Syntheses of heteroaryl-benzotriazoles by Mannich condensations

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Abstract

Efficient one step syntheses of *N*-substituted-2-(benzotriazol-1-yl) [isoindoles and pyrroles] are effected by reactions of primary amines with *o*-phthalaldehyde and 2,5-dimethoxy-2,5-dihydrofuran, respectively, in the presence of benzotriazole. Reaction of 2,5-dimethoxy-2,5-dihydrofuran with benzotriazole gave 2-(benzotriazol-1-yl)furan.

Keywords: Mannich reaction, benzotriazoles, 4-benzotriazolyl benzotriazoles, 4-benzotriazolyl pyroles

Introduction

Aryl benzotriazoles are useful synthons in thermal and photochemical Graebe-Ullmann reactions leading to carbazoles,[1] pyridoacridines,[2] carbolines,[3] benzocarbolines,[4] and fused tetraazapentalenes.[5]

N-Arylbenzotriazoles have been synthesized by three pathways: (i) Arylation of benzotriazole. Direct arylation of the benzotriazole anion succeeds only for activated aryl halides.[6] For the less reactive aryl halides, Cu-catalyzed reactions of benzotriazole with $ArPb(OAc)_3$,[7] or Pd-catalyzed reactions in the presence of a copper salt under phase transfer conditions[8] are used. (ii) Construction of the benzotriazole ring from an aromatic substituent. This usually involves three steps, the arylation of an ortho-nitroaniline, reduction of the nitro-group and diazotization followed by cyclization.[4] An alternative is the reaction of aryl azides with benzynes.[9] (iii) The direct synthesis of an aromatic system bearing a benzotriazole substituent. To our knowledge, the only such example was using 2-(benzotriazol-1-yl)vinamidinium salt to prepare 5-(benzotriazol-1-yl)pyrimidines, 4-(benzotriazol-1-yl)pyrazoles and 4-(benzotriazol-1-yl)pyrroles.[10] We now report a facile route to pyrryl-, furyl-, and isoindolyl-benzotriazoles via Mannich condensations of *o*-phthalaldehyde and 2,5-dimethoxy-2,5-dihydrofuran with primary amines.

Results and Discussion

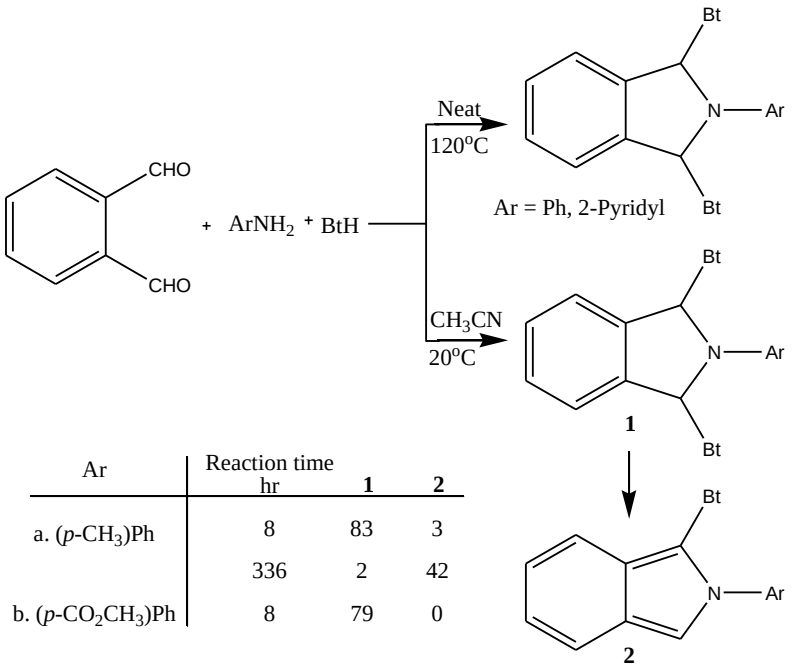
1. Preparation and reactivity of *N*-substituted-2-(benzotriazol-1-yl)isoindoles

Isoindoles have attracted considerable theoretical and synthetic interest.[11] Previous work showed that double Mannich condensation of *o*-phthalaldehyde with primary aromatic amines in the presence of excess (3 or 4 equivalents) of benzotriazole in acetonitrile[12] or at 120 ºC without solvent[13] gave exclusively or mainly benzotriazole-substituted isoindoline derivatives (1). The para substituent in the arylamine affects the product outcome. Thus *p*-methylaniline gave 3% 2*H*-isoindole (2a), while no formation of 2*H*-isoindole (2b) was detected with *p*-methoxycarbonylaniline. More 2*H*-isoindole (2a) was formed by extending the reaction time to 336 h (Scheme 1).[12]

We now find, somewhat surprisingly, that using benzylamine (instead of an aniline) in methylene chloride at room temperature gives *N*-benzyl-2-(benzotriazol-1-yl)isoindole 3a in 60% yield; none of the corresponding bis(benzotriazol-1-yl)isoindoline was isolated. Other *N*-substituted-2-(benzotriazol-1-yl)isoindoles (3b-g) were obtained in moderate to good yields (47-80%) by extending this reaction to a range of aliphatic primary amines.

In the absence of benzotriazole, primary amines are known to react with *o*-phthalaldehyde to produce the addition products (4), which can undergo dehydration to the corresponding isoindolinone (5) in low yield.[14] When benzotriazole and b -mercaptoethanol were used as dual synthetic auxiliaries[15] or there was an intramolecular auxiliary, *e.g*. amino acid or amino alcohol,[16] isoindolinone products (5) were obtained in good yield.

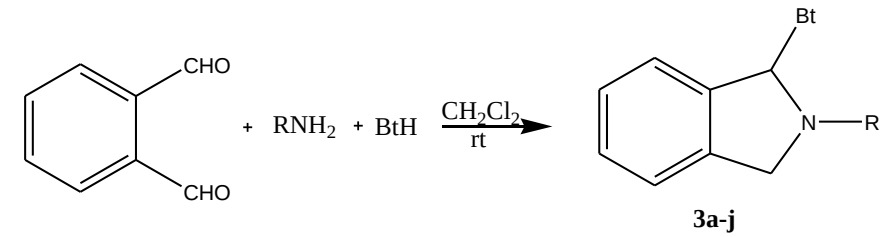
Under our reaction conditions the amino alcohol, (2*S*)-2-phenyl-2-aminoethanol, and amino acid esters also gave the corresponding isoindole products in good yields. However, the ^{1}H and ^{13}C NMR for compound 3i were not well defined due to lone pair interactions. The structure of 3h was further confirmed by X-ray crystallography (Scheme 2). Not shown in the diagram is the fact that the hydroxyl group is disordered over two positions, each of which involves hydrogen bonding to a nitrogen of a benzotriazole ring in an adjacent molecule.



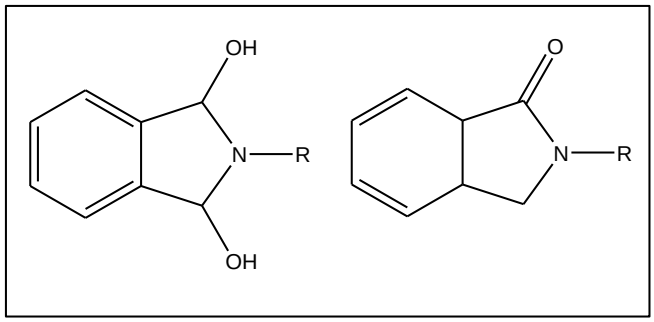
Ar	Reaction time hr	1	2
a. (*p*-CH_3)Ph	8	83	3
	336	2	42
b. (*p*-CO_2CH_3)Ph	8	79	0

Scheme 1

The 2-(benzotriazol-1-yl)isoindoles (3) are quite stable (at room temperature for several months without any change). Heating 3g in biphenyl ether to 250° C led via benzotriazole thermolysis to phenylimine (6), which was further hydrolyzed to isoindolinone (5a). Interestingly, the thermolysis of 3h in biphenyl ether under similar conditions gave the unusual benzotriazole migration products 9 (benzotriazol-1-yl) and 10 (benzotriazol-2-yl) in the ratio of 1:2, which is postulated to proceed through intermediate 7, along with minor tricyclic lactam product 8 (Scheme 3). The structure of 10 was unambiguously determined by X-ray crystallography. The crystals of 10 contain two independent molecules in the asymmetric unit, one of which is shown in Scheme 3.



3a-j



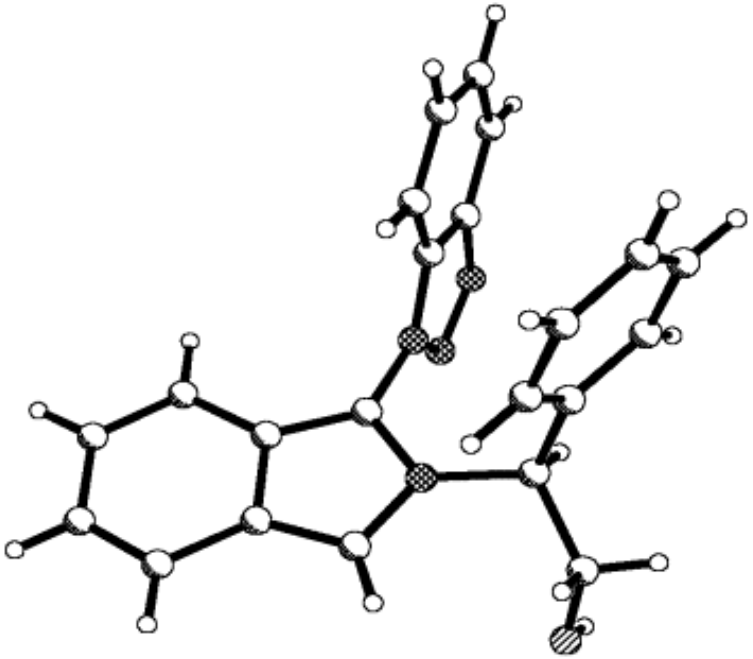
R = a. $PhCH_2$
b. $PhCh_2CH_2$
c. $CH_3(CH_2)_3$
d. $CH_3(CH_2)_2(CH_3)CH$
e. $CH_3(CH_2)_7$
f. 3-$PyCH_2$
g. (*S*)-$Ph(CH_3)CH$
h. (*S*)-$Ph(CH_2OH)CH$
i. (*S*)-$PhCH_2(CO_2CH_3)CH$
j. (S)-$CH_3(CO_2CH_3)CH$

Scheme 3

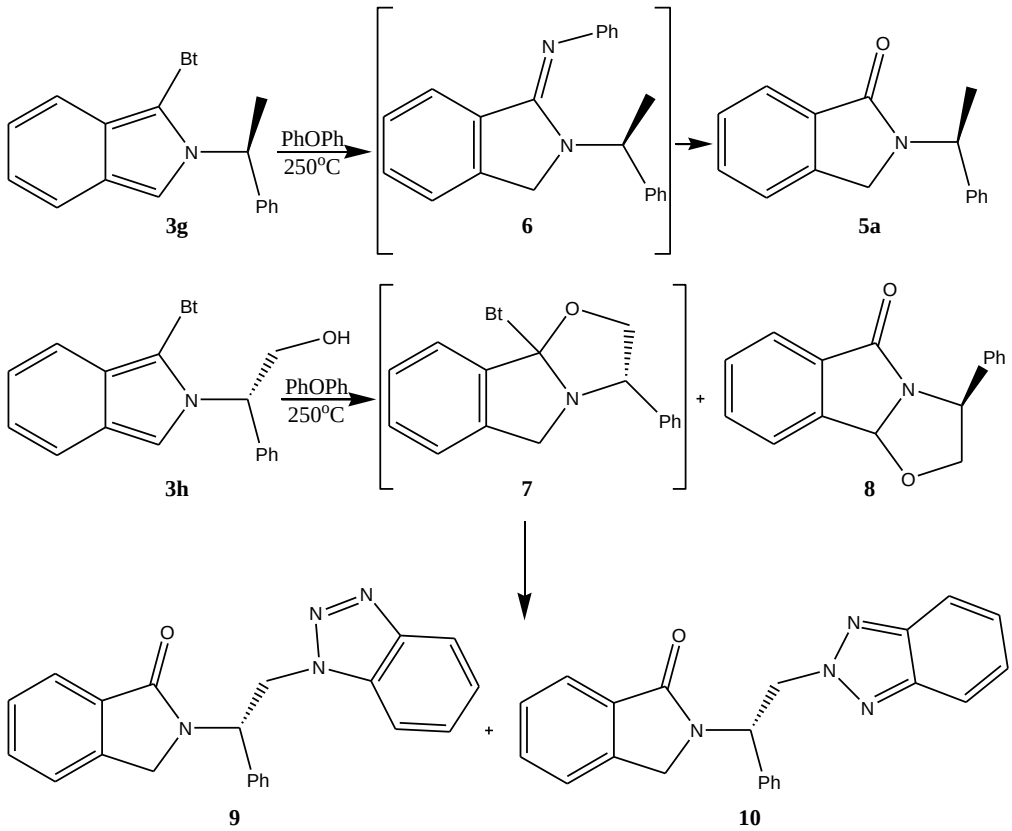
2. *N*-Substituted-2-(benzotriazol-1-yl)pyrroles and 2-(benzotriazol-1-yl)furan

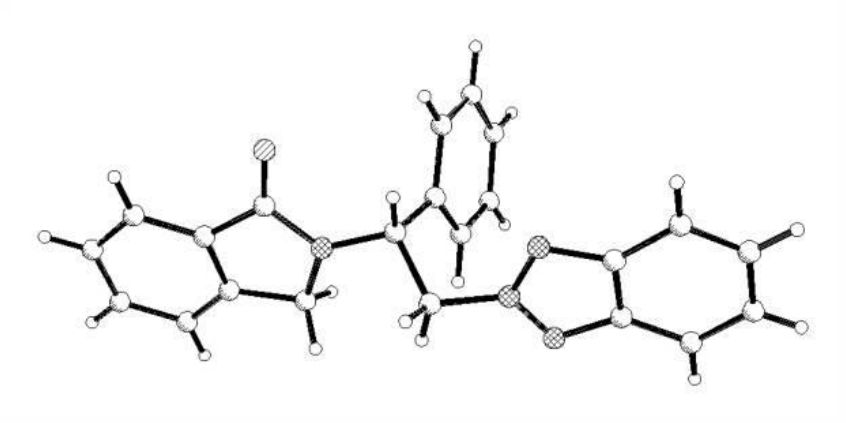
N-Substituted pyrroles are important intermediates with a wide variety of applications. They can be formed from primary amines by reaction with 2,5-dimethoxy-tetrahydrofuran or the reactive functional equivalent, 1,4-dichloro-1,4dimethoxybutane.[17]

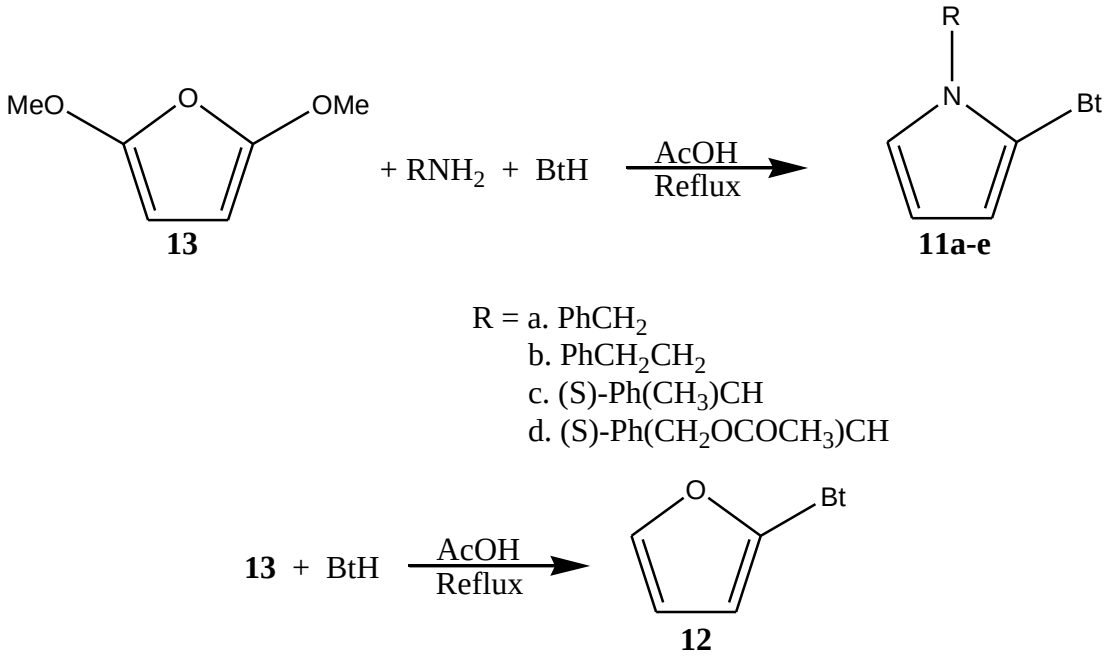
We now find that primary amines and benzotriazole condense with 2,5-dimethoxy-2,5-dihydrofuran (11), a useful polyfunctionalized C_4 synthon,[18] in acetic acid to give *N*-substituted-2-(benzotriazol-1-yl)pyrroles (12) in low yield (13) was obtained in moderate yield (65%) by heating 11 with benzotriazole in the absence of primary amines (Scheme 4).



The X-ray structure of 3h







Scheme 4

In summary, heteroaryl-benzotriazole compounds, *N*-substituted-2-(benzotriazol-1-yl)isoindoles, pyrroles, and 2-(benzotriazol-1-yl)furan were prepared in one step from *o*-phthalaldehyde and 2,5-dimethoxy-2,5-dihydrofuran by Mannich condensations.

Experimental Section

General Procedures. Melting points were determined on a hot-stage apparatus without correction. Column chromatography was carried out on silica gel (230-400 mesh). The ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ solution (300 MHz and 75 MHz respectively), with TMS or $CDCl_3$ as internal references.

General procedure for preparation of compounds 3a-j

A mixture of *o*-phthalic dicarboxaldehyde (1.34 g, 10 mmol), primary amine (10 mmol) and benzotriazole (2.38 g, 20 mmol) in CH_2Cl_2 (50 mL) was stirred with molecular sieves (4 Å) at room temperature overnight. The molecular sieves were removed by filtration, and the filtrate washed with 2 N NaOH (3 x 30 mL) and brine (3 x 30 mL). The organic phase was dried and concentrated to give a residue, which was purified by column chromatography (eluent: hexane/EtOAc) to afford compounds 3a-j.

1-(2-Benzyl-2*H*-isoindole-1-yl)-1*H*-1,2,3-benzotriazole (3a). Yield: 56.5%; Brown powder; mp 154- 155 °C; ^{1}H NMR δ : 5.19 (d, *J* = 10.0 Hz, 2H), 6.82- 6.83 (m, 2H), 6.94- 7.06 (m, 7H), 7.28- 7.36 (m, 3H), 7.58 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR δ : 51.7, 109.9, 111.4, 112.3, 116.6, 119.9, 120.0, 120.6, 121.6, 122.6, 123.2, 124.2, 127.0, 127.8, 128.2, 128.4, 135.1, 135.5, 145.0. Anal. Calcd for $C_{21}H_{16}N_4$: C, 77.76; H, 4.97; N, 17.27. Found: C, 77.78; H, 4.93; N, 17.30.

1-(2-Phenylethyl-2*H*-isoindole-1-yl)-1*H*-1,2,3-benzotriazole (3b). Yield: 47.0%; Brown oil; ^{1}H NMR δ : 2.94- 2.96 (m, 2H), 4.11- 4.17 (m, 1H), 4.30- 4.40 (m, 1H), 6.84- 6.86 (m, 2H), 6.93- 7.17 (m, 8H), 7.41- 7.43 (m, 2H), 7.54 (d, *J* = 8.2 Hz, 1H), 8.17 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR δ : 37.9, 49.3, 110.2, 111.0, 111.7, 116.7, 120.0, 120.1, 121.4, 122.4, 122.9, 124.4, 126.6, 128.3, 128.4, 135.0, 137.1, 145.1. Anal. Calcd for $C_{22}H_{18}N_4$: C, 78.08; H, 5.36; Found: C, 78.09; H, 5.58.

1-(2-Butyl-2*H*-isoindole-1-yl)-1*H*-1,2,3-benzotriazole (3c). Yield: 52.0%; Pale yellow microcrystals; mp 76-77° C;^{1}H NMR δ : 0.73 (t, *J* = 7.4 Hz, 3H), 1.13- 1.18 (m, 2H), 1.57- 1.67 (m, 2H), 3.92- 3.94 (m, 1H), 4.05- 4.20 (m, 1H), 6.95- 7.07 (m, 3H), 7.24- 7.32 (m, 2H), 7.42- 7.52 (m, 2H), 7.59 (d, *J* = 8.2 Hz, 1H), 8.18 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR δ : 13.3, 19.6, 33.0, 47.5, 110.1, 111.0, 111.6, 116.6, 119.9, 120.2, 120.3, 121.4, 122.5, 122.9, 124.4, 128.5, 135.3, 145.1. Anal. Calcd for $C_{18}H_{18}N_4$: C, 74.46; H, 6.25; N, 19.29. Found: C, 74.31; H, 6.14; N, 19.07.

1-[2-(1-Methylbutyl)-2*H*-isoindole-1-yl]-1*H*-1,2,3-benzotriazole (3d). Yield: 56.0%; Pale yellow microcrystals; mp 109-111 °C;(Two isomers, the data of minor isomer are in brackets). ^{1}H NMR δ : 0.53 (t, *J* = 6.3 Hz, 2H), 0.81 (t, *J* = 6.2 Hz, 3H), 1.14- 1.93 (m, 5H), 3.94- 4.03 (m, 1H), 6.90- 7.15 (m, 3H), 7.20- 7.29 (m, 1H), 7.38- 7.55 (m, 3H), 7.61 (d, *J* = 7.7 Hz, 1H), 8.18 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR δ : 13.3[13.6], 19.1[19.3], 22.8[22.9], 39.7[39.9], 52.7[52.8], 107.6[107.7], 109.9, 110.1, 116.6[116.7], 119.8[119.9], 120.0[120.1], 120.3, 121.3[121.4], 122.7[122.8], 122.9, 124.3, 128.5, 135.5, 145.2. Anal. Calcd for $C_{19}H_{20}N_4$: N, 18.41. Found: N, 18.53.

1-(2-Octyl-2*H*-isoindole-1-yl)-1*H*-1,2,3-benzotriazole (3e). Yield: 64.0%; Yellow oil; ^{1}H NMR δ : 0.82 (t, *J* = 7.2 Hz, 3H), 1.07- 1.29 (m, 10H), 1.61- 1.80 (m, 2H), 3.92- 4.12 (m, 2H), 6.94- 7.07 (m, 3H), 7.27- 7.31 (m, 2H), 7.42- 7.51 (m, 2H), 7.59 (d, *J* = 9.1 Hz, 1H), 8.17 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR δ : 13.9, 22.4, 26.3, 28.7, 28.8, 31.0, 31.5, 47.8, 110.1, 111.0, 111.5, 116.6,

119.9, 120.1, 120.2, 121.4, 122.5, 122.8, 124.4, 128.5, 135.2, 145.1. HRMS Calcd for $C_{22}H_{27}N_4$: 347.2235 (M^++1). Found: 347.2241 (M^++1).

1-[2-(3-Pyridinylmethyl)-2*H*-isoindole-1-yl]-1*H*-1,2,3-benzotriazole (3f). Yield: 53.0%; Brown microcrystals; mp 125- 127 ºC; ^{1}H NMR δ : 5.22- 5.28 (m, 2H), 6.94- 7.07 (m, 5H), 7.15 (d, *J* = 6.9 Hz, 1H), 7.30- 7.40 (m, 3H), 7.59 (d, *J* = 7.8 Hz, 1H), 8.10- 8.16 (m, 2H), 8.30 (d, *J* = 4.5 Hz, 1H); ^{13}C NMR δ : 49.1, 109.7, 111.3, 112.2, 116.5, 120.0, 120.4, 121.9, 122.7, 123.2, 123.4, 124.4, 128.5, 131.3, 134.6, 134.8, 144.9, 148.2, 149.2. Anal. Calcd for $C_{20}H_{15}N_5$: C, 73.83; H, 4.65; N, 21.52. Found: C, 73.83; H, 5.01; N, 21.70.

1-{2-[(1*S*)-1-phenylethyl]-2*H*-isoindole-1-yl}-1*H*-1,2,3-benzotriazole (3g). Yield: 80.0%; Yellow oil; (Two isomers, the data of minor isomer are in brackets). ^{1}H NMR δ : 1.96 (d, *J* = 6.9 Hz, 3H) [1.76 (d, *J* = 6.9 Hz, 3H)], 5.54 (q, *J* = 6.9 Hz, 1H) [5.36 (q, *J* = 6.9 Hz, 1H)], 6.64- 7.68 (m, 13H), 8.06 (d, *J* = 8.1 Hz, 1H) [8.18 (d, *J* = 8.1 Hz, 1H)]; ^{13}C NMR δ : 22.0[21.6], 56.4[55.7], 108.9, 110.0, 116.6[116.8], 119.7, 120.3, 121.5[121.6], 123.1[123.2], 124.0, 125.2, 126.7, 127.5, 128.0, 128.4, 128.5, 128.6, 135.5, 141.4, 145.0. Anal. Calcd for $C_{22}H_{18}N_4$: C, 78.07; H, 5.37; N, 16.56. Found: C, 77.83; H, 5.42; N, 16.62.

(2*S*)-2-[1-(1*H*-1,2,3-Benzotriazol-1-yl)-2*H*-isoindole-2-yl]-2-phenyl-1-ethanol (3h). (Two isomers, the data of minor isomer are in brackets). Yield: 61.0%; Dark brown microcrystals; mp 187- 188 ºC; ^{1}H NMR δ : 2.50- 2.60 (m, 1H) [2.20- 2.30 (m, 1H)], 4.30- 4.40 (m, 2H) [4.15- 4.25 (m, 2H)], 5.45- 5.50 (m, 1H) [5.30- 5.40 (m, 1H)], 6.70- 6.85 (m, 2H), 6.90- 7.10 (m, 5H), 7.20- 7.80 (m, 6H), 8.00- 8.10 (m, 1H); ^{13}C NMR δ : 62.7[62.2], 63.0, 109.7, 110.6[110.5], 111.2[111.0], 115.9[116.2], 119.7[119.4], 120.3[120.0], 120.7[120.4], 121.1[121.0], 122.3[121.8], 122.9[123.2], 124.3[124.6], 126.1[127.1], 128.0[127.6], 128.2, 128.5[128.4], 135.6[134.8], 137.8[137.7], 144.6[144.3]. Anal. Calcd for $C_{22}H_{18}N_4O$: C, 74.56; H, 5.12; N, 15.81. Found: C, 74.54; H, 5.06; N, 15.90.

Methyl-2(*S*)-[1-(1*H*-1,2,3-benzotriazol-1-yl)-2*H*-isoindole-2-yl]-3-phenyl propanoate (3i). (Two isomers, the data of minor isomer are in brackets). Yield: 72.4%; Pale brown oil; ^{1}H NMR d : 3.36- 3.45 (m, 3H), 3.60- 3.70 (m, 2H), 4.90- 5.00 (m, 1H), 6.50- 6.64 (m, 1H), 6.85- 7.01 (m, 5H), 7.18- 7.44 (m, 5H), 7.56- 7.63 (m, 2H), 8.10- 8.16 (m, 1H); ^{13}C NMR d : 41.2[40.5], 54.7[54.2], 62.4[61.5], 112.0, 118.5, 121.5[121.2], 122.0[121.9], 123.6, 124.6, 125.0[125.1], 126.0[126.2], 128.7[128.9], 129.8, 130.0, 130.2, 130.7, 136.9[136.8], 146.7, 171.1. Anal. Calcd for $C_{24}H_{20}N_4O_2$: C, 72.71; H, 5.09; N, 14.13. Found: C, 72.68; H, 5.10; N, 13.81.

Methyl-2(*S*)-[1-(1*H*-1,2,3-benzotriazol-1-yl)-2*H*-isoindole-2-yl]-propanoate (3j). (Two isomers, the data of minor isomer are in brackets). Yield: 43.0%; Pale yellow oil; ^{1}H NMR δ : 1.88 (d, *J* = 5.1 Hz, 3H) [1.77 (d, *J* = 5.1 Hz, 3H)], 3.39 (s, 3H) [3.70 (s, 3H)], 4.90- 5.05 (m, 1H) [4.70- 4.80 (m, 1H)], 6.97- 7.10 (m, 3H), 7.25- 7.30 (m, 1H), 7.43- 7.58 (m, 3H), 7.62- 7.76 (m, 1H), 7.93- 8.20 (m, 1H); ^{13}C NMR δ : 17.8, 52.5, 53.9, 109.3, 110.0, 110.4, 116.6, 120.2, 121.8, 122.8, 123.5, 124.5, 128.5, 130.9, 133.6, 135.3, 145.1, 170.1. HRMS Calcd for $C_{18}H_{17}N_4O_2$: 321.1352 (M^++1) Found: 321.1352 (M^++1)

General procedure for thermolysis of compound 3g and 3h. Compound 3g (or 3h) (0.2 g) was mixed with biphenyl ether (10 g) and the mixture was heated at reflux temperature (250 ^{o}C) until TLC analysis showed that all the starting material had been consumed (generally 2 h). The mixture was added to the top of a silica gel column and the column eluted with hexane to remove biphenyl ether. The product was then eluted with hexane/EtOAc to give 5a or 8.

2-[(1*S*)-1-Phenylethyl]-1-isoindolinone (5a).[19] From 3g, yield: 70.0%; Yellow oil; ^{1}H NMR δ : 1.70 (d, *J* = 7.2 Hz, 3H), 3.99 (d, *J* = 17.1 Hz, 1H), 4.33 (d, *J* = 17.1 Hz, 1H), 5.82 (q, *J* = 7.2 Hz, 1H), 7.26- 7.36 (m, 6H), 7.42- 7.52 (m, 2H), 7.88 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR δ : 17.3, 45.6, 49.1, 122.7, 123.8, 127.1, 127.5, 128.0, 128.6, 131.1, 132.9, 140.6, 141.3, 168.0. MS (EI): 237 (M^{+}, 70), 222 (100), 160 (30), 119 (40).

(3*S*)-3-Phenyl-2,3-dihydro[1,3]oxazolo[2,3-a]isoindol-5(9b*H*)-one (8). [20] From 3h, yield: 10.0%; Brown oil; ^{1}H NMR δ : 4.17 (t, *J* = 8.1 Hz, 1H), 4.84 (t, *J* = 8.1 Hz, 1H), 5.23 (t, *J* = 7.5 Hz, 1H), 6.06 (s, 1H), 7.30- 7.51 (m, 5H), 7.56- 7.66 (m, 2H), 7.74- 7.86 (m, 2H); ^{13}C NMR δ : 58.0, 78.0, 91.8, 124.0, 124.5, 126.0, 127.6, 128.8, 130.7, 132.9, 139.6, 142.0, 153.4, 174.0. MS (EI): 251 (M^{+}, 5), 221 (100), 193 (30), 165 (15).

2-[(1*S*)-2-(2*H*-1,2,3-Benzotriazol-1-yl)-1-phenylethyl]-1-isoindolinone (9). From 3h, yield: 20.0%; Pale brown oil; ^{1}H NMR δ : 4.10 (d, *J* = 16.8 Hz, 1H), 4.61 (d, *J* = 16.8 Hz, 1H), 5.29 (dd, *J* = 6.3 Hz, 14.1 Hz, 1H), 5.65 (dd, *J* = 9.3 Hz, 14.1 Hz, 1H), 6.03 (dd, *J* = 6.6 Hz, 9.0 Hz, 1H), 7.20- 7.68 (m, 10H), 7.73 (t, *J* = 7.8 Hz, 2H), 7.97 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR δ : 47.8, 48.6, 55.5, 109.5, 119.9, 122.8, 123.7, 124.0, 127.7, 127.8, 128.0, 128.7, 129.1, 131.6, 132.0, 133.1, 136.2, 141.2, 145.8, 168.9. Anal. Calcd for $C_{22}H_{18}N_4O$: C, 74.55; H, 5.13; N, 15.81. Found: C, 74.26; H, 4.95; N, 15.56.

2-[(1*S*)-2-(2*H*-1,2,3-Benzotriazol-2-yl)-1-phenylethyl]-1-isoindolinone (10). From 3h, yield: 40.0%; Brown oil; ^{1}H NMR δ : 4.20 (d, *J* = 16.2 Hz, 1H), 4.71 (d, *J* = 16.2 Hz, 1H), 5.38 (dd, *J* = 5.4 Hz, 15.0 Hz, 1H), 5.60 (dd, *J* = 10.5 Hz, 13.2 Hz, 1H), 6.34 (dd, *J* = 5.1 Hz, 10.8 Hz, 1H), 7.30- 7.41 (m, 7H), 7.46- 7.51 (m, 3H), 7.70- 7.78 (m, 3H); ^{13}C NMR δ : 46.9, 55.5, 56.3, 118.1, 122.8, 123.9, 126.4, 127.5, 127.9, 128.6, 129.1, 131.4, 132.2, 136.5, 141.2, 144.5, 168.5. Anal. Calcd for $C_{22}H_{18}N_4O$: C, 74.55; H, 5.13; N, 15.81. Found: C, 74.63; H, 5.02; N, 15.63.

General procedure for the preparation of compounds 12a-e

Primary amine (10 mmol), 2,5-dimethoxy-2,5-dhydrofuran (1.3 mL, 10 mmol), and benzotriazole (2.6 g, 22 mmol) were added to 25 mL of acetic acid and refluxed for 24 h. The mixture was cooled, CH_2Cl_2 (50 mL) was added and the solution was washed with 2 N NaOH (3 x 30 mL). The organic layer was dried over Na_2SO_4, and the solvent was removed by evaporation. The crude product was purified by column with hexane/EtOAc as eluent.

1-(1-Benzyl-1*H*-pyrrol-2-yl)-1*H*-1,2,3-benzotriazole (12a). Yield: 3.0%; Brown oil; ^{1}H NMR δ : 5.14 (s, 2H), 6.59- 6.60 (m, 1H), 6.80- 6.81 (m, 1H), 7.15- 7.16 (m, 1H), 7.21-7.25 (m, 2H), 7.32- 7.39 (m, 4H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 8.08 (d, *J* = 8.1 Hz, 1H);

^{13}C NMR δ : 54.1, 103.6, 110.4, 114.2, 119.9, 121.3, 122.2, 123.9, 127.3, 127.5, 128.1, 128.9, 132.7, 136.8, 145.8. Anal. Calcd for $C_{17}H_{14}N_4$: C, 74.42; H, 5.15. Found: C, 74.21; H, 5.24.

1-(1-Phenethyl-1*H*-pyrrol-2-yl)-1*H*-1,2,3-benzotriazole (12b). Yield: 1.1%; Brown oil; ^{1}H NMR δ : 3.10 (t, *J* = 6.8 Hz, 2H), 4.17 (t, *J* = 6.8 Hz, 2H), 6.55- 6.60 (m, 1H), 6.65- 6.70 (m, 1H), 6.98- 6.99 (m, 1H), 7.10- 7.15 (m, 2H), 7.20- 7.39 (m, 4H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 7.2 Hz, 1H), 8.07 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR δ : 38.1, 51.8, 103.3, 110.4, 113.7, 119.7, 120.7, 121.6, 123.8, 126.8, 127.4, 128.6, 128.7, 132.7, 137.8, 145.7. MS (EI): 288 (M^+, 10), 260 (10), 169 (100). HRMS Calcd for $C_{18}H_{17}N_4$: 289.1453 (M^++1) Found: 289.1451 (M^++1).

1-{1-[(1*S*)-1-Phenylethyl]-1*H*-pyrrol-2-yl}-1*H*-1,2,3-benzotriazole (12c). Yield: 2.1%; Brown oil; ^{1}H NMR δ : 1.90 (d, *J* = 7.2 Hz, 3H), 5.32 (m, 1H), 6.56- 6.58 (m, 1H), 6.83- 6.85 (m, 1H), 7.17- 7.20 (m, 3H), 7.27- 7.37 (m, 4H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 8.06 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR δ : 21.9, 58.9, 103.2, 110.5, 112.8, 119.7, 119.9, 123.9, 125.9, 127.5, 127.9, 128.8, 132.7, 142.2, 145.8. HRMS Calcd for $C_{18}H_{17}N_4$: 289.1453 (M^++1) Found: 289.1451 (M^++1).

(2*S*)-2-[2-(1*H*-1,2,3-Benzotriazol-1-yl)-1*H*-pyrrol-1-yl]-2-phenylethyl acetate (12d). Yield: 9.9%; Brown oil; ^{1}H NMR δ : 2.07 (s, 3H), 4.72- 4.78 (m, 2H), 5.50- 5.51 (m, 1H), 6.63- 6.64 (m, 1H), 6.89- 6.92 (m, 1H), 7.25- 7.27 (m, 3H), 7.36- 7.40 (m, 4H), 7.51 (t, *J* = 8.1 Hz, 1H), 7.67 (d, *J* = 8.1 Hz, 1H), 8.09 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR δ : 20.8, 62.3, 65.1, 103.7, 110.4, 111.1, 113.3, 120.0, 120.4, 123.9, 126.7, 127.6, 128.8, 129.1, 136.8, 142.2, 145.8, 170.5. HRMS Calcd for $C_{20}H_{18}N_4O_2$: 347.1508 (M^++1) Found: 347.1525 (M^++1).

1-(2-Furyl)-1*H*-1,2,3-benzotriazole (13). 2,5-Dimethoxy-2,5-dihydrofuran (1.3 mL, 10 mmol) and benzotriazole (2.6 g, 22 mmol) were added to 25 mL acetic acid, and the mixture was refluxed for 24 h. The mixture was cooled, CH_2Cl_2 (50 mL) added and the solution was washed with 2 N NaOH (3 ´ 30 mL). The organic layer was dried over Na_2SO_4, the solvent evaporated and the crude mixture was purified by column with hexane/EtOAc as eluent to give 15 in 67.0% yield. Brown oil; ^{1}H NMR δ : 6.63 (d, *J* = 1.5 Hz, 1H), 6.69 (d, *J* = 3.0 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.50 (br s, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR δ : 100.5, 110.6, 111.8, 120.1, 124.7, 128.8, 129.7, 132.2, 140.4, 145.4. Anal. Calcd for $C_{10}H_7N_3$: C, 64.85; H, 3.82. Found: C, 65.09; H, 3.83.

X-Ray crystallography

Data were collected with a Siemens SMART CCD area detector, using graphite monochromatized Mo Kα radiation (λ = 0.7107 Å). The structures were solved by direct methods and refined on F^2 using all data by full-matrix least-squares procedures. Hydrogen atoms were included in calculated positions except for the OH hydrogens, which were located from a difference map.

Crystal Data for 3h at 23 °C: $C_{22}H_{18}N_4O$, *M* = 354.4, orthorhombic, space group $P2_12_12_1$; *a* = 9.685(1), *b* = 10.709(1), *c* = 17.169(2); V = 1780.8(2), Z = 4, F(000) = 744, D_x = 1.322 g cm^{-3};

colorless block, 0.62 x 0.52 x 0.26 mm; m = 0.08 mm^{-1}, 2θ_{max} 54°; 3196 unique reflections, 255 parameters, wR = 0.1107 for all data, R = 0.0475 for 2203 data with I > 2σ(I).
Crystal Data for 10 at -115 °C: $C_{22}H_{18}N_4O$, *M* = 354.4, triclinic, space group *P*1; *a* = 6.410(1), *b* = 10.612(2), *c* = 13.621(3) A, α = 102.995(4), β = 93.814, γ = 99.126(4) °; V = 886.3(1), Z = 2, F(000) = 372, D_x = 1.328 g cm^{-3}; colorless block, 0.71 x 0.58 x 0.20 mm; m = 0.08 mm^{-1}, 2θ_{max} 53°; 5818 unique reflections, 487 parameters, wR = 0.1175 for all data, R = 0.0469 for 4917 data with I > 2s(I).

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