

A. H. Abd el Rahman and E. M. Kandeel

Faculty of Science, Mansoura University, Mansoura, Egypt

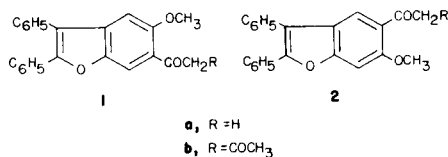
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When 6-acetoacetyl-5-methoxy- (**1b**) and 5-acetoacetyl-6-methoxy-2,3-diphenylbenzofuran (**2b**) were treated with cyanoacetamide, the corresponding pyridinecarbonitriles were obtained. Compounds **1b** and **2b** reacted with ethyl cyanoacetate in the presence of ammonium acetate to give the benzofuran-yl-pyrone derivatives. This reaction, when carried out in presence of diethylamine, led to the formation of furochromones. Hydrazine hydrate, phenylhydrazine and semicarbazide hydrochloride reacted with **1b** and **2b** with the formation of the corresponding pyrazoles. The corresponding isoxazole derivatives were formed by the reaction of **1b** and **2b** with hydroxylamine hydrochloride.

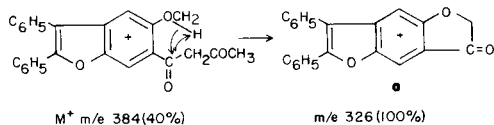
J. Heterocyclic Chem., **18**, 371 (1981).

It is well known that pyridine, pyrazole, pyrone, isoxazole and benzofuran derivatives show marked biological activity (1-5). Thus, the present investigation deals with the combination of pyridine, pyrone, pyrazole and isoxazole nuclei with a benzofuran ring in order to obtain new compounds of potential biological activity.

Both compounds 6-acetyl-5-methoxy- (**1a**) and 5-acetyl-6-methoxy-2,3-diphenylbenzofuran (**2a**) (6) undergo Claisen condensation with ethyl acetate in the presence of sodium metal to give 6-acetoacetyl-5-methoxy- (**1b**) and 5-acetoacetyl-6-methoxy-2,3-diphenylbenzofuran (**2b**), respectively. The ir spectra of compounds **1b** and **2b** showed bands at 1622 and 1618 cm^{-1} due to the tautomeric keto-enol forms (7).



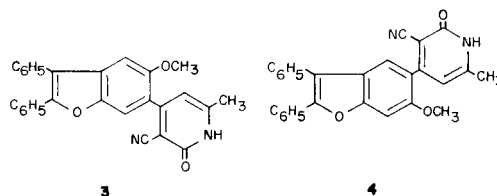
The ms of compound **1b** exhibited a molecular ion M^+ at m/e 384 (40%). The major fragmentation was the elimination of one mole of acetone yielding ion **a** as the base peak at m/e 326 (100%), due to the *ortho* effect of functional groups attached to the benzene ring of the benzofuran molecule (8). The ion **a** decomposed further by expulsion of carbon monoxide; a reasonable structure for this ion can be illustrated by the following mechanism.



The pmr spectrum of compound **1b** showed singlets at δ 2.20 (3H, CH₃), 3.88 (3H, OCH₃), 7.00 (1H, C-4), 8.17 (1H, C-7) and 6.62 (1H, olefinic); 10 aromatic protons also appeared as multiplets at δ 7.30-7.50. The spectrum of compound **2b** revealed the signals at δ 2.10 s (3H, CH₃), 3.96 s

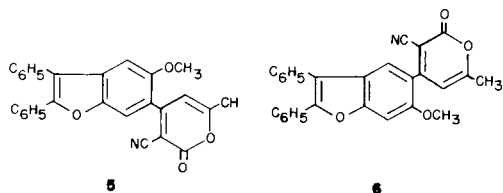
(3H, OCH₃), 7.06 s (1H, C-4), 7.96 s (1H, C-7), 6.40 s (1H, olefinic) and 7.40-7.60 m (10H, aromatic).

When compounds **1b** and **2b** were treated with cyanoacetamide in the presence of ammonium acetate, 4-(2',3'-diphenyl-5'-methoxy-6'-benzofuran-yl)- (**3**) and 4-(2',3'-diphenyl-6'-methoxy-5'-benzofuran-yl)-1,2-dihydro-2-oxo-6-methylpyridinecarbonitriles (**4**) were formed.



The ir spectra of compounds **3** and **4** revealed the presence of a carbonyl group at 1630 and 1625 cm^{-1} (tautomeric pyridone) a carbonitrile group at 2230 and 2225 cm^{-1} and an NH group at 3150 and 3160. These later absorptions are characteristic for the -NH stretching frequency in substituted 2-pyridone (9,10). The ms of compound **3** showed a molecular ion M^+ at m/e 432. The pmr spectra of compounds **3** and **4** were in agreement with the assigned structures. The spectrum for compound **3** showed signals at δ 2.68 s (3H, CH₃), 3.97 s (3H, OCH₃), 7.15 (s, 1H, C'-4), 7.85 s (1H, C'-7), 7.07 s (1H, C-5) and 7.30-7.70 m (10H, aromatic). Compound **4** revealed singlets at δ 2.51 (3H, CH₃), 4.05 (3H, OCH₃), 7.25 (1H, C'-4), 7.61 (1H, C'-7) and 7.12 (1H, C-5); 10 aromatic protons also appeared as multiplets at δ 7.30-7.55.

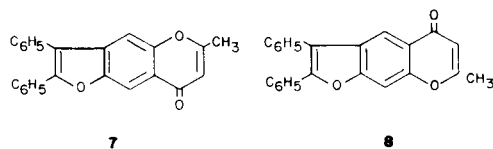
The behaviour of the diketones **1b** and **2b** with ethyl cyanoacetate was also investigated. When the reaction was carried out in the presence of ammonium acetate, 4-(2',3'-diphenyl-5'-methoxy-6'-benzofuran-yl)- (**5**) and 4-(2',3'-diphenyl-6'-methoxy-5'-benzofuran-yl)-3-cyano-6-methylpyran-2-one (**6**) were obtained.



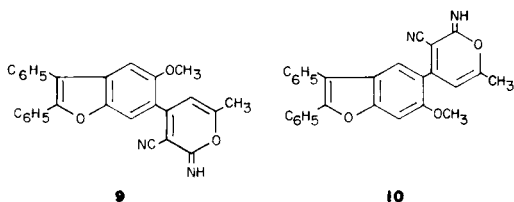
On the other hand, when the above reaction was carried out in presence of diethylamine or piperidine as a catalyst, 2,3-diphenyl-7-methyl-8H-furo[2,3-g][1]benzopyran-8-one (11) (**7**) and 2,3-diphenyl-7-methyl-5H-furo[3,2-g][1]benzopyran-5-one (11) (**8**) (m.p. and mixed m.p. with an authentic sample gave no depression) were obtained. The furochromones **7** and **8** were also formed by refluxing **1b** and **2b** with diethylamine or piperidine in ethanol, probably *via* demethylation followed by cyclodehydration (13).

The ir spectra of compounds **5** and **6** showed bands at 1750 and 1745 cm^{-1} , characteristic of α,β -unsaturated- δ -lactones (14). The bands at 2220 and 2235 cm^{-1} were due to the carbonitrile group.

The pmr spectrum of compound **7** has not been reported. The spectrum showed singlets at δ 7.32 (1H, C-4), 6.15 (1H, C-6), 8.28 (1H, C-9) and 2.37 (3H, CH_3); 10 aromatic protons also appeared as multiplets at δ 7.38-7.65. The ms of compound **7** showed a molecular ion M^+ at m/e 352 as the base peak.



The present investigation also describes the synthesis of 4-(2',3'-diphenyl-5'-methoxy-6'-benzofuranyl)- (**9**) and 4-(2',3'-diphenyl-6-methoxy-5'-benzofuranyl)-3-cyano-6-methyl-2-pyranimine (**10**), by the reaction of compounds **1b** and **2b** with malononitrile in presence of ammonium acetate, respectively.

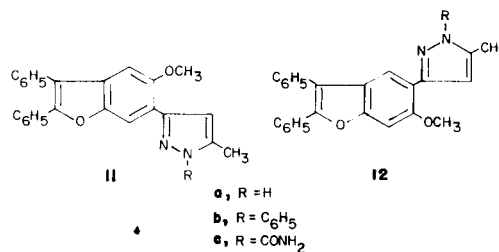


The infrared spectra of compounds **9** and **10** showed the absence of a carbonyl group and revealed bands at 1630 and 1625 cm^{-1} due to the $-\text{C}=\text{N}$ group, and bands at 2230 and 2225 cm^{-1} , characteristic for a carbonitrile group.

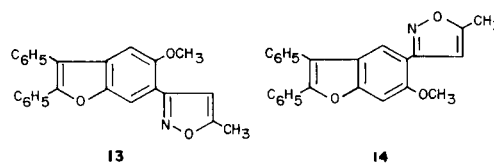
The diketones **1b** and **2b** reacted with hydrazine hydrate in ethanol or in acetic acid to yield 3-(2',3'-diphenyl-5'-methoxy-6'-benzofuranyl)- (**11a**) and 3-(2',3'-diphenyl-6'-methoxy-5'-benzofuranyl)-5-methylpyrazole (**12a**), respectively.

N-phenylpyrazoles **11b** and **12b** were formed by the reaction of **1b** and **2b** with phenyl hydrazine. The ir spectra of compounds **11a**, **11b**, **12a** and **12b** showed bands at 1620-1630 cm^{-1} due to the $-\text{C}=\text{N}$ group.

The reaction of compounds **1b** and **2b** with semicarbazide hydrochloride led to the formation of the corresponding pyrazoles **11c** and **12c**, respectively.



Compounds 3-(2',3'-diphenyl-5'-methoxy-6'-benzofuranyl)- (**13**) and 3-(2',3'-diphenyl-6'-methoxy-5'-benzofuranyl)-5-methylisoxazole were furnished by the reaction of **1b** and **2b** with hydroxylamine hydrochloride, respectively.



EXPERIMENTAL

Melting points were not corrected. Pmr spectra were obtained at 60 MHz in deuteriochloroform with TMS as an internal standard. Mass spectra were run at 70 eV. The infra-red spectra were carried out in potassium bromide on a Unicam infra-red spectrophotometer Model SP 2000.

Preparation of 6-Acetoacetyl-5-methoxy-2,3-diphenylbenzofuran (**1b**).

A solution of 4 g. of **1a** in 50 ml. of ethyl acetate was slowly added to 4 g. of powdered sodium metal. The reaction mixture was refluxed for 5 hours and then left to cool. Following the work up, the aqueous layer was acidified with acetic acid and the solid that separated was crystallized from ethanol to give compound **1b** as yellow needles, m.p. 158°, yield 80%.

Anal. Calcd. for $\text{C}_{25}\text{H}_{20}\text{O}_4$: C, 78.13; H, 5.21. Found: C, 78.23; H, 5.45.

5-Acetoacetyl-6-methoxy-2,3-diphenylbenzofuran (**2b**).

Compound **2b** was prepared from 4 g. of **2a** in 50 ml. of ethyl acetate and 4 g. of powdered sodium as in the case of **1b**. Compound **2b** was obtained as yellow needles from ethanol, m.p. 153-155°, yield 85%.

Anal. Calcd. for $\text{C}_{25}\text{H}_{20}\text{O}_4$: C, 78.13; H, 5.21. Found: C, 78.10; H, 5.41.

4-(2',3'-Diphenyl-5'-methoxy-6'-benzofuranyl)-1,2-dihydro-2-oxo-6-methylpyridinecarbonitrile (**3**).

A mixture of **1b** (1 g.), cyanoacetamide (1 g.) and ammonium acetate (2 g.) in 20 ml. of acetic acid was refluxed for one hour and then left to cool. The solid that separated was crystallized from ethanol to give **3** as yellow crystals, m.p. 265°, yield 75%.

Anal. Calcd. for $C_{28}H_{20}N_2O_3$: C, 77.78; H, 4.63; N, 6.48. Found: C, 77.49; H, 4.35; N, 6.56.

4-(2',3'-Diphenyl-6'-methoxy-5'-benzofuranyl)-1,2-dihydro-2-oxo-6-methylpyridinecarbonitrile (**4**).

In a manner similar to the preparation of **3**, 1 g. of **2b**, 1 g. of cyanoacetamide and 2 g. of ammonium acetate in 20 ml. of acetic acid gave **4** as yellow crystals from ethanol, m.p. 294°, yield 80%.

Anal. Calcd. for $C_{28}H_{20}N_2O_3$: C, 77.78; H, 4.63; N, 6.48. Found: C, 77.81; H, 4.89; N, 6.67.

4-(2',3'-Diphenyl-5'-methoxy-6'-benzofuranyl)-3-cyano-6-methylpyran-2-one (**5**).

A mixture of **1b** (1 g.), ethyl cyanoacetate (1 ml.) and ammonium acetate (2 g.) in 20 ml. of acetic acid was refluxed for 3 hours and then left to cool. The solid so obtained was crystallized from ethanol to give compound **5** as cream fibers, m.p. 105°, yield 80%.

Anal. Calcd. for $C_{29}H_{19}NO_4$: C, 77.60; H, 4.39; N, 3.23. Found: C, 77.83; H, 4.59; N, 3.42.

4-(2',3'-Diphenyl-6'-methoxy-5'-benzofuranyl)-3-cyano-6-methylpyran-2-one.

A mixture of **2b** (1 g.), ethyl cyanoacetate (1 ml.) and ammonium acetate (2 g.) in 20 ml. of acetic acid gave 75% of **6** as cream needles from ethanol, m.p. 142°.

Anal. Calcd. for $C_{29}H_{19}NO_4$: C, 77.60; H, 4.39; N, 3.23. Found: C, 77.65; H, 4.42; N, 3.45.

2,3-Diphenyl-7-methyl-8H-furo[2,3-g][1]benzopyran-8-one (**7**).

To a mixture of **1b** (1 g.) and ethyl cyanoacetate in 50 ml. of ethanol diethylamine (1 ml.) (or piperidine) was added. The reaction mixture was refluxed for 3 hours and left to cool. The solid that separated was crystallized from ethanol to give compound **7** as white crystals, m.p. 213°, yield 90% (m.p. and mixed m.p. with the known compound (**11**) gave no depression).

2,3-Diphenyl-7-methyl-5H-furo[3,2-g][1]benzopyran-5-one (**8**).

As in case of **7**, 1 g. of **2b** gave compound **8** as white crystals, m.p. 204°, yield 80% (m.p. and mixed m.p. with an authentic sample (**12**) gave no depression).

4-(2',3'-Diphenyl-5'-methoxy-6'-benzofuranyl)-3-cyano-6-methyl-2-pyranimine (**9**).

A mixture of **1b** (1 g.), malononitrile (1 g.) and ammonium acetate (2 g.) in 20 ml. of acetic acid was refluxed for 3 hours and then left to cool. The solid so obtained was crystallized from ethanol to give **9** as white crystals, m.p. 180°, yield 60%.

Anal. Calcd. for $C_{28}H_{20}N_2O_3$: C, 77.78; H, 4.63; N, 6.48. Found: C, 77.97; H, 4.69; N, 6.64.

4-(2,3,3'-Diphenyl-6-methoxy-5'-benzofuranyl)-3-cyano-6-methyl-2-pyranimine (**10**).

In a similar manner as the case of **9**, **2b** (1 g.), malononitrile (1 g.) and ammonium acetate (2 g.) in 20 ml. of acetic acid gave 55% of **10** as cream crystals from ethanol, m.p. 170°.

Anal. Calcd. for $C_{28}H_{20}N_2O_3$: C, 77.78; H, 4.63; N, 6.48. Found: C, 77.62; H, 4.34; N, 6.72.

Reaction of **1b** and **2b** with Hydrazine Hydrate or Phenylhydrazine.

A mixture of 1 g. of **1b** or **2b** and 0.5 ml. of hydrazine hydrate (99%) or phenylhydrazine in 50 ml. of ethanol or 20 ml. of acetic acid was refluxed for 5 hours and then concentrated to about 10 ml., diluted with water and left to cool, and the solid so obtained was crystallized from ethanol. The pyrazole **11a** was obtained as colourless crystals, m.p. 222°, yield 75%; pmr (trifluoroacetic acid): δ 2.60 s (3H, CH₃), 4.07 s (3H, OCH₃), 7.17 s (1H, C'-4), 7.95 s (1H, C'-7), 6.87 s (1H, C-4) and 7.30-7.60 m (10H, aromatic); ms: m/e M⁺ 380.

Anal. Calcd. for $C_{25}H_{20}N_2O_2$: C, 78.95; H, 5.26; N, 7.37. Found: C, 78.65; H, 5.55; N, 7.56.

Compound **12a** was formed in 75% yield as cream crystals, m.p. 190°; pmr: δ 3.94 s (3H, OCH₃), 2.27 s (3H, CH₃), 7.20 s (1H, C'-4), 7.63 s (1H, C'-7), 7.08 s (1H, C-4) and 7.30-7.55 m (10H, aromatic).

Anal. Calcd. for $C_{25}H_{20}N_2O_2$: C, 78.95; H, 5.26; N, 7.37. Found: C, 78.80; H, 5.20; N, 7.33.

The compound **11b** was formed as cream crystals, m.p. 218°, yield 70% pmr: δ 2.43 s (3H, CH₃), 3.33 s (3H, OCH₃), 6.36 (1H, C'-4), 6.83 s (1H, C'-7), 7.40 s (1H, C-4) and 7.30-7.60 m (15H, aromatic); ms: m/e M⁺ 456.

Anal. Calcd. for $C_{31}H_{24}N_2O_2$: C, 81.58; H, 5.26; N, 6.14. Found: C, 81.74; H, 5.05; N, 5.80.

N-Phenylpyrazole **12b** was furnished as cream crystals, m.p. 110°, yield 60%; δ 2.36 s (3H, CH₃), 3.40 s (3H, OCH₃), 6.25 s (1H, C'-4), 6.95 s (1H, C'-7), 7.30 s (1H, C-4) and 7.20-7.60 m (15H, aromatic).

Anal. Calcd. for $C_{31}H_{24}N_2O_2$: C, 81.58; H, 5.26; N, 6.14. Found: C, 81.32; H, 5.41; N, 6.27.

Preparation of Pyrazoles **11c** and **12c**.

A solution of 0.004 mole of **1b** or **2b** in the minimum amount of ethanol was added to a solution of semicarbazide hydrochloride in a minimum amount of water. The reaction mixture was refluxed for 3 hours and then cooled, and the solid that separated was crystallized from ethanol. The pyrazole **11c** was obtained as colourless crystals, m.p. 220°, yield 80%.

Anal. Calcd. for $C_{26}H_{21}N_3O_3$: C, 73.76; H, 4.96; N, 9.93. Found: C, 73.53; H, 5.33; N, 9.99.

Compound **12c** was formed as colorless crystals, m.p. 265°, yield 78%.

Anal. Calcd. for $C_{26}H_{21}N_3O_3$: C, 73.76; H, 4.96; N, 9.93. Found: C, 73.49; H, 4.81; N, 9.84.

3-(2',3'-Diphenyl-5'-methoxy-6'-benzofuranyl)-5-methylisoxazole (**13**).

A solution of 0.5 g. of hydroxylamine hydrochloride and 0.2 g. of sodium acetate in least amount of water was added to a suspension of 1.9 g. of **1b** in 50 ml. of ethanol. The reaction mixture was refluxed for 5 hours. On cooling and addition of water, a solid separated was crystallized from ethanol to give **13** as colourless crystals, m.p. 200°, yield 80% δ 2.38 s (3H, CH₃), 3.93 s (3H, OCH₃), 7.00 s (1H, C'-4), 8.18 s (1H, C'-7), 6.72 s (1H, C-4) and 7.40-7.60 m (10H, aromatic).

Anal. Calcd. for $C_{25}H_{19}NO_3$: C, 78.74; H, 4.99; N, 3.67. Found: C, 78.66; H, 5.10; N, 3.82.

3-(2',3'-Diphenyl-6'-methoxy-5'-benzofuranyl)-5-methylisoxazole (**14**).

In a similar manner as in case of **13**, **2b** (1.9 g.) gave **14** as colourless crystals, m.p. 163°, yield 80%; pmr: δ 2.33 s (3H, CH₃), 4.00 s (3H, OCH₃), 7.02 s (C'-4, 1H), 8.04 s (1H, C'-7), 6.65 s (1H, C-4) and 7.30-7.65 m (10H, aromatic).

Anal. Calcd. for $C_{25}H_{19}NO_3$: C, 78.74; H, 4.99; N, 3.67. Found: C, 78.54; H, 5.22; N, 3.82.

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