration of the solution the 9-methoxy derivative separated in crystalline form.

When the various methoxyphenylanthrones were heated with acetic and hydrobromic acids in attempts to demethylate them, dark colored, resinous, alkali-insoluble substances were obtained.

TABLE I

2-, 3- AND 4-METHOXY-9-PHENYLANTHRACENE ($C_{21}H_{16}O$)

		M. p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
1	2-Methoxy	94–96[a]	88.70	88.30	5.68	5.60
2	3-Methoxy	106–108[b]	88.70	88.52	5.68	5.68
3	4-Methoxy	164–166	88.70	88.58	5.68	5.76
	2-, 3- AND 4-METHOXY-9-HYDROXY-9-PHENYLANTHRONE-10 ($C_{21}H_{16}O_3$)					
4	2-Methoxy	183–185	79.71	79.51	5.10	5.18
5	3-Methoxy	177–178	79.71	79.64	5.10	5.04
6	4-Methoxy	228–230	79.71	79.72	5.10	5.14
	2-, 3- AND 4-METHOXY-9-METHOXY-9-PHENYLANTHRONE-10 ($C_{22}H_{18}O_3$)					
7	2-Methoxy	115–117	79.96	79.63	5.50	5.53
8	3-Methoxy	142–144	79.96	79.96	5.50	5.36
9	4-Methoxy	194–195	79.96	79.98	5.50	5.51

[a] Since 2-methoxyanthrone-9 melts at 96–98° a portion of the latter was mixed with the anthracene; mixed m. p. 70–80°.

[b] 3-Methoxyanthrone-9 melts at 105–106°; a mixture of the anthrone and the anthracene melted at 80–90°.

Compounds 1, 4, 5 and 6 were recrystallized from acetic acid, compound 2 from ethyl alcohol, compounds 7, 8 and 9 from methyl alcohol and compound 3 from a mixture of alcohol and ethyl acetate. Compounds 1, 2 and 3 were colored red by contact with concd. sulfuric acid and yield solutions which possess a blue fluorescence when dissolved in organic solvents. Compounds 4–9 turn blue when moistened with sulfuric acid.

4′,4″-Dimethoxydiphenylphthalin and Thionyl Chloride.—To 17.5 g. of the phthalin there was added 100 cc. of dry benzene and 10 g. of thionyl chloride. After twelve hours the deep red solution was steam distilled, the yellow, granular residue washed with water and digested for several hours with hot sodium carbonate solution to remove unchanged phthalin. The product, 17 g., dissolved in organic solvents to form green fluorescent solutions due, undoubtedly, to the presence of a small amount of 2,5-di-(*p*-methoxyphenyl)-3,4-benzofuran.[14] After recrystallization from alcohol and several recrystallizations from acetic acid 2-(4″-methoxybenzoyl)-4′-methoxybenzophenone was obtained in the form of colorless needles; mixed m. p. 154–157°.

4′-Methoxydiphenylphthalin and Thionyl Chloride.—To 3 g. of the phthalin[15] there was added 75 cc. of benzene and 2 g. of thionyl chloride. After four days the benzene was removed and the residue digested with sodium carbonate solution. The undissolved material became partially crystalline after several days. The crystalline product was washed free from gum with acetone and recrystallized from alcohol. The product was 3-methoxy-9-hydroxy-9-phenylanthrone-10; mixed m. p. 176–178°.

In a second experiment 20 g. of the phthalin was mixed with an equal weight of thionyl chloride. After twelve hours the pasty mass was heated with sodium carbonate solution for several hours and the insoluble portion dissolved in acetone. After several days 4 g. of crystalline 9-hydroxy-9-(4′-methoxyphenyl)-anthrone-10 had separated; mixed m. p. 206–207°.[16]

Treatment of 4′-Methoxydiphenylphthalin with Sulfuric Acid and Subsequent Oxidation of the Product Formed.—A mixture of 20 g. of the phthalin and 25 cc. of concd. sulfuric acid was stirred for five minutes, poured into 800 cc. of water, with vigorous agitation of the mixture, the yellow, amorphous product dissolved in 150 cc. of acetic acid and heated for a few minutes with 10 g. of sodium dichromate, dissolved in 10 cc. of water. The crystalline oxidation product, which separated, weighed 7.5 g. Upon recrystallization from acetic acid 2-(4″-methoxybenzoyl)-benzophenone was obtained; mixed m. p. 132–134°.[17] Careful dilution of the acetic acid filtrate yielded 3.5 g. of crystalline 9-hydroxy-9-(4′-methoxyphenyl)-anthrone-10 which was recrystallized three times from acetic acid; mixed m. p. 205–206°.[18]

---

[13] Graebe and Bernhard [*Ann.*, **349**, 225 (1906)] reported 169.5°.

[14] Ref. 3, p. 1458.

[15] Blicke and Swisher, THIS JOURNAL, **56**, 924 (1934).

[16] Blicke and Weinkauff [*ibid.*, **54**, 1462 (1932)] reported the melting point as 206–207°.

[17] Blicke and Swisher, *ibid.*, **56**, 925 (1934), reported 133–135°.

[18] The recorded m. p. is 206–207° [Blicke and Weinkauff, *ibid.*, **54**, 1461 (1932)].

Summary

The following new compounds have been prepared; 4-methoxyanthrone-9, 2-, 3- and 4- methoxy-9-phenylanthracene, 2-, 3- and 4-methoxy-9-hydroxy-9-phenylanthrone-10 and 2-, 3- and 4-methoxy-9-methoxy-9-phenylanthrone-10. The interaction of 4′-methoxy- and 4′,4″-dimethoxydiphenylphthalin with thionyl chloride and the action of sulfuric acid on 4′-methoxydiphenylphthalin has been investigated.

ANN ARBOR, MICHIGAN RECEIVED APRIL 7, 1934

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF KANSAS]

The Preparation and Hydrolysis of Mono- and Disubstituted Benzoylthioureas[1]

BY IRWIN B. DOUGLASS AND F. B. DAINS

Benzoyl isothiocyanate unites readily with most[2] primary and secondary amines to form substituted benzoylthioureas. From these compounds the benzoyl group can be removed by hydrolysis leaving the corresponding mono- or α,α-disubstituted thiourea. This hydrolysis is readily accomplished in the case of those thioureas derived from primary amines, but less readily with those from secondary.

Since the benzoyl isothiocyanate and acyl thioureas are easily made, the procedure affords a method for the identification of amines and also for the rapid preparation of monosubstituted thioureas.

Experimental

Benzoyl isothiocyanate and thioureas were prepared by a method already described.[3]

Hydrolysis of the monosubstituted benzoylthioureas was accomplished by boiling for five minutes with 10% sodium hydroxide. After neutralizing and making the cooled solutions faintly basic with ammonia the monosubstituted thioureas separated and were removed by filtering.[4] The yields were 80–90%.

MONOSUBSTITUTED BENZOYLTHIOUREAS

No.	Compound, thiourea	Formula	M. p., °C.	N analyses, % Calcd.	N analyses, % Found
I	α-Benzoyl-β-(*o*-chlorophenyl)-	$C_{14}H_{11}ClN_2OS$	145–146	9.64	9.65
II	α-Benzoyl-β-(*p*-chlorophenyl)-	$C_{14}H_{11}ClN_2OS$	140	9.64	9.74
III	α-Benzoyl-β-(2,4-dichlorophenyl)-	$C_{14}H_{10}Cl_2N_2OS$	152–153	8.62	8.41
IV	α-Benzoyl-β-(3,4-dichlorophenyl)-	$C_{14}H_{10}Cl_2N_2OS$	155–156	8.62	8.61
V	α-Benzoyl-β-(2,5-dichlorophenyl)-	$C_{14}H_{10}Cl_2N_2OS$	189–190	8.62	8.75
VI	α-Benzoyl-β-(*p*-bromophenyl)-	$C_{14}H_{11}BrN_2OS$	149–150	8.36	8.50
VII	α-Benzoyl-β-(2,4-dibromophenyl)-	$C_{14}H_{10}Br_2N_2OS$	160–161	6.75	6.75
VIII	α-Benzoyl-β-(2,6-dibromo-4-methylphenyl)-	$C_{15}H_{12}Br_2N_2OS$	195–196	6.55	6.46
IX	α-Benzoyl-β-(2,4,6-tribromophenyl)-	$C_{14}H_9Br_3N_2OS$	206–208	5.68	5.76
X	α-Benzoyl-β-(*p*-iodophenyl)-	$C_{14}H_{11}IN_2OS$	154	7.33	7.35
XI	α-Benzoyl-β-(*p*-fluorophenyl)-	$C_{14}H_{11}FN_2OS$	126–127	10.22	10.14
XII	α-Benzoyl-β-(*o*-nitrophenyl)-[a]	$C_{14}H_{11}N_3O_3S$	138–139	S 10.64	10.91
XIII	α-Benzoyl-β-(*o*-hydroxyphenyl)-	$C_{14}H_{12}N_2O_2S$	216	10.30	10.17
XIV	α-Benzoyl-β-(*p*-hydroxyphenyl)-	$C_{14}H_{12}N_2O_2S$	171–172	10.30	10.28
XV	(β-Benzoylthioureido)-benzoic acid	$C_{15}H_{12}N_2O_3S$	223 dec.	9.33	9.36

[a] Neither this compound nor the corresponding *m*-nitro derivative underwent satisfactory hydrolysis.

DISUBSTITUTED BENZOYLTHIOUREAS

No.	Compound, thiourea	Formula	M. p., °C.	N analyses, % . Calcd.	N analyses, % . Found
XVI	β-Benzoyl-α-methyl-α-phenyl-	$C_{15}H_{14}ON_2S$	138–139	10.37	10.44
XVII	β-Benzoyl-α-benzyl-α-phenyl-	$C_{21}H_{18}N_2OS$	156–157	8.09	8.00
XVIII	β-Benzoyl-α-methyl-α-(*p*-tolyl)-	$C_{16}H_{16}N_2OS$	124–125	9.86	9.93
XIX	β-Benzoyl-α-methyl-α-(*m*-tolyl)-	$C_{16}H_{16}N_2OS$	133–134	9.86	9.82
XX	β-Benzoyl-α-methyl-α-(*o*-tolyl)-	$C_{16}H_{16}N_2OS$	119–120	9.86	9.82
XXI	β-Benzoyl-α-ethyl-α-(*p*-tolyl)-	$C_{17}H_{18}N_2OS$	136	9.40	9.43

Disubstituted benzoylthioureas were more difficult to

---

[1] From part of a thesis presented by Irwin B. Douglass in partial fulfilment of the requirements for the Ph.D. degree.

[2] Benzoyl isothiocyanate could not be induced to react with 2,4-dinitroaniline, 2,4,6-trinitroaniline, or 2,6-dibromo-4-nitroaniline.

[3] Douglass and Dains, THIS JOURNAL, **56**, 719 (1934).

[4] This investigation was confined to thioureas derived from aryl amines. The recovery of monosubstituted alkylthioureas is less satisfactory.