Development and Application of Organic Reagents for Analysis. VI.[1] Synthesis and Fluorescence Spectral Properties of 2-(4-Substituted phenyl)benzofurans

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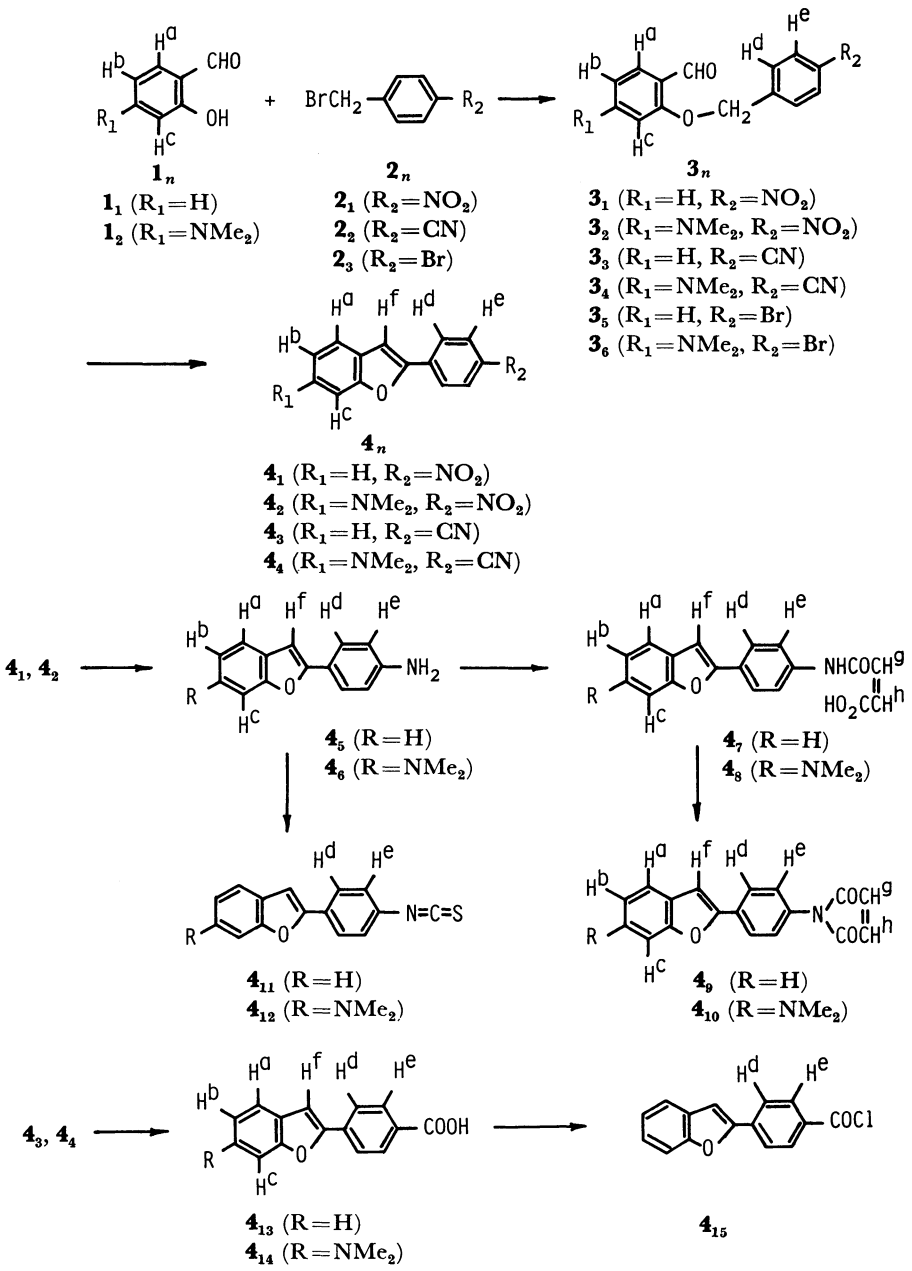
A synthesis of fifteen kinds of 2-(4-substituted phenyl)benzofurans (**4**$_n$) was carried out and their fluorescence spectral properties were investigated concerning their applicability as organic reagents for analyses.

In order to develop sensitive and useful fluorogenic reagents, our attention became directed toward the synthesis of derivatives of 2-phenylbenzofuran which were expected to exhibit strong fluorescence due to the presence of a latent *trans*-stilbene skeletone. The synthesis of 2-(4-substituted phenyl)benzofurans (**4**$_n$) was carried out and their fluorescence spectral properties were investigated in order to determine the applicability of **4**$_n$ as reagents for analyses. As shown Scheme 1, the construction of a benzofuran skeletone



Scheme 1.

of $\mathbf{4}_{1-4}$ was realized by a reaction of salicylaldehydes ($\mathbf{1}_1$ and $\mathbf{1}_2$) with *p*-nitro- and *p*-cyanobenzyl bromides ($\mathbf{2}_1$ and $\mathbf{2}_2$) in the presence of an alkali following cyclization to a furan ring.[2] The nitro compounds ($\mathbf{4}_1$ and $\mathbf{4}_2$) were reduced to corresponding amino compounds ($\mathbf{4}_5$ and $\mathbf{4}_6$). These could be converted to various other compounds ($\mathbf{4}_{7-12}$). In addition, the cyano compounds ($\mathbf{4}_3$ and $\mathbf{4}_4$) were transformed to acids ($\mathbf{4}_{13}$ and $\mathbf{4}_{14}$) and subsequently to the acid chloride ($\mathbf{4}_{15}$).

The electronic absorption and fluorescence spectra of these 2-phenylbenzofuran derivatives were measured and several characteristics were observed.

Results and Discussion

Synthesis of 2-(4-Substituted phenyl)benzofurans ($\mathbf{4}_n$). A synthesis of $\mathbf{4}_n$ was achieved according to Scheme 1. 2-(Benzyloxy)benzaldehydes ($\mathbf{3}_1$, $\mathbf{3}_2$, and $\mathbf{3}_3$) were prepared by the reaction of $\mathbf{1}_n$ with $\mathbf{2}_n$ in the presence of KOH in EtOH (R_2=NO_2) or sodium ethoxide in dimethylformamide(DMF)–EtOH (R_2=CN). 2-(4-Substituted phenyl)benzofurans ($\mathbf{4}_{1-3}$) were obtained from the cyclization of $\mathbf{3}_{1-3}$ in the presence of sodium methoxide in DMF or KOH in DMF.[2] The nitrile ($\mathbf{4}_4$) could be directly synthesized by a reaction of $\mathbf{1}_2$ with $\mathbf{2}_2$ without the isolation of $\mathbf{3}_4$. Cyclizations of the bromides ($\mathbf{3}_5$ and $\mathbf{3}_6$) were unsuccessful under the above conditions.

The nitro compounds ($\mathbf{4}_1$ and $\mathbf{4}_2$) were easily reduced with iron(III) chloride–hydrazine hydrate to yield corresponding amino compounds ($\mathbf{4}_5$ and $\mathbf{4}_6$) in good yields.

From the purpose of the synthesis of the maleimides ($\mathbf{4}_9$ and $\mathbf{4}_{10}$), which could be expected as organic reagents for the selective determination of thiols, $\mathbf{4}_5$ and $\mathbf{4}_6$ were treated with maleic anhydride to give the maleamic acids ($\mathbf{4}_7$ and $\mathbf{4}_8$).[3] The cyclization of $\mathbf{4}_7$ and $\mathbf{4}_8$ in the presence of sodium acetate in acetic anhydride afforded $\mathbf{4}_9$ and $\mathbf{4}_{10}$.

The isothiocyanates ($\mathbf{4}_{11}$ and $\mathbf{4}_{12}$) were obtained by the treatment of $\mathbf{4}_5$ and $\mathbf{4}_6$ with an excess of thiophosgene.[4]

The nitriles ($\mathbf{4}_3$ and $\mathbf{4}_4$) were hydrolyzed with an alkali to give the carboxylic acids ($\mathbf{4}_{13}$ and $\mathbf{4}_{14}$), from which the acid chloride ($\mathbf{4}_{15}$) was derived.

Electronic Absorption Spectral Properties of $\mathbf{4}_n$. The longest wavelength absorption maxima of 2-phenylbenzofurans ($\mathbf{4}_n$) that were observed are given in Table 1. From the data it has become apparent that a dimethylamino substitution in $\mathbf{4}_n$ produces a red shift and a hypsochromic effect.

Fluorescence Spectral Properties. The fluorescence spectra of $\mathbf{4}_n$ were measured and the relative fluorescence intensities were compared with one another (Table 1). Red shifts were observed at the emission maxima (λ_{em}) of the dimethylamino substituted compounds relative to the corresponding unsubstituted ones. The isothiocyanates ($\mathbf{4}_{11}$ and $\mathbf{4}_{12}$) exhibited very little fluorescence and the nitro and *N*-maleimide compounds ($\mathbf{4}_1$, $\mathbf{4}_2$, $\mathbf{4}_9$, and $\mathbf{4}_{10}$) showed almost no fluorescence. These *N*-maleimides ($\mathbf{4}_9$ and $\mathbf{4}_{10}$) when combined with thiols showed strong fluorescence, *e.g.*, the adduct of $\mathbf{4}_9$ with *N*-acetyl-L-cysteine: λ_{ex} 320, λ_{em} 360 nm; the adduct of $\mathbf{4}_{10}$ with *N*-acetyl-L-cysteine: λ_{ex} 346, λ_{em} 470 nm (Fig. 1).[5] The large difference (124 nm) between λ_{ex} and λ_{em} in the latter seems to be an advantageous property as an analytical reagent for practical use. Recently, we have briefly reported on the fluorometric determination of glutathione using $\mathbf{4}_{10}$. This has proved to be useful as a new fluorigenic thiol-selective reagent.[6] Similarly, the isothiocyanates ($\mathbf{4}_{11}$ and $\mathbf{4}_{12}$) reacted with aliphatic amines to afford adducts which emitted strong fluorescence. An application of $\mathbf{4}_{11}$ and $\mathbf{4}_{12}$ to analytical reagents is now in progress.

Table 1. Spectral data of 2-(4-substituted phenyl) benzofurans

Compound	λ_{max}^{EtOH}	log ε	λ_{em}^{EtOH}	RFI[a]
$\mathbf{4}_1$	357	4.38	—	—
$\mathbf{4}_2$	438	4.34	—	—
$\mathbf{4}_3$	322	4.57	380	100
$\mathbf{4}_4$	392	4.48	512	36
$\mathbf{4}_5$	321	4.56	387	83
$\mathbf{4}_6$	345	4.52	400	71
$\mathbf{4}_9$	310	4.53	—	—
$\mathbf{4}_{10}$	355	4.50	—	—
$\mathbf{4}_{11}$	329	4.73	372	3.2
$\mathbf{4}_{12}$	375	4.59	430	8.5
$\mathbf{4}_{13}$	314	4.54	385	32
$\mathbf{4}_{14}$	366	4.48	465	31

a) Relative fluorescence intensity: the nitrile $\mathbf{4}_3$ is arbitrarily taken as 100 [concentration: 2μM (1 M= 1 mol dm^{-3})].

Experimental

Melting points are uncorrected. The ^{1}H NMR spectra (tetramethylsilane as an internal standard) were recorded on a JEOL FX 90Q spectrometer (chemical shifts given in ppm units). The IR spectra were taken using a JASCO IRA 2 spectrophotometer, the MS using a JEOL JMS-01SG mass spectrometer, and the UV using Hitachi 210 and Shimadzu UV-150 spectrophotometers. The fluorescence spectra were measured with a Shimadzu RF-540 fluorescence spectrophotometer.

4-(Dimethylamino)salicylaldehyde ($\mathbf{1}_2$). Aluminum chloride (18.8 g, 0.14 mol) was added to a solution of *m*-dimethylaminophenol (12.50 g, 0.094 mol) in chloroform (185 ml) and triethyl orthoformate (84 g, 0.57 mol) at room temperature and was mixed for 10 min. After the exothermic reaction had ceased, HCl (10%, 50 ml) was added and stirred to hydrolyze the resulting acetal. The mixture was neutralized with aq sodium hydroxide (10%). The resulting deposit was filtered off through a short column of Celite and washed with $CHCl_3$. The filtrate was combined with a cleaning solution, washed with saturated aq NaCl, dried over $MgSO_4$, and concentrated *in vacuo*. Recrystallization of the product from $CHCl_3$ gave 9.82 g (65%) of $\mathbf{1}_2$, mp 78—79 °C (79—80 °C[7]); ^{1}H NMR ($CDCl_3$): δ=2.81 (s, 6H, NMe_2), 5.8—6.1 (m, 2H, H^a and H^b), 7.13 (s, 1H, H^c), 9.20 (s, 1H, CHO); IR (Nujol): 1640

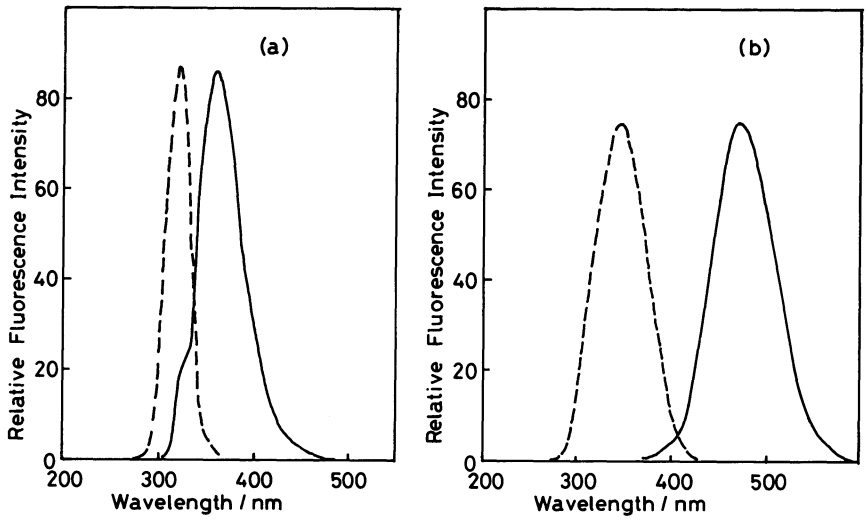


Fig. 1. Fluorescence spectra of the reaction mixtures of **4**$_9$ and **4**$_{10}$ with *N*-acetyl-L-cysteine (NAC).
(a): adduct of **4**$_9$ with NAC; (b): adduct of **4**$_{10}$ with NAC.
Procedure: A solution of **4**$_9$ or **4**$_{10}$ in acetone (0.5 mM 0.5 ml) was mixed with a solution of NAC-0.1 M H_3PO_4 (pH 7.0) (0.5 mM, 10 ml), stood for 1 h at room temperature, and then the fluorescence spectra were measured.

(C=O) cm^{-1}.

4-Dimethylamino-2-(4-nitrobenzyloxy)benzaldehyde (3$_2$*).* A solution of KOH (0.40 g, 7 mmol) in EtOH (3 ml) was added to a solution of 4-(dimethylamino)salicylaldehyde (**1**$_2$) (1.00 g, 6 mmol) and 4-nitrobenzyl bromide (**2**$_1$) in EtOH (12 ml). Then, the mixture was refluxed for 7 h. After the solution had been cooled, the resulting crystals were filtered off, washed with water, and dried *in vacuo*. Then, the crystals were recrystallized from EtOH; 1.02 g, 56%; mp 179—180 °C; ^{1}H NMR ($CDCl_3$): δ=3.06 (s, 6H, NMe_2), 5.27 (s, 2H, CH_2), 6.05 (d, J=3 Hz, 1H, H^c), 6.33 (J=3, 9 Hz, 1H, H^b), 7.44 (d, J=9 Hz, 1H, H^a), 7.64 (d, J=9 Hz, 2H, H^d), 8.25 (d, J=9 Hz, 2H, H^e), 10.23 (s, 1H, CHO); IR (Nujol): 1655 (C=O) cm^{-1}; MS: m/z 300 (M^+). Found: C, 63.91; H, 5.38; N, 9.26%. Calcd for $C_{16}H_{16}N_2O_4$: C, 63.99; H, 5.37; N, 9.33%.

2-(4-Nitrobenzyloxy)benzaldehyde (3$_1$*)*: Yield, 86%; mp 117 °C (118 °C[8]); ^{1}H NMR ($CDCl_3$): δ=5.28 (s, 2H, CH_2), 6.92—8.32 (m, 8H, aromatic H), 10.52 (s, 1H, CHO); IR (Nujol): 1680 (C=O) cm^{-1}; MS: m/z 257 (M^+). (Found: C, 65.37; H, 4.28; N, 5.60%).

2-(4-Bromobenzyloxy)benzaldehyde (3$_5$*)*: Yield, 81%; mp 94—94.5 °C; ^{1}H NMR ($CDCl_3$): δ=5.14 (s, 2H, CH_2), 6.95—7.91 (m, 8H, aromatic H), 10.52 (s, 1H, CHO); IR (Nujol): 1685 (C=O) cm^{-1}. Found: C, 57.58; H, 3.79%. Calcd for $C_{14}H_{11}BrO_2$: C, 57.76; H, 3.81%.

4-Dimethylamino-2-(4-bromobenzyloxy)benzaldehyde (3$_6$*)*: Yield, 36%; mp 126—128 °C; ^{1}H NMR ($CDCl_3$): δ=3.05 (s, 6H, NMe_2), 5.10 (s, 2H, CH_2), 6.04 (d, J=3 Hz, H^c), 6.29 (J=3, 9 Hz, H^b), 7.30 (d, J=9 Hz, 2H, H^e), 7.50 (d, J=9 Hz, 1H, H^a), 7.73 (d, J=9 Hz, 2H, H^d), 10.22 (s, 1H, CHO); IR (Nujol): 1645 (C=O) cm^{-1}. Found: C, 57.40; H, 4.82; N, 4.50%. Calcd for $C_{16}H_{16}BrNO_2$: C, 57.50; H, 4.83; N, 4.19%.

2-(4-Cyanobenzyloxy)benzaldehyde (3$_3$*)*: Yield, 79%; mp 103—104 °C (105—106 °C[9]); IR (Nujol): 2250 (C≡N), 1685 (C=O) cm^{-1}. (Found: C, 76.01; H, 4.66; N, 6.02%).

6-Dimethylamino-2-(4-nitrophenyl)benzofuran (4$_2$*).* A solution of **3**$_2$ (0.90 g, 3 mmol) in DMF (6 ml) was added to a solution of sodium methoxide (prepared from Na (69 mg, 3 mmol)) in MeOH (1 ml) and refluxed for 20 min. The crystals (**4**$_2$) deposited after adding MeOH (12 ml) to the mixture were filtered off and recrystallized from EtOH: red needles (0.73 g, 86%); mp 209.5—210.5 °C; ^{1}H NMR ($CDCl_3$): δ=3.04 (s, 6H, NMe_2), 6.76 (d, J=9 Hz, 1H, H^b), 6.81 (s, 1H, H^c), 7.10 (s, 1H, H^f), 7.43 (d, J=9 Hz, 1H, H^a), 7.85 (d, J=9 Hz, 2H, H^d), 8.24 (d, J=9 Hz, 2H, H^e); MS: m/z 282 (M^+). Found: C, 67.99; H, 4.97; N, 9.89%. Calcd for $C_{16}H_{14}N_2O_3$: C, 68.08; H, 5.00; N, 9.92%.

2-(4-Nitrophenyl)benzofuran (4$_1$*)*: Yield, 82% (yellow needles); mp 183.5—184.5 °C (182 °C[8]); ^{1}H NMR ($CDCl_3$): δ= 7.22—8.35 (m, 9H, aromatic H); MS: m/z 239 (M^+). (Found: C, 70.29; H, 3.71; N, 5.85%).

2-(4-Cyanophenyl)benzofuran (4$_3$*)*: Yield, 72%; mp 143—145 °C (145—146 °C[9]); ^{1}H NMR ($CDCl_3$): δ=7.15—7.97 (m, 5H, aromatic H), 7.69 (d, J=9 Hz, 2H, H^d), 7.93 (d, J=9 Hz, 2H, H^e); IR (Nujol): 2225 (C≡N) cm^{-1}; MS: m/z 219 (M^+). (Found: C, 82.28; H, 4.08; N, 6.44%).

6-Dimethylamino-2-(4-cyanophenyl)benzofuran (4$_4$*).* A solution of **1**$_2$ (2.00 g, 0.012 mol) in DMF (10 ml) was added to a solution of sodium ethoxide (prepared from Na (0.30 g, 0.013 mol)) in EtOH (8 ml) over a period of 20 min at room temperature. After the mixture had been stirred for 20 min, **2**$_1$ (2.62 g, 0.013 mol) in DMF (8 ml) was added. The resulting solution was heated the at 110 °C for 2 h and the EtOH was removed under reduced pressure. The condensed solution was poured into a mixture of ice-cold water (54 g) and MeOH (16 ml) and stirred at 0 °C for 1 h. Deposited crystals were collected, washed with water, and then dried *in vacuo*. Crude **4**$_4$ was recrystallized from petroleum benzine (bp 60—80 °C), 1.30 g, 41%: mp 164.5—166 °C; ^{1}H NMR ($CDCl_3$): δ=3.03 (s, 6H, NMe_2), 6.79 (J=3, 9 Hz, 1H, H^b), 6.89 (d, J=3 Hz, 1H, H^c), 7.04 (s, 1H, H^f), 7.42 (d, J=9 Hz, 1H, H^a), 7.63 (d, J=9 Hz, 2H, H^d), 7.83 (d, J=9 Hz, 2H, H^e); IR (Nujol): 2225 (C≡N) cm^{-1}; MS: m/z 262 (M^+). Found: C, 77.86; H, 5.34; N, 10.71%. Calcd for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68%.

6-Dimethylamino-2-(4-aminophenyl)benzofuran (4₆). A benzene (20 ml)–MeOH (18 ml) solution of **4₂** (1.00 g, 4 mmol), active carbon (0.08 g) and a catalytic amount of $FeCl_3 \cdot 6H_2O$ was refluxed for 10 min and then hydrazine hydrate (98%) (2.30 g) was added dropwise.[10] The mixture was refluxed for 7 h and filtered off under reduced pressure. A concentrate of the filtrate yielded a crude product which was recrystallized from cyclohexane to afford **4₆** (0.72 g, 81%, orange needles): mp 198.5—200 °C; ^{1}H NMR ($CDCl_3$): δ= 2.98 (s, 6H, NMe_2), 6.68 (s, 1H, H^c), 6.71 (d, J=9 Hz, 2H, H^e), 6.80 (d, J=9 Hz, 1H, H^b), 7.25 (s, 1H, H^f), 7.35 (d, J=9H, 1H, H^a), 7.59 (d, J=9 Hz, 2H, H^d): IR (KBr): 3420, 3340 (NH_2) cm^{-1}; MS: m/z 252 (M^+). Found: C, 76.42; H, 6.34; N, 11.11%. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.36; N, 11.10%.

2-(4-Aminophenyl)benzofuran (4₅): Yield, quantitative; mp 150—151 °C (152—154 °C[11]); ^{1}H NMR ($CDCl_3$): δ=3.81 (broad s, 2H, NH_2), 6.67—7.70 (m, 9H, aromatic H); IR (KBr): 3440, 3340 (NH_2) cm^{-1}; MS: m/z 209 (M^+). (Found: C, 80.64; H, 5.31; N, 6.72%).

N-[4-(2-benzofuranyl)phenyl]maleamic Acid (4₇). A mixture of **4₅** (0.50 g, 2.4 mmol) and maleic anhydride (0.23 g, 2.4 mmol) in $CHCl_3$ (5 ml) was stirred for 3 h at room temperature. The deposited crystals were filtered off, washed with a small amount of $CHCl_3$, and then recrystallized from EtOH to afford **4₇** (0.64 g, 86%, orange crystals): mp *ca.* 238.5 °C (dec.); ^{1}H NMR (DMSO-d_6): δ=3.59 (broad s, 1H, NH), 6.31 (d, J=12 Hz, 1H, H^g or H^h), 6.53 (d, J=12 Hz, 1H, H^g or H^h), 7.21—7.95 (m, 9H, aromatic H), 10.52 (s, 1H, COOH); IR (KBr): 1695 (COOH), 1625 (CONH) cm^{-1}; MS: m/z 307 (M^+). Found: C, 70.32; H, 4.21; N, 4.57%. Calcd for $C_{18}H_{13}NO_4$: C, 70.35; H, 4.26; N, 4.56%.

N-[4-(6-Dimethylamino-2-benzofuranyl)phenyl]maleamic Acid (4₈): Yield, 84%; mp 219.5—221 °C; ^{1}H NMR (DMSO-d_6): δ=2.95 (s, 6H, NMe_2), 3.80 (broad s, 1H, NH), 6.32 (d, J=12 Hz, 1H, H^g or H^h), 6.52 (d, J=12 Hz, 1H, H^g or H^h), 6.71—7.45 (m, 4H, H^{a-c} and H^f), 7.76 (s, 4H, $H^{d,e}$), 10.56 (s, 1H, COOH); IR (KBr): 1695 (COOH), 1620 (CONH) cm^{-1}; MS: m/z 350 (M^+). Found: C, 68.56; H, 5.14; N, 7.88%. Calcd for $C_{20}H_{18}N_2O_4$: C, 68.56, H, 5.18; N, 8.00%.

N-[4-(6-Dimethylamino-2-benzofuranyl)phenyl]maleimide (4₁₀): A mixture of **4₈** (1.17 g, 3.3 mmol) and sodium acetate (0.03 g, 0.3 mmol) in acetic anhydride (18 ml) was refluxed and cooled in an ice bath. The deposited crystals of **4₁₀** were collected and washed with water while the filtrate was neutralized with aq NaOH (20%) and extracted with $CHCl_3$ (30 ml×2). The organic phase was washed with saturated aq NaCl, dried over $MgSO_4$, and concentrated *in vacuo* to afford **4₁₀**. The combined products were recrystallized from acetone to give reddish purple crystals (0.51 g, 46%): mp 203—204 °C; ^{1}H NMR ($CDCl_3$): δ=3.01 (s, 6H, NMe_2), 6.84 (s, 2H, $H^{g,h}$), 6.68—7.91 (m, 8H, aromatic H); IR (Nujol): 1710 (C=O) cm^{-1}; MS: m/z 332 (M^+). Found: C, 72.15; H, 4.81; N, 8.28%. Calcd for $C_{20}H_{16}N_2O_3$: C, 72.28; H, 4.85; N, 8.43%.

N-[4-(2-Benzofuranyl)phenyl]maleimide (4₉): Yield, 45%, mp 250.5—251.5 °C; ^{1}H NMR ($CDCl_3$): δ=6.87 (s, 2H, $H^{g,h}$), 7.06 (s, 1H, H^f), 7.45 (d, J=9 Hz, 2H, H^d or H^e), 7.20—7.88 (m, 4H, *o*-disubstituted benzene H), 7.95 (d, J=9 Hz, 2H, H^d or H^e); IR (Nujol): 1710 (C=O) cm^{-1}; MS: m/z 289 (M^+). Found: C, 74.52; H, 3.80; N, 4.81%. Calcd for $C_{18}H_{11}NO_3$: C, 74.43; H, 3.83; N, 4.84%.

4-(6-Dimethylamino-2-benzofuranyl)phenyl Isothiocyanate (4₁₂). A benzene solution of thiophosgene (1 ml) was added to a solution of **4₆** (1.00 g, 4 mmol) in acetone (10 ml). The mixture was refluxed for 1 h and cooled in an ice bath. The crystals which were separated were filtered off and recrystallized from cyclohexane to afford yellow leaflets (0.56 g, 48%). mp 140—140.5 °C; ^{1}H NMR ($CDCl_3$): δ=3.01 (s, 6H, NMe_2), 6.67—7.44 (m, 4H, aromatic H), 7.22 (d, J=9 Hz, 2H, H^d), 7.77 (d, J=9 Hz, 2H, H^e); IR (Nujol): 2070, 2110, 2280 (N=C=S) cm^{-1}; MS: m/z 294 (M^+). Found: C, 69.45; H, 4.79; N, 9.44; S, 10.90%. Calcd for $C_{17}H_{14}N_2OS$: C, 69.39; H, 4.79; N, 9.52; S, 10.89%.

4-(2-Benzofuranyl)phenyl Isothiocyanate (4₁₁): Yield, 45%; mp 127—129.5 °C; ^{1}H NMR ($CDCl_3$): δ=7.26 (d, J=9 Hz, 2H, H^d), 7.01—7.76 (m, 5H, benzofuran ring H), 7.81 (d, J=9 Hz, 2H, H^e); IR (Nujol): 2170, 2150 (N=C=S) cm^{-1}; MS: m/z 251 (M^+). Found: C, 71.82; H, 3.55; N, 5.44; S, 12.86%. Calcd for $C_{15}H_9NOS$: C, 71.69; H, 3.61; N, 5.57; S, 12.76%.

4-(2-Benzofuranyl)benzoic Acid (4₁₃). A solution of **4₃** (0.30 g, 1.3 mmol) and powdered KOH (1.00 g, 18 mmol) in ethylene glycol (25 ml) was refluxed for 6 h, cooled to room temperature, and poured into a mixture of ice-water (50 ml) and concd HCl (0.5 ml). The deposited crystals were filtered off, washed with water, and dried *in vacuo*. Any crude crystals were recrystallized from EtOH to give colorless needles (0.27 g, 83%). mp *ca.* 293 °C (dec) (301—302 °C[12]); ^{1}H NMR (DMSO-d_6): δ=7.19—7.75 (m, 5H, benzofuran ring H), 8.04 (s, 4H, $H^{d,e}$); IR (Nujol): 1680 (C=O) cm^{-1}; MS: m/z 238 (M^+). (Found: C, 75.54; H, 4.14%).

4-(6-Dimethylamino-2-benzofuranyl)benzoic Acid (4₁₄): Yield, 59%; mp *ca.* 157 °C (dec); ^{1}H NMR (DMSO-d_6): δ=3.39 (s, 6H, NMe_2), 6.80 (d, J=9 Hz, 1H, H^b), 6.90 (s, 1H, H^c), 7.39 (s, 1H, H^f), 7.46 (d, J=9 Hz, 1H, H^a), 7.88 (d, J=9 Hz, 2H, H^d), 8.01 (d, J=9 Hz, 2H, H^e); IR (Nujol): 1675 (C=O) cm^{-1}; MS: m/z 281 (M^+). Found: C, 72.43; H, 5.43; N, 4.92%. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98%.

4-(2-Benzofuranyl)benzoyl Chloride (4₁₅). A mixture of **4₁₃** (1.00 g, 4.2 mmol) and thionyl chloride (25 ml) was refluxed for 15 min and concentrated *in vacuo*. Purification of the residue by recrystallization from cyclohexane gave **4₁₅** as light yellow needles (1.01 g, 94%). mp 159—160 °C; ^{1}H NMR ($CDCl_3$): δ=7.18—7.69 (m, 5H, benzofuran ring H), 7.95 (d, J=9 Hz, 2H, H^d), 8.18 (d, J=9 Hz, 2H, H^e); IR (Nujol): 1760, 1725 (C=O) cm^{-1}; MS: m/z 256 (M^+). Found: C, 70.49; 3.47; Cl, 13.58%. Calcd for $C_{15}H_9ClO_2$: C, 70.19; H, 3.53; Cl, 13.81%.

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