Phenalenones. IV (1). Heterocycles from 3-Hydroxyphenalenone (I)

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3-Hydroxyphenalenone reacts with *o*-disubstituted benzenes (substituents: NH_2, OH, CH_2OH and SH), aliphatic and aromatic aldehydes to give the various heterocyclic compounds which are fused with phenalene ring. These reactions resemble those of 1,3-cyclohexanediones in many respects.

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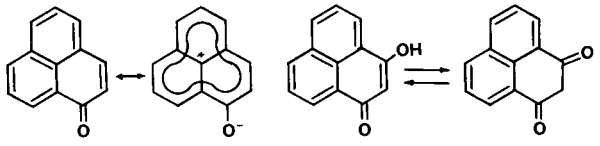
Phenalenone **1** has received wide attention because of its specific properties as a non-benzenoid aromatic compound (2). Not only the aromatic character of the ring bearing the carbonyl group but also the high basicity and large dipole moment are believed to be due to the contribution of the pi-electron delocalized structure **1b**. Therefore, 3-hydroxyphenalenone **2** is expected to have properties similar to a phenol. This assumption is probably correct since **2** undergoes electrophilic substitutions, such as halogenations (3), nitration (4) and coupling with aryl diazonium salts (3), at the 2-position. However,

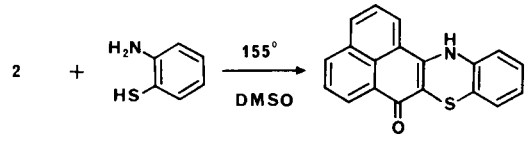


1a **1b** **2**

2 can be considered to be a naphtho derivative of 3-hydroxycyclohexenone or 1,3-cyclohexanedione. In fact, 2 resembles the alicyclic diketone in many respects; that is, **2** is easily dissolved in weak bases such as ammonium hydroxide, and its coloration with ferric chloride resembles that of cyclohexanediones rather than phenols. In addition to this, the existence of keto-enol tautomerism of **2** was suggested based on infra-red spectroscopy (3).

In this paper, further evidences for the similarity of **2** to the cyclohexanediones will be presented based on the synthesis of various heterocyclic compounds from **2**.

The first example is a thiazine ring formation. Miyano, *et al.* (5), reported that cyclic 1,3-diones react with *o*-aminothiophenol to give 3,4-dihydro-1*H*-phenothiazin-(10*H*)ones. Applying this reaction to **2** we obtained 7*H*-naphtho[1,8-*ab*]phenothiazin-7-one **3** in 55% yield.



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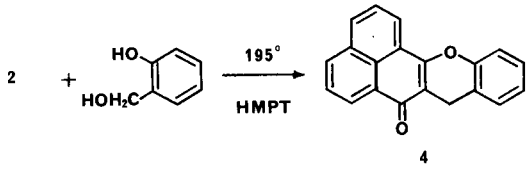

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Application of Yetes' pyran synthesis (6) to **2** was also successful. When **2** was heated with *o*-hydroxybenzyl alcohol in hexamethylphosphoric triamide (HMPT), 7*H*,8*H*-benzo[*b*]phenaleno[2,1-*e*]pyran-7-one **4** was obtained in 64% yield.

These two results indicate that the ring formations take place through attack of the amino and the alcohol hydroxyl group at the 2- and 3-positions of phenalene ring, respectively. Consequently, a new heterocyclic ring formation was expected for the reaction of **2** with *o*-aminobenzyl alcohol. When the reaction was carried out in dimethyl sulfoxide (DMSO) at 155°, 8,13-dihydro-7*H*-phenaleno-[1,2-*b*]quinolin-7-one **5** was obtained as expected. The same reaction carried out in HMPT at 195°, on the contrary, gave the dihydroquinolinone **5** in rather low yield; the main product was 7*H*-phenaleno[1,2-*b*]quinolin-7-one **6**. This difference can be attributed to the dehydrogenation of the dihydro compound **5** at higher temperature. Owing to its relatively low stability, **5** was converted partly to **6** during purifications by chromatography on alumina or by vacuum sublimation. Dehydrogenation of **5** with palladium charcoal catalyst in boiling trimethylbenzene afforded **6** in quantitative yield.

A similar reaction with 3-aminopropanol instead of *o*-aminobenzyl alcohol resulted in the formation of three different types of products **7-9a**; the expected ring closure could not be attained. The difference in pattern can be explained in terms of the flexibility of the carbon chain, which should diminish the chance of ring closure. More remarkable is the formation of bis(3-hydroxy-1-oxo-2-phenalenyl)methane **9a**. The methylene group of **9a** was shown to arise from the formyl group of the solvent *N*,*N*-dimethylformamide. Details of this reaction will be reported in the near future (7). Another interesting feature is that the two phenalene rings were connected with the

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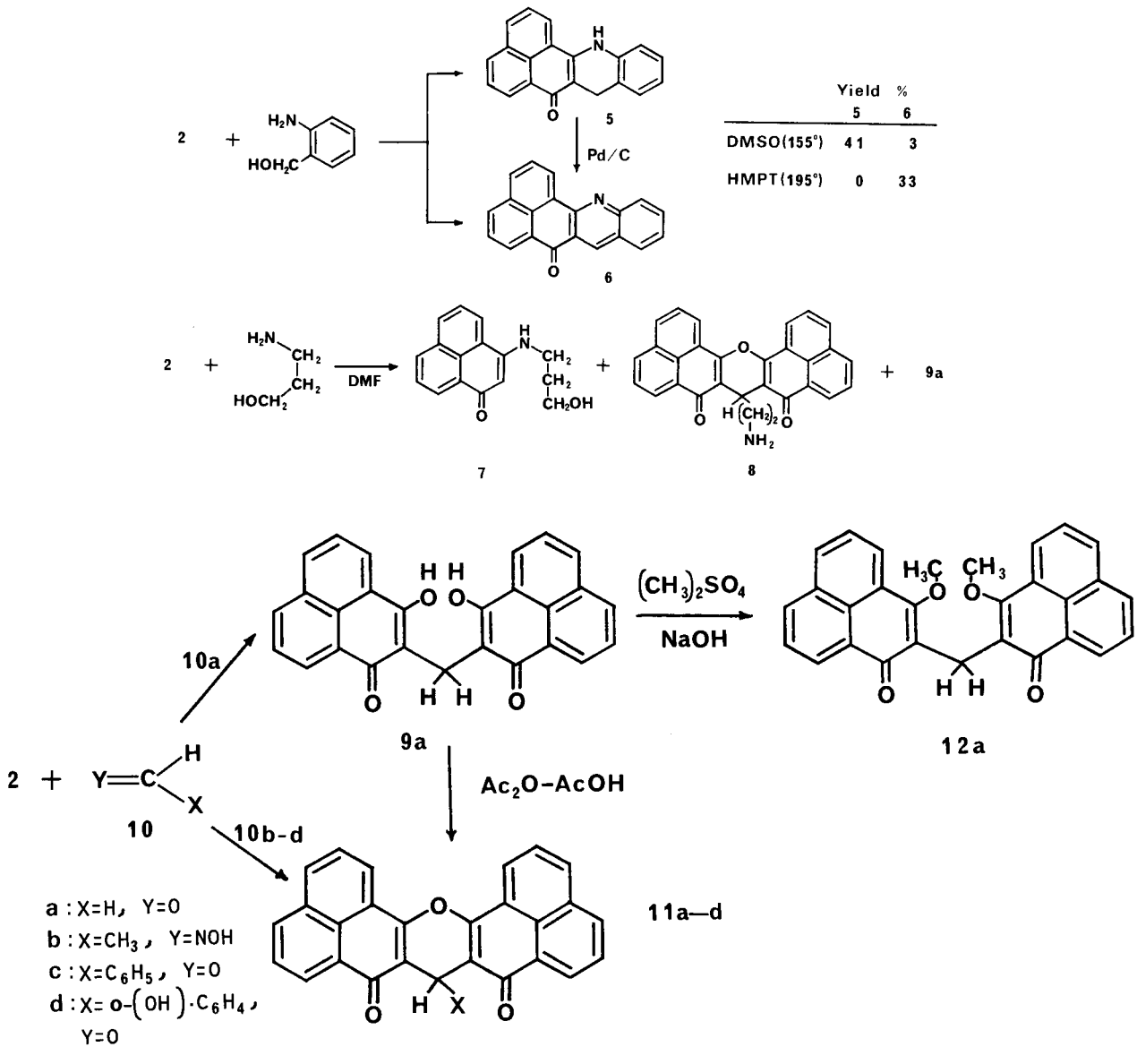

terminal carbon atom of the aliphatic amine in **8**. Although there is no conclusive evidence as to the reaction mechanism, it is probable that the phenalene rings were connected by 3-aminopropanal, which arose from the aminoalcohol by oxidation or dehydrogenation. Aldehydes react readily with **2** to give diphenalenylmethane derivatives, as described below.

It is well known that the dimedone is particularly useful for isolation and identification of small amounts of aldehydes (8). Analogously, **2** reacted with aliphatic and aromatic aldehydes, and also with acetaldoxime to give diphenalenylmethane or pyran derivatives. Bis(3-hydroxy-1-oxo-2-phenalenyl)methane **9a** was converted to 7*H*,8*H*,9*H*-diphenaleno[1,2-*b*,2',1'-*e*]pyran-7,9-dione **11a** by boiling in acetic anhydride-acetic acid mixture. Similar pyran derivatives **11b,c,d** were directly obtained in the reactions of **2** with aromatic aldehydes, **10c,d**, and acetaldoxime **10b**.

EXPERIMENTAL

All melting points were determined on a Yanagimoto hot-stage type apparatus and were uncorrected. The spectra obtained were recorded on a Jasco IRA-1 spectrophotometer (ir), a Jeol JNM-PS-100 and Hitachi R-600 spectrometers (nmr), an Hitachi EPS-3T spectrophotometer (uv) and an Hitachi RMU-7M mass spectrometer.

7*H*-Naphtho[1,8-*ab*]phenothiazin-7-one (**3**).

A solution of **2** (5.85 g) and *o*-aminobenzenethiol (6.30 g) in 15 ml of DMSO was heated at 155° for 2 hours. A filtered precipitate was treated with a sodium carbonate solution (5%) and washed with water and dried. Recrystallization from DMF gave 4.95 g (55%) of deep blue crystals, m.p. 286-295°; ir (potassium bromide): 3320 (N-H), 1636 (C=O); nmr (DMSO-d_6): δ 6.81-7.05 (4H, m), 7.70-7.85 (2H, t), 8.23-8.39 (3H, m), 8.55 (1H, dd, J = 7.8 and 1.0 Hz, 6-H), 8.92 (1H, broad, N-H); uv (dioxane): nm, ε 243

Table I

Compound No.	Yield %	M.p. °C	Ir cm^{-1} (potassium bromide)	Uv nm, ε (dichloroethane)	Nmr ppm (DMSO-d_6)	Ms m/e (relative intensities)	Formula	Elemental Analysis Calcd. C	Calcd. H	Found C	Found H
9a	53	darkens at 314-315	2930, 2880, 2800-2560 br, 1643	239.5 (52,500) 257.5 sh (24,900), 265.5 sh (19,500), 340 sh (22,000), 357.5 (23,000), 372 sh (21,700), 410 (8,800)		404.1053 (M^+, 42), 221 (3), 209 (20), 208 (100), 197 (17)	$C_{27}H_{16}O_4$	80.19	3.99	79.91	3.79
11a	50	>330	2920, 2870, 1672, 1648, 1636	231.5 (30,600), 239 (30,900), 251 (30,600), 347 (18,500), 359 (19,700), 364 sh (16,900), 384 sh (10,300)		386 (M^+, 100), 385 (55), 357 (29), 329 (5), 300 (18)	$C_{27}H_{14}O_3$	83.93	3.65	83.76	3.61
11b	10	308.5-314	3000, 2970, 2950, 2930, 1665, 1635	231.5 (38,800), 237.5 sh (36,800), 248 sh (32,220), 346.5 (25,600), 362 sh (23,200)	1.46 (3H, d, 6.6), 4.40 (1H, q, 6.6), 7.80-8.07 (4H, m), 8.33-8.85 (8H, m)	400 (M^+, 10), 399 (13), 386 (31), 385 (100)	$C_{28}H_{16}O_3$	83.98	4.03	83.82	3.98
11c	18	>330	1660, 1636	230 sh (38,800), 239.5 (37,300), 250.5 sh (35,000), 346 (23,400), 363 (22,700)	5.51 (1H, s), 7.06-7.76 (5H, m), 7.83-7.99 (4H, m), 8.31-8.78 (6H, m), 8.82 (2H, d, 7.4)	462 (M^+, 66), 385 (100), 300 (10)	$C_{33}H_{18}O_3$	85.70	3.92	85.64	3.90
11d	33	295-297	3020, 1638	241 (48,400), 265 sh (19,800), 355 (22,000), 373 sh (19,500), 386 (18,600)	5.94 (1H, s), 7.06-7.41 (4H, m), 7.63-7.96 (4H, m), 8.19-8.66 (8H, m)	478 (M^+, 26), 385 (7), 284 (35), 283 (100)	$C_{33}H_{18}O_4$	82.83	3.79	82.80	3.69
12a	29	239.5-241.6	2935, 2840, 1635	230.2 (35,200), 238.2 (34,600), 253.2 (37,500), 329.5 (12,900), 343.5 (13,500), 357 (17,700), 397 (14,000)	4.01 (6H, s), 4.20 (2H, s), 7.23-8.11 (10H, m), 8.54 (2H, d)	432 (M^+, 36), 417 (100), 401 (15), 386 (36), 385 (38), 373 (6), 357 (14)	$C_{29}H_{20}O_4$	80.54	4.66	80.61	4.68

(38,300), 302.5 (10,800), 352 (14,500), 369 (14,400), 387 sh (11,200), 611 (1,000); ms: m/e (relative intensities) 301 (M^+, 100), 273 (41), 241 (12).

Anal. Calcd. for $C_{19}H_{11}NOS$: C, 75.72; H, 3.68; N, 4.65. Found: C, 75.70; H, 3.62; N, 4.72.

7*H*,8*H*-Benzo[*b*]phenaleno[2,1-*e*]pyran-7-one (**4**).

o-Hydroxybenzyl alcohol (1.24 g) and **2** (2.00 g) were heated in 5 ml of HMPT at 195° for 3 hours. The reaction mixture was taken up in 200 ml of chloroform, and a small amount of dark powder was filtered. The chloroform solution was shaken with 200 ml of hydrochloric acid (15%), then with a sodium hydroxide solution (5%) and finally with water. From the dried solution, 1.15 g (64%) of brown crystals was obtained by concentration of the volume of solution to 15 ml, m.p. 169-185°. An analytical sample was sublimed at 150° (10^{-4} torr), and recrystallized from benzene, giving pale yellow crystals, m.p. 197-198°; ir (potassium bromide): 2890 (CH_2), 1638 (C=O); nmr (DMSO-d_6): δ 3.80 (2H, s, CH_2), 7.12-7.41 (4H, m, ring protons at positions 9-12), 7.71-7.91 (2H, m, ring protons), 8.23-8.51 (4H, m, ring protons); uv (ethanol): nm, ε 242 (28,500), 256 sh (12,300), 346 (13,800), 361 (13,600); ms: m/e (relative intensities) 284 (M^+, 100), 283 (75), 256 (44), 226 (17).

Anal. Calcd. for $C_{20}H_{12}O_2$: C, 84.49; H, 4.25. Found: C, 84.38; H, 4.18.

8,13-Dihydro-7*H*-phenaleno[1,2-*b*]quinolin-7-one (**5**).

A crude product (1.30 g) was obtained as a reddish brown powder by heating **2** (1.00 g) and *o*-aminobenzyl alcohol (0.95 g) in 2.5 ml of DMSO at 155° for an hour. Pure **5** (600 mg, 44%) from chloroform gave reddish purple crystals of m.p. 208-209°; ir (potassium bromide): 3305 (N-H), 2880 (CH_2), 1625 (C=O); nmr (DMSO-d_6): δ 3.92 (2H, s, CH_2), 6.96-7.24 (4H, m, ring protons 1-H - 4-H), 7.76-8.19 (3H, m, ring protons), 8.27-9.27 (3H, m, ring protons); uv (ethanol): nm, ε 245.5 (36,800), 248.5 (37,700), 305 sh (9,700), 321 (12,600), 337 sh (11,300), 345 (12,400), 360 (12,000), 373 sh (9,900), 391 sh (8,400), 504 (3,100); ms: m/e (relative intensities) 283 (M^+, 100), 282 (102), 281 (58), 254 (37).

Anal. Calcd. for $C_{20}H_{13}NO$: C, 84.78; H, 4.63; N, 4.94. Found: C, 84.66; H, 4.68; N, 4.79.

7*H*-Phenaleno[1,2-*b*]quinolin-7-one (**6**).

A mixture of **2** (2.00 g), *o*-aminobenzyl alcohol (1.50 g) and HMPT (5 ml) was heated at 195° for 30 minutes. A reddish brown solid, which mainly consists of **5** was removed, and the filtrate was treated with hydrochloric acid (5%). The solid which precipitated was digested with ammonium hydroxide and washed with water. Recrystallization from ethanol gave 950 mg (33%) of **6** as yellow needles, m.p. 223-224°; ir (potassium bromide): 1663, 1623; nmr (pyridine-d_5): δ 7.75-8.43 (8H, m, ring protons), 8.87 (1H, dd, J = 7.4 and 1.4 Hz), 9.40 (1H, s, 8-H), 9.50 (1H, dd, J = 7.4 and 1.4 Hz, 6-H); uv (ethanol): nm, ε 283.5 (58,600), 245.5 (57,400), 257 (34,900), 321.5 (30,300), 338.5 sh (18,300), 360 (16,300), 397 (5,800), 416 (5,800); ms: m/e (relative intensities) 281 (M^+,

100), 253 (20).

Anal. Calcd. for $C_{20}H_{11}NO$: C, 85.39; H, 3.94; N, 4.98. Found: C, 85.30; H, 3.89; N, 4.79.

Dehydrogenation of **5** (100 mg) by boiling with 5% palladium charcoal (10 mg) in 1,3,4-trimethylbenzene (40 ml) for 2 hours gave **6** (98%).

Reaction of **2** with 3-Aminopropanol.

A mixture of **2** (2.00 g), 3-aminopropanol (0.75 g) and DMF (5 ml) was stirred at 155° for 3.5 hours. The reaction mixture was treated with a sodium carbonate solution (5%) and extracted by chloroform. A small amount of insoluble part was removed by filtration, and the solvent was evaporated to dryness. The residual solid was refluxed with 100 ml of ethanol and filtered while hot. From the ethanol insoluble portion, 100 mg of bis(3-hydroxy-1-oxo-2-phenalenyl)methane **9a** was obtained. The ethanol solution was concentrated to 15 ml to give 400 mg of crude 8-(2-aminoethyl)-7*H*,8*H*,9*H*-diphenaleno[1,2-*b*:2,1-*e*]pyran-7,9-dione **8**. Vacuum sublimation (200°/10^{-6} torr) and subsequent recrystallization from chloroform afforded yellow crystals. This compound darkened at 295-315° without melting; ir (potassium bromide): 3320, 3240 (NH_2), 1640 (C=O), 770 (NH_2); uv (dichloroethane): nm, ϵ 237 (37,900), 321 (25,200), 442 sh (4,100); ms: m/e (relative intensities) 429 (M^+, 100), 401 (7), 400 (7), 384 (4), 383 (20).

Anal. Calcd. for $C_{29}H_{19}NO_3$: C, 81.10; H, 4.46; N, 3.26. Found: C, 81.12; H, 4.37; N, 3.26.

Further concentration of the mother liquor of *9* gave 180 mg of 3-(3-hydroxypropylamino)phenalen-1-one **7**. The filtrate was evaporated to dryness, and chromatographed on alumina. Three fractions were separated by chloroform elution. From the first and third fractions, 120 mg of **7** and trace amount of **9** were isolated, respectively. Two crops of **7** were combined and recrystallized from chloroform to give pure **7** as yellow needles, m.p. 174-174.8°; ir (potassium bromide): 3300 (N-H), 3280 (O-H), 2950, 2900 (CH_2), 1639 (C=O); nmr (DMSO-d_6): δ 1.87 (2H, t, -O-CH_2-), 3.27-3.60 (4H, m, -CH_2-CH_2-), 4.64 (1H, broad, NH), 5.60 (1H, s, 2-H), 7.50-7.69 (2H, m, ring protons), 8.04-8.31 (4H, m, ring protons); uv (ethanol): nm, ϵ 257 (49,300), 324.5 sh (9,600), 340 (16,900), 354 sh (14,000), 368 sh (12,200), 435 (450); ms: m/e (relative intensities) 253 (M^+, 21), 236 (1), 209 (66), 208 (100), 196 (21).

Anal. Calcd. for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.78; H, 5.90; N, 5.38.

Reactions of **2** with Aldehydes and Acetaldoxime.

Reactions of aldehydes or acetaldoxime (2.2 mmoles) with **2** (2.0 mmoles) in DMSO (5 ml) were carried out at 155° for 3 hours under nitrogen. After removal of **2** by treatment with a sodium carbonate solution, the products were purified by vacuum sublimation and recrystallization. The results are listed in Table I.

7*H*,8*H*,9*H*-Diphenaleno[1,2-*b*:2′,1′-*e*]pyran-7,9-dione (**11a**).

The diphenalenlylmethane **9a** (20 mg) was refluxed in an acetic anhydride-acetic acid mixture (1:1, 100 ml) for 2 hours.

Bis(3-methoxy-1-oxo-2-phenalenyl)methane (**12a**).

A mixture of **9a** (1.00 g), 50% sodium hydroxide (0.21 ml) and DMSO (90 ml) was warmed at 60° to giva a clear red solution. This solution was cooled to room temperature, added to dimethyl sulfate (0.63 ml) portionwise, and stirred for one hour. Then additional sodium hydroxide solution (0.10 ml) and dimethyl sulfate (0.30 ml) were added and the mixture was stirred for 18 hours. The reaction mixture was poured into ammonium hydroxide; 0.87 g of precipitate was recrystallized twice from acetone to give 0.31 g of **12a**.

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(4) Russian investigators reported that nitration of **2** gave 3-hydroxy-2-nitrophenalenone [E. Gudriniece, E. Dreimanis and G. Vanags, *J. Gen. Chem. USSR*, **26**, 289 (1956); *Chem. Abstr.*, **50**, 13857 (1956); E. Gudriniece and E. Karlsone, *Latv. PSR Zinat. Akad. Vestis, Kim, Ser.*, 339 (1963); *Chem. Abstr.*, **60**, 1668 (1964)]. However, Eistert, *et al.* (3), obtained naphthalic anhydride solely, instead of the nitro compound.

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