Synthesis of 2,1-Benzisoxazoles by Nucleophilic Substitution of Hydrogen in Nitroarenes Activated by the Azole Ring

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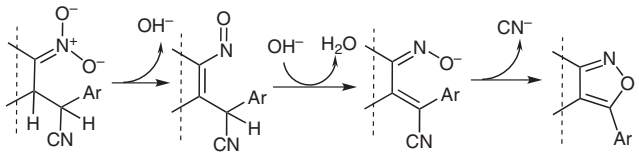
Abstract: Reaction of 1-nitro-4-(1,2,3-triazolyl/tetrazolyl)benzenes with arylacetonitriles in an alcoholic medium in the presence of excess alkali gives novel 2,1-benzisoxazoles. These findings indicate a high reactivity of nitroarenes activated by the azole ring due to their electron-deficient character. Moreover, it was found that annulation of the isoxazole ring occurred regioselectively in disubstituted nitroarenes. In the case of 1-(4-nitrophenyl)-1*H*-tetrazole, the tetrazole ring cleaved faster than the σ^H-adduct was formed.

Key words: 1*H*-1,2,3-triazole, tetrazole, nucleophilic substitution, 2,1-benzisoxazole, annulation

One of the most convenient methods for the synthesis of 2,1-benzisoxazoles (reagents for bioactive substances[1]), is the reaction of nitroarenes with arylacetonitriles under conditions found by Davis.[2] The mechanism of the reaction is a nucleophilic aromatic substitution (S_NAr).[3] It is noteworthy, that S_NAr reactions of hydrogen occur rarely in contrast to S_EAr reactions, because of the fact that the hydride ion has a small electronegativity and is unfavorable in reactions as a nucleofuge. In addition, the hydride ion, which does not form hydrogen bonds and solvates, is not fixed as a kinetically independent particle in the reactions of organic compounds.

Probably, the most general transformation of σ^H-adducts into products of nucleophilic substitution of hydrogen occurs when the reacting nucleophiles contain a leaving group X at the nucleophilic center (β-elimination of HX gives anionic products, which give products of hydrogen replacement with the nucleophile moiety via protonation). In contrast, anionic σ^H-adducts, formed by addition of nucleophiles to the aromatic ring, undergo oxidation with external or internal oxidants.[3]

Herein, we describe the reactions of arylacetonitriles with *para*-substituted nitrobenzenes by elimination of water in the σ^H-adducts to produce nitroso compounds, and subsequent cyclization with elimination of hydrogen cyanide to form 2,1-benzisoxazoles (Scheme 1). It is known, that such reactions are sensitive to electronic effects of substituents in the aromatic ring. The addition of nucleophilic agents to the aromatic ring occurs more effectively in the case of electron-deficient character of the ring. It can be possible due to the presence of strongly electron-withdrawing substituents in the ring, such as the nitro group. Electron-donor substituents do not generally allow the reaction to proceed.[4–7]



Scheme 1 Mechanism of the isoxazole ring annulation in nitroaromatic substrates

Compounds containing an aromatic or heterocyclic ring in the *para*-position to the nitro group have been insufficiently studied for 2,1-benzisoxazole synthesis. For example, reaction of 2-(4-nitrophenyl)-5-phenyl-1,3,4-oxadiazole with phenylacetonitrile gave 3-phenyl-5-(5-phenyl-1,3,4-oxadiazol-2-yl)-2,1-benzisoxazole in 80% yield. However, 4-nitrobiphenyl in such a reaction gave 3,5-diphenyl-2,1-benzisoxazole in only 44% yield.[5,6]

In the current work, nitroarenes, activated by the azole (tetrazole or triazole) ring, were selected for the synthesis of 2,1-benzisoxazoles. The starting nitroarenes were synthesized from commercially available 4-nitroanilines **1a–c** by several procedures (Scheme 2). Some new 1*H*-1,2,3-triazol-4-yl ketones **4a**,**b** and 1*H*-1,2,3-triazole-4-carboxylic acids **4c–k** were synthesized by base-catalyzed cyclocondensation of aryl azides **2a–c** (prepared from sodium azide and diazonium salts obtained from anilines **1a–c**) with β-diketones **3a**,**b** and β-keto esters **3c–i** according to the procedure described in the literature.[8] By decarboxylation of acids **4c**,**k** at temperatures 20 °C higher than their melting points, 1*H*-1,2,3-triazoles **5a**,**b** were obtained.[8] The reaction required strict control of the temperature; rapid decomposition of the triazole ring occurred when the reaction was overheated.

1-(4-Nitrophenyl)-1*H*-tetrazole (**6**) was synthesized by the reaction of 4-nitroaniline (**1a**) with triethyl orthoformate and sodium azide in acetic acid.[9] 1*H*-Tetrazoles **7a–c** were prepared by a two-step procedure: anilines **1a** were acylated by acid chlorides, the obtained acylanilides were converted into imidoyl chlorides by phosphorus oxychloride and then one-pot reaction with sodium azide gave the tetrazole ring. We have found that this reaction gave 5-substituted tetrazoles **7a–c** in 67–84% isolated yield.

2-(4-Nitrophenyl)-2*H*-tetrazole-5-carboxylic acid (**9**), as a type of 2,5-disubstituted tetrazole, was synthesized by the Boulton–Katritzky rearrangement[10] of 3-triazenoisox-

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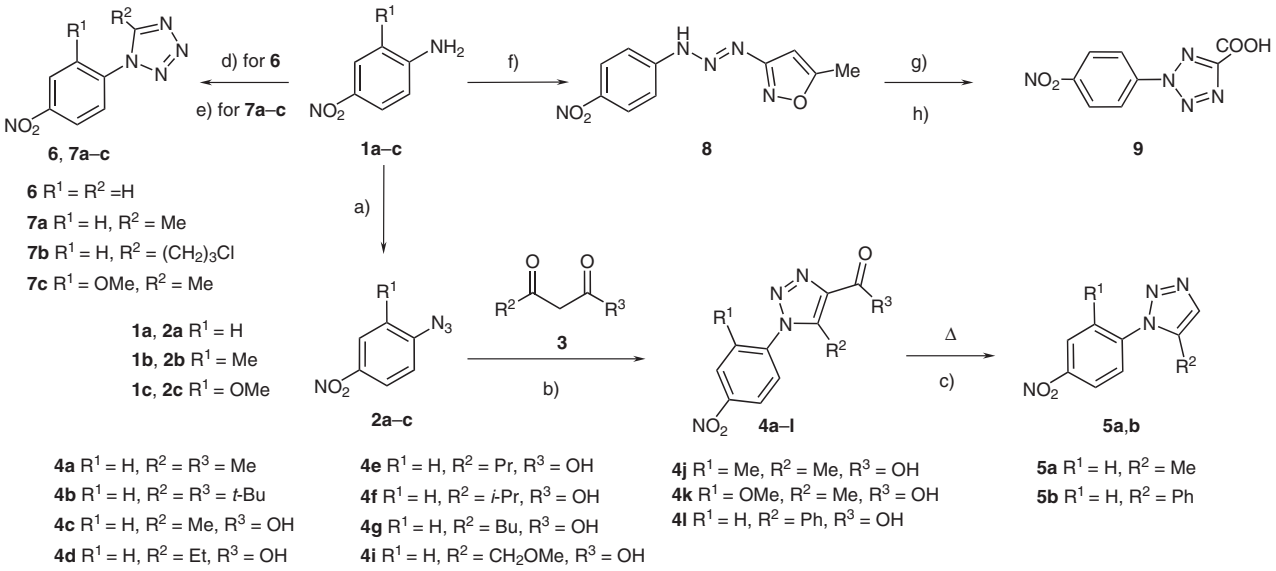
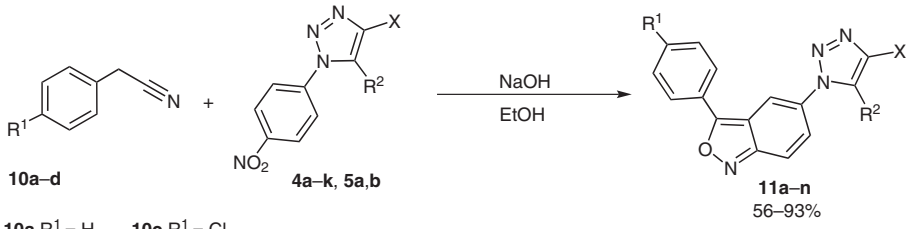


Scheme 2 *Reagents and conditions*: (a) $NaNO_2$, HCl, then NaN_3, 0 °C; (b) Na, MeOH, r.t., 1 d (for **4a**), 61%; 65 °C, 1 h (for **4b**–**k**), 54–94%; (c) 20 °C above mp, 10 min, 85–91%; (d) $CH(OEt)_3$, NaN_3, AcOH, 100 °C, 4 h; (e) 1. R^2COCl, dioxane, Et_3N, r.t., 1 h; 2. $POCl_3$, NaN_3, MeCN, 100 °C, 4 h, 67–84%; (f) $NaNO_2$, HCl, then 5-methylisoxazol-3-amine, NaOAc, H_2O, r.t., 1 h; (g) NH_3, acetone, 56 °C, 5 min; (h) $KMnO_4$, 68% (from **1a**).

Table 1 2,1-Benzisoxazoles **11a**–**n**



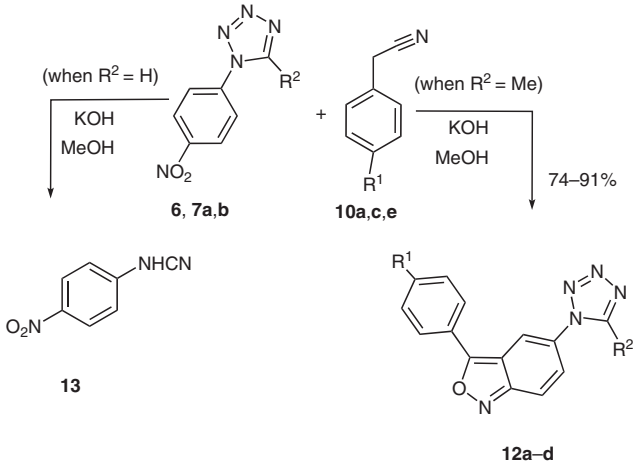
Entry	Product	X	R^1	R^2	Yield[a] (%)
1	**11a**	H	H	Me	70
2	**11b**	H	Cl	Me	84
3	**11c**	H	H	Ph	88
4	**11d**	COMe	H	Me	–[b]
5	**11e**	CO*t*-Bu	H	*t*-Bu	87
6	**11f**	CO_2H	H	Me	91
7	**11g**	CO_2H	F	Me	84
8	**11h**	CO_2H	Cl	Me	93
9	**11i**	CO_2H	Br	Me	90
10	**11j**	CO_2H	H	Et	88
11	**11k**	CO_2H	H	Pr	73
12	**11l**	CO_2H	H	*i*-Pr	70
13	**11m**	CO_2H	H	Bu	69
14	**11n**	CO_2H	H	CH_2OMe	56

[a] Isolated yields are based on a single experiment and yields were not optimized.
[b] Mixture of products.

azole **8** and oxidation of the acetone fragment to the corresponding acid by the action of potassium permanganate.

We found that the reaction of 4-nitroarenes **4**, **5** with arylacetonitriles **10a–d** in ethanol in the presence of excess sodium hydroxide formed compounds **11a–n** in good yield (Table 1). Formation of byproducts was not observed. Moreover, the reaction occurred with sterically shielded ketone **4b**. However, the ketone **4a** gave a mixture of products.

In the reaction of 1,5-disubstituted 1*H*-tetrazoles **7a–c** with arylacetonitriles **10a**,**c**,**e**, 2,1-benzisoxazoles **12a–d** were obtained as the main products. The reaction was carried out using a methanolic potassium hydroxide solution (Scheme 3); it exhibited an appreciable exothermal effect and was complete within 5–10 min. In general, the product of the reaction formed immediately after mixing the reagents. The polycyclic compounds **12a–d** were isolated in good yields (74–91%) (Table 2). High yields were possible due to the presence of strongly electron-withdrawing substituents in the arene ring, such as the electron-deficient tetrazole ring. However, 1-(4-nitrophenyl)-1*H*-tetrazole (**6**) did not react with arylacetonitriles **10** to yield 2,1-benzisoxazoles. It was found that under the reaction conditions the tetrazole ring cleaved and lost a molecule of nitrogen. The product of the reaction was (4-nitrophenyl)cyanamide (**13**). Obviously, the cyanamide group was formed faster than the nucleophile attacked the aryl ring and formed the σ^H-adduct. In fact, the change of the character of substituents and the electronic configuration of the ring made subsequent transformation impossible. We were unsuccessful in our attempts to annulate the isoxazole ring in the reaction of (4-nitrophenyl)cyanamide (**13**) with phenylacetonitrile.



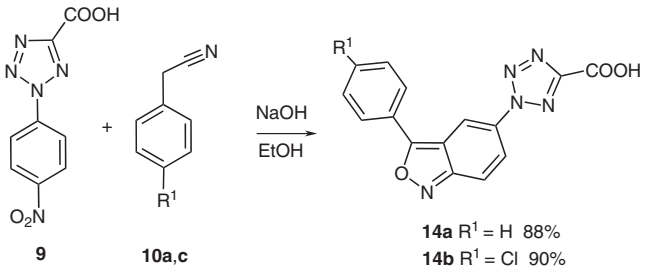
Scheme 3

Furthermore, we have subsequently obtained 2,1-benzisoxazoles **14a**,**b** in the highest yields (88–90%) from the reaction of 2*H*-tetrazole **9** with arylacetonitriles **10a**,**c** (Scheme 4). It cannot be validly argued that the tetrazole ring is suitable in such reactions due to a strong *I*-effect of the ring, mostly exhibited in 2-substituted 2*H*-tetrazoles.

Table 2 2,1-Benzisoxazoles **12a–d**

Entry	Product	R^1	R^2	Yield[a] (%)
1	**12a**	H	Me	87
2	**12b**	Me	Me	84
3	**12c**	Cl	Me	91
4	**12d**	H	$(CH_2)_3Cl$	74

[a] Isolated yields.



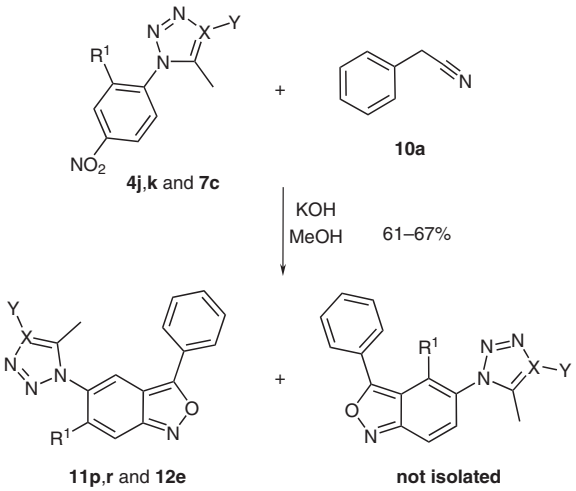
Scheme 4

The structures of all new compounds were confirmed by analytical and spectroscopic data. In the ^{1}H NMR spectra of 2,1-benzisoxazoles **11a–n**, **12a–d**, **14a**,**b** there was a large difference in chemical shift values for the H4, H6, and H7 protons which is typical for the 2,1-benzisoxazole system.[11] Spin-spin coupling constant values between the H6 and H7 protons were J = 9.2, 9.6 Hz. It is important to emphasize that the chemical shift value for the H4 proton, found in a low field, increased according to the *I*-effect of the heterocycle in the position 3 of the aryl ring in order: 2*H*-tetrazole, 1*H*-tetrazole, and 1*H*-1,2,3-triazole derivatives correspondingly.

In addition, it is necessary to point out that the reaction of nucleophiles with asymmetric arenes occurred regioselectively. It was found that in the reaction of 4-nitroarenes **4i**,**j**, **7c** with phenylacetonitrile only one of two possible isomers (**11o**,**p**, **12e**) was isolated (Table 3). The phenylacetonitrile carbanion attacked the aryl ring in the *para*-position to an electron-donor methyl or methoxy group. In fact, electron-donor substituents had a negative influence on the rate of the reaction. Thus, the less sterically hindered position (with a low electron density) was preferable for the nucleophilic attack. Therefore, we have presumed that regioselectivity can be achieved in similar reactions of 2,1-benzisoxazole synthesis. The formation of regioisomeric mixtures was excluded by the NMR spectral data. In ^{1}H NMR spectroscopic data there were two singlet signals at δ = 7.2–7.8 and δ = 8.1–8.6 of the H7 and H4 protons of 2,1-benzisoxazoles.

In conclusion, this method is very effective and allows the preparation of 5-(tetrazolyl/1*H*-1,2,3-triazolyl)-2,1-benzisoxazoles under mild reaction conditions and with good yields and regioselectivity. Moreover, the reaction displays an approach to the study of tetrazole and 1*H*-1,2,3-triazole properties as substituents in the aromatic ring.

Table 3 2,1-Benzisoxazoles **11o**,**p**, **12e**



Entry	Product	X–Y	R^1	Yield[a] (%)
1	**11o**	C–CO_2H	Me	67
2	**11p**	C–CO_2H	OMe	61
3	**12e**	N	OMe	65

[a] Isolated yields.

Further investigations on other azoles are in progress in our laboratory.

All melting points were determined in capillary tubes in a Thiele apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Varian Mercury 400 instrument (400 MHz for ^{1}H) with TMS or deuterated solvent as an internal reference. Mass spectra were run using Agilent 1100 series LC/MSD with an API-ES/APCI ionization mode. The evolution of the reactions and purity of the synthesized compounds were monitored chromatographically on Silufol UV-254 plates. Aryl azides **2a**–**c** were prepared from commercially available 4-nitroanilines **1a**–**c** according to the procedures described in the literature.[12] We used the following abbreviations in NMR spectra presentation: Bis = 2,1-benzisoxazole, Tr = triazole.

1-[5-Methyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl]ethanone (4a)

To a soln of NaOMe (540 mg, 10.0 mmol) in anhyd MeOH (20 mL) was added pentane-2,4-dione (**3a**, 1 mL, 10.0 mmol). To this soln 1-azido-4-nitrobenzene (**2a**, 1.6 g, 10.0 mmol) in anhyd MeOH (2 mL) was added dropwise. The mixture was stirred at r.t. for 24 h. The resulting suspension was filtered and the solid product was washed with H_2O and MeOH to give **4a** as light yellow crystals; yield: 1.50 g (61%); mp 132–133 °C (Lit.[13] 133–134 °C).

MS (CI): *m*/*z* (%) = 247 (100) [M + H$^+$].

1-[5-*tert*-Butyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl]-2,2-dimethylpropan-1-one (4b)

To the soln of NaOMe (540 mg, 10.0 mmol) in anhyd MeOH (20 mL) was added 2,2,6,6-tetramethylheptane-3,5-dione (2.1 mL, 10.0 mmol) and 1-azido-4-nitrobenzene (**2a**, 1.6 g, 10.0 mmol). The mixture was kept in an ice-water bath for 30 min and then slowly heated under reflux for 1 h. The mixture was cooled and the solid started to precipitate. The solid product was filtered and washed with H_2O and MeOH to give **4b** as white crystals; yield: 3.10 g (94%), mp 135–136 °C.

^{1}H NMR (DMSO-d_6): δ = 1.21 (s, 9 H, *t*-Bu), 1.38 (s, 9 H, *t*-Bu), 7.86 (d, ^3J = 8.8 Hz, 2 H, $H3_{Ar}$, $H5_{Ar}$), 8.45 (d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$).

MS (CI): *m*/*z* (%) = 331 (100) [M + H$^+$].

Anal. Calcd for $C_{17}H_{22}N_4O_3$ (330.38): C, 61.80; H, 6.71; N, 16.96. Found: C, 61.92; H, 6.67; N, 16.85.

5-Substituted 1-Aryl-1*H*-1,2,3-triazole-4-carboxylic Acids 4c–k; General Procedure

Na (0.23 g, 10 mmol) was added to abs MeOH (20 mL). β-Keto ester **3** (10 mmol) and the appropriate azide **2** (10 mmol) were slowly added (cooling with ice-water) to the obtained NaOMe soln. The mixture was kept in an ice-water bath for 30 min and then slowly heated under reflux for 1 h; the solid precipitated. Hot H_2O was added to dissolve the precipitate (50 mL), if necessary the soln of NaOH can be adjusted to pH 11–12 and heated under reflux for 1 h. The hot soln was poured into concd HCl (10 mL) and left crystallized. The obtained solid was filtered, washed with H_2O (2 ×), and crystallized (EtOH).

5-Methyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-4-carboxylic Acid (4c)

White crystals; yield: 1.66 g (67%); mp 190–191 °C (Lit.[8] 188–189 °C).

MS (CI): *m*/*z* (%) = 249 (100) [M + H$^+$].

5-Ethyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-4-carboxylic Acid (4d)

White crystals; yield: 2.22 g (85%); mp 180–181 °C.

^{1}H NMR (DMSO-d_6): δ = 1.11 (t, ^3J = 7.2 Hz, 3 H, Et), 3.02 (q, ^3J = 7.2 Hz, 2 H, Et), 7.91 (d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.48 (d, ^3J = 8.8 Hz, 2 H, $H3_{Ar}$, $H5_{Ar}$).

MS (CI): *m*/*z* (%) = 263 (100) [M + H$^+$].

Anal. Calcd for $C_{11}H_{10}N_4O_4$ (262.22): C, 50.38; H, 3.84; N, 21.37. Found: C, 50.24; H, 3.72; N, 21.41.

1-(4-Nitrophenyl)-5-propyl-1*H*-1,2,3-triazole-4-carboxylic Acid (4e)

White crystals; yield: 2.29 g (83%); mp 175–176 °C.

^{1}H NMR (DMSO-d_6): δ = 0.82 (t, ^3J = 7.2 Hz, 3 H, Pr), 1.43–1.51 (m, 2 H, Pr), 3.00 (t, ^3J = 7.6 Hz, 2 H, Pr), 7.91 (d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.48 (d, ^3J = 8.8 Hz, 2 H, $H3_{Ar}$, $H5_{Ar}$).

MS (CI): *m*/*z* (%) = 277 (100) [M + H$^+$].

Anal. Calcd for $C_{12}H_{12}N_4O_4$ (276.25): C, 52.17; H, 4.38; N, 20.28. Found: C, 51.97; H, 4.54; N, 20.39.

5-Isopropyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-4-carboxylic Acid (4f)

White crystals; yield: 1.49 g (54%); mp 164–165 °C;

^{1}H NMR (DMSO-d_6): δ = 1.29 (d, ^3J = 7.2 Hz, 6 H, *i*-Pr), 3.26 (m, 1 H, *i*-Pr), 7.92 (d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.48 (d, ^3J = 8.8 Hz, 2 H, $H3_{Ar}$, $H5_{Ar}$).

MS (CI): *m*/*z* (%) = 277 (100) [M + H$^+$].

Anal. Calcd for $C_{12}H_{12}N_4O_4$ (276.25): C, 52.17; H, 4.38; N, 20.28. Found: C, 52.02; H, 4.28; N, 20.17.

5-Butyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-4-carboxylic Acid (4g)

White crystals; yield: 1.62 g (56%); mp 158–159 °C.

^{1}H NMR (DMSO-d_6): δ = 0.81 (t, ^3J = 7.6 Hz, 3 H, Me), 1.22 (m, 2 H, CH_2), 1.43 (m, 2 H, CH_2), 3.03 (t, ^3J = 7.6 Hz, 2 H, CH_2), 7.92

(d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.49 (d, ^3J = 8.8 Hz, 2 H, $H3_{Ar}$, $H5_{Ar}$).

MS (CI): *m*/*z* (%) = 291 (100) [M + H^+].

Anal. Calcd for $C_{13}H_{14}N_4O_4$ (290.27): C, 53.79; H, 4.86; N, 19.30. Found: C, 53.84; H, 4.93; N, 19.15.

5-(Methoxymethyl)-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-4-carboxylic Acid (4h)

White crystals; yield: 1.81 g (65%); mp 161–162 °C.

^{1}H NMR (DMSO-d_6): δ = 3.31 (s, 3 H, Me), 4.85 (s, 2 H, CH_2), 8.03 (d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.47 (d, ^3J = 8.8 Hz, 2 H, $H3_{Ar}$, $H5_{Ar}$).

MS (CI): *m*/*z* (%) = 279 (100) [M + H^+].

Anal. Calcd for $C_{11}H_{10}N_4O_5$ (278.22): C, 47.49; H, 3.62; N, 20.14. Found: C, 47.76; H, 3.44; N, 20.36.

5-Methyl-1-(2-methyl-4-nitrophenyl)-1*H*-1,2,3-triazole-4-carboxylic Acid (4i)

White crystals; yield: 1.94 g (74%); mp 183–184 °C;

^{1}H NMR (DMSO-d_6): δ = 2.07 (s, 3 H, Me), 2.46 (s, 3 H, Me), 7.93 (d, ^3J = 8.8 Hz, 1 H, $H6_{Ar}$), 8.23 (s, 1 H, $H3_{Ar}$), 8.48 (d, ^3J = 8.8 Hz, 1 H, $H5_{Ar}$).

MS (CI): *m*/*z* (%) = 263 (100) [M + H^+].

Anal. Calcd for $C_{11}H_{10}N_4O_4$ (262.22): C, 50.38; H, 3.84; N, 21.37. Found: C, 50.61; H, 3.67; N, 21.55.

1-(2-Methoxy-4-nitrophenyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxylic Acid (4j)

White crystals; yield: 1.92 g (69%); mp 160–161 °C.

^{1}H NMR (DMSO-d_6): δ = 2.43 (s, 3 H, Me), 3.91 (s, 3 H, OMe), 7.76 (d, ^3J = 8.8 Hz, 1 H, $H6_{Ar}$), 8.38 (s, 1 H, $H3_{Ar}$), 8.48 (d, ^3J = 8.8 Hz, 1 H, $H5_{Ar}$).

MS (CI): *m*/*z* (%) = 279 (100) [M + H^+].

Anal. Calcd for $C_{11}H_{10}N_4O_5$ (278.22): C, 47.49; H, 3.62; N, 20.14. Found: C, 47.56; H, 3.38; N, 20.06.

1-(4-Nitrophenyl)-5-phenyl-1*H*-1,2,3-triazole-4-carboxylic Acid (4k)

White crystals; yield: 2.82 g (91%); mp 182–183 °C.

^{1}H NMR (DMSO-d_6): 7.34–7.43 (m, 5 H, H_{Ph}), 7.89 (d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.49 (d, ^3J = 8.8 Hz, 2 H, $H3_{Ar}$, $H5_{Ar}$).

MS (CI): *m*/*z* (%) = 311 (100) [M + H^+].

Anal. Calcd for $C_{15}H_{10}N_4O_4$ (310.26): C, 58.07; H, 3.25; N, 18.06. Found: C, 57.73; H, 3.18; N, 17.97.

Decarboxylation of 1*H*-1,2,3-triazole-4-carboxylic Acids 4c,k; General Procedure

Compound **4c** or **4k** (10 mmol) was heated at the temperature 20 °C higher than its mp until evolution of CO_2 ceased. The triazoles **5a**,**b** obtained were crystallized (EtOH).

5-Methyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazole (5a)

White crystals; yield: 1.85 g (91%); mp 139–140 °C (Lit.[8] 140 °C).

MS (CI): *m*/*z* (%) = 205 (100) [M + H^+].

1-(4-Nitrophenyl)-5-phenyl-1*H*-1,2,3-triazole (5b)

White crystals; yield: 2.26 g (85%); mp 103–104 °C.

^{1}H NMR (DMSO-d_6): 7.37–7.47 (m, 5 H, H_{Ph}), 7.89 (d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.02 (s, 1 H, H_{Tr}), 8.49 (d, ^3J = 8.8 Hz, 2 H, $H3_{Ar}$, $H5_{Ar}$).

MS (CI): *m*/*z* (%) = 367 (100) [M + H^+].

Anal. Calcd for $C_{14}H_{10}N_4O_2$ (266.25): C, 63.15; H, 3.79; N, 21.04. Found: C, 63.28; H, 3.62; N, 21.17.

1-(4-Nitrophenyl)-1*H*-tetrazole (6)

Prepared according to the procedure described previously in the literature.[9]

5-Substituted 1-(4-Nitrophenyl)-1*H*-tetrazoles 7a–c; General Procedure

The 4-nitroaniline **1** (0.1 mol) was dissolved in dioxane and Et_3N (7 mL, 0.1 mol) was added. The mixture was cooled to 0 °C and the corresponding acyl chloride (0.025 mol) was added keeping the temperature below 5 °C. The soln was left at r.t. for 1 h and H_2O (50 mL) was then added. The obtained solid was filtered, washed with H_2O (2 ×), crystallized (EtOH), and dried in vacuo.

A mixture of acylaniline (0.02 mol) with NaN_3 (2.6 g, 0.04 mol) and $POCl_3$ (15.4 g, 0.1 mol) in MeCN (200 mL) was stirred under reflux for 10 h. The solvent and excess $POCl_3$ were removed under reduced pressure. The residue was cooled, neutralized with sat. $NaHCO_3$ soln, and evaporated to dryness. Compounds **7a–e** were crystallized (EtOH).

5-Methyl-1-(4-nitrophenyl)-1*H*-tetrazole (7a)

White crystals; yield: 3.46 g (84%); mp 107–108 °C.

^{1}H NMR (DMSO-d_6): δ = 2.66 (s, 3 H, CH_3), 8.01 (d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.47 (d, ^3J = 8.8 Hz, 2 H, $H3_{Ar}$, $H5_{Ar}$).

MS (CI): *m*/*z* (%) = 206 (100) [M + H^+].

Anal. Calcd for $C_8H_7N_5O_2$ (205.17): C, 46.83; H, 3.44; N, 34.13. Found: C, 46.66; H, 3.60; N, 34.04.

5-(3-Chloropropyl)-1-(4-nitrophenyl)-1*H*-tetrazole (7b)

White crystals; yield: 3.58 g (67%); mp 80–81 °C.

^{1}H NMR (DMSO-d_6): δ = 2.24 (m, 2 H, CH_2), 3.10 (t, ^3J = 7.2 Hz, 2 H, CH_2), 3.69 (t, ^3J = 7.2 Hz, 2 H, CH_2), 7.98 (d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.45 (d, ^3J = 8.8 Hz, 2 H, $H3_{Ar}$, $H5_{Ar}$).

MS (CI): *m*/*z* (%) = 268 (100) [M + H^+].

Anal. Calcd for $C_{10}H_{10}ClN_5O_2$ (267.67): C, 44.87; H, 3.77; N, 26.16. Found: C, 44.72; H, 3.49; N, 26.21.

1-(2-Methoxy-4-nitrophenyl)-5-methyl-1*H*-tetrazole (7c)

White crystals; yield: 3.52 g (75%); mp 138–139 °C;

^{1}H NMR (DMSO-d_6): δ = 2.43 (s, 3 H, Me), 3.91 (s, 3 H, OMe), 7.76 (d, ^3J = 8.8 Hz, 1 H, $H6_{Ar}$), 8.38 (s, 1 H, $H3_{Ar}$), 8.48 (d, ^3J = 8.8 Hz, 1 H, $H5_{Ar}$).

MS (CI): *m*/*z* (%) = 236 (100) [M + H^+].

Anal. Calcd for $C_9H_9N_5O_3$ (235.20): C, 45.96; H, 3.86; N, 29.78. Found: C, 46.07; H, 3.69; N, 29.64.

2-(4-Nitrophenyl)-2*H*-tetrazole-5-carboxylic Acid (9)

$NaNO_2$ (1.4 g, 20.3 mmol) was added to the soln of 4-nitroaniline (**1a**, 2.8 g, 20.3 mmol) in 16% HCl (22 mL) keeping the temperature below 5 °C. The resulting diazonium salt was added to a soln of 5-methylisoxazol-3-amine (2 g, 20.4 mmol) and NaOAc (5.6 g, 68.3 mmol) in H_2O (100 mL). The mixture was stirred at r.t. for 24 h. The resulting suspension was filtered and the solid product was washed with H_2O to give the corresponding triazene **8** (mp 169–171 °C). Compound **8** was heated in 5% NH_3 in acetone soln for 5 min. The mixture was diluted with H_2O and 1-[2-(4-nitrophenyl)-2*H*-tetrazol-5-yl]propan-2-one started to precipitate (mp 132–134 °C). To the soln [acetone (30 mL) and H_2O (10 mL)] of 2*H*-tetrazole (10 mmol), $KMnO_4$ (3.2 g, 20.3 mmol) was added in portions. The soln was heated to discoloration. The hot soln was filtered, cooled and

acidified with HCl. Acid **9** was filtered, washed with H_2O, and dried; yield: 1.60 g (68%); mp 184 °C (Lit.[14] 184 °C).[14]

MS (CI): *m*/*z* (%) = 236 (100) [M + H$^+$].

3-Aryl-2,1-benzisoxazoles 11a–p; General Procedure

To a warm soln of NaOH (5.0 g, 0.125 mol) in EtOH (40 mL) was added arylacetonitrile **10** (11.25 mmol) and a soln of nitroarene **4**, **5** (10 mmol) in EtOH (25 mL). The mixture was stirred at 60 °C for 4 h and at r.t. for 1 d. The soln was diluted with H_2O and acidified with HCl. The precipitate was isolated by filtration, washed with hot H_2O, and dried.

5-(5-Methyl-1*H*-1,2,3-triazol-1-yl)-3-phenyl-2,1-benzisoxazole (11a)

White crystals; yield: 1.93 g (70%); mp 148–149 °C (EtOH–H_2O).

^{1}H NMR (DMSO-d_6): δ = 2.37 (s, 3 H, CH_3), 7.57–7.66 (m, 3 H, H_{Ph}), 7.72 (d, ^3J = 9.2 Hz, 1 H, $H7_{Bis}$), 7.92 (m, 2 H, $H6_{Bis}$, H_{Tr}), 8.17 (m, 2 H, H_{Ph}), 8.36 (s, 1 H, $H4_{Bis}$).

MS (CI): *m*/*z* (%) = 277 (100) [M + H$^+$].

Anal. Calcd for $C_{16}H_{12}N_4O$ (276.29): C, 69.55; H, 4.38; N, 20.28. Found: C, 69.39; H, 4.49; N, 20.19.

3-(4-Chlorophenyl)-5-(5-methyl-1*H*-1,2,3-triazol-1-yl)-2,1-benzisoxazole (11b)

White crystals; yield: 2.61 g (84%); mp 189–190 °C (EtOH).

^{1}H NMR (DMSO-d_6): δ = 2.49 (s, 3 H, CH_3), 7.61–7.70 (m, 3 H, $H6_{Bis}$, $H3_{Ar}$, $H5_{Ar}$), 7.73 (s, 1 H, H_{Tr}), 7.92 (d, ^3J = 8.8 Hz, 1 H, $H7_{Bis}$), 8.19 (d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.34 (s, 1 H, $H4_{Bis}$).

MS (CI): *m*/*z* (%) = 311 (100) [M + H$^+$].

Anal. Calcd for $C_{16}H_{11}ClN_4O$ (310.74): C, 61.84; H, 3.57; N, 18.03. Found: C, 61.98; H, 3.38; N, 17.86.

3-Phenyl-5-(5-phenyl-1*H*-1,2,3-triazol-1-yl)-2,1-benzisoxazole (11c)

White crystals; yield: 2.97 g (88%); mp 214–215 °C (EtOH).

^{1}H NMR (DMSO-d_6): δ = 7.27 (d, ^3J = 9.6 Hz, 1 H, $H6_{Bis}$), 7.39–7.45 (m, 5 H, H_{Ph}), 7.52–7.61 (m, 3 H, H_{Ph}), 7.70 (d, ^3J = 9.6 Hz, 1 H, $H7_{Bis}$), 7.98 (d, ^3J = 8.0 Hz, 2 H, $H2_{Ph}$, $H6_{Ph}$), 8.00 (s, 1 H, H_{Tr}), 8.18 (s, 1 H, $H4_{Bis}$).

MS (CI): *m*/*z* (%) = 339 (100) [M + H$^+$].

Anal. Calcd for $C_{21}H_{14}N_4O$ (338.36): C, 74.54; H, 4.17; N, 16.56. Found: C, 74.40; H, 4.03; N, 16.39.

1-[5-*tert*-Butyl-1-(3-phenyl-2,1-benzisoxazol-5-yl)-1*H*-1,2,3-triazol-4-yl]-2,2-dimethyl-1-propanone (11e)

White crystals; yield: 3.5 g (87%); mp 178–179 °C (EtOH).

IR (KBr): 1650 cm^{-1} (s, C=O).

^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.25 (s, 9 H, *t*-Bu), 1.40 (s, 9 H, *t*-Bu), 7.59 (d, ^3J = 9.3 Hz, 1 H, $H6_{Bis}$), 7.60–7.65 (m, 3 H, $H3_{Ph}$, $H4_{Ph}$, $H5_{Ph}$), 7.89 (d, ^3J = 9.3 Hz, 1 H, $H7_{Bis}$), 8.21 (d, ^3J = 7.8 Hz, 2 H, $H2_{Ph}$, $H6_{Ph}$), 8.60 (s, 1 H, $H4_{Bis}$).

MS: (CI) *m*/*z* (%) = 403 (100) [M + H$^+$].

Anal. Calcd for $C_{24}H_{26}N_4O_2$ (402.49): C, 71.62; H, 6.51; N, 13.92. Found: C, 74.40; H, 4.03; N, 16.39.

5-Methyl-1-(3-phenyl-2,1-benzisoxazol-5-yl)-1*H*-1,2,3-triazole-4-carboxylic Acid (11f)

White crystals; yield: 2.91 g (91%); mp 210–211 °C (dec.) (EtOH).

^{1}H NMR (DMSO-d_6): δ = 2.56 (s, 3 H, Me), 7.58–7.66 (m, 4 H, $H6_{Bis}$, $H3_{Ph}$, $H4_{Ph}$, $H5_{Ph}$), 7.93 (d, ^3J = 9.6 Hz, 1 H, $H7_{Bis}$), 8.16 (d, ^3J = 7.8 Hz, 2 H, $H2_{Ph}$, $H6_{Ph}$), 8.45 (s, 1 H, $H4_{Bis}$).

MS (CI): *m*/*z* (%) = 321 (100) [M + H$^+$].

Anal. Calcd for $C_{17}H_{12}N_4O_3$ (320.30): C, 63.75; H, 3.78; N, 17.49. Found: C, 63.70; H, 3.81; N, 17.35.

1-[3-(4-Fluorophenyl)-2,1-benzisoxazol-5-yl]-5-methyl-1*H*-1,2,3-triazole-4-carboxylic Acid (11g)

White crystals; yield: 2.3 g (84%); mp 235–236 °C (dec.) (EtOH).

^{1}H NMR (DMSO-d_6): δ = 2.84 (s, 3 H, Me), 7.37 (t, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 7.56 (d, ^3J = 9.2 Hz, 1 H, $H6_{Bis}$), 7.85 (d, ^3J = 9.2 Hz, 1 H, $H7_{Bis}$), 8.24 (dd, $^3J_{HH}$ = 8.8, $^4J_{HF}$ = 4.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.42 (s, 1 H, $H4_{Bis}$), 12.96 (s, 1 H, COOH).

MS (CI): *m*/*z* (%) = 339 (100) [M + H$^+$].

Anal. Calcd for $C_{17}H_{11}FN_4O_3$ (338.29): C, 60.36; H, 3.28; N, 16.56. Found: C, 60.58; H, 3.37; N, 16.64.

1-[3-(4-Chlorophenyl)-2,1-benzisoxazol-5-yl]-5-methyl-1*H*-1,2,3-triazole-4-carboxylic Acid (11h)

White crystals; yield: 3.29 g (93%); mp 244–245 °C (dec.) (EtOH).

^{1}H NMR (DMSO-d_6): δ = 2.61 (s, 3 H, Me), 7.58 (d, ^3J = 9.6 Hz, 1 H, $H6_{Bis}$), 7.61 (d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 7.87 (d, ^3J = 9.6 Hz, 1 H, $H7_{Bis}$), 8.19 (d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.44 (s, 1 H, $H4_{Bis}$), 12.99 (s, 1 H, COOH).

MS (CI): *m*/*z* (%) = 355 (100) [M + H$^+$].

Anal. Calcd for $C_{17}H_{11}ClN_4O_3$ (354.75): C, 57.56; H, 3.13; N, 15.79. Found: C, 57.42; H, 3.01; N, 15.63.

1-[3-(4-Bromophenyl)-2,1-benzisoxazol-5-yl]-5-methyl-1*H*-1,2,3-triazole-4-carboxylic Acid (11i)

White crystals; yield: 3.59 g (90%); mp 230–231 °C (dec.) (EtOH).

^{1}H NMR (DMSO-d_6): δ = 2.59 (s, 3 H, Me), 7.66 (d, ^3J = 9.6 Hz, 1 H, $H6_{Bis}$), 7.83 (d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 7.96 (d, ^3J = 9.6 Hz, 1 H, $H7_{Bis}$), 8.14 (d, ^3J = 8.8 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.49 (s, 1 H, $H4_{Bis}$), 13.28 (s, 1 H, COOH).

MS (CI): *m*/*z* (%) = 399 (100) [M + H$^+$], 401 (89) [M + H$^+$].

Anal. Calcd for $C_{17}H_{11}BrN_4O_3$ (399.20): C, 51.15; H, 2.78; N, 14.03. Found: C, 51.24; H, 2.56; N, 14.19.

5-Ethyl-1-(3-phenyl-2,1-benzisoxazol-5-yl)-1*H*-1,2,3-triazole-4-carboxylic Acid (11j)

White crystals; yield: 2.94 g (88%); mp 182–183 °C (dec.) (EtOH).

^{1}H NMR (DMSO-d_6): δ = 1.12 (t, ^3J = 7.2 Hz, 3 H, Et), 3.03 (q, ^3J = 7.2 Hz, 2 H, Et), 7.50 (d, ^3J = 9.2 Hz, 1 H, $H6_{Bis}$), 7.56–7.64 (m, 3 H, $H3_{Ph}$, $H4_{Ph}$, $H5_{Ph}$), 7.86 (d, ^3J = 9.2 Hz, 1 H, $H7_{Bis}$), 8.14 (d, ^3J = 7.8 Hz, 2 H, $H2_{Ph}$, $H6_{Ph}$), 8.42 (s, 1 H, $H4_{Bis}$), 12.95 (s, 1 H, COOH).

MS (CI): *m*/*z* (%) = 335 (100) [M + H$^+$].

Anal. Calcd for $C_{18}H_{14}N_4O_3$ (334.33): C, 64.66; H, 4.22; N, 16.76. Found: C, 64.46; H, 4.34; N, 16.42.

1-(3-Phenyl-2,1-benzisoxazol-5-yl)-5-propyl-1*H*-1,2,3-triazole-4-carboxylic Acid (11k)

White crystals; yield: 2.54 g (73%); mp 193–194 °C (dec.) (EtOH).

^{1}H NMR (DMSO-d_6): δ = 0.82 (t, ^3J = 7.2 Hz, 3 H, Pr), 1.50–1.55 (m, 2 H, Pr), 3.00 (t, ^3J = 8.0 Hz, 2 H, Pr), 7.50 (d, ^3J = 9.2 Hz, 1 H, $H6_{Bis}$), 7.56–7.64 (m, 3 H, $H3_{Ph}$, $H4_{Ph}$, $H5_{Ph}$), 7.86 (d, ^3J = 9.2 Hz, 1 H, $H7_{Bis}$), 8.14 (d, ^3J = 7.8 Hz, 2 H, $H2_{Ph}$, $H6_{Ph}$), 8.42 (s, 1 H, $H4_{Bis}$), 12.95 (s, 1 H, COOH).

MS (CI): *m*/*z* (%) = 349 (100) [M + H$^+$].

Anal. Calcd for $C_{19}H_{16}N_4O_3$ (348.36): C, 65.51; H, 4.63; N, 16.08. Found: C, 65.30; H, 4.78; N, 16.00.

5-Isopropyl-1-(3-phenyl-2,1-benzisoxazol-5-yl)-1*H*-1,2,3-triazole-4-carboxylic Acid (11l)
White crystals; yield: 2.4 g (70%); mp 175–176 °C (dec.) (EtOH).

^{1}H NMR (DMSO-d_6): δ = 1.35 (d, ^3J = 7.2 Hz, 6 H, *i*-Pr), 3.30–3.35 (m, 1 H, *i*-Pr), 7.42 (d, ^3J = 9.2 Hz, 1 H, $H6_{Bis}$), 7.55–7.61 (m, 3 H, $H3_{Ph}$, $H4_{Ph}$, $H5_{Ph}$), 7.83 (d, ^3J = 9.2 Hz, 1 H, $H7_{Bis}$), 8.13 (d, ^3J = 7.8 Hz, 2 H, $H2_{Ph}$, $H6_{Ph}$), 8.39 (s, 1 H, $H4_{Bis}$), 12.95 (s, 1 H, COOH).

MS (CI): *m*/*z* (%) = 349 (100) [M + H$^+$].

Anal. Calcd for $C_{19}H_{16}N_4O_3$ (348.36): C, 65.51; H, 4.63; N, 16.08. Found: C, 65.44; H, 4.48; N, 16.21.

5-Butyl-1-(3-phenyl-2,1-benzisoxazol-5-yl)-1*H*-1,2,3-triazole-4-carboxylic Acid (11m)
White crystals; yield: 2.5 g (69%); mp 246–247 °C (dec.) (EtOH).

^{1}H NMR (DMSO-d_6): δ = 0.76 (t, ^3J = 7.2 Hz, 3 H, Me), 1.34 (m, 2 H, CH_2), 1.46 (m, 2 H, CH_2), 3.15 (t, ^3J = 8.0 Hz, 2 H, CH_2), 7.47–7.64 (m, 4 H, $H6_{Bis}$, $H3_{Ph}$, $H4_{Ph}$, $H5_{Ph}$), 7.83 (d, ^3J = 9.2 Hz, 1 H, $H7_{Bis}$), 8.14 (d, ^3J = 7.6 Hz, 2 H, $H2_{Ph}$, $H6_{Ph}$), 8.32 (s, 1 H, $H4_{Bis}$), 12.95 (s, 1 H, COOH).

MS: (CI) *m*/*z* (%) = 363 (100) [M + H$^+$].

Anal. Calcd for $C_{20}H_{18}N_4O_3$ (362.38): C, 66.29; H, 5.01; N, 15.46. Found: C, 66.33; H, 4.89; N, 15.34.

5-(Methoxymethyl)-1-(3-phenyl-2,1-benzisoxazol-5-yl)-1*H*-1,2,3-triazole-4-carboxylic Acid (11n)
White crystals; yield: 1.96 g (56%); mp 201–202 °C (dec.) (EtOH).

^{1}H NMR (DMSO-d_6): δ = 3.34 (s, 3 H, Me), 4.85 (s, 2 H, CH_2), 7.55–7.65 (m, 3 H, $H3_{Ph}$, $H4_{Ph}$, $H5_{Ph}$), 7.68 (d, ^3J = 9.6 Hz, 1 H, $H6_{Bis}$), 7.85 (d, ^3J = 9.6 Hz, 1 H, $H7_{Bis}$), 8.11 (d, ^3J = 7.2 Hz, 2 H, $H2_{Ph}$, $H6_{Ph}$), 8.47 (s, 1 H, $H4_{Bis}$), 13.35 (s, 1 H, COOH).

MS (CI): *m*/*z* (%) = 351 (100) [M + H$^+$].

Anal. Calcd for $C_{18}H_{14}N_4O_4$ (350.33): C, 61.71; H, 4.03; N, 15.99. Found: C, 61.51; H, 4.17; N, 15.81.

5-Methyl-1-(6-methyl-3-phenyl-2,1-benzisoxazol-5-yl)-1*H*-1,2,3-triazole-4-carboxylic Acid (11o)
White crystals; yield: 2.24 g (67%); mp 209–210 °C (dec.) (EtOH);

^{1}H NMR (DMSO-d_6): δ = 2.04 (s, 3 H, Me), 2.46 (s, 3 H, Me), 7.54–7.61 (m, 3 H, $H3_{Ph}$, $H4_{Ph}$, $H5_{Ph}$), 7.68 (s, 1 H, $H7_{Bis}$), 8.14 (d, ^3J = 8.0 Hz, 2 H, $H2_{Ph}$, $H6_{Ph}$), 8.41 (s, 1 H, $H4_{Bis}$), 12.99 (s, 1 H, COOH).

MS (CI): *m*/*z* (%) = 335 (100) [M + H$^+$].

Anal. Calcd for $C_{18}H_{14}N_4O_3$ (334.33): C, 64.66; H, 4.22; N, 16.76. Found: C, 64.49; H, 4.41; N, 16.52.

1-(6-Methoxy-3-phenyl-2,1-benzisoxazol-5-yl)-5-methyl-1*H*-1,2,3-triazole-4-carboxylic Acid (11p)
White crystals; yield: 2.13 g (61%); mp 205–206 °C (dec.) (EtOH).

^{1}H NMR (DMSO-d_6): δ = 2.42 (s, 3 H, Me), 3.91 (s, 3 H, OMe), 7.17 (s, 1 H, $H7_{Bis}$), 7.52–7.62 (m, 3 H, $H3_{Ph}$, $H4_{Ph}$, $H5_{Ph}$), 8.11 (d, ^3J = 8.0 Hz, 2 H, $H2_{Ph}$, $H6_{Ph}$), 8.38 (s, 1 H, $H4_{Bis}$), 12.97 (s, 1 H, COOH).

MS (CI): *m*/*z* (%) = 351 (100) [M + H$^+$].

Anal. Calcd for $C_{18}H_{14}N_4O_4$ (350.33): C, 61.71; H, 4.03; N, 15.99. Found: C, 61.59; H, 3.92; N, 15.82.

3-Aryl-2,1-benzisoxazoles 12a–e, 14a,b; General Procedure
To the soln of KOH (9.8 g, 0.17 mol) in MeOH (25 mL) was added with stirring arylacetonitrile **10** (11 mmol) and a soln of nitroarene **6**, **7** (10 mmol) in MeOH (15 mL). The mixture was stirred at r.t. for 1 h. The precipitate was isolated by filtration, washed with H_2O, and dried. Compounds **12a–e** and **14a**,**b** were crystallized (EtOH–DMF).

5-(5-Methyl-1*H*-tetrazol-1-yl)-3-phenyl-2,1-benzisoxazole (12a)
White crystals; yield: 2.41 g (87%); mp 154–155 °C (EtOH).

^{1}H NMR (DMSO-d_6): δ = 2.64 (s, 3 H, Me), 7.56–7.64 (m, 4 H, $H6_{Bis}$, $H3_{Ph}$, $H4_{Ph}$, $H5_{Ph}$), 7.86 (d, ^3J = 9.6 Hz, 1 H, $H7_{Bis}$), 8.14 (d, ^3J = 7.2 Hz, 2 H, $H2_{Ph}$, $H6_{Ph}$), 8.51 (s, 1 H, $H4_{Bis}$).

MS (CI): *m*/*z* (%) = 278 (100) [M + H$^+$].

Anal. Calcd for $C_{15}H_{11}N_5O$ (277.28): C, 64.97; H, 4.00; N, 25.26. Found: C, 64.81; H, 4.14; N, 25.03.

3-(4-Methylphenyl)-5-(5-methyl-1*H*-tetrazol-1-yl)-2,1-benzisoxazole (12b)
White crystals; yield: 2.44 g (84%); mp 171–172 °C (EtOH).

^{1}H NMR (DMSO-d_6): δ = 2.46 (s, 3 H, CH_3), 2.63 (s, 3 H, CH_3), 7.41 (d, ^3J = 8.0 Hz, 2 H, $H3_{Ar}$, $H5_{Ar}$), 7.57 (d, ^3J = 9.2 Hz, 1 H, $H6_{Bis}$), 7.83 (d, ^3J = 9.2 Hz, 1 H, $H7_{Bis}$), 8.03 (d, ^3J = 8.0 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.49 (s, 1 H, $H4_{Bis}$).

MS (CI): *m*/*z* (%) = 292 (100) [M + H$^+$].

Anal. Calcd for $C_{16}H_{13}N_5O$ (291.31): C, 65.97; H, 4.50; N, 24.04. Found: C, 65.64; H, 4.36; N, 23.92.

3-(4-Chlorophenyl)-5-(5-methyl-1*H*-tetrazol-1-yl)-2,1-benzisoxazole (12c)
White crystals; yield: 2.84 g (91%); mp 163–164 °C (EtOH).

^{1}H NMR (DMSO-d_6): δ = 2.65 (s, 3 H, CH_3), 7.57–7.64 (m, 3 H, $H6_{Bis}$, $H3_{Ar}$, $H5_{Ar}$), 7.87 (d, ^3J = 9.2 Hz, 1 H, $H7_{Bis}$), 8.18 (d, ^3J = 8.4 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.53 (s, 1 H, $H4_{Bis}$).

MS (CI): *m*/*z* (%) = 312 (100) [M + H$^+$].

Anal. Calcd for $C_{15}H_{10}ClN_5O$ (311.72): C, 57.79; H, 3.23; N, 22.47. Found: C, 57.99; H, 3.07; N, 22.58.

5-[5-(3-Chloropropyl)-1*H*-tetrazol-1-yl]-3-phenyl-2,1-benzisoxazole (12d)
White crystals; yield: 2.51 g (74%); mp 163–164 °C (EtOH).

^{1}H NMR (DMSO-d_6): δ = 2.26 (m, 2 H, CH_2), 3.10 (t, ^3J = 7.2 Hz, 2 H, CH_2), 3.70 (t, ^3J = 7.2 Hz, 2 H, CH_2), 7.54–7.64 (m, 4 H, $H6_{Bis}$, $H3_{Ar}$, $H4_{Ar}$, $H5_{Ar}$), 7.86 (d, ^3J = 9.6 Hz, 1 H, $H7_{Bis}$), 8.15 (d, ^3J = 8.4 Hz, 2 H, $H2_{Ar}$, $H6_{Ar}$), 8.52 (s, 1 H, $H4_{Bis}$).

MS (CI): *m*/*z* (%) = 340 (100) [M + H$^+$].

Anal. Calcd for $C_{10}H_{14}ClN_5O$ (339.79): C, 60.09; H, 4.15; N, 20.61. Found: C, 59.89; H, 4.01; N, 20.70.

6-Methoxy-5-(5-methyl-1*H*-tetrazol-1-yl)-3-phenyl-2,1-benzisoxazole (12e)
White crystals; yield: 2.0 g (65%); mp 247–248 °C (EtOH).

^{1}H NMR (DMSO-d_6): δ = 2.46 (s, 3 H, Me), 3.89 (s, 3 H, OMe), 7.29 (s, 1 H, $H7_{Bis}$), 7.59–7.67 (m, 3 H, $H3_{Ph}$, $H4_{Ph}$, $H5_{Ph}$), 8.15 (d, ^3J = 8.0 Hz, 2 H, $H2_{Ph}$, $H6_{Ph}$), 8.62 (s, 1 H, $H4_{Bis}$).

MS (CI): *m*/*z* (%) = 308 (100) [M + H$^+$].

Anal. Calcd for $C_{16}H_{13}N_5O_2$ (307.31): C, 62.53; H, 4.26; N, 22.79. Found: C, 62.20; H, 4.04; N, 22.91.

2-(3-Phenyl-2,1-benzisoxazol-5-yl)-2*H*-tetrazole-5-carboxylic Acid (14a)
White crystals; yield: 2.7 g (88%); mp 209–210 °C (dec.) (EtOH).

^{1}H NMR (DMSO-d_6): δ = 7.59–7.71 (m, 3 H, $H3_{Ph}$, $H4_{Ph}$, $H5_{Ph}$), 7.96 (d, ^3J = 9.6 Hz, 1 H, $H6_{Bis}$), 8.15 (d, ^3J = 7.2 Hz, 2 H, $H2_{Ph}$, $H6_{Ph}$), 8.20 (d, ^3J = 9.6 Hz, 1 H, $H7_{Bis}$), 8.75 (s, 1 H, $H4_{Bis}$).

MS (CI): *m*/*z* (%) = 308 (100) [M + H$^+$].

Anal. Calcd for $C_{15}H_9N_5O_3$ (307.26): C, 58.63; H, 2.95; N, 22.79. Found: C, 58.86; H, 2.75; N, 22.83.

2-[3-(4-Chlorophenyl)-2,1-benzisoxazol-5-yl]-2*H*-tetrazole-5-carboxylic Acid (14b)

White crystals; yield: 3.01 g (90%); mp 220–221 °C (dec.) (EtOH).

^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.76 (d, ^3J = 8.0 Hz, 2 H, $H3_{Ph}$, $H5_{Ph}$), 8.02 (d, ^3J = 9.6 Hz, 1 H, $H6_{Bis}$), 8.20–8.23 (m, 3 H, $H2_{Ph}$, $H6_{Ph}$, $H7_{Bis}$), 8.64 (s, 1 H, $H4_{Bis}$), 13.28 (s, 1 H, COOH).

MS (CI): *m*/*z* (%) = 342 (100) [M + H$^+$].

Anal. Calcd for $C_{15}H_8ClN_5O_3$ (341.71): C, 52.72; H, 2.36; N, 20.50. Found: C, 52.44; H, 2.18; N, 20.41.

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