methylamino)benzohiazole[4] (8) in 39.7% yield in addition to 3-(dimethylcarbamoyl)benzothiazolin-2-one (11) in 60.2% yield. The structure of 11 is supported by elemental analysis, infrared spectroscopy, nmr and mass spectrum. Evidence for the structural assignment of 11 includes C=O absorption at 1755 cm^{-1} in the infrared spectrum. The nmr spectrum contains two unsplit methyl signals at 3.05 and 3.15 ppm, whereas the aromatic region displays a multiplet at 7.1 ppm. In the mass spectrum of 11, the molecular ion is observed at *m/e* 222 (M^+). The initial fragmentation pattern is characterized by the loss from the parent ion of a carbonyl (C=O) and dimethylcarbamoyl group, $(CH_3)_2NCO$ (base peak), to give *m/e* 122.

The reaction of urea 5 with phosgene follows two major pathways. Initial attack by the urea oxygen (path a), similar to that which occurs in the anilide–carbonyl chloride reaction, gives chloroformamidine 7, as an intermediate *via* 6, which cyclocondenses to give 2-(dimethylamino)benzothiazole (8). Alternately, attack of phosgene by the urea nitrogen atom (N^3) affords the intermediate allophanoyl chloride 10 by way of 9; loss of methyl chloride from 10 gives 11 directly. The formation of intermediates analogous to 7 and 10 is well documented in the literature.[1,5]

Experimental Section

2′-(Methylthio)acetanilide (1a). This compound was prepared in 90.1% yield from 2-aminothioanisole and acetyl chloride in tetrahydrofuran in the presence of triethylamine as acceptor for hydrogen chloride; colorless crystalline solid, mp 111–113° (lit.[6] mp 114–115°).

4′-Chloro-2′-(methylthio)cyclopropanecarboxanilide (1b). This compound was prepared in 95% yield from 2-amino-5-chlorothioanisole[7] and cyclopropanecarbonyl chloride as outlined above for 1a: mp 117–119°; ir (KBr) 3260 (NH) and 1655 cm^{-1} (C=O); nmr ($CDCl_3$) δ 0.7–1.8 (5, m, cyclopropyl), 2.4 (3, s, CH_3), and 7–9 ppm (3, m, C_6H_3); mass spectrum (70 eV) *m/e* 243 (M^+), 196, 194 ($M^+ - CH_3S$), 175, 173 ($M^+ - C_3H_5CO$), 69 (C_3H_5CO), 41 (C_3H_5).

Anal. Calcd for $C_{11}H_{12}ClNOS$: C, 54.7; H, 5.0; N, 5.8. Found: C, 54.5; H, 5.4; N, 5.6.

2′-(Methylthio)-2,2,2-trifluoroacetanilide (1c). This compound was prepared analogously in 89.4% yield from 2-aminothioanisole and trifluoroacetyl chloride in the presence of 1 molar equiv of triethylamine: mp 45–47°; ir (KBr) 3220 (NH) and 1740 cm^{-1} (C=O); nmr (DMSO-d_6) δ 2.4 (3, s, CH_3), 7.3 (4, q, C_6H_4), and 11.0 ppm (1, s, NH).

Anal. Calcd for $C_9H_8F_3NOS$: C, 46.0; H, 3.4; N, 6.0. Found: C, 45.7; H, 3.3; N, 5.7.

2-Methylbenzothiazole Hydrochloride and 2-Methylbenzothiazole (4a). To a stirred solution of 13.5 g (0.075 mol) of 1a in 200 ml of *p*-dioxane was added dropwise a solution of 30.0 g (0.30 mol) of phosgene (*caution: highly toxic*) in 50 ml of *p*-dioxane. The resulting yellow solution was heated to reflux (80–85°). After 3.5 hr, a sample was withdrawn, cooled, filtered, and dried to give a crystalline solid: mp 180–183°; ir (KBr) 2600 cm^{-1} (HX-salt); nmr (DMSO-d_6) δ 2.9 (3, m, CH_3), 7–8.2 (4, m, aromatic H), and 12.2 ppm (1, m, HCl); mass spectrum (70 eV) *m/e* 149 (M^+ – HCl, base peak), 121, 117 ($M^+ - S$), 108 ($C_6H_4S^+$), 82, 75, 69, 63, 50, 45, 39.

Anal. Calcd for C_8H_8ClNS: C, 51.8; H, 4.3; N, 7.5; Cl, 19.1. Found: C, 51.4; H, 4.2; N, 7.3; Cl, 19.1.

After a heating period of 8 hr at 80–98°, thin layer chromatography indicated the complete disappearance of starting material, and hydrogen chloride evolution had ceased. The reaction mixture was concentrated under reduced pressure, washed with water, dissolved in ether, dried ($MgSO_4$), concentrated, and distilled to give 9.5 g (86%) of a colorless liquid: bp 128–130° (35 mm); bp 236° (760 mm) (lit.[8] bp 238°); nmr ($CDCl_3$) δ 2.8 (3, s, CH_3), and 7–8 ppm (4, m, aromatic H).

Anal. Calcd for C_8H_7NS: C, 64.4; H, 4.7; N, 9.4. Found: C, 64.4; H, 4.7; N, 9.4.

6-Chloro-2-cyclopropylbenzothiazole (4b). A solution of 19.0 g (0.079 mol) of 1b in 200 ml of ethyl acetate containing 30.0 g (0.30 mol) of phosgene was refluxed at 50–55° for 8 hr. In order to contain the low-boiling phosgene in the reaction flask, the reflux condenser was topped with a Dry Ice–acetone condenser. The solvent and excess phosgene were removed by distillation leaving a residue which crystallized from ethyl acetate to give 2.0 g (10%) of 4b, a colorless crystalline solid: mp 65–67°; nmr ($CDCl_3$) δ 1.2 [4, s, $(CH_2)_2$ cyclopropyl], 2.4 (1, m, CH cyclopropyl), and 7–8 ppm (3, m, CH aromatic); mass spectrum (70 eV) *m/e* 211, 209 (M^+, base peak), 210, 208 (M^+ – H), 196, 194, 185, 183 (M^+ – HCl), 142 ($ClC_6H_4S^+$), 107, 92, 75, 69, 63, 45, 41, 39; ir (KBr) no carbonyl bands, mostly phenyl bands.

Anal. Calcd for $C_{10}H_8ClNS$: C, 57.3; H, 3.8; N, 6.7. Found: C, 57.4; H, 3.9; N, 6.6.

1,1-Dimethyl-3-(2′-(methylthio)phenyl)urea (5). Reaction of 2-(methylthio)phenyl isocyanate with dimethylamine in benzene afforded 5 in 97% yield, mp 98–100°.

Anal. Calcd for $C_{10}H_{14}N_2OS$: N, 13.3; S, 15.3. Found: N, 13.5; S, 15.5.

2-(Dimethylamino)benzothiazole (8) and 3-(Dimethylcarbamoyl)benzothiazolin-2(3*H*)-one (11). A solution of 15.7 g (0.075 mol) of 5 in 200 ml of *p*-dioxane containing 30.0 g (0.30 mol) of phosgene was refluxed at 70° with stirring. After approximately 15 min, a colorless solid began to precipitate. After 12 hr, the mixture was cooled to 20° and filtered to give 6.4 g (39.7%) of the hydrochloride of 8: mp 234–235°; ir (KBr) 3500, 3420 (NH or OH), 2800 cm^{-1} (bonded OH, NH, HX); nmr (DMSO-d_6, TFA-d) δ 3.6 [6, s, $(CH_3)_2$], and 7.5 ppm (4, m, aromatic H).

Anal. Calcd for $C_9H_{11}ClN_2S$: C, 50.3; H, 5.2; Cl, 16.5; N, 13.1. Found: C, 47.9; H, 5.4; Cl, 16.0; N, 12.5.

The above salt was dissolved in 50 ml of water and the solution was made basic by addition of aqueous sodium hydroxide to give 6.0 g (37.5%) of 8, a colorless crystalline solid: mp 82–83° and 88–90° (lit.[4] mp 87°); ir (KBr) bands at 1560, 1570, and 1605 cm^{-1} (aromatic H); nmr ($CDCl_3$) δ 3.2 [6, s, $(CH_3)_2$], and 6.8–7.7 ppm (4, m, aromatic H).

Anal. Calcd for $C_9H_{10}N_2S$: C, 60.7; H, 5.6; N, 15.7. Found: C, 60.6; H, 5.7; N, 15.8.

The original filtrate was concentrated to dryness and triturated with hexane to give 10.0 g (60.2%) of 11, as a colorless crystalline solid: mp 80–82°; ir (KBr) 1600 (C=) and 1755 cm^{-1} (C=O); nmr ($CDCl_3$) δ 3.05 and 3.15 [6, s, $(CH_3)_2$], and 7.1 ppm (4, m, aromatic H); mass spectrum (70 eV) *m/e* 222 (M^+), 150 [$M^+ - (CH_3)_2NCO$], 122 (C_6H_4NS), 106, 95, 78, 72 [$(CH_3)_2NCO$, base peak], 69, 56, 51, 45, 44, 42, 38, 15.

Anal. Calcd for $C_{10}H_{10}N_2SO_2$: C, 54.1; H, 4.5; N, 12.6. Found: C, 53.8; H, 4.5; N, 12.3.

Registry No.—1a, 6310-41-4; 1b, 52260-23-8; 1c, 52260-24-9; 4a, 120-75-2; 4a HCl, 52260-25-0; 4b, 52260-26-1; 5, 52260-27-2; 8, 4074-74-2; 8 HCl, 52260-28-3; 11, 52260-29-4; 2-aminothioanisole, 2987-53-3; acetyl chloride, 75-36-5; cyclopropanecarbonyl chloride, 4023-34-1; trifluoroacetyl chloride, 354-32-5; 2-(methythio)phenyl isocyanate, 52260-30-7; dimethylamine, 124-40-3.

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Syntheses of Some Derivatives of Pyrrolo- and Thieno[2,3-*c*]quinoxaline and -quinoline

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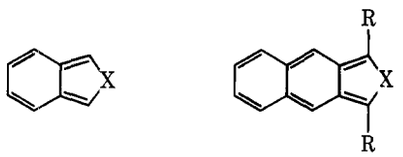
The recent isolation of the elusive isobenzofuran (1a) and isoindole (1b) rounds out the identification of all the parent benzo[*c*] heterocycles 1.[1-3] In contrast, none of the parent naphtho[2,3-*c*] heterocycles 2 has been reported, although transient formation of 2b (R = H) and 2c (R = H) was demonstrated by trapping them with *N*-phenylmaleimide.[4,5] 1,3-Diphenylnaphtho[2,3-*c*]furan (2a, R = Ph)



1 2

a, X = O
b, X = NH
c, X = S

and 1,3-diphenylnaphtho[2,3-*c*]thiophene (**2c**, R = Ph) were synthesized by Cava and Van Meter.[6] **2a** (R = Ph) was found to be rather unstable and quite reactive in Diels–Alder reactions.

We report the syntheses of some analogs of **2** containing more than one heteroatom (**3c–f**). Key intermediates in these syntheses were 2,3-dibenzoylquinoxaline (**7a**) and 2,3-dibenzoylquinoline (**7b**), whose preparations are described below.

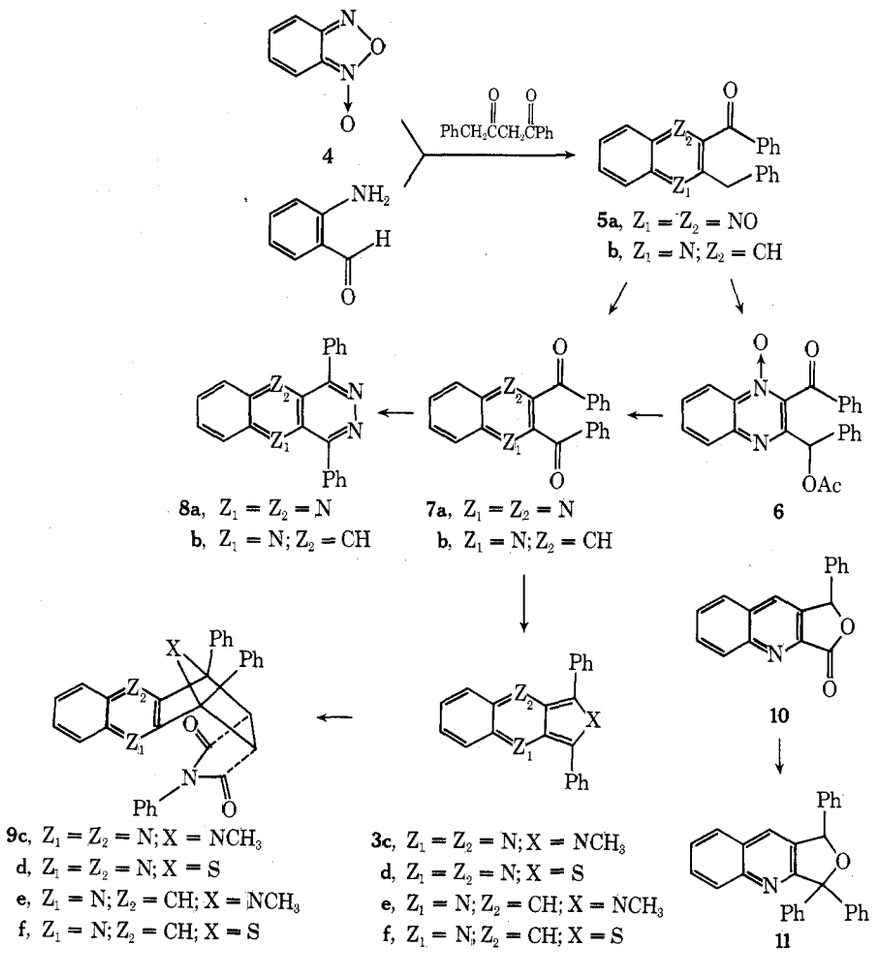
Treatment of benzofurazan oxide (**4**) with phenylacetylacetophenone in triethylamine gave 2-benzyl-3-benzoylquinoxaline 1,4-dioxide (**5a**), which was converted by refluxing acetic anhydride into 2-benzoyl-3-α-acetoxybenzylquinoxaline 1-oxide (**6**) in 50% yield. Hydrolysis of **6** in hot methanolic potassium hydroxide gave 2,3-dibenzoylquinoxaline (**7a**) in 63% yield. The rearrangement of **6** into **7a** is analogous to that reported recently for quinoxaline 1,4-dioxides with an α-methylene group.[7] The identity of **7a** was established by comparison with an authentic sample prepared by photolysis of 1,3-diphenylfuro[2,3-*c*]quinoxaline in the presence of oxygen.[8] As expected, **7a** reacted readily with hydrazine to give 1,4-diphenylpyridazino[4,5-*b*]quinoxaline (**8a**).[9]

Friedlander condensation of *o*-aminobenzaldehyde with phenylacetylacetophenone gave in good yield 2-benzyl-3-benzoylquinoline (**5b**) from which **7b** could be obtained by oxidation with chromic oxide in acetic anhydride. Quinoline **7b** was also obtained by adaptation of the recent method of Potts and Elliot.[10] The structure of **7b** was confirmed by its reaction with hydrazine to give 1,4-diphenylpyridazino[4,5-*b*]quinoline (**8b**).

Treatment of a hot methanolic solution of **7a** and methylamine with sodium borohydride or sodium dithionite brought about swift development of a blue color and subsequent precipitation of blue 1,3-diphenyl-2-methylpyrrolo[2,3-*c*]quinoxaline (**3c**) in 90% yield. Similarly, 1,3-diphenyl-2-methylpyrrolo[2,3-*c*]quinoline (**3e**)[11] was obtained as a red solid in high yield from **7b**. These reactions are essentially an adaptation of the Leuckart reductive amination of an *o*-dibenzoyl aromatic system which was employed by Emmett and Lwowski in the synthesis of 1,3-diphenylisoindoles.[12]

The reaction of **7a** in pyridine with phosphorus pentasulfide[13] gave, after chromatography, 1,3-diphenylthieno[3,4-*b*]quinoxaline (**3d**) as a blue solid. Similarly, red 1,3-diphenylthieno[3,4-*b*]quinoline (**3f**) was obtained from **7b** in 55% yield.

The products are formulated as **3c–f** on the basis of their elemental analyses, spectroscopic properties, and addition reactions to *N*-phenylmaleimide. The Diels–Alder adducts (**9c–f**), which partially reversed to starting materials before melting, were predominantly endo as inferred from their nmr signals in the 3.70–4.0 ppm region.[14] Adduct formation occurred at room temperature with **3e** (4 min) and **3c** (5 hr), but required prolonged heating at 78° with **3f** (50 hr) and **3d** (150 hr).



The *N*-methyl protons of **3c** (τ 5.82) and **3e** (τ 5.92) are deshielded compared with those of 1,3-diphenyl-2-methylisoindole (τ 6.25). The deshielding is apparently due to the electron-withdrawing effect of the nitrogen atoms in the adjacent six-membered ring and is, therefore, more pronounced in **3c** (quinoxaline ring) than in **3e** (quinoline ring). Electron withdrawal by the two nitrogen atoms in **3c** is also responsible for the observed sluggishness of the diene to react with *N*-phenylmaleimide.

Finally, in an effort to synthesize 1,3-diphenylfuro-[2,3-*c*]quinoline we treated lactone[7] **10** with phenylmagnesium bromide. Acidification of the reaction product yielded furan **11**.

Experimental Section[15]

2-Benzyl-3-benzoylquinoxaline 1,4-Dioxide (5a). A warm solution of benzofurazan oxide (**4**, 16.3 g) in triethylamine (50 ml) was mixed with a warm solution of phenylacetylacetophenone[16] (29 g) in triethylamine (50 ml). The solution was allowed to stand at room temperature for 5 days, during which a dark brown oil appeared. The supernatant liquid was decanted and the oily residue was rubbed with methanol to yield **5a** as a yellow solid. Recrystallization from methanol furnished yellow needles that melted at 167–168: 8.4 g (20%); ir 1670, 1350, 1040, 950, 765, 700, and 680 cm^{-1}; nmr τ 1.55 (m, 2 H), 2.5 (m, 12 H), 5.8 (s, 2 H).

Anal. Calcd for $C_{22}H_{16}N_2O_3$: C, 74.14; H, 4.53; N, 7.86. Found: C, 74.11; H, 4.50; N, 7.73.

2-Benzoyl-3-α-acetoxybenzylquinoxaline 1-Oxide (6). 2-Benzyl-3-benzoylquinoxaline 1,4-dioxide (5 g) was dissolved in acetic anhydride–acetic acid (10:5 ml) and the solution was refluxed for 0.5 hr. The cold solution was poured onto ice–water and the resulting brownish solid was purified by chromatography on an alumina column (benzene elution). Recrystallization from methanol yielded colorless prisms (2.5 g, 45%): mp 150–152; ir 1740, 1670, 1400, 1350, 1230, 1030, 960, 770, 750, 720, 700, and 690 cm^{-1}; nmr τ 1.6 (m, 1 H) 2.5 (m, 13 H), 3.1 (s, 1 H), 8.25 (s, 3 H).

Anal. Calcd for $C_{24}H_{18}N_2O_4$: C, 72.35; H, 4.55; N, 7.03. Found: C, 72.63; H, 4.57; N, 7.02.

2,3-Dibenzoylquinoxaline (7a). 2-Benzoyl-3-α-acetoxybenzylquinoxaline 1-oxide (2 g) was placed in 10% methanolic potassium hydroxide (40 ml). The solution was heated until all the solid dissolved, after which it was cooled and diluted with water. The precipitate was collected and recrystallized from methanol: 1.2 g (63%); mp 169–170; ir 1660, 1595, 1450, 1320, 1280, 1240, 930, 920, 880, 760, and 720 cm^{-1}; nmr τ 2.3 (m). The product was identical with that obtained from the photolysis of 1,3-diphenylfuro-[2,3-*c*]quinoxaline in the presence of oxygen. 1,4-Diphenylpyridazino[4,5-*b*]quinoxaline obtained from the reaction of **7a** with hydrazine melted at 237–238° (lit.[9] mp 239–240°).

2-Benzyl-3-benzoylquinoline (5b). *o*-Aminobenzaldehyde (6.2 g) and phenylacetylacetophenone (12.2 g) were dissolved in absolute ethanol (100 ml). Piperidine (0.5 ml) was added and the solution was refluxed for 48 hr. The solution was concentrated to half its volume and cooled in an ice–salt bath. The product appeared as a yellowish solid which was recrystallized from ethanol, 7 g (43%), mp 79–80°. In some cases where the product appeared as an oil, prolonged cooling resulted in a solid which was purified by chromatography on alumina and benzene elution: ir 1660, 1615, 1590, 1560, 1485, 1440, 1410, 1280, 1260, 1245, 1200, 1100, 1070, 940, 910, 870, 790, 775, 760, 720, 710, and 700 cm^{-1}; nmr τ 2.6 (m, 15 H), 5.55 (s, 2 H).

Anal. Calcd for $C_{23}H_{17}NO$: C, 85.42; H, 5.30; N, 4.33. Found: C, 84.95; H, 5.31; N, 4.34.

2,3-Dibenzoylquinoline (7b). 2-Benzyl-3-benzoylquinoline (3.3 g) was dissolved in acetic anhydride (10 ml). Concentrated sulfuric acid (2 ml) was added and the solution was cooled in an ice bath. A solution of chromic oxide (3 g) in water (2 ml) and acetic anhydride (13 ml) was cooled to 0° and added to the above solution. The mixture was allowed to stand at room temperature for 1 hr and poured onto ice–water. The resulting solid was chromatographed on alumina (benzene elution). Product **7b** (2 g, 58%) was recrystallized from methanol: mp 118–120°; ir 1665, 1450, 1405, 1330, 1235, 960, 935, 920, 870, 760–750, 710, and 700 cm^{-1}; nmr τ 2.38 (s, 1 H), 2.8 (m, 14 H).

Anal. Calcd for $C_{23}H_{15}NO_2$: C, 81.88; H, 4.48; N, 4.15. Found: C, 81.84; H, 4.52; N, 4.12.

Product **7b** was identical with a sample prepared by the condensation of dibenzoylacetylene with *o*-aminobenzaldehyde (30%).[10]

1,4-Diphenylpyridazino[4,5-*b*]quinoline (8b). 2,3-Dibenzoylquinoline (100 mg) was dissolved in hot methanol (10 ml). Addition of 80% hydrazine hydrate (3 ml) brought about the precipitation of **8b** which was recrystallized from methanol: 50 mg (50%); mp 232–233°; ir 1450, 1380, 1370, 920, 780, 765, 750, and 700 cm^{-1}.

Anal. Calcd for $C_{23}H_{15}N_3$: C, 82.86: H, 4.54; N, 12.61. Found: C, 82.84; H, 4.33; N, 12.55.

1,3-Diphenyl-2-methylpyrrolo[3,4-*b*]quinoline (3e). 2,3-Dibenzoylquinoline (100 mg) was dissolved in hot methanol (10 ml). An aqueous solution of 40% methylamine (5 ml) was added. Heating was continued for another minute. Sodium borohydride was added (30 mg) and a deep red color developed. On cooling **3e** separated as a red solid which was recrystallized from methanol: 75 mg (75%); mp 196–198°; ir 1600, 1480, 1450, 1280, 1220, 760, and 750 cm^{-1}; nmr τ 2.3 and 2.7 (m, 15 H), 5.92 (s, 3 H).

Anal. Calcd for $C_{24}H_{18}N_2$: C, 86.20; H, 5.43; N, 8.38. Found: C, 86.09; H, 5.37; N, 8.03.

1,3-Diphenyl-2-methylpyrrolo[3,4-*b*]quinoxaline (3c). The above procedure was applied to the synthesis of **3c**. 2,3-Dibenzoylquinoxaline (100 mg) yielded 90 mg of blue **3c** which was recrystallized from methanol: mp 224–225°; ir 1600, 1470, 1420, 760, and 700 cm^{-1}; nmr τ 2.2 and 2.6 (m, 14 H), 5.82 (s, 3 H).

Anal. Calcd for $C_{23}H_{17}N_3$: C, 82.38; H, 5.11; N, 12.53. Found: C, 81.46; H, 5.07; N, 12.33.

1,3-Diphenylthieno[3,4-*b*]quinoxaline (3d). 2,3-Dibenzoylquinoxaline (100 mg) was dissolved in pyridine (5 ml). Phosphorus pentasulfide (70 mg) was added and the mixture was refluxed for 2 hr. Evaporation of the solvent gave a solid which was extracted with benzene and chromatographed on alumina (benzene elution). Evaporation of the blue fractions gave **3d**, which was recrystallized from acetic acid: 60 mg (60%); mp 174–175°; ir 1590, 1530, 1500, 1470, 1430, 1410, 1300, 760, 710, 690, and 660 cm^{-1}.

Anal. Calcd for $C_{22}H_{14}N_2S$: C, 78.09; H, 4.17; N, 8.28; S, 9.46. Found: C, 77.83; H, 4.17; N, 8.05; S, 9.59.

1,3-Diphenylthieno[3,4-*b*]quinoline (3f). The above procedure was used to prepare **3f**. 2,3-Dibenzoylquinoline (200 mg) gave 110 mg (55%) of **3f**, which was recrystallized from methanol: mp 162–163°; ir 1600, 1500, 1470, 1450, 1420, 900, 750, and 700 cm^{-1}.

Anal. Calcd for $C_{23}H_{15}NS$: C, 81.88; H, 4.48; N, 4.15; S, 9.49. Found: C, 81.25; H, 4.56; N, 4.08; S, 9.44.

Adducts with *N*-Phenylmaleimide. General Procedure. The specific diene was dissolved in benzene and an equimolar quantity of *N*-phenylmaleimide was added to the solution. The reaction mixture was worked up when the color of diene disappeared. The adducts (Table I) did not melt sharply owing to dissociation to starting materials.

1,3-Dihydro-1,3,3-triphenylfuro[3,4-*b*]quinoline (11). Treat-

Table I

Adduct	Time and temp, °C	Ir, cm^{-1}	Nmr, τ	Mp, °C
9e	4 min, room temp	1715, 770, 700, 770, 700	4 (m, 2 H), 5.5 (s, 2 H), 8 (s, 3 H)	215–222
9c	5 hr, 78	1710, 770, 700	3.92 (m, 2 H), 5.55 (s, 2 H), 8 (s, 3 H)	205–242
9f	50 hr, 78	1715, 770, 700	3.92 (m, 2 H) 5.12 (s, 2 H)	235–242
9d	150 hr, 78	1720, 770, 700	3.65 (m, 2 H), 4.95 5.87 (s, 2 H)	217–225

ment of 1,3-dihydro-1-phenylfuro[3,4-*b*]quinolin-3-one[7] (**10**) with phenylmagnesium bromide according to the procedure of Cava and Van Meter[6] gave the title compound in 48% yield: mp 210–211° (from ethanol); ir 1625, 1600, 1025, 770, 750, and 700 cm^{-1}; nmr τ 2.5 (m, 20 H), 3.8 (s, 1 H).

Anal. Calcd for $C_{29}H_{21}NO$: C, 87.19; H, 5.30; N, 3.51. Found: 87.39; H, 5.24; N, 3.48.

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Registry No.—**3c,** 52260-31-8; **3d,** 52260-32-9; **3e,** 52260-33-0; **3f,** 52260-34-1; **4,** 480-96-6; **5a,** 52260-35-2; **5b,** 52260-36-3; **6,** 52260-37-4; **7a,** 19029-35-7; **7b,** 52260-38-5; **8b,** 52260-39-6; **9c,** 52260-40-9; **9d,** 52260-41-0; **9e,** 52341-46-5; **9f,** 52260-42-1; **10,** 52260-43-2; **11,** 52260-44-3; phenylacetylacetophenone, 3442-15-7; *o*-aminobenzaldehyde, 529-23-7; hydrazine, 302-01-2; *N*-phenylmaleimide, 941-69-5.

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A New Synthesis of Maltol[1]

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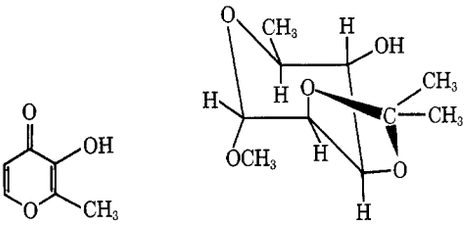
Maltol (2-methyl-3-hydroxy-4*H*-pyran-4-one), **1,** is known to exist in several plants, *e.g.*, fern leaves and larch bark, and in food materials, *e.g.*, roasted chicory, coffee, caramel, and corn.[3] Streptomycin on alkaline hydrolysis also yields up to 30% maltol.[4,5] It was isolated in 1894 by Brand and its structure was established by Peratoner and Tamburello in 1905.[3]

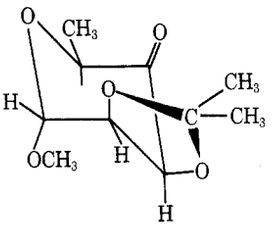
Although maltol is of great value as a flavoring agent in food industry, its reported laboratory syntheses proceed in poor yields and under severe experimental conditions.[6,7]

The purpose of this work was to provide a facile synthesis of **1** from readily available materials in reasonable yields under mild experimental conditions.

Oxidation of methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**2**)[8,9] with chromium trioxide–pyridine complex, prepared at room temperature, according to the procedure of Poos and coworkers,[10] gave a syrupy material, identified as methyl 2,3-*O*-isopropylidene-6-deoxy-α-L-*lyxo*-hexopyranos-4-ulose (**3**) in 55% yield. Its ir and nmr spectra and the elemental analysis of its crystalline oxime confirmed its structure.



1 **2**



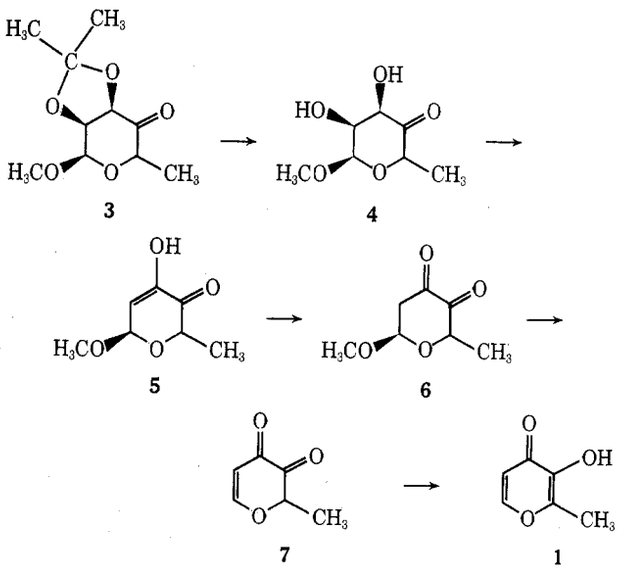
3

Compound **3** was heated on a steam bath with Dowex 50 (H^+) and Dowex 1 (OH^-) ion exchange resins, in water and in benzene, and the appearance of maltol was determined colorimetrically at 540 nm at given intervals.[11] Maximum yields were obtained by hydrolysis of **3** in aqueous medium by means of Dowex 50 (H^+) ion exchange resin: 72% in 60 hr. The final product was characterized as maltol (**1**) by its nmr and ir spectra, its elemental analysis, and by comparison of its tlc behavior with a commercial sample of maltol.

The yield of maltol by reaction of **3** with Dowex 1 (OH^-) ion exchange resin in aqueous medium was poor (15% yield). In benzene, the hydrolysis did not proceed to any significant extent (<1% yield) in the presence of acidic or basic ion exchange resins.

The following pathway is suggested for the degradation of **3** to maltol under the conditions of hydrolysis (Scheme I). The pathway involves elimination of acetone under the

Scheme I



influence of Dowex 50 (H^+) ion exchange resin (known lability of the isopropylidene group to mild acid conditions),[12] followed by β elimination of water in which H atom α to the carbonyl function is lost (**4** and **5**). After tau-