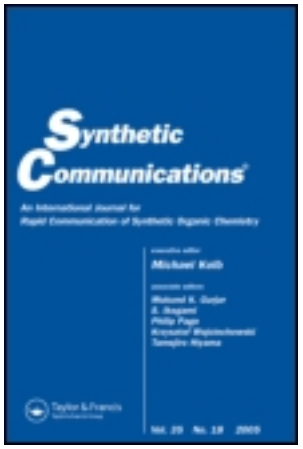


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Convenient Synthesis of 1H-Benzotriazolylalkylphenols

Vitalij A. Osyanin [a], Natalia E. Sidorina [a] & Yuri N. Klimochkin [a]

[a] Organic Chemistry Division, Samara State Technical University, Samara, Russia

Available online: 31 Oct 2011

To cite this article: Vitalij A. Osyanin, Natalia E. Sidorina & Yuri N. Klimochkin (2012): Convenient Synthesis of 1H-Benzotriazolylalkylphenols, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 42:18, 2639-2647

To link to this article: http://dx.doi.org/10.1080/00397911.2011.563452

Synthetic Communications®, 42: 2639–2647, 2012

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397911.2011.563452

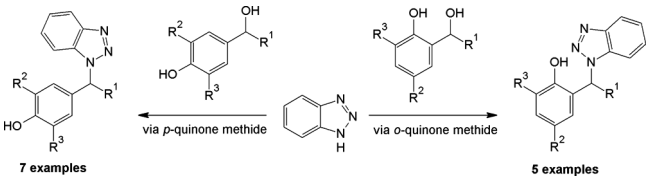
Taylor & Francis
Taylor & Francis Group

CONVENIENT SYNTHESIS OF 1*H*-BENZOTRIAZOLYLALKYLPHENOLS

Vitalij A. Osyanin, Natalia E. Sidorina, and Yuri N. Klimochkin

Organic Chemistry Division, Samara State Technical University, Samara, Russia

GRAPHICAL ABSTRACT



Abstract *A simple, efficient, and environmentally benign method has been developed for the exclusive formation of synthetically significant 1*H*-benzotriazol-1-ylalkylphenols from hydroxybenzyl alcohols and benzotriazole.*

Keywords Aza-Michael reaction; benzotriazole; 1*H*-benzotriazol-1-ylalkylphenols; 2- and 4-hydroxybenzyl alcohols; quinone methides

INTRODUCTION

In recent years, much attention has been focused on the use of benzotriazole (BtH) methodology as a versatile synthetic tool.[1–3] In this respect, an important application of the benzotriazole methodology is the use of 1*H*-benzotriazol-1-ylalkylphenols as intermediates for the preparation of chromane and benzofuran derivatives,[4,5] condensed sulfur heterocycles,[6] substituted phenols,[7,8] and 1,1-bis(2-hydroxyaryl)alkanes.[9] It was found that 2-(1-benzotriazolylalkyl)phenols react with a variety of nucleophiles including alcohols, Grignard reagents, thiols, amines, amides, and active methylene compounds through *o*-quinone methide formation and Michael addition to give *o*-substituted phenols.[7,9,10] Besides, the methylene groups in 2-(1*H*-benzotriazol-1-ylalkyl)phenols are capable of undergoing lithiation and the resultant anions can be quenched with various electrophiles such as alkyl halides, aldehydes, and ketones to give substituted 2-(1*H*-benzotriazol-1-ylalkyl)phenols.[10]

Received January 9, 2011.

Address correspondence to Vitalij A. Osyanin, Samara State Technical University, Samara, Russia. E-mail: vosyanin@mail.ru

o-Quinone methides are important intermediates in many chemical and biological processes. These reactive species are efficient DNA alkylating and cross-linking agents, and play a key role in the biological action of several antibiotics such as mitomycin and anthracyclines.[11] *o*-Quinone methides act as heterodienes in inter- and intramolecular cycloadditions with olefins to give various substituted chromanes. Like vinyl ketones, *o*- and *p*-quinone methides also act as acceptors in Michael additions to afford *ortho*- and *para*-substituted phenols. Most of the methods reported to date for generating quinone methides involve photolysis, high-temperature thermolysis, and/or use of highly derivatized or structurally complex precursors.[12–14] One effective approach for the generation of quinone methides is the use of 1*H*-benzotriazolylalkylphenols.[9,10]

Preparation of 2-(1*H*-benzotriazol-1-ylmethyl)phenols has been previously effected by refluxing of 1-hydroxymethylbenzotriazole with phenols in acetic acid.[7] It should be noted that phenols with electron-withdrawing substituents in the ring remain inert under the reaction conditions and do not give the corresponding 2-(1*H*-benzotriazol-1-ylmethyl)phenols. In addition, *para*-isomers can be prepared only from 2,6-disubstituted phenols.

Unsubstituted 2-(1*H*-benzotriazol-1-ylmethyl)phenol has been also obtained from 2-(1*H*-benzotriazol-1-ylmethyl)aniline.[15] Another method for the preparation of these compounds is the base-catalyzed reaction of benzotriazole with 2- and 4-hydroxybenzyl halogenides. However, preparation of such precursors by direct halogenmethylation is difficult because of their instability.[16]

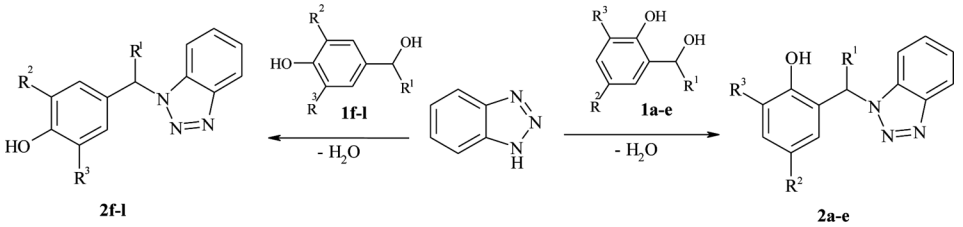
We now report a general, simple procedure for the synthesis of 2- and 4-(1*H*-benzotriazol-1-ylalkyl)phenols (**2a–I**) from the corresponding 2- and 4-hydroxybenzyl alcohols and benzotriazole (Scheme 1).

The reaction has been carried out by heating equimolar amounts of the reagents at 160 °C for 15 min (method A) under solvent-free conditions. Refluxing in dimethylformamide (DMF) was also found to be a successful procedure in the preparation of 1*H*-benzotriazol-1-ylalkylphenols (method B). The isolated yields are reasonable, between 68% and 86%. Products can be easily purified from impurities by single recrystallization. The reaction was repeated on several different scales (up to 100 mmol), all with comparable yields. The results are summarized in Table 1.

A mechanism accounting for the formation of 1*H*-benzotriazol-1-ylalkylphenols is depicted in Scheme 2.

The hydroxybenzyl alcohol loses a molecule of water to give the quinone methide. A nucleophilic attack on the methylene group of quinone methide by the nitrogen atom of the benzotriazole produces the corresponding 1*H*-benzotriazol-1-ylalkylphenols. The driving force of the reaction is the resulting rearomatization of the molecule.

It is known that hydroxybenzyl alcohols are termally unstable, and at temperatures above 100 °C they rapidly undergo polycondensation. Nevertheless, in this case the crude products contained only negligible impurities of polymeric products. *o*-Quinone methides are known to be very reactive and unstable intermediates. As a consequence of this reactivity, di- and trimerization in which one molecule acts as heterodiene and another as dienophile has led to some chroman fused-ring systems.[17] However, in all experiments no *o*-quinone methide dimer or trimer was encountered. Besides, no 2*H*-isomers were isolated from reaction mixtures.



Scheme 1. Synthesis of 1H-benzotriazol-1-ylalkylphenols. $R^1{=}R^2{=}R^3{=}H$ (**a**); $R^1{=}R^3{=}H$, $R^2{=}NO_2$ (**b**); $R^1{=}CH_3$, $R^2{=}NO_2$, $R^3{=}H$ (**c**); $R^1{=}R^3{=}H$, $R^2{=}Br$ (**d**); $R^1{=}CH_3$, $R^2{=}H$, $R^3{=}NO_2$ (**e**); $R^1{=}R^2{=}R^3{=}H$ (**f**); $R^1{=}R^2{=}H$, $R^3{=}NO_2$ (**g**); $R^1{=}CH_3$, $R^2{=}R^3{=}H$ (**h**); $R^1{=}R^2{=}H$, $R^3{=}OCH_3$ (**i**); $R^1{=}H$, $R^2{=}Br$, $R^3{=}OCH_3$ (**j**); $R^1{=}CH_3$, $R^2{=}OCH_3$, $R^3{=}H$ (**k**); $R^1{=}R^3{=}H$, $R^2{=}CHO$ (**l**).

Although it is known that *p*-quinone methides that are more stable and consequently are formed more readily than their corresponding *o*-quinone methides, no differences between them were found under reaction conditions.

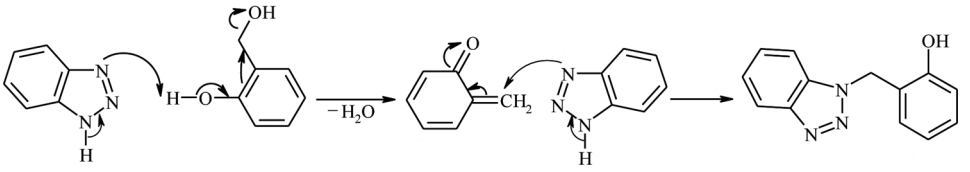
Both the generation of quinone methides and the thermodynamic stability of the resulting adducts were shown to be highly responsive to both the presence of substituents on the aromatic ring and the nature of the leaving group at the benzylic position of their precursors.[18] Electron-donating groups facilitate quinone methide generation, wheras electron-withdrawing groups strongly suppress initial formation of quinone methide, making the resulting 1*H*-benzotriazol-1-ylalkylphenols more stable. At the same time, the leaving-group ability of benzotriazole is not sufficient to regenerate the quinone methide. Thus, the 1*H*-benzotriazol-1-ylalkylphenols, electron-donating and electron-withdrawing substituents remain stable under reaction conditions.

It is known that quinone methides can be generated by elimination of phenol Mannich base methiodides, so 2-(1*H*-benzotriazol-1-ylmethyl)-4-methoxyphenol (**2m**) was prepared from benzotriazole and (2-hydroxy-5-methoxybenzyl)trimethylammonium iodide by heating in DMF (Scheme 3).

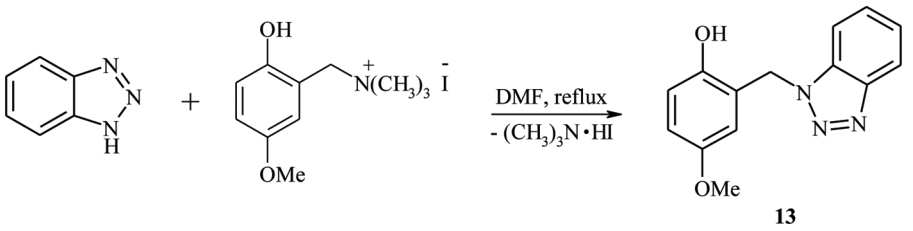
Table 1. 1*H*-Benzotriazol-1-ylalkylphenols (**2a**–**l**)

Compound	Yield (%)[a] (method)
2a	77 (A), 62 (B)
2b	86 (A)
2c	69 (A)
2d	72 (A)
2e	68 (A)
2f	82 (A)
2g	81 (A)
2h	82 (A)
2i	81 (A)
2j	71 (A)
2k	78 (B)
2l	68 (B)

[a]Isolated yield.



Scheme 2. Plausible mechanism for the synthesis of 1*H*-benzotriazol-1-ylalkylphenols.



Scheme 3. Synthesis of 2-(1*H*-benzotriazol-1-ylmethyl)-4-methoxyphenol (**2m**).

The structures of **2a–m** were confirmed by their infrared (IR), ^{1}H NMR spectral data, and elemental analysis. The IR spectra of **1–13** contain strong absorption bands at 3400–2500 cm^{-1} characteristic of O-H stretching vibrations, associated by the intermolecular hydrogen bond. The methylene and methine (in compounds **2c, 2e, 2h, 2k, 2l**) signals in ^{1}H NMR spectra shift downfield because of the electron-withdrawing benzotriazole group and appear at δ 5.47–6.60 ppm. Broad singlets at δ 8.91–11.05 ppm were assigned to OH protons.

An easy ecofriendly laboratory procedure under solvent-free conditions is presented for the hydroxybenzylation of the benzotriazole with *o*- and *p*-hydroxybenzyl alcohols. Synthesis of **2a–m** by the suggested procedures takes less time, does not require an excess of any reagents or the use of any metal catalysts, and can be performed under neutral reaction conditions. The method is general for *o*- and *p*-hydroxybenzyl alcohols containing both electron-withdrawing and electron-donating substituents; it allows preparation of 1*H*-benzotriazol-1-ylalkylphenols of high purity in good yields.

EXPERIMENTAL

FTIR spectra were taken on a Shimadzu FTIR-8400S spectrophotometer in KBr pellets. ^{1}H NMR spectra were recorded on a Brucker AM 400-MHz spectrometer in dimethylsulfoxide (DMSO-d_6) using tetramethylsilane (TMS) as an internal reference. Chemical shifts and coupling constants were recorded in units of parts per million (ppm) and hertz (Hz), respectively. Melting points were determined on an Electrothermal melting-point apparatus and are uncorrected. Elemental analyses were performed on a EuroVector EA-3000 instrument. Electrospray ionization–mass spectrometry (EI-MS) spectra were obtained on a Finnigan Trace DSQ spectrometer (70 eV). Thin-layer chromatography (TLC) was carried out on

aluminium-backed silica-gel plates (Merck 60 F_{254}) with visualization of components by ultraviolet (UV) light (254 nm) or exposure to I_2. Noncommercial hydroxybenzyl alcohols were prepared according to the well-known methods.[19–21]

General Experimental Procedures for the Synthesis of 1*H*-Benzotriazolylalkylphenols (2a–l)

Method A. A mixture of 1 g (8.4 mmol) of benzotriazole and 8.4 mmol of the appropriate hydroxybenzyl alcohol was added to a opened round-bottom flask equipped with a mechanical stirrer and thermometer. The flask was placed in a preliminary heated metal bath, and the reaction mixture was stirred at 160 °C for 15 min. After completion of the reaction, the mixture was cooled to room temperature and washed with cold dichloromethane, and the crude product was purified by recrystallization.

Method B. A mixture of 1 g (8.4 mmol) of benzotriazole and 8.4 mmol of the appropriate hydroxybenzyl alcohol in DMF (10 ml) was refluxed for 2 h. The resulting solution was cooled to room temperature and then poured into 50 ml of rapidly stirred water to yield a solid product, which was dried and purified by recrystallization.

Characterization Data of the 1*H*-Benzotriazolylalkylphenols (2a–m)

2-(1H-1,2,3-Benzotriazol-1-ylmethyl)phenol (2a). Colorless crystals; mp 171–172 °C (ethylacetate) (lit. mp 168–170 °c)[7], ^{1}H NMR, δ, ppm: 5.85 (s, 2H, CH_2), 6.74 (t, 1H, H-4, $J = 7.4$ Hz), 6.87 (d, 1H, H-6, $J = 7.4$ Hz), 7.05 (d, 1H, H-3, $J = 7.7$ Hz), 7.13 (dd, 1H, H-5, $J = 8.0$ Hz, $J = 1.8$ Hz), 7.35 (t, 1H, H_{Bt}-5, $J = 8.2$ Hz), 7.48 (t, 1H, H_{Bt}-6, $J = 7.9$ Hz), 7.77 (d, 1H, H_{Bt}-7, $J = 8.4$ Hz), 8.03 (d, 1H, H_{Bt}-4, $J = 8.4$ Hz), 9.95 (s, 1H, OH); IR, ν, cm^{-1}: 3300–2500 (OH), 1601, 1508, 1497, 1464, 1433, 1400, 1352, 1319, 1267, 1229, 1161, 1136, 1086, 852, 770, 760, 746; EI-MS (70 eV) *m/z* (% int.): 225 (M^+, 59), 196 (M^+ – CHO, 65), 180 (10), 168 (M^+ – CHO – N_2, 33), 167 (20), 119 $C_6H_5N_3^+$, 8), 117 (16), 107 (C_7H_7O, 100). Anal. calcd. for $C_{13}H_{11}N_3O$, %: C, 69.32; H, 4.92; N, 18.66. Found, %: C, 69.37; H, 4.88; N, 18.71.

2-(1H-1,2,3-Benzotriazol-1-ylmethyl)-4-nitrophenol (2b). Yellow crystals; mp 241–242 °C (ethanol–DMF); ^{1}H NMR, δ, ppm: 5.95 (s, 2H, CH_2), 7.03 (d, 1H, H-6, $J = 8.3$ Hz), 7.41 (t, 1H, H_{Bt}-6, $J = 8.4$ Hz), 7.55 (t, 1H, H_{Bt}-5, $J = 8.4$ Hz), 7.81–7.84 (m, 2H, H_{Bt}-7, H-5), 7.92 (s, 1H, H-3), 8.02 (d, 1H, H_{Bt}-4, $J = 8.3$ Hz), 11.05 (s, 1H, OH); IR, ν, cm^{-1}: 3300–2500 (OH), 1620, 1593, 1527 (NO_2), 1497, 1447, 1339 (NO_2), 1300, 1273, 1088, 748; EI-MS (70 eV) *m/z* (% int.): 270 (M^+, 39), 241 (M^+ – CHO, 10), 196 (14), 195 (M^+ – CHO – NO_2, 26), 167 (M^+ – CHO – NO_2 – N_2, 24), 152 ($C_7H_6NO_3^+$, 100), 139 (7), 106 ($C_7H_6O^+$, 40), 105 ($C_7H_5O^+$, 17). Anal. calcd. for $C_{13}H_{10}N_4O_3$, %: C, 57.78; H, 3.70; N, 20.74. Found, %: C, 57.85; H, 3.64; N, 20.63.

2-[1-(1H-1,2,3-Benzotriazol-1-yl)ethyl]-4-nitrophenol (2c). Yellow crystals; mp 246–248 °C (ethanol–DMF); ^{1}H NMR, δ, ppm: 1.73 (d, 3H, CH_3,

$J = 7.7$ Hz), 5.82 (q, 1H, CH, $J = 7.7$ Hz), 7.15 (d, 1H, H-6, $J = 8.0$ Hz), 7.38 (t, 1H, H_{Bt}-6, $J = 8.0$ Hz), 7.50 (t, 1H, H_{Bt}-5, $J = 8.0$ Hz), 7.68–7.72 (m, 2H, H_{Bt}-7, H-5), 7.91 (s, 1H, H-3), 8.38 (d, 1H, H_{Bt}-4, $J = 7.6$ Hz), 9.94 (s, 1H, OH); IR, ν, cm^{-1}: 3300–2500 (OH), 1620, 1593, 1524 (NO_2), 1497, 1458, 1435, 1385, 1335 (NO_2), 1296, 1277, 1242, 1153, 1103, 756; EI-MS (70 eV) m/z (% int.): 284 (M^+, 80), 255 (M^+ – CHO, 12), 241 (66), 209 (37), 195 (46), 166 ($C_8H_8NO_3^+$, 100), 149 (23), 120 ($C_8H_8O^+$, 76), 119 $C_6H_5N_3^+$, 43). Anal. calcd. for $C_{14}H_{12}N_4O_3$, %: C, 59.15; H, 4.23; N, 19.72. Found, %: C, 59.23; H, 4.18; N, 19.65.

2-(1H-1,2,3-Benzotriazol-1-ylmethyl)-4-bromophenol (2d). Colorless crystals; mp 184–185 °c (ethanol–ethylacetate); ^{1}H NMR, δ, ppm: 5.84 (s, 1H, CH_2), 6.83 (d, 1H, H-6, $J = 8.7$ Hz), 7.24 (d, 1H, H-3, $J = 2.5$ Hz), 7.31 (dd, 1H, H-5, $J = 8.7$ Hz, $J = 2.5$ Hz), 7.39 (t, 1H, H_{Bt}-5, $J = 7.5$ Hz), 7.53 (t, 1H, H_{Bt}-6, $J = 7.5$ Hz), 7.79 (d, 1H, H_{Bt}-7, $J = 8.4$ Hz), 8.03 (d, 1H, H_{Bt}-4, $J = 8.4$ Hz), 10.16 (br. s, 1H, OH); IR, ν, cm^{-1}: 3200–2500 (OH), 1593, 1497, 1454, 1420, 1346, 1277, 1227, 1169, 1126, 1092, 814, 771, 744; EI-MS (70 eV) m/z (% int.) (for ^{79}Br isotope): 303 (M^+, 47), 274 (M^+ – CHO, 27), 196 (M^+ – CO – Br, 78), 185 ($C_7H_6BrO^+$, 100), 168 (26), 167 (44), 139 (13), 117 (53), 106 ($C_7H_6O^+$, 14). Anal. calcd. for $C_{13}H_{10}BrN_3O$, %: C, 51.32; H, 3.29; N, 13.82. Found, %: C, 51.40; H, 3.24; N, 13.68.

2-[1-(1H-1,2,3-Benzotriazol-1-yl)ethyl]-6-nitrophenol (2e). Yellow crystals; mp 91–92 ° (ethanol); ^{1}H NMR, δ, ppm: 2.07 (d, 3H, CH_3, $J = 7.2$ Hz), 6.60 (q, 1H, CHCH$_3$, $J = 7.2$ Hz), 7.06 (t, 1H, H-4, $J = 8.1$ Hz), 7.39 (t, 1H, H_{Bt}-5, $J = 8.1$ Hz), 7.50 (t, 1H, H_{Bt}-6, $J = 8.1$ Hz), 7.59 (d, 1H, H-3, $J = 7.5$), 7.69 (d, 1H, H_{Bt}-7, $J = 8.4$ Hz), 7.97 (d, 1H, H-5, $J = 8.4$ Hz), 8.04 (d, 1H, H_{Bt}-4, $J = 8.1$ Hz), 10.78 (br. s, 1H, OH); IR, ν, cm^{-1}: 3271 (OH), 3094, 3055, 1612, 1589, 1539 (NO_2), 1447, 1381, 1350 (NO_2), 1300, 1273, 1246, 1196, 1122, 899, 841, 760, 744; EI-MS (70 eV) m/z (% int.): 284 (M^+, 79), 255 (M^+ – CHO, 4), 241 (32), 221 (8), 209 (10), 195 (13), 180 (23), 166 ($C_8H_8NO_3^+$, 16), 139 (8), 119 $C_6H_5N_3^+$, 16), 118 (100). Anal. calcd. for $C_{14}H_{12}N_4O_3$, %: C, 59.15; H, 4.23; N, 19.72. Found, %: C, 59.33; H, 4.16; N, 19.75.

4-(1H-1,2,3-Benzotriazol-1-ylmethyl)phenol (2f). Colorless crystals; mp 170–171 °c (ethanol); ^{1}H NMR, δ, ppm: 5.60 (s, 2H, CH_2), 6.79 (d, 2H, H-2,6, $J = 7.1$ Hz), 7.36 (d, 2H, H-3,5, $J = 7.1$ Hz), 7.50–7.70 (m, 2H, H_{Bt}-5,6), 7.83–8.10 (m, 2H, H_{Bt}-4,7), 9.65 (br. s, 1H, OH); IR, ν, cm^{-1}: 3300–2600 (OH), 1632, 1603, 1515, 1457, 1382, 1365, 1321, 1269, 1233; EI-MS (70 eV) m/z (% int.): 225 (M^+, 99), 196 (M^+ – CHO, 100), 180 (27), 168 (M^+ – CHO – N_2, 27), 167 (19), 119 $C_6H_5N_3^+$, 32), 107 (C_7H_7O, 98), 106 (C_7H_6O, 16). Anal. calcd. for $C_{13}H_{11}N_3O$, %: C, 69.32; H, 4.92; N, 18.66. Found, %: C, 69.38; H, 4.85; N, 18.72.

4-(1H-1,2,3-Benzotriazol-1-ylmethyl)-2-nitrophenol (2g). Yellow crystals; mp 187–189 ° (ethanol); ^{1}H NMR, δ, ppm: 5.96 (s, 2H, CH_2), 7.12 (d, 1H, H-6, $J = 8.1$ Hz), 7.38–7.58 (m, 2H, H_{Bt}), 7.90 (d, 1H, H-5, $J = 8.1$ Hz), 8.01–8.07 (m, 2H, H_{Bt}), 8.47 (s, 1H, H-3), 11.02 (br. s, 1H, OH); IR, ν, cm^{-1}: 3256 (OH), 1632, 1574, 1539 (NO_2), 1489, 1454, 1442, 1423, 1339 (NO_2), 1285, 1254, 1219, 1153, 1122, 1088, 748; EI-MS (70 eV) m/z (% int.): 270 (M^+, 100), 241 (M^+ – CHO, 23), 196 (22), 195 (M^+ – CHO – NO_2, 36), 167 (M^+ – CHO – NO_2 – N_2, 56), 152 ($C_7H_6NO_3^+$, 89), 139 (12), 119 $C_6H_5N_3^+$, 10), 106 ($C_7H_6O^+$, 66), 105 ($C_7H_5O^+$, 26).

Anal. calcd. for $C_{13}H_{10}N_4O_3$, %: C, 57.75; H, 3.70; N, 20.74. Found, %: C, 57.85; H, 3.64; N, 20.80.

4-[1-(1H-1,2,3-Benzotriazol-1-yl)ethyl]phenol (2h). Colorless crystals; mp 68–70 °c (ethanol–water); ^{1}H NMR, δ, ppm: 2.03 (d, 3H, CH_3, $J = 7.3$ Hz), 6.19 (q, 1H, CHCH$_3$, $J = 7.3$ Hz), 6.72 (d, 2H, H-2,6, $J = 8.4$ Hz), 7.20 (d, 2H, H-3,5, $J = 8.4$ Hz), 7.36 (t, 1H, H_{Bt}-5, $J = 7.0$ Hz), 7.46 (t, 1H, H_{Bt}-6, $J = 7.0$ Hz), 7.68 (d, 1H, H_{Bt}-7, $J = 8.4$ Hz), 8.02 (d, 1H, H_{Bt}-4, $J = 8.1$ Hz), 9.38 (br. s, 1H, OH); IR, ν, cm^{-1}: 3400–2500 (OH), 1612, 1593, 1516, 1450, 1377, 1269, 1238, 1207, 1169, 1103, 1061, 833, 783, 744; EI-MS (70 eV) *m/z* (% int.): 239 (M^+, 59), 210 (M^+ – CHO, 18), 196 (30), 167 (11), 121 ($C_8H_9O^+$, 88), 120 ($C_8H_8O^+$, 59), 119 $C_6H_5N_3^+$, 100), 91 (99). Anal. calcd. for $C_{14}H_{13}N_3O$, %: C, 70.29; H, 5.44; N, 17.57. Found, %: C, 70.35; H, 5.37; N, 17.65.

4-(1H-1,2,3-Benzotriazol-1-ylmethyl)-2-methoxyphenol (2i). Colorless crystals; mp 75–76 °c (ethanol); ^{1}H NMR, δ, ppm: 3.73 (s, 3H, CH_3O), 5.83 (s, 2H, CH_2), 6.73–6.78 (m, 2H, H-5,6), 7.02 (s, 1H, H-3), 7.38 (t, 1H, H_{Bt}-5, $J = 7.5$ Hz), 7.51 (t, 1H, H_{Bt}-6, $J = 7.5$ Hz), 7.81 (d, 1H, H_{Bt}-7, $J = 8.6$ Hz), 8.03 (d, 1H, H_{Bt}-4, $J = 8.6$ Hz), 8.96 (br. s, 1H, OH); IR, ν, cm^{-1}: 3400–2600 (OH), 1612, 1524, 1454, 1431, 1273, 1246, 1223, 1157, 1130, 1111, 1038, 960, 849, 829, 802, 787, 741; EI-MS (70 eV) *m/z* (% int.): 255 (M^+, 100), 226 (M^+ – CHO, 22), 211 (25), 196 (43), 183 (22), 167 (18), 166 (14), 137 ($C_8H_9O_2^+$, 80), 122 (25), 119 $C_6H_5N_3^+$, 100). Anal. calcd. for $C_{14}H_{13}N_3O_2$, %: C, 65.88; H, 5.10; N, 16.47. Found, %: C, 66.78; H, 5.06; N, 16.40.

4-(1H-1,2,3-Benzotriazol-1-ylmethyl)-2-bromo-6-methoxyphenol (2j). Colorless crystals; mp 158–159 °c (ethanol); ^{1}H NMR, δ, ppm: 3.78 (s, 3H, CH_3O), 5.85 (s, 2H, CH_2), 7.05 and 7.09 (d, 2H, H-3,5, $J = 1.2$ Hz), 7.40 (t, 1H, H_{Bt}-5, $J = 6.8$ Hz), 7.54 (t, 1H, H_{Bt}-6, $J = 6.8$ Hz), 7.87 (d, 1H, H_{Bt}-7, $J = 8.4$ Hz), 8.04 (d, 1H, H_{Bt}-4, $J = 8.4$ Hz), 9.45 (br. s, 1H, OH); IR, ν, cm^{-1}: 3300–2500 (OH), 1605, 1582, 1501, 1454, 1423, 1288, 1273, 1231, 1184, 1103, 1049, 787, 741; EI-MS (70 eV) *m/z* (% int.) (for ^{79}Br isotope): 333 (M^+, 95), 304 (M^+ – CHO, 17), 289 (M^+ – CHO – CH_3, 15), 274 (23), 215 ($C_8H_8BrO_2^+$, 71), 211 (61), 183 (57), 172 (14), 166 (20), 154 (22), 135 ($C_8H_7O_2^+$, 12), 120 (18), 119 $C_6H_5N_3^+$, 27). Anal. calcd. for $C_{14}H_{12}BrN_3O_2$, %: C, 50.33; H, 3.59; N, 12.57. Found, %: C, 50.43; H, 3.39; N, 12.63.

4-[1-(1H-1,2,3-Benzotriazol-1-yl)ethyl]-2-methoxyphenol (2k). Colorless crystals; mp 155–156 °c (ethanol–water); ^{1}H NMR, δ, ppm: 2.05 (d, 3H, CH_3, $J = 6.9$ Hz), 3.72 (s, 3H, CH_3O), 6.16 (q, 1H, CHCH$_3$, $J = 6.9$ Hz), 6.72 (d, 1H, H-6, $J = 8.1$ Hz), 6.78 (dd, 1H, H-5, $J = 8.1$ Hz, $J = 1.2$ Hz), 6.99 (d, 1H, H-3, $J = 1.2$ Hz), 7.36 (t, 1H, H_{Bt}-5, $J = 7.7$ Hz), 7.46 (t, 1H, H_{Bt}-6, $J = 8.4$ Hz), 7.70 (d, 1H, H_{Bt}-7, $J = 8.4$ Hz), 8.02 (d, 1H, H_{Bt}-4, $J = 7.7$ Hz), 8.91 (s, 1H, OH); IR, ν, cm^{-1}: 3300–2700 (OH), 1612, 1524, 1454, 1435, 1292, 1273, 1242, 1157, 1126, 1038, 783, 742, 733; EI-MS (70 eV) *m/z* (% int.): 269 (M^+, 93), 240 (M^+ – CHO, 3), 226 (12), 211 (20), 208 (12), 183 (15), 180 (11), 151 ($C_9H_{11}O_2^+$, 100), 150 ($C_9H_{10}O_2^+$, 80), 135 (36), 121 (26), 119 $C_6H_5N_3^+$, 35). Anal. calcd. for $C_{15}H_{15}N_3O_2$, %: C, 66.91; H, 5.58; N, 15.61. Found, %: C, 67.01; H, 5.64; N, 15.54.

5-(1H-1,2,3-Benzotriazol-1-ylmethyl)-2-hydroxybenzaldehyde (2l). Colorless crystals; mp 138–140 °c (ethanol); ^{1}H NMR, δ, ppm: 5.93 (s, 2H, CH_2), 6.99 (d, 1H, H-3, $J = 8.0$ Hz), 7.40 (t, 1H, H_{Bt}, $J = 8.1$ Hz), 7.51–7.56 (m, 2H, H_{Bt}), 7.69 (s, 1H, H-6), 7.85 (d, 1H, H-4, $J = 8.0$ Hz), 8.05 (d, 1H, H_{Bt}, $J = 8.1$ Hz), 10.23 (s, 1H, CHO), 10.76 (br. s, 1H, OH); IR, ν, cm^{-1}: 3230–2950 (OH), 2851, 1682 (CO), 1612, 1501, 1450, 1381, 1350, 1300, 1277, 1254, 1231, 1157, 1134, 1111, 945, 833, 783, 760, 741; EI-MS (70 eV) *m/z* (% int.): 253 (M^+, 100), 224 (M^+ – CHO, 57), 196 (62), 168 (16), 167 (15), 135 ($C_8H_7O_2^+$, 82), 133 ($C_8H_5O_2^+$, 58), 119 $C_6H_5N_3^+$, 16), 105 (C_7H_5O, 13). Anal. calcd. for $C_{14}H_{11}N_3O_2$, %: C, 66.40; H, 4.35; N, 16.60. Found, %: C, 66.50; H, 4.28; N, 16.53.

2-(1H-1,2,3-Benzotriazol-1-ylmethyl)-4-methoxyphenol (2m). A mixture of 1 g (8.4 mmol) of benzotriazole and 2.8 g (8.4 mmol) of (2-hydroxy-5-methoxybenzyl)trimethylammonium iodide in DMF (15 ml) was refluxed for 2 h. The resulting solution was cooled to room temperature and then poured into 50 ml of rapidly stirred saturated water solution of sodium chloride to yield a solid product, which was dried, and purified by recrystallization from toluene to give 1.18 g (55%) of colorless crystals, m.p. 138–140 °C. ^{1}H NMR, δ, ppm: 3.66 (s, 3H, OCH_3), 5.47 (s, 2H, CH_2), 7.08 (d, 1H, H-6, $J = 8.3$ Hz), 7.44 (t, 1H, H_{Bt}-6, $J = 8.4$ Hz), 7.50 (t, 1H, H_{Bt}-5, $J = 8.4$ Hz), 7.70–7.78 (m, 2H, H_{Bt}-7, H-5), 7.88 (s, 1H, H-3), 8.02 (d, 1H, H_{Bt}-4, $J = 8.2$ Hz), 9.42 (br. s, 1H, OH). IR, ν, cm^{-1}: 3300–2500 (OH), 1601, 1512, 1454, 1435, 1311, 1273, 1254, 1227, 1215, 1157, 1092, 1041, 806, 768, 744; EI-MS (70 eV) *m/z* (% int.): 255 (M^+, 73), 226 (M^+ – CHO, 35), 212 (26), 184 (25), 167 (18), 156 (10), 154 (9), 137 ($C_8H_9O_2^+$, 89), 136 ($C_8H_8O_2^+$, 27), 117 (100). Anal. calcd. for $C_{14}H_{13}N_3O_2$, %: C, 65.88; H, 5.10; N, 16.47. Found, %: C, 66.77; H, 5.04; N, 16.38.

ACKNOWLEDGMENT

The study was financially supported by the Federal Program Scientific and Pedagogical Staff of Innovative Russia in 2009–2013 (Projects N P1104 and 02.740.11.0632).

REFERENCES

1. Katritzky, A. R.; Lan, X.; Yang, J. Z.; Denisko, O. V. Properties and synthetic utility of N-substituted benzotriazoles. *Chem. Rev.* **1998**, *98*, 409–548.
2. Katritzky, A. R.; Rogovoy, B. V. Benzotriazole: An ideal synthetic auxiliary. *Chem. Eur. J.* **2003**, *9*, 4586–4593.
3. Katritzky, A. R.; Manju, K.; Singh, S. K.; Meher, N. K. Benzotriazole-mediated amino-, amido, alkoxy-, and alkylthio-alkylation. *Tetrahedron* **2005**, *61*, 2555–2581.
4. Katritzky, A. R.; Lan, X.; Zhang, Z. Novel routes to 1-aryl-1,4-dihydro-3(2H)-isoquinolinones and 2-substituted or 2,3-disubstituted benzofurans by intramolecular cyclizations. *J. Heterocycl. Chem.* **1993**, *30*, 381–387.
5. Katritzky, A. R.; Lan, X. *o*-(α-Benzotriazolylalkyl)phenols: Novel precursors of *o*-quinone methides. *Synthesis* **1992**, *8*, 761–764.
6. Rumpf, N.; Gröschl, D.; Meier, H.; Oniciu, D. C.; Katritzky, A. R. An alternative route to 2H-naphtho[1,2-b]thiete and its cycloaddition products. *J. Heterocycl. Chem.* **1998**, *35*, 1505–1508.

7. Katrizky, A. R.; Lan, X.; Lam, J. N. o-(α-Benzotriazolylalkyl)phenols: Versatile intermediates for the synthesis of substituted phenols. *Chem. Ber.* **1991**, *124*, 1809–1817.
8. Rivera, A.; Duarte, Y.; Gonzalez-Salas, D.; Rios-Motta, J.; Zaragoza, G. X-ray and hydrogen-bonding properties of 1-((1H-benzotriazol-1-yl)methyl)naphthalen-2-ol. *Molecules* **2009**, *14*, 1234–1244.
9. Katritzky, A. R.; Zhang, Z.; Lang, H.; Lan, X. o-(α-Benzotriazolylalkyl)phenols: Novel precursors for the preparation of 1,1-bis(2-hydroxyaryl)alkanes. *J. Org. Chem.* **1994**, *59*, 7209–7213.
10. Katritzky, A. R.; Zhang, Z.; Lan, X.; Lang, H. o-(α-Benzotriazolylalkyl)phenols: Novel precursors for the preparation of ortho-substituted phenols via intermediate o-quinone methide. *J. Org. Chem.* **1994**, *59*, 1900–1903.
11. Rokita, S. E., Ed., *Quinone Methides*; Hoboken, NJ: Wiley, 2009.
12. Van De Water, R. W.; Pettus, T. R. R. o-Quinone methides: Intermediates underdeveloped and underutilized in organic synthesis. *Tetrahedron* **2002**, *58*, 5367–5405.
13. Wan, P.; Barker, B.; Diao, L.; Fisher, M.; Shi, Y.; Yang, C. Quinone methides: relevant intermediates in organic chemistry. *Can. J. Chem.* **1996**, *74*, 465–475.
14. Wan, P.; Brousmiche, D. W.; Chen, C. Z.; Cole, J.; Lukeman, M.; Xu, M. Quinone methide intermediates in organic photochemistry. *Pure Appl. Chem.* **2001**, *73*, 529–534.
15. Biagi, G.; Giorgi, I.; Livi, O.; Scartoni, V.; Barili P. L.; Calderone, V.; Martinotti, E. New 5-substituted-1-(2-hydroxybenzoyl)-benzotriazoles, potassium channel activators. *Farmaco* **2001**, *56*, 827–834.
16. Taylor, L. D.; Grasshoff, J. M.; Pluhar, M. Use of *o*- and *p*-hydroxybenzyl functions as blocking groups which are removable with base. *J. Org. Chem.* **1978**, *43*, 1197–1200.
17. Bolon, D. A. Generation of *o*-quinone methides in solution: Trimerization. *J. Org. Chem.* **1970**, *35*, 715–719.
18. Weinert, E. E.; Dondi, R.; Colloredo-Melz, S.; Frankenfield, K. N.; Mitchell, C. H.; Freccero, M.; Rokita, S. E. Substituents on quinone methides strongly modulate formation and stability of their nucleophilic adducts. *J. Am. Chem. Soc.* **2006**, *128*, 11940–11947.
19. Osyanin, V. A.; Sidorina, N. E. Synthesis of imidazo[2,1-*b*][1,3]benzoxazines from 2-halogenimidazoles and salicylic alcohols. *Izv. Vuzov. Khimiya I Khim. Tekhnologiya*, **2005**, *48* 10, 83–85.
20. Stoermer, R.; Behn, K. Synthese aromatischer aikohole mit formaldehyd. *Chem. Ber.*, **1901**, *34*, 2455–2460.
21. Treadwell, E. M.; Neighbors, J. D.; Wiermer, D. F. A cascade cyclyzation appoach to Schweinfurthin B. *Org. Lett.* **2002**, *4*, 3639–3642.