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Synthesis of Indoles by Domino Reaction of 2-(Tosylamino)benzyl Alcohols with Furfurylamines: Two Opposite Reactivity Modes of the α-Carbon of the Furan Ring in One Process

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An unusual domino reaction where the same furan α-carbon atom reacts initially as a nucleophile and then as an electrophile is reported. In the presence of acid, *N*-tosylfurfurylamines react with 2-(tosylamino)benzyl alcohols to afford 2-(2-acylvinyl)indoles. The reaction proceeds by Friedel–Crafts alkylation at the C(2) atom of furan followed by acid-catalyzed intramolecular nucleophilic attack of the *ortho*-amino group onto the same carbon atom. The replacement of the tosylamino leaving group by phthalimide enables generation of a different type of indole yet allows the ambiphilic nature of C(2) to be retained. Both types of indoles were obtained when *N*-furfurylbenzamides were employed.

Introduction

In recent years furans have increasingly attracted the attention of researchers from various areas of chemistry. For industrial chemists, furfural, 5-hydroxymethylfurfural, and furan-2,5-dicarboxylic acid are among the most important synthetic platforms produced by biomass processing.[1] The interest in furans is stimulated by a wide variety of potential applications in polymer chemistry,[2] the chemistry of materials,[3] and in medicinal chemistry. Notably, multiple drugs such as, azimilide, dantrolene, furacin, furosemide, nifuratel, ranitidine, and others, contain the furan ring as a key structural element. To increase the scope of furan utility in various areas of science and industry, organic chemists have developed numerous approaches for the transformation of furans into a broad spectrum of products, from alkanes which can be utilized as high-quality diesel fuels,[4] to other heterocyclic systems.[5]

Due to the multifaceted reactivity of furans, these investigations are now experiencing exponential growth. Indeed, as heteroaromatic compounds, furans demonstrate typical arene reactivity trends.[6] However, due to the low aromaticity of the furan ring, they can also react as alkene, 1,3-diene, 1,4-diketone, and enol ether equivalents, to name just a few. Some of these transformations, being quite different in both mechanism and reaction products, can be carried out under similar reaction conditions. For instance, Friedel–Crafts alkylation of furans is catalyzed by Bronsted or Lewis acids and usually proceeds with excellent regioselectivity at the more nucleophilic α-carbon (Scheme 1, panel a). Meanwhile, acid catalysis is also utilized in the Piancatelli reaction[7,8] and related processes[9] where the furan α-carbon reacts as an electrophile (Scheme 1, panel b). Recognizing these two different modes of reactivity, under the qualitatively same reaction conditions, inspired us to design an acid-catalyzed domino reaction in which the alkylation step is combined with Piancatelli-like intramolecular rearrangement. To realize this idea, the nucleophilic moiety of the alkylating agent should tolerate the internal electrophilic center. 2-(Tosylamino)benzyl alcohols **1** were selected for this purpose due to the weakly nucleophilic character of the tosylamino group. Despite this quality of the tosylamino moiety, it also was envisioned to be sufficiently reactive in intramolecular processes such as acid-catalyzed rearrangements of 2-[2-(tosylamino)benzyl]furans.[10] Furthermore, it was hypothesized that the leaving group at the α-position of the furan side chain should have moderate nucleofugacity to minimize acid-induced side reactions related to furfuryl cation generation. Furfuryl alcohols and furfuryl halides do not satisfy this demand. We considered the tosylamino group as an appropriate substituent because: a) tosylamines are good leaving groups in Bronsted and Lewis acid-catalyzed reactions;[11] and b) *N*-tosylfurfurylamine (**2**) is relatively stable under acidic conditions; thus, it can be acyl-

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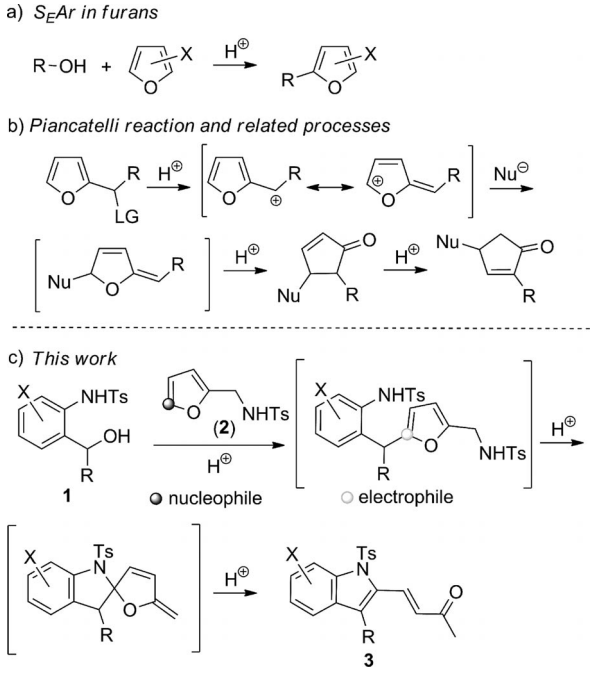
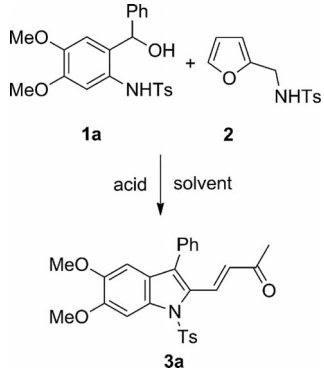
ated with benzoyl chloride in the presence of $AlCl_3$.[12] The additional advantage of this combination of substrates was postulated to be that it would enable facile access to useful indole derivatives **3** (Scheme 1, panel c).[13] Thus, we designed the domino reaction sequence to include Friedel–Crafts alkylation of furan **2** with 2-(tosylamino)benzyl alcohols **1** to afford 5-tosylamino-2-[2-(tosylamino)benzyl]-furans followed by Piancatelli-like intramolecular rearrangement and aromatization into 3-aryl(alkyl)-2-(2-acylvinyl)indoles **3**. Herein, we report the results of our investigation into this domino reaction inclusive of leaving group effects observed in dictating the specific furan product structures formed.



Scheme 1. Examples of nucleophilic and electrophilic reactivity of α-carbon atom of furan.

Table 1. Optimization of reaction conditions.[a]



Entry	Solvent	Acid	*T* [°C]	*t* [h]	Yield [%][b]
1	CH_2Cl_2	CF_3CO_2H	20	4	35
2	CH_2Cl_2	CF_3CO_2H	reflux	1	25
3	CH_2Cl_2	$BF_3{\cdot}OEt_2$	0	0.25	8
4	CH_2Cl_2	$BF_3{\cdot}OEt_2$	–20	0.5	10
5	CH_2Cl_2	PPA-Et[c]	reflux	12	19
6	benzene	CF_3CO_2H	reflux	1	68
7	benzene	CF_3CO_2H	40	48	63
8	benzene	Me_3SiCl	40	48	55
9	benzene	Me_3SiCl	reflux	8	26
10	benzene	TsOH	reflux	0.25	40
11	benzene	Amberlyst 15	reflux	1	52
12	benzene	PPA-Et[c]	reflux	2	24
13	AcOH	H_2SO_4	40	1	21
14	AcOH	H_3PO_4	40	48	14
15	AcOH	H_3PO_4	reflux	11	39
16	AcOH	$HClO_4$	40	3	31
17	AcOH	HCl	40	40	64
18	AcOH	HCl	reflux	0.166	44
19	AcOH	$CuSO_4{\cdot}5H_2O$[d]	reflux	4	69
20	AcOH	$CuSO_4$	reflux	2	40
21	AcOH	$Cu(OAc)_2{\cdot}2H_2O$[d]	reflux	4	17
22	AcOH	$Cu(OTf)_2$[e]	reflux	0.33	14
23	AcOH	$Yb(OTf)_3$[e]	reflux	0.166	52
24	dioxane	$HClO_4$	40	72	17

[a] All reactions were performed on 2 mmol scale using 1.1 equiv. of **2**. [b] Isolated yields. [c] Ethyl polyphosphate. [d] 200 mol-% of Lewis acid was used. [e] 10 mol-% of Lewis acid was used.

Results and Discussion

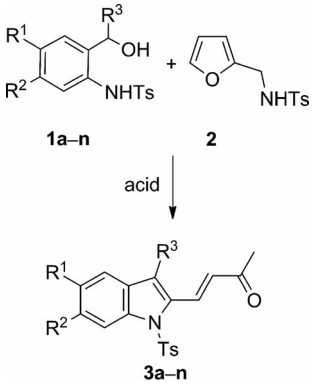
We started this investigation by optimizing reaction conditions for the synthesis of indole **3a** from *N*-tosylfurfurylamine (**2**) and 2-(tosylamino)benzhydryl alcohol **1a**. During extensive survey of various acidic conditions (Table 1), we found that good yields could be achieved using CF_3CO_2H in benzene, AcOH/HCl at 40 °C or refluxing $CuSO_4{\cdot}5H_2O$ in AcOH (Table 1, Entries 6, 17, and 19, respectively). The use of other strong Bronsted ($HClO_4$, H_2SO_4, H_3PO_4) or Lewis acids ($Cu(OTf)_2$, $Yb(OTf)_3$), in combination with AcOH proved to be much less efficient at inducing the desired domino reaction. The use of a CF_3CO_2H/benzene system gave much better results than other acids in benzene or CF_3CO_2H in other solvents.

The structure of **3a** was determined by analysis of the spectroscopic data. It is worth noting that **3a** was obtained as a single (*E*)-isomer as deduced on the basis of ^3J values for the olefinic protons.

Optimization data revealed that a fine balance of acid strength, reaction temperature and solvent polarity is required to achieve good yields. In principle, this is not unexpected since both starting compounds have ambiphilic character. Therefore, it is difficult to predict which method would give the best results for reactions between furfurylamine **2** and other 2-aminobenzyl alcohols **1**. Keeping this in mind, we investigated the reaction scope using the three sets of conditions identified above (Table 2).

We found that a broad range of 2-(tosylamino)benzyl alcohols **1** reacted with *N*-tosylfurfurylamine (**2**) affording corresponding indoles **3**. Overall, indole products were obtained in reasonable yields using all three procedures for benzhydryl alcohols containing electron-donating substituents. Replacement of the aromatic group in the α-position with alkyl moieties had no impact on reaction efficiency when the process was initiated with CF_3CO_2H in benzene or $CuSO_4{\cdot}5H_2O$/AcOH (methods **B** and **C**, respectively).

Table 2. Scope of benzyl alcohols **1** in domino reaction with *N*-tosylfurfurylamine (**2**).[a]



Entry	1,3	R^1	R^2	R^3	Yield [%][b] A[c]	B[d]	C[e]
1	**a**	OMe	OMe	Ph	64	68	69
2	**b**	OMe	OMe	4-MeC_6H_4	56	64	66
3	**c**	OMe	OMe	4-ClC_6H_4	70	67	61
4	**d**	OMe	OMe	4-BrC_6H_4	71	55	69
5	**e**	OMe	OMe	Me	32	62	64
6	**f**	OMe	OMe	Et	30	67	65
7	**g**	H	H	Ph	41	60	63
8	**h**	H	H	Me		17	
9	**i**	Cl	H	Ph		16[f, g]	
10	**j**	NO_2	H	Ph		12[h, g]	
11	**k**	–OCH_2CH_2O–		Ph	57	61	65
12	**l**	–OCH_2CH_2O–		Me	33	59	62
13	**m**	–OCH_2CH_2O–		Et	31	52	56
14	**n**	–OCH_2O–		H	35	42	47

[a] All reactions were performed on 2 mmol scale using 1.1 equiv. of **2**. [b] Isolated yields. [c] AcOH/HCl, 40 °C, 24–48 h. [d] Benzene/CF_3CO_2H, reflux, 1–2 h. [e] AcOH/$CuSO_4 \cdot 5H_2O$, reflux, 4 h. [f] *trans*-Isomer was isolated from the reaction mixture. [g] A small quantity of unseparated mixture of *cis*/*trans*-isomers was also obtained. [h] *cis*-Isomer was isolated from the reaction mixture.

However, much lower yields were obtained using the AcOH/HCl system (method **A**) (Table 2, Entries 5, 6, 12, 13). Similarly, removal of the electron-donating alkoxy group in **1**, as in 2-(tosylamino)benzhydryl alcohol (**1g**), had no significant influence on the reaction yield when methods **B** and **C**, but not **A**, were applied (Table 2, Entry 7). In contrast, the combination of both effects (as in **1h**) dramatically decreased the reaction efficiency (Table 2, Entry 8). When primary benzyl alcohol **1n** was utilized, indole **3n** was formed in moderate yield regardless of which reaction conditions were employed (Table 2, Entry 14). This observation can be explained by the low stability of a primary carbocation that leads to its oligomerization and, as a result, significant tarring of the reaction. Electron-withdrawing substituents situated *para*- to the tosylamino group reduce substrate nucleophilicity resulting in reduced product generation (Table 2, Entries 9, 10). Moreover, in these cases, both *cis*- and *trans*-isomers of indoles **3** were obtained. Isomeric product mixtures can be attributed to the fact that indoles **3** are *push-pull* alkenes and undergo a relatively fast *cis-trans* isomerization due to their capacity to assume a zwitterionic form. Introduction of an electron-withdrawing substituent into the indole ring reduces this *push-pull* character of the alkenes and decelerates *cis-trans* isomerization.

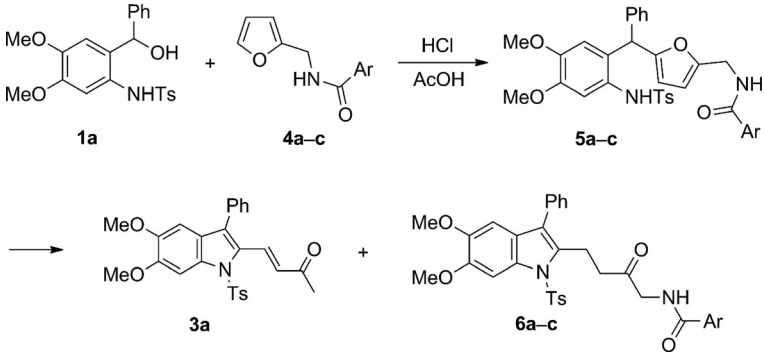
N-Tosylfurfurylamine was selected as a reaction component due, as noted before, to its good balance of acid stability and leaving group ability of the tosylamino moiety. The use of furfuryl derivatives with better leaving groups, such as furfuryl alcohol and furfuryl chloride, was found to be unproductive due to their high capacity for oligomerization. Consequently, we next turned our attention to the use of *N*-furfurylbenzamides **4a**–**c**. The logic of this decision was supported by previous reports in which benzamide was employed as a leaving group in alkylations of active methylene compounds[14a] and Friedel–Crafts reactions[14b] (Table 3).

We found that reaction of amides **4** with benzhydryl alcohol **1a** proceeded in the presence of HCl in AcOH at 40 °C. However, in every instance, target compound **3a** was formed as a minor product; the major products were indole derivatives **6** bearing the 4-aroylamino-3-oxobutyl substituent at the indole C(2). When the reaction between **1a** and **4a** was performed under refluxing conditions, the yield of **3a** was increased and found to coincide with a diminished yield of **6a** (Table 3, Entries 1, 2). On the basis of this observation, we reasoned that **6** may actually be an intermediate en route to indole **3**. To verify this hypothesis, α-aminoketones **6** were treated with HCl in AcOH under the same reaction conditions used to generate improved yields of **3a**. However, no transformation of **6** into **3a** was observed. This finding suggests that **3** and **6** are likely produced through different pathways. In contrast, the intermediacy of alkylated furans **5** was unambiguously demonstrated by their isolation from the reaction mixture and subsequent conversion into the same **3/6** mixtures previously noted by treatment with the HCl/AcOH system.

These results can be rationalized by competitive protonation of **5** at either the amide group or C(5) of the furan ring (Scheme 2). Protonation of the amide group (Scheme 2, path *a*) significantly increases its nucleofugacity (cation **A**) affording carbocation **B** by amide elimination. Nucleophilic attack by the 2-tosylamino group onto the C(2) atom of the furan followed by opening of the spirodihydrofuran ring in **C** establishes indole **3**. Protonation of furanyl C(5) (Scheme 2, path *b*) produces cation **D**, thus enabling generation of spiro-intermediate **E**. Rearrangement of **E** is completed by furan ring scission and tautomerization to **F**. It is has to be noted that, in this pathway, the furan C(2) also exhibits two opposite modes of reactivity being a nucleophile in the alkylation step leading to intermediate **5** and then serving as an electrophile in its reaction with the 2-tosylamino group leading to intermediate **E**.[15]

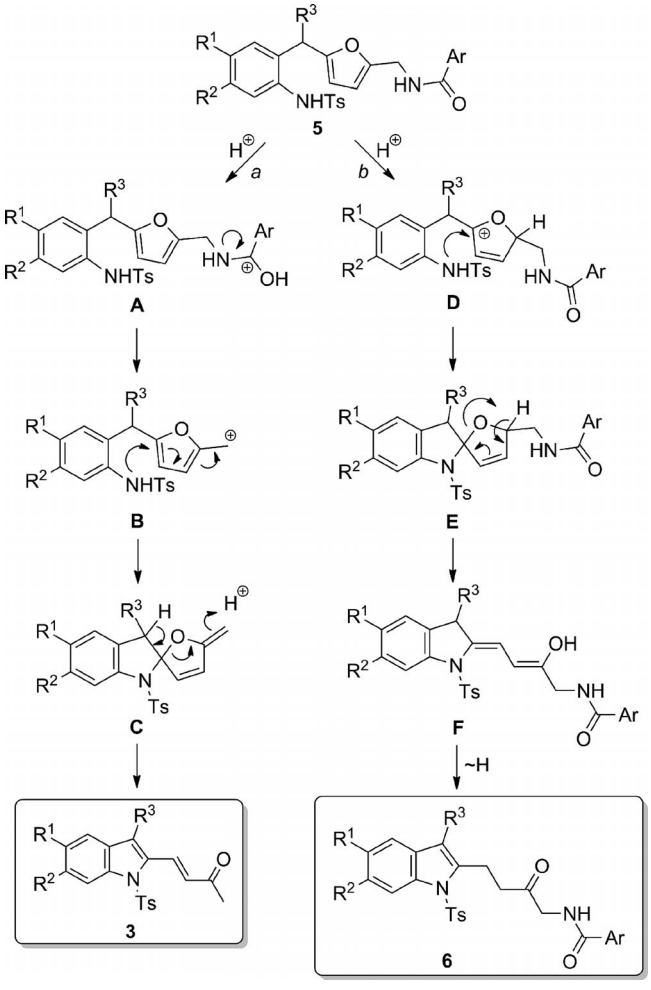
Finally, the reaction of **1a** with *N*-furfurylphthalimide **9** was investigated. In this case 4-phthalimido-3-oxobutylindole **10** was isolated exclusively (Scheme 3). This reaction is likely to proceed through a mechanism analogous to that described for formation of **6**. The formation of **3** in trace amounts is possibly related to the much lower rate of protonation of phthalimide O atoms relative to furan ring pro-

Table 3. Reaction of *N*-furfurylbenzamides **4** with benzhydryl alcohol **1a**.[a]



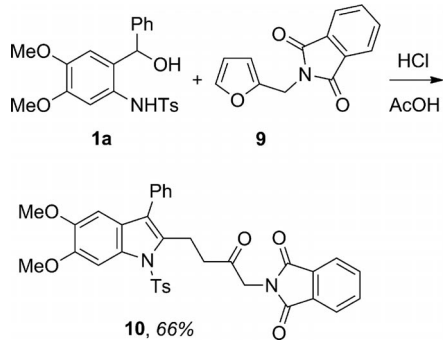
Entry	4,6	Ar	*T* [°C]	*t*	Yield [%][b]	
					3a	**6**
1	**a**	Ph	40	2 d	12	62
2	**a**	Ph	reflux	10 min	16	48
3	**b**	4-$O_2NC_6H_4$	40	2d	6	63
4	**b**	4-$O_2NC_6H_4$	reflux	10 min	9	44
5	**c**	3,4-$(MeO)_2C_6H_3$	40	2d	12	50
6	**c**	3,4-$(MeO)_2C_6H_3$	reflux	10 min	9	45

[a] All reactions were performed on 2 mmol scale using 1.1 equiv. of **4** in 15 mL of solvent. [b] Isolated yields.



Scheme 2. Possible mechanisms for generation of indoles **3** and **6**.

tonation encountered in generating intermediates like **5**. Again, the furan C(2) reacts initially as a nucleophile, and then as an electrophile.



Scheme 3. Reaction of **1a** with *N*-furfurylphthalimide **9**.

This result was quite unexpected given the better leaving group ability of phthalimide relative to benzamides. Moreover, the clear-cut dependence of the **3a/6** ratio on the nature of substituents on **4** could be expected at the first glance. In all likelihood, these results can be explained by a change in the **5**-to-**3** rate-limiting step that occurs with a change of *N*-protecting group. Namely, the electron-donating *para*-methoxy substituent in **4c** accelerates protonation of the amide oxygen affording very stable cation **A** (Scheme 2, path *a*). However, the high stability of this cation significantly decelerates amide elimination that furnishes cation **B**. Oppositely, *para*-nitrobenzamide and phthalimide are better leaving groups than the unsubstituted benzamide. However, in these cases, protonation of the amide oxygen producing cation **A** is quite inefficient. As a result, formation of **3** is decelerated and protonation of the furan ring leading to cation **D** (Scheme 2, path *b*) and then to **6** (or **10**) predominates.

Conclusions

In conclusion, we have developed a domino reaction of *N*-tosylfurfurylamine with 2-tosylaminobenzyl alcohols affording 2-(2-acetylvinyl)indoles. The specific feature of this reaction is related to the unusual behaviour of the α-carbon of the furan, which reacts initially as a nucleophile in the Friedel–Crafts alkylation and then as an electrophile in the Piancatelli-like rearrangement, which is accompanied by aromatization of the rearranged product.

Such ambiphilic behaviour is typical for isocyanides but quite unusual for aromatic carbon atoms. Furans are the most appropriate substrates to realize this dual reactivity due to the known ambiphilic properties of the furan ring. Further efforts to unveil other examples of analogous ambiphilic reactivity of aromatic carbons are currently underway.

Substitution of the tosylamino group in the furan side chain by the phthalimide moiety changes chemoselectivity of the reaction; 2-(4-phthalimido-3-oxobutyl)-indole was exclusively formed in this case. At the same time, the α-carbon in the furan demonstrates the same ambiphilic behaviour. *N*-furfurylbenzamides represent the intermediate case producing both types of products. Control experiments suggested two independent pathways for the formation of these indole derivatives.

Experimental Section

General Remarks: ^{1}H and ^{13}C NMR spectra were recorded with a Bruker Avance-600 (600 MHz for ^{1}H and 150 MHz for ^{13}C NMR) and Agilent 400-MR DD2 (400 MHz for ^{1}H and 100 MHz for ^{13}C NMR) spectrometers at room temperature; the chemical shifts (δ) were measured in ppm with respect to the solvent ($CDCl_3$, ^{1}H: δ = 7.26 ppm, ^{13}C: δ = 77.2 ppm; [D$_6$]DMSO, ^{1}H: δ = 2.50 ppm, ^{13}C: δ = 39.5 ppm). Coupling constants (J) are given in Hertz. Splitting patterns of an apparent multiplet associated with an averaged coupling constants were designed as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets) and br (broadened). IR spectra were measured as KBr plates using Prestige-21 FT-IR and Perkin–Elmer FT-IR Spectrum Two spectrophotometers. Mass spectra were recorded with a Kratos MS-30 instrument using 70 eV electron impact ionization at 200 °C. Elemental analyses were performed with a Fisons EA-1108 CHNS elemental analyser instrument. High resolution mass spectra were measured with a Bruker microTOF II instrument. Melting points are uncorrected. Column chromatography was performed using silica gel KSK (50–160 μm, LTD Sorbpolymer). All the reactions were carried out using freshly distilled and dry solvents from solvent stills. Starting 2-(tosylamino)benzhydryl and 2-(tosylamino)benzyl alcohols **1a**–**n**, *N*-furfuryl-4-methylbenzenesulfonamide (**2**), and *N*-furfurylbenzamides **4** were synthesized according to published procedures.[10b,12,16,17]

General Procedure for the Synthesis of Indoles 3a–n, 6a–c, 10

Method A: A mixture of 2-(tosylamino)benzyl alcohol **1** (2 mmol), *N*-protected furfurylamine **2**, **4**, or **9** (2.2 mmol), HCl (2.5 mL) and AcOH (15 mL) was stirred at 35–40 °C for 24–48 h (TLC control). Then the reaction mixture was poured into cold water (100 mL) and $NaHCO_3$ was added until neutral reaction. The precipitate formed was filtered. The product was purified by column chromatography on silica gel using CH_2Cl_2/hexane (1:5) mixture as an eluent and recrystallized from a mixture of $CHCl_2$/hexane.

Method B: A mixture of 2-(tosylamino)benzyl alcohol **1** (2 mmol), *N*-tosylfurfurylamine (**2**) (2.2 mmol), CF_3CO_2H (1 mL) and benzene (20 mL) was refluxed for 1–2 h (TLC control). Then reaction mixture was poured into cold water (100 mL) and $NaHCO_3$ was added until neutral reaction. The resulting mixture was extracted with ethyl acetate (3× 30 mL). The combined organic fractions were dried with Na_2SO_4 and concentrated under reduced pressure. Products were purified by column chromatography on silica gel using CH_2Cl_2/hexane (1:5) mixture as an eluent and recrystallized from a mixture of CH_2Cl_2/hexane.

Method C: A mixture of 2-(tosylamino)benzyl alcohol **1** (2 mmol), *N*-tosylfurfurylamine (**2**) (2.2 mmol), $CuSO_4{\cdot}5H_2O$ (1 g, 4 mmol) and AcOH (15 mL) was refluxed for 4 h (TLC control). Then the reaction mixture was treated as described in Method A.

Method D: A mixture of 2-(tosylamino)benzhydryl alcohol **1a** (2 mmol), *N*-benzoylfurfurylamine **4** (2.2 mmol), HCl (2.5 mL) and AcOH (15 mL) was refluxed for 10 min (TLC control). Then the reaction mixture was poured into cold water (100 mL) and $NaHCO_3$ was added until neutral reaction. The precipitate formed was filtered. The product was purified by column chromatography on silica gel using CH_2Cl_2/hexane (1:5) mixture as an eluent and recrystallized from a mixture of $CHCl_2$/hexane.

(3*E*)-4-[5,6-Dimethoxy-1-(4-methylphenyl)sulfonyl-3-phenyl-1*H*-indol-2-yl]but-3-en-2-one (3a): Yellow solid. R_f = 0.55 (acetone/petroleum ether, 1:1), m.p. 176–177 °C. ^{1}H NMR (600 MHz, [D$_6$]-DMSO): δ = 8.00 (d, ^3J = 16.4 Hz, 1 H, CH=), 7.71 (s, 1 H, Ind), 7.65–7.62 (m, 2 H, Ar), 7.53–7.48 (m, 2 H, Ar), 7.47–7.43 (m, 1 H, Ar), 7.38–7.31 (m, 4 H, Ar), 6.60 (s, 1 H, Ind), 5.91 (d, ^3J = 16.4 Hz, 1 H, CH=), 3.93 (s, 3 H, CH_3O), 3.65 (s, 3 H, CH_3O), 2.30 (s, 3 H, CH_3), 2.20 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 197.1, 149.7, 148.0, 145.6, 133.4, 132.0, 131.7, 131.4, 130.2 (2 C), 130.1, 130.0, 129.4 (2 C), 129.3 (2 C), 129.2, 128.4, 126.5 (2 C), 123.2, 101.1, 98.7, 56.0, 55.5, 27.0, 21.0 ppm. IR (KBr): $\tilde{\nu}$ = 1668, 1608, 1546, 1489, 1368, 1317, 1292, 1244, 1227, 1163, 1028, 766 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 475 (100) [M]$^+$, 320 (70), 278 (98), 263 (64), 247 (82), 234 (25), 219 (28), 91 (40), 76 (76), 43 (68). $C_{27}H_{25}NO_5S$ (475.56): calcd. C 68.19, H, 5.30, N, 2.95, S, 6.74; found C, 68.29, H, 5.29, N, 3.04, S, 6.64.

(3*E*)-4-[5,6-Dimethoxy-3-(4-methylphenyl)-1-(4-methylphenyl)sulfonyl-1*H*-indol-2-yl]but-3-en-2-one (3b): Beige solid. R_f = 0.56 (acetone/petroleum ether, 1:1), m.p. 157–158 °C. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.98 (d, ^3J = 16.4 Hz, 1 H, CH=), 7.70 (s, 1 H, Ind), 7.65–7.58 (m, 2 H, Ar), 7.37–7.33 (m, 2 H, Ar), 7.32–7.28 (m, 2 H, Ar), 7.25–7.18 (m, 2 H, Ar), 6.60 (s, 1 H, Ind), 5.97 (d, ^3J = 16.4 Hz, 1 H, CH=), 3.92 (s, 3 H, CH_3O), 3.66 (s, 3 H, CH_3O), 2.37 (s, 3 H, CH_3), 2.31 (s, 3 H, CH_3), 2.21 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 197.1, 149.6, 148.0, 145.5, 137.8, 133.3, 131.8, 131.5, 130.1 (2 C), 129.9, 129.8, 129.7 (2 C), 129.4, 129.3 (2 C), 128.8, 126.4 (2 C), 123.4, 101.2, 98.8, 55.9, 55.5, 26.9, 21.0, 20.8 ppm. IR (KBr): $\tilde{\nu}$ = 1663, 1483, 1368, 1321, 1290, 1242, 1225, 1190, 1159, 1047, 1007, 856, 787 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 489 (100) [M]$^+$, 334 (60), 292 (98), 276 (46), 261 (42), 233 (29), 166 (17), 139 (14), 118 (19), 91 (21), 76 (30), 57 (21), 43 (59). $C_{28}H_{27}NO_5S$ (489.58): calcd. C 68.69, H, 5.56, N, 2.86, S, 6.55; found C, 68.86, H, 5.42, N, 2.77, S, 6.29.

(3*E*)-4-[3-(4-Chlorophenyl)-5,6-dimethoxy-1-(4-methylphenyl)sulfonyl-1*H*-indol-2-yl]but-3-en-2-one (3c): Yellow solid. R_f = 0.57 (acetone/petroleum ether, 1:1), m.p. 201–202 °C. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.98 (d, ^3J = 16.4 Hz, 1 H, CH=), 7.70

(s, 1 H, Ind), 7.66–7.62 (m, 2 H, Ar), 7.57–7.53 (m, 2 H, Ar), 7.40–7.33 (m, 4 H, Ar), 6.64 (s, 1 H, Ind), 5.91 (d, ^3J = 16.4 Hz, 1 H, CH=), 3.92 (s, 3 H, CH_3O), 3.68 (s, 3 H, CH_3O), 2.31 (s, 3 H, CH_3), 2.23 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 197.1, 149.7, 148.0, 145.6, 133.9, 133.0, 131.6, 131.4 (2 C), 131.2, 130.8, 130.5, 130.1 (2 C), 130.0, 129.2 (2 C), 127.3, 126.4 (2 C), 122.9, 101.1, 98.6, 55.9, 55.6, 27.0, 21.0 ppm. IR (KBr): $\tilde{\nu}$ = 1674, 1497, 1379, 1304, 1254, 1200, 1096, 1022, 854, 791 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 511/509 (33/100) [M]$^+$, 356/354 (18/36), 312 (32), 281 (30), 277 (32), 91 (35), 43 (15). $C_{27}H_{24}ClNO_5S$ (510.00): calcd. C 63.59, H, 4.74, N, 2.75, S, 6.29; found C, 63.54, H, 4.78, N, 2.77, S, 6.39.

(3*E*)-4-[3-(4-Bromophenyl)-5,6-dimethoxy-1-(4-methylphenyl)sulfonyl-1*H*-indol-2-yl]but-3-en-2-one (3d): Yellow solid. R_f = 0.56 (acetone/petroleum ether, 1:1), m.p. 215–216 °C. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.97 (d, ^3J = 16.4 Hz, 1 H, CH=), 7.72–7.67 (m, 3 H, Ar + Ind), 7.66–7.62 (m, 2 H, Ar), 7.38–7.33 (m, 2 H, Ar), 7.33–7.29 (m, 2 H, Ar), 6.64 (s, 1 H, Ind), 5.91 (d, ^3J = 16.4 Hz, 1 H, CH=), 3.92 (s, 3 H, CH_3O), 3.68 (s, 3 H, CH_3O), 2.31 (s, 3 H, CH_3), 2.23 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 197.1, 149.7, 148.0, 145.6, 133.4, 132.2 (2 C), 131.7 (2 C), 131.6, 131.3, 131.2, 130.6, 130.1 (2 C), 130.0, 127.3, 126.5 (2 C), 122.8, 121.7, 101.1, 98.6, 56.0, 55.6, 27.0, 21.0 ppm. IR (KBr): $\tilde{\nu}$ = 1674, 1557, 1495, 1377, 1256, 1094, 1020, 845, 793 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 555/553 (100/100) [M]$^+$, 400/398 (27/27), 341 (12), 277 (22), 234 (14), 43 (28). $C_{27}H_{24}BrNO_5S$ (554.45): calcd. C 58.49, H, 4.36, N, 2.53, S, 5.78; found C, 58.56, H, 4.42, N, 2.47, S, 5.79.

(3*E*)-4-[5,6-Dimethoxy-3-methyl-1-(4-methylphenyl)sulfonyl-1*H*-indol-2-yl]but-3-en-2-one (3e): Yellow solid. R_f = 0.54 (acetone/petroleum ether, 1:1), m.p. 166–167 °C. ^{1}H NMR (600 MHz, [D$_6$]-DMSO): δ = 8.03 (d, ^3J = 16.3 Hz, 1 H, CH=), 7.63 (s, 1 H, Ind), 7.55–7.51 (m, 2 H, Ar), 7.31–7.27 (m, 2 H, Ar), 7.09 (s, 1 H, Ind), 6.42 (d, ^3J = 16.3 Hz, 1 H, CH=), 3.90 (s, 3 H, CH_3O), 3.80 (s, 3 H, CH_3O), 2.38 (s, 3 H, CH_3), 2.29 (s, 3 H, CH_3), 2.28 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 197.3, 149.4, 147.6, 145.3, 133.5, 132.3, 131.1, 130.1, 130.0 (2 C), 128.8, 126.3 (2 C), 125.2, 124.3, 101.8, 98.5, 55.8, 55.7, 27.6, 20.9, 11.1 ppm. IR (KBr): $\tilde{\nu}$ = 1659, 1555, 1354, 1285, 1244, 1165, 1005, 853 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 413 (92) [M]$^+$, 258 (100), 243 (18), 215 (95), 201 (60), 185 (21), 91 (20), 65 (18), 43 (47). $C_{22}H_{23}NO_5S$ (413.49): calcd. C 63.90, H, 5.61, N, 3.39, S, 7.75; found C, 64.21, H, 5.53, N, 3.36, S, 7.51.

(3*E*)-4-[3-Ethyl-5,6-dimethoxy-1-(4-methylphenyl)sulfonyl-1*H*-indol-2-yl]but-3-en-2-one (3f): Yellow solid. R_f = 0.51 (acetone/petroleum ether, 1:1), m.p. 204–205 °C. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.97 (d, ^3J = 16.4 Hz, 1 H, CH=), 7.61 (s, 1 H, Ind), 7.53–7.48 (m, 2 H, Ar), 7.31–7.27 (m, 2 H, Ar), 7.06 (s, 1 H, Ind), 6.36 (d, ^3J = 16.4 Hz, 1 H, CH=), 3.89 (s, 3 H, CH_3O), 3.79 (s, 3 H, CH_3O), 2.73 (q, ^3J = 7.5 Hz, 2 H, CH_2), 2.39 (s, 3 H, CH_3), 2.27 (s, 3 H, CH_3), 1.09 (t, ^3J = 7.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 197.4, 149.4, 147.7, 145.3, 133.2, 132.5, 131.5, 131.4, 129.9 (2 C), 129.7, 128.2, 126.3 (2 C) 123.4, 101.6, 98.8, 55.9, 55.8, 27.5, 21.0, 17.8, 14.1 ppm. IR (KBr): $\tilde{\nu}$ = 1657, 1545, 1491, 1358, 1319, 1250, 1167, 1009, 964, 845, 785 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 427 (42) [M]$^+$, 398 (20), 272 (100), 230 (22), 77 (15), 43 (32). $C_{23}H_{25}NO_5S$ (427.51): calcd. C 64.62, H, 5.89, N, 3.28, S, 7.50; found C, 64.83, H, 5.72, N, 3.38, S, 7.53.

(3*E*)-4-[1-(4-Methylphenyl)sulfonyl-3-phenyl-1*H*-indol-2-yl]but-3-en-2-one (3g): White solid. R_f = 0.62 (acetone/petroleum ether, 1:1), m.p. 146–147 °C. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 8.22–8.15 (m, 1 H, Ar), 8.03 (d, ^3J = 16.5 Hz, 1 H, CH=), 7.69–7.64 (m, 2 H, Ar), 7.53–7.49 (m, 3 H, Ar), 7.48–7.43 (m, 1 H, Ar), 7.38–7.33 (m, 4 H, Ar), 7.32–7.28 (m, 1 H, Ar), 7.28–7.25 (m, 1 H, Ar), 5.97 (d, ^3J = 16.5 Hz, 1 H, CH=), 2.30 (s, 3 H, CH_3), 2.23 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 197.2, 145.8, 136.5, 133.7, 132.2, 131.7, 131.6, 131.5, 130.3 (2 C), 130.1, 129.6 (2 C), 129.1 (2 C), 128.4, 127.6, 126.9, 126.5 (2 C), 124.9, 120.5, 115.0, 27.1, 21.0 ppm. IR (KBr): $\tilde{\nu}$ = 1674, 1447, 1379, 1250, 1171, 1088, 976, 750 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 415 (35) [M]$^+$, 276 (100), 260 (55), 218 (55), 118 (25), 91 (30), 76 (45), 43 (43). $C_{25}H_{21}NO_3S$ (415.50): calcd. C 72.27, H, 5.09, N, 3.37, S, 7.72; found C, 72.45, H, 4.95, N, 3.38, S, 7.63.

(3*E*)-4-[3-Methyl-1-(4-methylphenyl)sulfonyl-1*H*-indol-2-yl]but-3-en-2-one (3h): Cream solid. R_f = 0.57 (acetone/petroleum ether, 1:1), m.p. 141–142 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.24–8.16 (m, 1 H, Ar), 8.14 (d, ^3J = 16.6 Hz, 1 H, CH=), 7.54–7.47 (m, 2 H, Ar), 7.45–7.41 (m, 1 H, Ar), 7.40–7.34 (m, 1 H, Ar), 7.31–7.22 (m, 1 H, Ar), 7.15–7.07 (m, 2 H, Ar), 6.33 (d, ^3J = 16.6 Hz, 1 H, CH=), 2.48 (s, 3 H, CH_3), 2.29 (s, 3 H, CH_3), 2.28 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.8, 145.1, 137.4, 134.8, 134.4, 131.8, 131.7, 131.6, 129.7 (2 C), 126.7, 126.6 (2 C), 124.3, 124.0, 120.0, 115.6, 26.5, 21.6, 11.1 ppm. IR (KBr): $\tilde{\nu}$ = 1661, 1450, 1367, 1256, 1171, 1124, 1086, 974, 758 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 353 (35) [M]$^+$, 198 (100), 182 (45), 156 (56), 91 (52), 77 (25), 43 (28). $C_{20}H_{19}NO_3S$ (353.43): calcd. C 67.97, H, 5.42, N, 3.96, S, 9.07; found C, 67.92, H, 5.45, N, 3.85, S, 8.95.

(3*E*)-4-[5-Chloro-1-(4-methylphenyl)sulfonyl-3-phenyl-1*H*-indol-2-yl]but-3-en-2-one (3i): Cream solid. R_f = 0.65 (acetone/petroleum ether, 1:1), m.p. 202–203 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 (d, ^3J = 8.9 Hz, 1 H, Ind), 8.08 (d, ^3J = 16.5 Hz, 1 H, CH=), 7.64–7.55 (m, 2 H, Ar), 7.47–7.39 (m, 3 H, Ar), 7.35 (dd, ^4J = 2.1, ^3J = 8.9 Hz, 1 H, Ind), 7.25–7.17 (m, 5 H, Ar), 6.05 (d, ^3J = 16.5 Hz, 1 H, CH=), 2.35 (s, 3 H, CH_3), 2.30 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.0, 145.7, 135.8, 134.8, 133.2, 132.9, 132.2, 132.0, 131.8, 130.5, 130.0 (2 C), 129.6 (2 C), 129.3 (2 C), 128.7, 127.6, 126.9, 126.8 (2 C), 120.3, 116.8, 27.2, 21.8 ppm. IR (KBr): $\tilde{\nu}$ = 1676, 1445, 1377, 1248, 1188, 1088, 978, 811, 770 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 451/449 (33/91) [M]$^+$, 296/294 (35/80), 280/278 (7/22), 252/250 (35/75), 217 (100), 91 (72), 65 (20), 43 (38). $C_{25}H_{20}ClNO_3S$ (449.95): calcd. C 66.73, H, 4.48, N, 3.11, S, 7.13; found C, 66.96, H, 4.57, N, 3.16, S, 6.92.

(3*Z*)-4-[1-(4-Methylphenyl)sulfonyl-5-nitro-3-phenyl-1*H*-indol-2-yl]but-3-en-2-one (3j): Pale yellow solid. R_f = 0.63 (acetone/petroleum ether, 1:1), m.p. 181–182 °C. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 8.32 (d, ^3J = 9.2 Hz, 1 H, Ind), 8.25 (dd, ^4J = 2.2, ^3J = 9.2 Hz, 1 H, Ind), 8.13 (d, ^4J = 2.2 Hz, 1 H, Ind), 7.95–7.90 (m, 2 H, Ar), 7.53–7.45 (m, 3 H, Ar), 7.44–7.32 (m, 4 H, Ar), 7.18 (d, ^3J = 12.0 Hz, 1 H, CH=), 6.49 (d, ^3J = 12.0 Hz, 1 H, CH=), 2.33 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 198.1, 146.3, 144.1, 138.0, 134.8, 134.7, 133.8, 130.8, 130.3 (2 C), 129.7 (2 C), 129.0 (2 C), 128.9, 127.9, 127.3 (2 C), 126.4, 123.1, 120.3, 115.5, 114.8, 28.6, 21.1 ppm. IR (KBr): $\tilde{\nu}$ = 1698, 1521, 1342, 1239, 1167, 1087, 1021, 929, 750 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 460 (100) [M]$^+$, 417 (22), 305 (95), 289 (60), 261 (88), 246 (90), 228 (75), 216 (70), 190 (20), 155 (31), 91 (88), 65 (18), 43 (24). $C_{25}H_{20}N_2O_5S$ (460.50): calcd. C 65.20, H, 4.38, N, 6.08, S, 6.96; found C, 65.27, H, 4.42, N, 5.93, S, 6.73.

(3*E*)-4-[6-(4-Methylphenyl)sulfonyl-8-phenyl-2,3-dihydro-6*H*-[1,4]-dioxino[2,3-*f*]indol-7-yl]but-3-en-2-one (3k): Pale yellow solid. R_f = 0.59 (acetone/petroleum ether, 1:1), m.p. 233–234 °C. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.96 (d, ^3J = 16.4 Hz, 1 H, CH=), 7.63–7.58 (m, 3 H, Ar), 7.51–7.41 (m, 3 H, Ar), 7.40–7.36 (m, 2 H, Ar), 7.31–7.27 (m, 2 H, Ar), 6.59 (s, 1 H, Ar), 5.92 (d, ^3J = 16.4 Hz,

1 H, CH=), 4.32–4.29 (m, 2 H, CH_2), 4.25–4.22 (m, 2 H, CH_2), 2.32 (s, 3 H, CH_3), 2.20 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 197.1, 145.6, 143.9, 142.3, 133.5, 131.7, 131.6, 131.5, 130.8, 130.7, 130.2 (2 C), 129.3 (2 C), 129.1 (2 C), 128.4, 128.2, 126.4 (2 C), 124.4, 106.7, 103.4, 64.3, 63.9, 27.0, 21.1 ppm. IR (KBr): $\tilde{\nu}$ = 1672, 1555, 1460, 1368, 1335, 1244, 1163, 1069, 847, 700 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 473 (100) [M]$^+$, 319 (35), 276 (45), 220 (31), 91 (40), 43 (34). $C_{27}H_{23}NO_5S$ (473.54): calcd. C 68.48, H, 4.90, N, 2.96, S, 6.77; found C, 68.39, H, 4.92, N, 2.93, S, 6.76.

(3*E*)-4-[8-Methyl-6-(4-methylphenyl)sulfonyl-2,3-dihydro-6*H*-[1,4]dioxino[2,3-*f*]indol-7-yl]but-3-en-2-one (3l): Beige solid. R_f = 0.57 (acetone/petroleum ether, 1:1), m.p. 186–187 °C. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.98 (d, ^3J = 16.4 Hz, 1 H, CH=), 7.52 (s, 1 H, Ind), 7.51–7.48 (m, 2 H, Ar), 7.34–7.29 (m, 2 H, Ar), 7.06 (s, 1 H, Ind), 6.42 (d, ^3J = 16.4 Hz, 1 H, CH=), 4.32–4.29 (m, 2 H, CH_2), 4.27–4.24 (m, 2 H, CH_2), 2.37 (s, 3 H, CH_3), 2.28 (s, 3 H, CH_3), 2.22 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 197.3, 145.3, 143.7, 141.9, 133.6, 132.1, 131.3, 130.8, 130.1 (2 C), 129.6, 126.2 (2 C), 125.3, 124.3, 107.0, 103.1, 64.3, 63.8, 27.6, 21.0, 10.8 ppm. IR (KBr): $\tilde{\nu}$ = 1668, 1566, 1477, 1360, 1331, 1250, 1171, 1146, 1063, 887, 814 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 411 (100) [M]$^+$, 256 (92), 213 (53), 185 (15), 157 (30), 91 (18), 43 (17). $C_{22}H_{21}NO_5S$ (411.47): calcd. C 64.22, H, 5.14, N, 3.40, S, 7.79; found C, 64.05, H, 4.97, N, 3.39, S, 7.71.

(3*E*)-4-[8-Ethyl-6-(4-methylphenyl)sulfonyl-2,3-dihydro-6*H*-[1,4]-dioxino[2,3-*f*]indol-7-yl]but-3-en-2-one (3m): Beige solid. R_f = 0.58 (acetone/petroleum ether, 1:1), m.p. 136–137 °C. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.93 (d, ^3J = 16.4 Hz, 1 H, CH=), 7.50 (s, 1 H, Ind), 7.49–7.47 (m, 2 H, Ar), 7.33–7.27 (m, 2 H, Ar), 7.06 (s, 1 H, Ind), 6.35 (d, ^3J = 16.4 Hz, 1 H, CH=), 4.31–4.28 (m, 2 H, CH_2), 4.27–4.24 (m, 2 H, CH_2), 2.66 (q, ^3J = 7.5 Hz, 2 H, CH_2), 2.38 (s, 3 H, CH_3), 2.27 (s, 3 H, CH_3), 1.06 (t, ^3J = 7.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 197.4, 145.3, 143.6, 141.9, 133.4, 132.3, 131.7, 130.5, 130.4, 130.0 (2 C), 129.0, 126.3 (2 C), 124.4, 107.0, 103.4, 64.3, 63.8, 27.5, 21.0, 17.8, 14.1 ppm. IR (KBr): $\tilde{\nu}$ = 1676, 1483, 1375, 1263, 1198, 1094, 939, 876, 700 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 425 (100) [M]$^+$, 396 (60), 270 (95), 227 (42), 190 (20), 43 (29). $C_{23}H_{23}NO_5S$ (425.50): calcd. C 64.92, H, 5.45, N, 3.29, S, 7.54; found C, 64.95, H, 5.47, N, 3.39, S, 7.41.

(3*E*)-4-[5-(4-Methylphenyl)sulfonyl-5*H*-[1,3]dioxolo[4,5-*f*]indol-6-yl]-but-3-en-2-one (3n): Beige solid. R_f = 0.57 (acetone/petroleum ether, 1:1), m.p. 206–207 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.11 (d, ^3J = 16.1 Hz, 1 H, CH=), 7.66–7.61 (m, 2 H, Ar), 7.60 (s, 1 H, Ind), 7.40–7.36 (m, 2 H, Ar), 7.35 (s, 1 H, Ind), 7.06 (s, 1 H, Ind), 6.75 (d, ^3J = 16.1 Hz, 1 H, CH=), 6.10 (s, 2 H, OCH_2O), 2.34 (s, 3 H, CH_3), 2.31 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 197.2, 147.7, 145.8, 145.7, 134.8, 133.9, 132.9, 131.2, 130.3 (2 C), 127.8, 126.3 (2 C), 123.7, 113.6, 101.8, 99.9, 95.9, 27.6, 21.0 ppm. IR (KBr): $\tilde{\nu}$ = 1656, 1528, 1455, 1364, 1314, 1238, 1163, 1084, 1035, 945, 799 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 383 (41) [M]$^+$, 228 (100), 213 (12), 198 (15), 186 (18), 91 (35), 43 (25). $C_{20}H_{17}NO_5S$ (383.42): calcd. C 62.65, H, 4.47, N, 3.65, S, 8.36; found C, 62.64, H, 4.62, N, 3.67, S, 8.15.

***N*-{4-[5,6-Dimethoxy-1-(4-methylphenyl)sulfonyl-3-phenyl-1*H*-indol-2-yl]-2-oxobutyl}benzamide (6a):** Beige solid. R_f = 0.52 (acetone/petroleum ether, 1:1), m.p. 139–140 °C. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 8.80 (t, ^3J = 5.7 Hz, 1 H, NH), 7.90–7.84 (m, 2 H, Ar), 7.72–7.67 (m, 2 H, Ar), 7.66 (s, 1 H, Ind), 7.57–7.45 (m, 5 H, Ar), 7.44–7.38 (m, 1 H, Ar), 7.37–7.32 (m, 4 H, Ar), 6.68 (s, 1 H, Ind), 4.11 (d, ^3J = 5.7 Hz, 2 H, CH_2N), 3.86 (s, 3 H, CH_3O), 3.66 (s, 3 H, CH_3O), 3.23–3.09 (m, 2 H, CH_2), 3.02–2.92 (m, 2 H, CH_2), 2.29 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 205.3, 166.4, 147.7, 147.4, 145.3, 134.7, 134.0, 133.8, 132.3, 131.4, 130.2 (2 C), 129.8, 129.5 (2 C), 128.9 (2 C), 128.4 (2 C), 127.8, 127.3 (2 C), 126.2 (2 C), 124.2, 122.7, 100.9, 99.2, 56.0, 55.5, 48.8, 40.6, 21.0, 20.9 ppm. IR (KBr): $\tilde{\nu}$ = 3399, 1711, 1655, 1526, 1489, 1369, 1225, 1163, 1024, 714 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 596 (28) [M]$^+$, 441 (100), 423 (20), 320 (18), 279 (25), 266 (31), 234 (15), 220 (24), 188 (25), 162 (40), 105 (90), 91 (55), 65 (30), 43 (28). $C_{34}H_{32}N_2O_6S$ (596.69): calcd. C 68.44, H, 5.41, N, 4.69, S, 5.37; found C, 68.51, H, 5.58, N, 4.66, S, 5.05.

***N*-{4-[5,6-Dimethoxy-1-(4-methylphenyl)sulfonyl-3-phenyl-1*H*-indol-2-yl]-2-oxobutyl}-4-nitrobenzamide (6b):** Beige solid. R_f = 0.50 (acetone/petroleum ether, 1:1), m.p. 171–172 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 9.14 (t, ^3J = 5.7 Hz, 1 H, NH), 8.37–8.29 (m, 2 H, Ar), 8.11–8.04 (m, 2 H, Ar), 7.69–7.67 (m, 2 H, Ar), 7.66 (s, 1 H, Ind), 7.50–7.46 (m, 3 H, Ar), 7.44–7.39 (m, 1 H, Ar), 7.38–7.32 (m, 3 H, Ar), 6.68 (s, 1 H, Ind), 4.17 (d, ^3J = 5.7 Hz, 2 H, CH_2N), 3.86 (s, 3 H, CH_3O), 3.66 (s, 3 H, CH_3O), 3.22–3.10 (m, 2 H, CH_2), 3.04–2.90 (m, 2 H, CH_2), 2.30 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 204.8, 164.9, 149.2, 147.7, 147.4, 145.3, 139.4, 134.7, 134.0, 132.3, 130.2 (2 C), 129.8, 129.5 (2 C), 129.0 (2 C), 128.8 (2 C), 127.8, 126.3 (2 C), 124.3, 123.7 (2 C), 122.7, 100.9, 99.2, 56.0, 55.5, 48.9, 40.7, 21.0, 20.9 ppm. IR (KBr): $\tilde{\nu}$ = 3362, 1711, 1663, 1522, 1486, 1343, 1303, 1157, 1089, 1024, 845, 717 cm^{-1}. HRMS (ESI) calcd. for $C_{34}H_{31}N_3O_8S^+$ [M]$^+$ 641.1832, found 641.1826.

***N*-{4-[5,6-Dimethoxy-1-(4-methylphenyl)sulfonyl-3-phenyl-1*H*-indol-2-yl]-2-oxobutyl}-3,4-dimethoxybenzamide (6c):** Beige solid. R_f = 0.40 (acetone/petroleum ether, 1:1), m.p. 183–184 °C. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 8.66 (t, ^3J = 5.6 Hz, 1 H, NH), 7.71–7.67 (m, 2 H, Ar), 7.66 (s, 1 H, Ind), 7.51–7.47 (m, 3 H, Ar), 7.46 (d, ^4J = 1.9 Hz, 1 H, Ar), 7.44–7.39 (m, 1 H, Ar), 7.37–7.31 (m, 4 H, Ar), 7.03 (d, ^3J = 8.5 Hz, 1 H, Ar), 6.68 (s, 1 H, Ind), 4.07 (d, ^3J = 5.6 Hz, 2 H, CH_2N), 3.86 (s, 3 H, CH_3O), 3.81 (s, 3 H, CH_3O), 3.80 (s, 3 H, CH_3O), 3.66 (s, 3 H, CH_3O), 3.20–3.11 (m, 2 H, CH_2), 3.00–2.90 (m, 2 H, CH_2), 2.30 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 205.5, 166.0, 151.4, 148.3, 147.7, 147.4, 145.2, 134.8, 134.0, 132.2, 130.1 (2 C), 129.8, 129.4 (2 C), 128.9 (2 C), 127.7, 126.2 (2 C), 126.0, 124.2, 122.7, 120.5, 110.9, 110.7, 101.0, 99.3, 56.0, 55.6, 55.5, 55.4, 48.8, 40.6, 21.0, 20.9 ppm. IR (KBr): $\tilde{\nu}$ = 3433, 1722, 1657, 1599, 1468, 1358, 1263, 1223, 1155, 1018, 852, 766 cm^{-1}. HRMS (ESI) calcd. for $C_{36}H_{36}N_2O_8S^+$ [M]$^+$ 656.2192, found 656.2187.

2-{4-[5,6-Dimethoxy-1-(4-methylphenyl)sulfonyl-3-phenyl-1*H*-indol-2-yl]-2-oxobutyl}isoindole-1,3(2*H*)-dione (10): Method A. Pale yellow solid. R_f = 0.52 (acetone/petroleum ether, 1:1), m.p. 186–187 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.96–7.89 (m, 2 H, Ar), 7.88–7.81 (m, 2 H, Ar), 7.74–7.67 (m, 2 H, Ar), 7.66 (s, 1 H, Ind) 7.54–7.45 (m, 2 H, Ar), 7.44–7.31 (m, 5 H, Ar), 6.69 (s, 1 H, Ind), 4.60 (s, 2 H, CH_2N), 3.87 (s, 3 H, CH_3O), 3.66 (s, 3 H, CH_3O), 3.23–3.13 (m, 2 H, CH_2), 3.12–3.02 (m, 2 H, CH_2), 2.29 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, DMSO): δ = 202.2, 167.4 (2 C), 147.8, 147.4, 145.3, 134.8 (2 C), 134.4, 133.9, 132.2, 131.5 (2 C), 130.2 (2 C), 129.8, 129.5 (2 C), 129.0 (2 C), 127.8, 126.3 (2 C), 124.4, 123.3 (2 C), 122.7, 100.9, 99.2, 56.0, 55.5, 46.3, 40.7, 21.0, 20.8 ppm. IR (KBr): $\tilde{\nu}$ = 1713, 1487, 1431, 1362, 1304, 1231, 1190, 1159, 1090, 1028, 997, 847, 760 cm^{-1}. $C_{35}H_{30}N_2O_7S$ (622.69): calcd. C 67.51, H, 4.86, N, 4.50, S, 5.15; found C, 67.27, H, 4.70, N, 4.30, S, 5.29.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of **3a**–**n**, **6a**–**c** and **10**.

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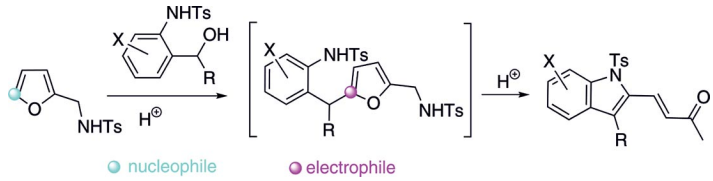

Furfurylamines react with 2-(tosylamino)-benzyl alcohols affording 2-(2-acylvinyl)-indoles by a domino reaction sequence in which the same furan α-carbon atom behaves initially as an electron-rich center and then as an electron deficient one. In addition, substitution of the tosylamino leaving group with a phthalimido group furnishes a change in chemoselectivity.

Keywords: Oxygen heterocycles / Electrophilic substitution / Nucleophilic substitution / Nitrogen heterocycles

