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A Convenient Synthesis of 2-Substituted Benzofurans from Salicylaldehydes

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Base-mediated cyclocondensation of 2-hydroxybenzaldehydes with 3-bromo-1-(arylsulfonyl)propenes and 4-bromocrotonates afforded (*E*)-2-(2-sulfonylvinyl)benzofurans and (*E*)-2-benzofuranyl-3-acrylates respectively. Previous reports of benzoxepine formation in the latter case were found to be incorrect.

Introduction

As part of a program in screening heterocycles for developing new anticancer therapeutics, we were interested in investigating the cytotoxicity profile of 4-sulfonyl-1-benzoxepine derivatives **1** (Figure 1). The benzoxepine framework is found in a number of important natural products[1] and 1-benzoxepine derivatives are known to exhibit biological activities such as estrogen regulator modulation.[2]

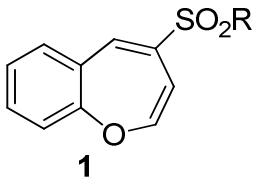
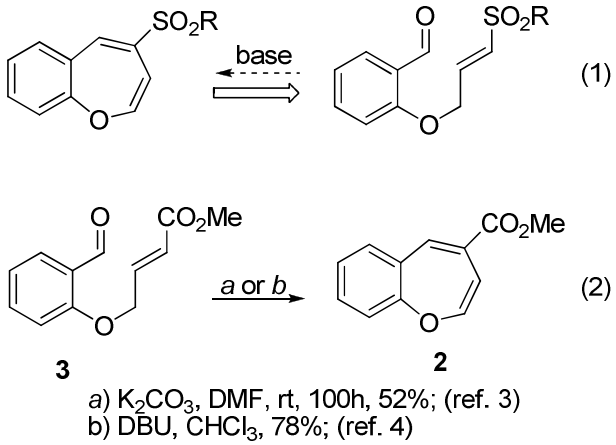


Figure 1: 4-sulfonyl-1-benzoxepine framework

A straightforward assembly of the 1-benzoxepine framework was envisaged as depicted in Scheme 1 (eq. 1) in order to generate a library of derivatives for biological screening. This synthetic plan was adapted from the reports by Ciganek[3] and Zeitler[4] that described the formation of the corresponding carboxylate esters (eq. 2, Scheme 1). For example, 4-methoxycarbonyl-1-benzoxepine **2** has been synthesized by base-mediated cyclization of the salicylaldehyde-derived ester **3**.

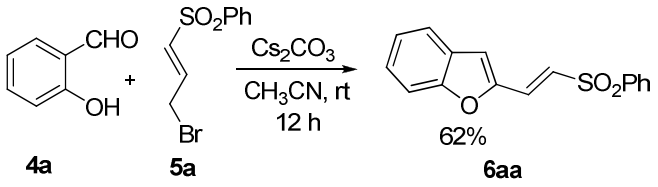


Scheme 1: Planned synthesis of 1 (eq.1) and reported syntheses of its carboxy-analogue 2 (eq.2)

Results and Discussion

The attempted synthesis of **1** began with base-mediated O-alkylation of salicylaldehyde **4a** with the previously described bromide **5a**.[5] This seemingly straightforward O-alkylation, however, afforded a mixture of products that were difficult to separate from each other by chromatography (The mixture of products arises presumably due to the base-catalyzed isomerization of the vinyl sulfone moiety into the corresponding allyl sulfone[6] subsequent to the alkylation) Pleasingly, it was found that this mixture can be converted into a single product by exposing it again to base for a longer period of time. Further experiments revealed that the isolation of the O-alkylated intermediate was not necessary, as prolonged treatment of salicylaldehyde **4a** and the bromosulfone **5a** with 2 equivalents of cesium carbonate in acetonitrile for 12h resulted in the formation of a single product. Spectroscopic analysis,

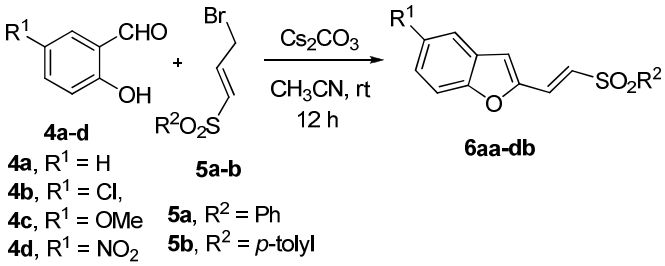
however, indicated that the product is the benzofuran derivative **6aa** (Scheme 2).



Scheme 2: Formation of 2-substituted benzofuran from salicylaldehyde

In the ^{1}H NMR spectrum of **6aa**, the olefinic proton adjacent to the sulfonyl group resonated at δ 7.57 as a doublet with coupling constant of 15.0 Hz, confirming the presence of a *trans* double bond. The remaining olefinic hydrogen resonated along with four of the aromatic protons (δ 7.65-7.55). A singlet resonance corresponding to the benzofuran-3-H was discernible at δ 7.04 (1H). All other signals were in agreement with the assigned structure.

Natural and manmade molecules containing the benzofuran nucleus exhibit a wide range of biological activities.[7] This includes, inter alia, antifungal,[8a] analgesic,[8b] antipsychotic[8c] and antimitotic[8d] activities. Therefore, the above-described annulation reaction that affords a benzofuran **6** endowed with a functionalizable handle at the 2-position appeared worth pursuing. Thus, a number of substituted salicylaldehydes **4a-d** was treated with γ-bromovinyl sulfones **5a-b** under the optimized reaction conditions. The results are summarized in table 1.



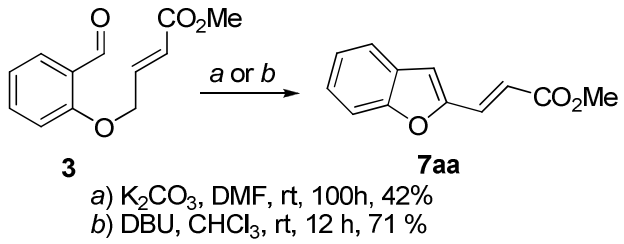
Entry	Aldehyde **4**	Bromide **5**	Product **6**	Yield[a]
1	**4a**	**5a**	**6aa**	62%
2	**4a**	**5b**	**6ab**	52%
3	**4b**	**5a**	**6ba**	55%
4	**4b**	**5b**	**6bb**	51%
5	**4c**	**5a**	**6ca**	53%
6	**4c**	**5b**	**6cb**	50%
7	**4d**	**5a**	**6da**	0[b]
8	**4d**	**5b**	**6db**	0[b]

[a]isolated yield after chromatography; [b]**4d** along with mixture of unidentified products were obtained.

Table 1: One-pot synthesis of 2-(2-sulfonylvinyl)benzofurans

The annulation reaction appears to be general affording 2-(2-sulfonylvinyl)benzofurans **6** in moderate to good yields. It is noteworthy that 2-functionalized benzofurans can be accessed in a one-pot operation from readily available starting materials, albeit in moderate yields. Out of the four substituted salicylaldehydes employed, 5-nitrosalicylaldehyde **4d** failed to react under the optimized conditions, presumably due to the sluggish *O*-alkylation of the rather stable *o*-formyl-*p*-nitrophenolate intermediate.

Thus it was evident that the approach[3-4] that led to 4-methoxycarbonyl-1-benzoxepins (Scheme 1) was not suitable for the construction of the corresponding sulfonyl derivatives. This was surprising when the known propensity of *E*-vinyl sulfones to undergo base-mediated isomerisation to *Z*-allyl sulfones[6] was taken into consideration. The unanticipated outcome of this reaction prompted us to investigate the previously described benzoxepine formation from salicylaldehyde and methyl-4-bromocrotonate. Thus, the ester **3**, derived from salicylaldehyde when subjected to the cyclocondensation conditions as reported by Ciganek[3] and Zeitler,[4] afforded the benzofuran derivative **7aa** (Scheme 4).

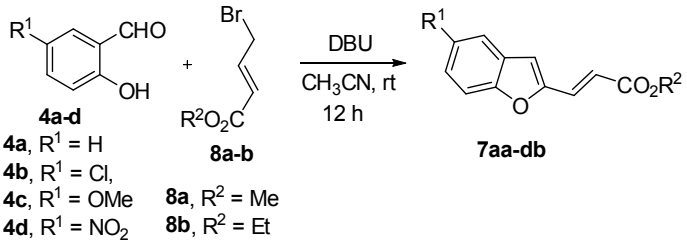


Scheme 4: Benzofuran formation via base-mediated annulation of **3**

The product **7aa** was characterized by spectroscopic analysis.[9] In the ^{1}H NMR, the olefinic protons were discernible as two mutually coupled doublets (J = 15.7 Hz) at δ 7.56 and 6.58. The 3-benzofuranyl hydrogen resonated at δ 6.94 as a singlet. It may be pointed out here that the spectroscopic data reported by Ciganek[3] for the compound **2** matches with that obtained for **7aa** in our laboratory. Most significantly, the presence of a mutually coupled pair of trans olefinic protons is inconsistent with the reported[3] benzoxepine structure **2**. Thus, in view of the new evidence, it may be concluded that the base-mediated cyclocondensation of **3** leads to the benzofuran derivative **7aa** instead of the benzoxepine **2**.[10]

Optimization experiments revealed that the substituted benzofuran derivatives could be prepared in a one-pot operation by treating substituted salicylaldehydes **4a-d** and 4-bromocrotonates **8a-b** with 2 equivalents of 1,8-diazabicycloundec-7-ene (DBU) in acetonitrile at room temperature (Table 2).

As depicted in table 2, the one-pot alkylation-annulation reaction can be extended to substituted salicylaldehydes. The benzofuran derivatives **7** are formed in moderate to good yields. It is important to note that the yields reported here correspond to the overall yield of two reactions, ie, O-alkylation and cyclization.



Entry	Aldehyde **4**	Bromide **8**	Product **7**	Yield[a]
1	**4a**	**8a**	**7aa**	61%
2	**4a**	**8b**	**7ab**	71%
3	**4b**	**8a**	**7ba**	57%
4	**4b**	**8b**	**7bb**	56%
5	**4c**	**8a**	**7ca**	53%
6	**4c**	**8b**	**7cb**	55%
7	**4d**	**8a**	**7da**	42%
8	**4d**	**8b**	**7db**	45%

[a]isolated yield after chromatography

Table 2: One-pot synthesis of (*E*)-2-benzofuranyl-3-acrylates

Additionally, unambiguous evidence for the assigned structure (**7**) was obtained from single crystal X-ray analysis of a representative compound **7cb** (Figure 2).[11]

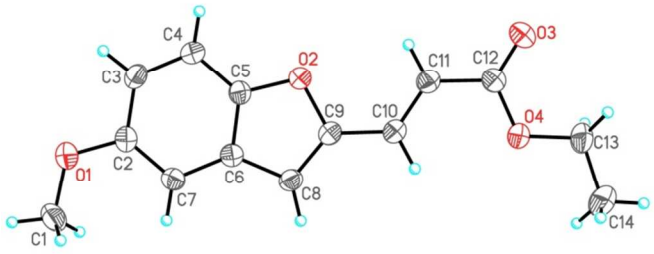
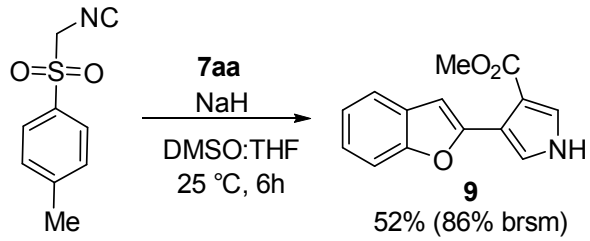


Figure 2: ORTEP diagram of **7cb**

The α,β-unsaturated ester functionality offers a number of possibilities of further synthetic manipulations. For example, treatment of the benzofuran **7aa** with van Leusen's reagent[12] (tosylmethyl isocyanide) in presence of base afforded the 3,4-disubstituted pyrrole derivative **9** in 86% isolated yield (based on recovered stating material).



Scheme 5: Synthesis of a 3,4-disubstituted pyrrole from **7aa**

Conclusions

In conclusion, a convenient one-pot method for the synthesis of 2-alkenyl substituted benzofurans from 3-bromo-1-(arylsulfonyl)propenes or 4-bromocrotonates and salicylaldehydes was developed. It is noteworthy that both the salicylaldehydes and 4-bromocrotonates are commercially available and the benzofurans generated are amenable to further functionalization. The "pluripotent" phenylsulfonyl functional group[13] has been termed as "arguably the most versatile functional group" and it is reasonable to assume that the benzofurans **6** possessing this functional group could also be employed in further transformations.

Experimental

General Information

All ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solvent on Varian Bruker 300 MHz, a Varian Unity 400 MHz and Avance 500 MHz spectrometer at ambient temperature. IR spectra were recorded on Nicolet 380 FT-IR spectrophotometer. Mass spectra were obtained on a Finnegan Mat1020B, a micromass VG 70-70H or an Agilent technologies LC/MSD treapSL spectrometer operating at 70eV using the direct inlet system and high resolution mass spectra (HRMS) were recorded on a QSTAR XL Hybrid MS/MS mass spectrometer. Melting points were recorded on an electrothermal apparatus and are uncorrected. All the reagents and solvents were used without further purification unless specified otherwise. Technical grade ethyl acetate and petroleum ether used for column chromatography were distilled prior to use. Column chromatography was carried out using silica gel (60-120 mesh and 100-200 mesh) packed in glass columns. All reactions were performed in oven-dried glassware with magnetic stirring. Salicylaldehydes (**4a-d**), methyl-4-bromocrotonates (**8a**, 85% technical grade) and ethyl-4-bromocrotonates (**8b**, 75% technical grade) used in the study were obtained from Aldrich and were used as received. 4-(2-Formylphenoxy)-but-2-enoate **3** was prepared by potassium carbonate-mediated alkylation of salicylaldehyde **4a** with **8a**.[3] *(E)*-3-bromo-1-(arylsulfonyl)propenes **5a-b** were prepared as described by Gallagher and Grayson.[14]

General procedure for the synthesis of 2-(β-sulfonylvinyl)benzofurans 6aa-cb

Cesium carbonate (326 mg, 1 mmol) was added to a solution of salicylaldehyde **4a-d** (0.5 mmol) and 3-bromo-1-(arylsulfonyl)propene **5a-b** (0.5 mmol) in anhydrous acetonitrile (5mL). The resulting solution was stirred at ambient temperature for 12h. The reaction mixture was then partitioned between dichloromethane and ice cold water, and aqueous

phase was extracted with ethyl acetate. The combined organic phases were dried with anhydrous sodium sulfate and concentrated under reduced pressure. Column chromatography on silica gel using petroleum ether-ethyl acetate as eluent afforded analytically pure samples of 2-(2-sulfonylvinyl)benzofurans **6aa-6cb**.

(*E*)-2-[2-(phenylsulfonyl)vinyl]benzofuran (**6aa**). Compound **6aa** (88 mg, 62%) was obtained as a yellow crystalline solid; Mp. 123-125 °C (CH_2Cl_2-hexane); IR ν_{max} (KBr): 3448, 2924, 2853, 1736, 1620, 1468, 1316, 1287, 1213, 1154, 1085, 1026, 954, 86, 827cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.97 (d, *J* = 8.7 Hz, 2H), 7.65-7.55 (m, 5H), 7.44-7.42 (m, 1H), 7.37 (dt, *J* = 7.2 Hz, 1.2 Hz, 1H), 7.27-7.24 (m, 1H), 7.04 (s, 1H), 7.01 (d, *J* = 15.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 155.7, 150.0, 140.4, 133.5, 129.4, 129.1, 127.9, 127.7, 127.6, 127.1, 123.6, 122.1, 113.2, 111.4; HRMS calcd for $C_{16}H_{13}O_3SNa$(M+Na) 307.0405; found 307.0392.

(*E*)-2-(2-tosylvinyl)benzofuran (**6ab**). Compound **6ab (**78 mg, 52%) was obtained as a pale yellow solid; Mp. 138-140 °C (CH_2Cl_2-hexane); IR ν_{max} (KBr): 2924, 2853, 1743, 1593, 1448, 1317, 1292, 1141, 1085, 954, 884, 852, 810, 795, 754 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.84 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 15.0 Hz, 1H), 7.42 (dd, *J* = 8.4 Hz, 0.8 Hz, 1H), 7.38-7.34 (m, 3H), 7.27-7.23 (m, 1H), 7.02 (s, 1H), 7.00 (d, *J* = 15.0 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.2, 144.5, 137.6, 133.3, 130.0, 128.6, 128.2, 128.0, 127.8, 127.0, 123.6, 122.0, 112.9, 111.4, 21.6; **HRMS** calcd for $C_{17}H_{14}O_3SNa$ (M+Na) 321.0561; found 321.0565.

(*E*)-5-chloro-2-[2-(phenylsulfonyl)vinyl]benzofuran (**6ba**). Compound **6ba (**87 mg, 55%) was obtained as a pale yellow solid; Mp. 164-166 °C (CH_2Cl_2-hexane); IR ν_{max} (KBr): 3442, 2924, 2853, 1741, 1624, 1445, 1321, 1149, 1085, 966, 951, 858, 827, 796 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.96 (d, *J* = 8.3 Hz, 2H), 7.67-7.52 (m, 5H), 7.37-7.32 (m, 2H), 7.02 (d, *J* = 15.1 Hz, 1H), 6.98 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 154.0, 151.4, 140.3, 133.6, 129.4, 129.2, 128.8, 128.6, 127.8, 127.3, 121.5, 112.5, 112.3; HRMS calcd for $C_{16}H_{11}ClO_3SNa$(M+Na) 341.0015; found 341.0007.

(*E*)-5-chloro-2-(2-tosylvinyl)benzofuran (**6bb**). Compound **6bb (**85 mg, 51%) was obtained as a brown solid; Mp. 157-159 °C (CH_2Cl_2-hexane); IR ν_{max} (KBr): 3436, 2924, 2853, 1743, 1626, 1595, 1465, 1300, 1152, 1084, 964, 856, 827, 801, 723 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.83 (d, *J* = 8.4 Hz, 2H), 7.56 (d, *J* = 2.6 Hz, 1H), 7.51 (d, *J* = 15.0 Hz, 1H), 7.37-7.34 (m, 3H), 7.31 (dd, *J* = 8.7 Hz, 2.0 Hz, 1H), 7.01 (d, *J* = 15.0 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 154.0, 151.5, 144.7, 138.7, 137.3, 130.1, 129.3, 129.2, 128.1, 127.8, 127.2, 121.5, 112.4, 112.0, 21.6; HRMS calcd for $C_{17}H_{14}ClO_3S$(M+H) 333.0352; found 333.0336.

(*E*)-5-methoxy-2-[2-(phenylsulfonyl)vinyl]benzofuran (**6ca**). Compound **6ca** (83 mg, 53%) was obtained as a dark yellow crystalline solid; Mp. 180-182 °C (CH_2Cl_2-hexane); IR ν_{max} (KBr): 3448, 2924, 2853, 1736, 1620, 1468, 1316, 1287, 1212, 1196, 1168, 1154, 1085, 1025, 954, 861, 827 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.96 (d, *J* = 8.7 Hz, 2H), 7.65-7.61 (m, 1H), 7.57-7.53 (m, 3H), 7.31 (d, *J* = 9.0 Hz, 1H), 7.01 (d, *J* = 2.7 Hz, 1H), 6.99-6.96 (m, 3H) 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 156.3, 150.8, 150.7, 133.4, 129.3, 129.1, 128.5, 127.7, 127.3, 116.6, 113.3, 112.0, 103.4, 55.8; HRMS calcd for $C_{17}H_{15}O_4SNa$ (M+Na) 337.0510; found 337.0498.

(*E*)-5-methoxy-2-(2-tosylvinyl)benzofuran (**6cb**). Compound **6cb (**82 mg, 50%) was obtained as a brown solid; Mp. 145-147 °C (CH_2Cl_2-hexane); IR ν_{max} (KBr): 3448, 3054, 2921, 2851, 1621, 1593, 1475, 1463, 1317, 1304, 1221, 1193, 1140, 1085, 964, 860, 832, 811, 785 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.83 (d, *J* = 8.2 Hz, 2H), 7.50 (d, *J* = 15.0 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 9.0 Hz, 1H), 7.01 (d, *J* = 2.4 Hz, 1H), 6.98-6.94 (m, 3H), 3.83 (s, 3H(, 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 156.4, 150.9, 144.5, 137.7, 130.0, 128.7, 128.6, 127.9, 127.7, 116.5, 113.0, 112.0, 103.6, 55.9, 21.6; HRMS calcd for $C_{18}H_{16}O_4SNa$ (M+Na) 351.0667; found 351.0664.

General procedure for the synthesis of 2-(β-alkoxycarbonylvinyl)benzofurans 7aa-db

DBU (152 mg, 1 mmol) was added to a solution of salicylaldehyde **4a-d** (0.5 mmol) and the 4-bromocrotonate ester **8** (0.5 mmol; 0.07 mL for **8a** and 0.09 mL for **8b**) in anhydrous acetonitrile (5mL). The resulting solution was stirred at ambient temperature for 12h. The reaction mixture was then partitioned between dichloromethane and ice cold water, and aqueous phase was extracted with ethyl acetate. The combined organic phases were dried with anhydrous sodium sulfate and concentrated under reduced pressure. Column chromatography on silica gel using petroleum ether-ethyl acetate as eluent afforded analytically pure samples of 2-substituted benzofurans **7aa-7db**.

(*E*)-methyl 3-(benzofuran-2-yl)acrylate (**7aa**). Compound **7aa** (62 mg, 61%) was obtained as an off-white solid; Mp. 83-85 °C[15] (CH_2Cl_2-hexane); IR ν_{max} (KBr): 3408, 2923, 2852, 1712, 1634, 1451, 1329, 1290, 1266, 1165, 1124, 1007, 977, 951, 826, 750 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.60-7.53 (m, 2H), 7.49 (d, *J* = 8.1 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.26-7.22 (m, 1H), 6.94 (s, 1H) 6.58 (d, *J* = 15.7 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 167.1, 155.5, 152.2, 131.5, 128.3, 126.4, 123.3, 121.7, 118.4, 111.4, 111.2, 51.8; HRMS calcd for $C_{12}H_{11}O_3$(M+H) 203.0708; found 203.0694.

(*E*)-ethyl 3-(benzofuran-2-yl)acrylate (**7ab**). Compound **7ab** (77 mg, 71%) was obtained as a pale yellow solid; Mp. 73-75 °C[16] (CH_2Cl_2-hexane); IR ν_{max} (KBr): 3411, 2922, 2851, 1717, 1643, 1550, 1450, 1367, 1299, 1290, 1257, 1161, 1123, 1022, 978, 949, 872, 826, 753 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.58 (d, *J* = 7.0 Hz, 1H), 7.54 (d, *J* = 15.7 Hz, 1H), 7.35 (t, *J* = 8.2 Hz, 1H), 7.26-7.21 (m, 1H), 6.93 (s, 1H), 6.58 (d, *J* = 15.7 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 155.5, 152.3, 131.2, 128.3, 126.4, 123.3, 121.7, 119.0, 111.4, 111.0, 60.6, 14.3; HRMS calcd for $C_{13}H_{13}O_3$ (M+H) 217.0865; found 217.0860.

(*E*)-methyl 3-(5-chlorobenzofuran-2-yl)acrylate (**7ba**). Compound **7ba** (67 mg, 57%) was obtained as a white solid; Mp. 160-162 °C (CH_2Cl_2-hexane); IR ν_{max} (KBr): 3412, 2923, 2852, 1729, 1642, 1488, 1441, 1304, 1253, 1089, 1168, 1059, 965, 859, 805cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.55 (d, *J* = 2.0 Hz, 1H), 7.53 (d, *J* = 15.7 Hz, 1H), 7.40 (d, J = 8.9 Hz, 1H), 7.31 (dd, *J* = 8.9, 2.0 Hz, 1H), 6.88 (s, 1H), 6.58 (d, *J* = 15.7 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.9, 153.8, 153.6, 131.0, 129.6, 128.9, 126.6, 121.2, 119.5, 112.4, 110.3, 51.9; HRMS calcd for $C_{12}H_{10}ClO_3$ (M+H) 237.0318; found 237.0312.

(*E*)-ethyl-3-(5-chlorobenzofuran-2-yl)acrylate (**7bb**). Compound **7bb** (70 mg, 56%) was obtained as a white solid; Mp. 123-125 °C (CH_2Cl_2-hexane); IR ν_{max} (KBr): 3432, 2924, 2853, 1738, 1489, 1464, 1260, 1162, 1090, 1034, 805 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.55-7.49 (m, 2H), 7.40 (d, *J* = 8.9 Hz, 1H), 7.30 (dd, *J* = 8.9, 2.0 Hz, 1H), 6.87 (s, 1H), 6.58 (d, *J* = 15.7 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 153.8, 153.6, 130.7,

129.5, 128.8, 126.5, 121.1, 119.9, 112.4, 110.1, 128.8, 60.7, 12.2; **HRMS** calcd for $C_{13}H_{12}ClO_3$ (M+H) 251.0475; found 251.0469.

(*E*)-methyl 3-(5-methoxybenzofuran-2-yl)acrylate (**7ca**). Compound **7ca** (62 mg, 53%) was obtained as a white solid; Mp. 98-100 °C (CH_2Cl_2-hexane); IR ν_{max} (KBr): 3423, 2924, 2853, 1702, 1638, 1610, 1478, 1436, 1318, 1273, 1206, 1175, 1124, 1041, 1024, 963, 938, 851. 817 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.53 (d, *J* = 15.7 Hz, 1H), 7.37 (d, *J* = 8.8 Hz, 1H), 7.01 (d, *J* = 2.5 Hz, 1H), 6.97 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.88 (s, 1H), 6.54 (d, *J* = 15.7 Hz, 1H), 3.84 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 167.2, 156.2, 153.0, 150.6, 131.5, 128.8, 118.2, 115.8, 111.9, 111.3, 103.4, 55.8, 51.8; HRMS calcd for $C_{13}H_{13}O_4$(M+H) 233.0814; found 233.0830.

(*E*)-ethyl-3-(5-methoxybenzofuran-2-yl)acrylate (**7cb**). Compound **7cb (**68 mg, 53%) was obtained as an off-white solid; Mp. 127-129 °C (CH_2Cl_2-hexane); IR ν_{max} (KBr): 3428, 2923, 2852, 1702, 1633, 1470, 1446, 1432, 1394, 1367, 1314, 1260, 1234, 1203, 1122, 1045, 1026, 960, 934, 848, 806, 766 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 7.51 (d, *J* = 15.7 Hz, 1H), 7.36 (d, *J* = 8.9 Hz, 1H), 7.01-6.94 (m, 2H), 6.86 (s, 1H), 6.54 (d, *J* = 15.7 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 3.84 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.7, 156.1, 153.0, 150.6, 131.2, 128.8, 118.7, 115.6, 111.9, 111.1, 103.3, 60.6, 55.8, 14.2; HRMS calcd for $C_{14}H_{14}O_4$ (M+H) 247.0970; found 247.0957.

(*E*)-methyl 3-(5-nitrobenzofuran-2-yl)acrylate (**7da**). Compound **7da** (52 mg, 42%) was obtained as an off-white solid; Mp. 163-165 °C (CH_2Cl_2-hexane); IR ν_{max} (KBr): 3417, 1721, 1642, 1525, 1454, 1426, 1347, 1317, 1253, 1193, 1175, 1133, 1026, 1008, 970, 818, 752 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 8.53 (d, *J* = 2.3 Hz, 1H), 8.29 (dd, *J* = 9.0, 2.3 Hz, 1H), 7.59-7.57 (m, 1H), 7.55 (s, 1H), 7.06 (s, 1H), 6.66 (d, *J* = 15.7 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (125 MHz, $(CD_3)_2SO$) δ 165.6, 161.4, 136.4, 130.9, 128.9, 128.8, 126.6, 125.4, 123.6, 123.5, 107.8, 52.4; HRMS calcd for $C_{12}H_{10}NO_5$ (M+H) 248.0559; found 248.0566.

(*E*)-ethyl 3-(5-nitrobenzofuran-2-yl)acrylate (**7db**). Compound **7db** (59mg, 45%) was obtained as an off-white solid; Mp. 157-159 °C (CH_2Cl_2-hexane); IR ν_{max} (KBr): 3418, 2924, 2853, 1714, 1643, 1520, 1464, 1344, 1269, 1179, 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.53 (d, *J* = 2.0 Hz, 1H), 8.29 (dd, *J* = 9.0 Hz, 1.9 Hz, 1H), 7.57 (d, *J* = 9.0 Hz, 1H), 7.55 (d, *J* = 15.9 Hz, 1H), 7.05 (s, 1H), 6.66 (d, *J* = 15.9 Hz, 1H), 4.30 (q, *J* = 7.2 Hz, 2H), 1.36 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.1, 155.4, 154.2, 144.5, 130.0, 128.7, 121.9, 121.5, 118.1, 111.8, 110.6, 61.0, 14.3; HRMS calcd for $C_{13}H_{12}NO_5$ (M+H) 262.0715; found 262.0722.

Conversion of 7aa into the pyrrole derivative 9

A solution of **7aa** (101 mg, 0.5 mmol) and tosylmethyl isocyanide (108 mg, 0.55 mmol) in anhydrous THF-DMSO (1 mL and 2 mL respectively) was added dropwise into a suspension of sodium hydride (60 % dispersion in mineral oil, 42 mg, 1.1 mmol) in THF (2mL). The mixture was stirred at room temperature for 6h. The reaction mixture was then treated with water and extracted with ethyl acetate. The combined extracts were dried over anhydrous sodium sulfate, solvent was removed on a rotavapor and the residue obtained was chromatographed on silica gel using petroleum ether-ethyl acetate as eluent to afford the pyrrole derivative **9** (63 mg) and unreacted **7aa** (40 mg).

Methyl-4-(benzofuran-2-yl)-1H-pyrrole-3-carboxylate (**9**). Compound **9** [63 mg, 52 % (86% brsm)] was obtained as a brown solid; Mp. 158-160 °C (CH_2Cl_2-hexane); IR (KBr) ν_{max}: 3286, 2922, 2851, 1693, 1616, 1531, 1458, 1440, 1321, 1288, 1257, 1208, 1156, 1121, 1083, 1014, 951, 815, 789 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 8.68 (br s, 1H), 7.60 (s, 1H), 7.58-7.55 (m, 1H), 7.52 (t, *J* = 2.5 Hz, 1H), 7.43 (d, *J* = 7.7 Hz, 1H), 7.38 (t, *J* = 2.5 Hz, 1H), 7.25-7.16 (m, 2H), 3.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$ and $(CD_3)_2SO$) δ: 164.3, 153.2, 151.2, 129.4, 126.2, 122.8, 121.9, 120.1, 119.1, 114.7, 111.2, 109.8, 102.8, 50.4; HRMS calcd for $C_{14}H_{12}NO_3$(M+H) 242.0817; found 242.0817.

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† Electronic Supplementary Information (ESI) available: [^1H and ^{13}C NMR spectra of all compounds and crystallographic data for compound **7cb** (CCDC 1020845)]. See DOI: 10.1039/b000000x/

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Graphical Abstract

Base-mediated cyclocondensation of 2-hydroxybenzaldehydes with 3-bromo-1-(arylsulfonyl)propenes and 4-bromocrotonates afforded (*E*)-2-(2-sulfonylvinyl)benzofurans and (*E*)-2-benzofuranyl-3-acrylates respectively. Previous reports of benzoxepine formation in the latter case were found to be incorrect.