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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/jo402543s • Publication Date (Web): 13 Jan 2014

Just Accepted

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Potassium trinitromethanide as 1,1-ambiphilic synthon equivalent: access to 2-nitroarenofurans

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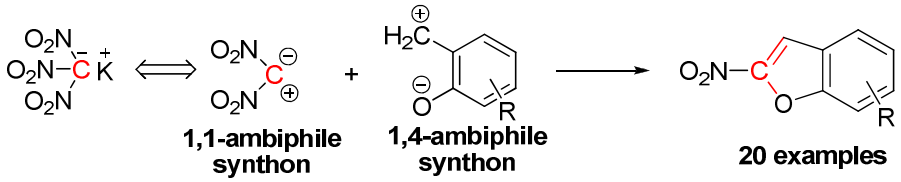


Abstract: The first example of using of potassium trinitromethanide as a 1,1-ambiphilic synthon equivalent for the construction of a benzofuran moiety mediated by triethylamine (TEA) has been developed. The method tolerates a variety of functional groups on the starting quaternary ammonium salt and has been successfully extended to polysubstituted benzofurans. Formation of a *o*-quinone methide intermediate is postulated as a key to the mechanism of this cascade process.

Keywords: *o*-Quinone methides, 2-nitrobenzofurans, potassium trinitromethanide, C1 building block, 1,1-ambiphile synthon.

Introduction

Ambiphilic synthons, which contain both electrophilic and nucleophilic centers in the same molecule, are widely used in organic synthesis as useful building blocks.[1] The development of new synthetic methods using ambiphiles have a great potential in elaboration of new high step economy reactions.[2] Moreover, 1,1-ambiphiles with reaction centers on the same carbon atom are promising for construction of cyclic molecules.[3] However, this reaction type remains undeveloped.

Use of polynitromethane derivatives in the synthesis of heterocycles are generally limited to

isoxazole and isoxazolidine units.[4] In these transformations polynitromethanes react as 1,3-dipoles and C, N, O atoms are incorporated into the structure of heterocycles. Potassium trinitromethanide (potassium nitroformate) is often used to introduce trinitromethyl group in organic molecules. The reaction of potassium trinitromethanide as a 1,1-ambiphilic reagent, wherein only the carbon atom was included into the formed heterocyclic structure, is unprecedented.

o-Quinone methides (*o*-QMs) are highly reactive and useful species which have been implicated as intermediates in the synthesis of natural products, usually as heterodynes, to form chromane systems.[5] They also react with nucleophiles as 1,4-Michael acceptors.[6] Reactions of *o*-QM precursors are exceptionally facile, compared with traditional Michael acceptors, because aromatization energy provides additional product and transition state stabilization in the case of the *o*-QM fragment. In addition, initial products of Michael-type reaction with *o*-QM may undergo further intramolecular cyclization with phenolic hydroxyl groups to provide a pathway to oxygen-containing heterocycles.[7] However, alike cascade protocols are rare and require further study.

In the process of an overall synthetic program aimed at the development of new cascade transformations utilizing *o*-QM[7b] we put our efforts on the study of reaction of potassium trinitromethanide with *o*-QM precursors. We have found that this reaction affords 2-nitroarenofurans, which has drawn extensive attention because of their varied biological activities. For example, many of these compounds exhibit antibacterial,[8] antiparasitic,[9] radiosensitizing,[10] mutagenic properties[11] and can be used as regulators of the nuclear receptor HNF4α.[12] Besides, 2-nitrobenzofurans are useful intermediates for the preparation of 2-halogenobenzofurans,[13] dibenzofurans[14] and benzofuro[2,3-*c*]pyrroles.[15]

A number of methods have been reported for the syntheses of 2-nitrobenzofurans. These compounds are generally prepared by the condensation between *o*-hydroxybenzaldehydes and bromonitromethane.[12,16] Although this reaction has already been performed under miscellaneous

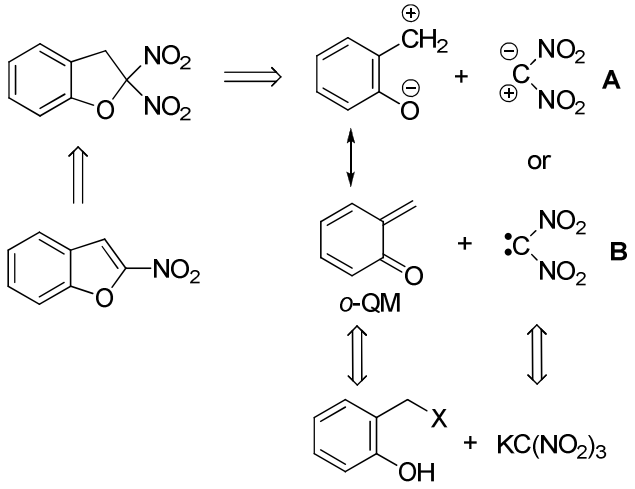
conditions with a large variety of aldehydes, its applicability is not completely versatile and leads to rather unsatisfactory yields in certain cases. The direct nitration of benzofurans in the 2-position usually leads to low yields and unwanted nitration products.[17]

3-Alkyl-2-nitrobenzofurans are also obtained by replacement of the acyl group in 2-acyl-3-alkylbenzofurans[18] and by treating 3-alkylbenzofurans successively with *t*-BuLi, then trimethyltin chloride and finally tetranitromethane in DMSO.[19] 2-Nitrobenzofuran has been prepared by *ipso*-nitration of 2-benzofuranboronic acid using bismuth (III) nitrate[20] and by nitration of benzofuran using sodium nitrite in the presence of cerium (IV) ammonium nitrate.[21] Recently, 3-alkyl-2-nitrobenzofurans were synthesized from 2-(2-nitroethyl)phenols via a hypervalent iodine-induced oxidative cyclization.[22]

Results and discussion

Potassium trinitromethanide reacts with *o*-QMs by carbon as a soft nuchleophilic center and acts as synthetic equivalent of a 1,1-dipole one-carbon synthon **A** or dinitrocarbene **B** (Scheme 1).

Scheme 1 Retrosynthetic approach to benzofuran moiety

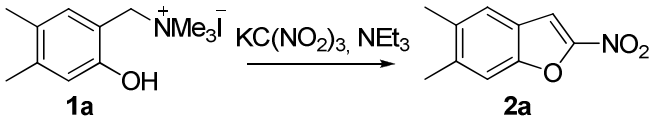


We first investigated the reaction between the *o*-QM precursor **1a** with potassium trinitromethanide under various conditions. Potassium trinitromethanide was obtained from the reaction of tetranitromethane with potassium hydroxide and ethanol in water solution.[23]

$$C(NO_2)_4 + KOH + C_2H_5OH \rightarrow KC(NO_2)_3 + C_2H_5ONO_2 + H_2O$$

When the reaction with potassium trinitromethanide was carried out in ethanol at room temperature in the absence of any base, no desired product formation was observed (Table 1, entry 1). The use of catalytic amount of TEA (0.1 equiv) at elevated temperature furnished only a trace amount (<5%) of the expected 2-nitrobenzofuran **2a** in 40 min (entry 2). Attempts to improve the yield by increasing the reaction time were unsuccessful. In order to achieve a high yield, we did further investigation on other parameters, such as solvent, temperature and ratio of components. If the ratio of **1a**:$KC(NO_2)_3$:TEA was adjusted from 1:1:1 to 1:3:3, a good yield (79%) was obtained (entry 8). A lower base loading caused a loss of reaction yield. No significant improvement was gained in the yield of **2a** when we employed more than 3 equiv of potassium trinitromethanide. The reaction was also performed at various temperatures and the best results were obtained at approximately 80 ºC. The reaction was not carried at higher temperatures since the onset temperature of the decomposition of potassium trinitromethanide was found to be 80 ºC.[23a] The influence of solvents was also examined. The results show that the same reaction can also be performed in aqueous THF, ethanol, or acetonitrile, which afforded the highest yield.

Table 1 The results of the optimization[a]



1a **2a**

Entry	Solvent	T, ºC	Ratio of **1a**:$KC(NO_2)_3$:TEA	Yield[a] (%)
1	EtOH	25	1:1:0	–
2	EtOH	78	1:1:0.1	<5
3	CH_3CN	25	1:1:1	20
4	CH_3CN	25	1:3:3	25
5	CH_3CN	81	1:1:1	55

6	CH_3CN	81	1:2:2	64
7	CH_3CN	81	1:2:3	63
8	CH_3CN	81	1:3:3	79
9	EtOH	78	1:3:3	74
10	THF–H_2O, 3:1	65	1:3:3	69
11	DMF	80	1:3:3	31
12	H_2O	80	1:3:3	26

[a] Reaction conditions: compound **1a** (1 mmol), $KC(NO_2)_3$, TEA, 20 mL of solvent, 40 min.

In order to evaluate the effect of the base on the reaction, a range of organic bases were examined (Table 2). Triethylamine proved to be a more efficient base. Thus, in optimal conditions, 3 equiv of the potassium trinitromethanide and 3 equiv of TEA in acetonitrile at 81 ºC provided the desired product in 79% yield in 40 min.

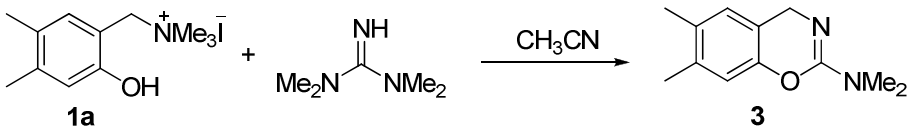
Table 2 Optimization of bases[a]

Entry	Base	pKa	Yield[b] (%)
1	TEA	10.75	79
2	DIPEA	11.4	54
3	NMM	7.38	54
4	N-methylimidazole	7.4	17
5	DMAP	9.2	14
6	DABCO	8.82	14
7	DBU	12.0	10
8	TMG	13.6	–[c]

[a] 1 equiv of **1a**, 3 equiv of potassium trinitromethanide, 3 equiv of base in CH_3CN under reflux are used. In all cases, the reaction times were 40 min.
[b] Isolated yields after silica gel chromatography.

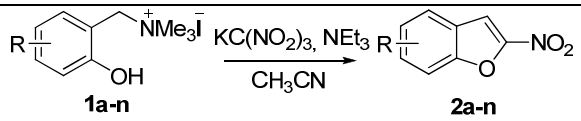
[c] Only 1,3-benzoxazine **3** was isolated.

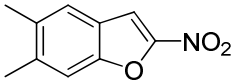
Scheme 2



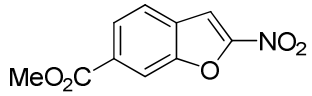
It is interesting to note that in the case of 1,1,3,3-tetramethylguanidine (TMG) only 2-dimethylamino-4*H*-1,3-benzoxazine **3** was isolated in 54% yield (Table 2, entry 8, Scheme 2).[24] Under the optimized reaction conditions, the scope and generality of this cascade process were then explored. A variety of electronically divergent *o*-benzoquinone methide precursors were examined, and the results are summarized in Table 3. The method turned out to be tolerant toward a broad range of functional groups. The reaction proceeded without any problems for a wide range of substrates bearing electron-donating (CH_3O, Alk) or electron-withdrawing (NO_2, Hal, CO_2CH_3, CHO) substituents on the aryl ring, providing 2-nitrobenzofurans in moderate to good yields. The sterically hindered adamantyl-substituted nitrobenzofuran **1f** was obtained in good yield, indicating that steric hindrance had no obvious influence on the efficiency of our method.

Table 3. Synthesis of 2-nitrobenzofurans **2a-n**.[a,b,c]

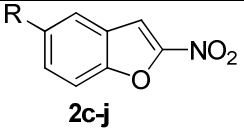




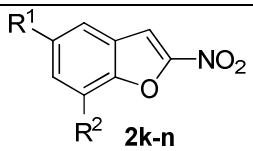
2a, 79%



2b, 51%



2c, R = OMe	59%	**2g**, R = Cl	57%
2d, R = t-Bu	36%	**2h**, R = CO_2Me	62%
2e, R = 1-Adamantyl	61%	**2i**, R = COMe	68%
2f, R = Bn	68%	**2j**, R = NO_2	50%



2k, R^1 = t-Bu, R^2 = NO_2	39%
2l, R^1 = Me, R^2 = 1-Adamantyl	73%
2m, R^1 = CHO, R^2 = OMe	59%
2n, R^1 = CO_2Me, R^2 = OMe	60%

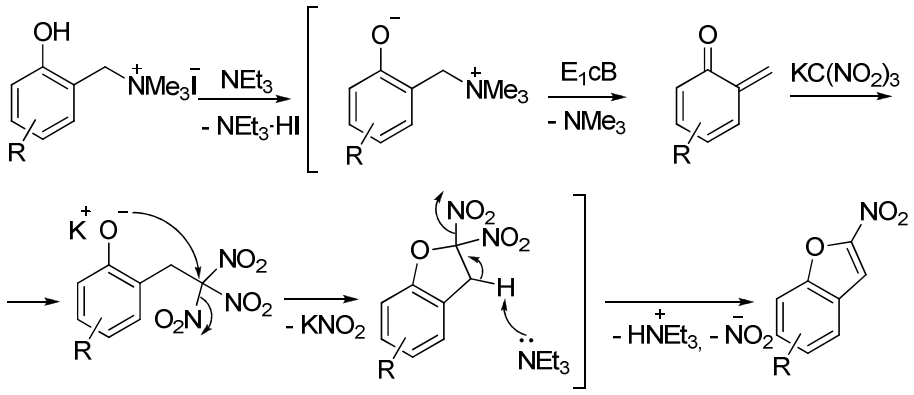
[a] Optimal conditions: 1 equiv of **1**, 3 equiv of potassium trinitromethanide, 3 equiv of TEA in CH_3CN under reflux.

[b] Isolated yields after silica gel chromatography.

[c] All reactions, except the first one, were carried out without additional optimization.

Scheme 3 outlines a proposed mechanism of the formation of 2-nitrobenzofurans. The mechanism involves initial elimination of trimethylamine from anion of quaternary ammonium salt by an E_1cB mechanism to afford an electrophilic *o*-QM. Subsequent a Michael-type addition of trinitromethanide anion, intramolecular nucleophilic substitution and elimination of nitro groups affords the 2-nitrobenzofuran. TEA promotes generation of *o*-QMs and further aromatization of intermediate dihydrobenzofurans. It also keeps the media basic which is necessary for avoidance of formation of side waxy products.

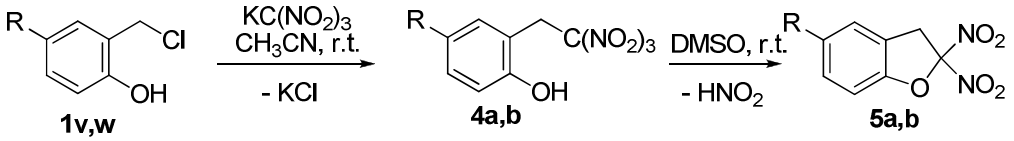
Scheme 3 Proposed mechanism for the synthesis of **2**



In support of the proposed mechanistic pathway, in some cases intermediate trinitroethyl derivatives and 2,2-dinitro-2,3-dihydrobenzofurans can be isolated. From 2-chloromethylphenols **1v,w** and potassium trinitromethanide the phenols **4a,b** were prepared in acetonitrile at room temperature. In DMSO solution the trinitroethyl derivatives **4a,b** undergo cyclization and form 2,2-dinitro-2,3-dihydrobenzofurans **5a,b** (Scheme 4). We have also found different reaction rates of these transformations depending on nature of the substituent in the aromatic core. Thuswise, full conversion of acetyl-substituted phenol **4b** to dihydrobenzofuran **5b** was accomplished in 5 days at room temperature. On the other hand, nitrophenol **4a** converted to **5a** in 5 hours (according to NMR monitoring). It should also be noted that compounds **5a,b** in DMSO or

acetonitrile solution slowly transform in 2-nitrobenzofurans **2j** and **2i**, respectively. At the same time, in non-polar solvents compounds **4a,b** and **5a,b** are more stable.

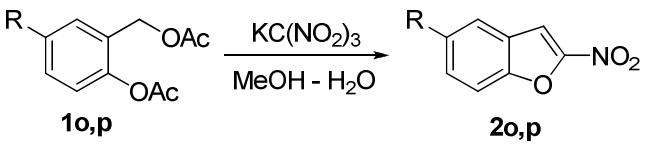
Scheme 4 Synthesis of dihydrobenzofurans **5a,b**



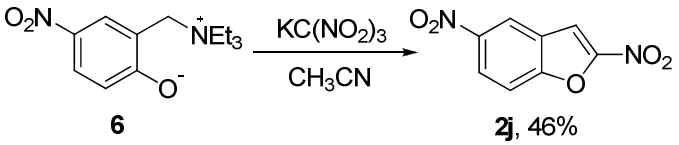
R = NO_2 (**1v,4a,5a**), COMe (**1w,4b,5b**)

Attempts to extend this reaction to the Mannich bases of simple phenols failed to furnish the expected products. The reason for failure may be due to the relatively greater thermal stability of Mannich bases compared to that of the quaternary ammonium salts. However, instead of quaternary salts 2-acetoxybenzyl acetates **1o,p** as well as ammoniophenolate **6** can be used (Scheme 5).

Scheme 5 Extention of developed methodology to another *o*-QM precursors

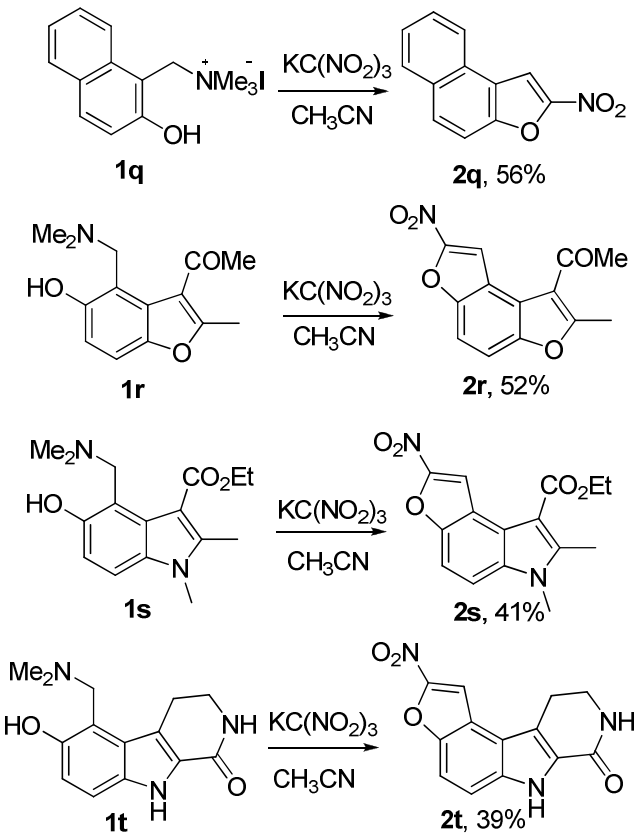


R = H (**1o, 2o**, 46%), Br (**1p, 2p**, 51%)



In order to broaden the scope of the present method, we attempted the present protocol for the naphthalene **1q** and heterocyclic **1r,s,t,** precursors of *o*-QMs. From Mannich bases **1r,s,t** heterocyclic systems benzo[1,2-*b*:4,3-*b*']difuran **2r**, furo[3,2-*e*]indole **2s** and furo[3,2-*e*]pyrido[3,4-*b*]indole **2t** were prepared in moderate yields (Scheme 6).

Scheme 6 Synthesis of condensed nitrobenzofurans



In summary, we have developed a simple and efficient method for the synthesis of 2-nitroarenofurans from quaternary ammonium salts, some phenolic Mannich bases or 2-acetoxybenzyl acetates and potassium trinitromethanide in moderate to good yields. This is the first example of using of potassium trinitromethanide as a 1,1-ambiphilic reagent. The tolerance of various substituents on the aromatic rings makes this protocol highly practical for diversity-oriented synthesis.

Experimental section

FTIR-spectra were taken in KBr pellets. ^{1}H, ^{13}C, and DEPT NMR spectra were recorded using a 400 MHz NMR spectrometer in CD_3CN, $CDCl_3$ or DMSO-d_6 solutions with TMS as internal standard. Chemical shifts and coupling constants were recorded in units of ppm and Hz, respectively. The melting points were uncorrected. Elemental analysis was carried out on an automatic CHNS-analyzer. Mass spectra were recorded with 70 eV electron ionization energy. Thin-layer chromatography was carried out on aluminium-backed silica gel plates with

visualisation of components by UV light (254 nm) or exposure to I_2. Known *o*-QM precursors were prepared according to the literature procedures.[25-29]

[2-Hydroxy-3-nitro-5-*tert*-butylbenzyl]trimethylammonium iodide (1k).

Dimethylamine (6 mL of 33% aqueous solution, 0.04 mol) and formaldehyde (3 mL of 37% aqueous solution, 0.04 mol) were added to a solution of 4-*tert*-butyl-2-nitrophenol (7 g, 0.036 mol) in ethanol (50 mL). The reaction mixture was stored at room temperature for 2 days. The solvent was evaporated *in vacuo*, the residue was dissolved in acetonitrile (20 mL) and treated with CH_3I (7 mL, 16 g, 0.11 mol). The resulting solution was stirred at room temperature for 2 days, the solvent was evaporated *in vacuo*, the residue was recrystallized from mixture ethanol–diethyl ether. Yield 62%; 8.77 g; orange crystals; mp 169–171 ºC (decomp.); ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.01 and 7.99 (d, ^4J = 2.3 Hz, 2H), 4.63 (s, 2H), 3.08 (s, 9H), 1.27 (s, 9H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 151.2 (C), 142.6 (C), 140.2 (CH), 136.7 (C), 124.0 (CH), 120.2 (C), 62.7 (CH_2), 55.5 (C), 52.9 ($3CH_3$), 34.7 (C), 31.2 ($3CH_3$); IR ν_{max} (KBr): 648, 887, 980, 1161, 1265, 1312, 1346, 1377, 1416, 1477, 1535 (NO_2), 1597, 1620, 2870, 2951, 3001, 3400–3100 (OH) cm^{-1}. Anal. Calcd (%) for $C_{14}H_{23}IN_2O_3$: C, 42.65; H, 5.88; N, 7.11. Found: C (%), 42.72; H, 5.90; N, 7.02.

Potassium trinitromethanide

Caution: Although we have encountered no difficulties in working with potassium trinitromethanide and tetranitromethane, full safety precautions (goggles, shields, fume hoods) should be taken whenever it possible due to explosive nature and toxicity of these compounds.

Potassium hydroxide (18.6 g, 0.332 mol) was dissolved in 22 mL of water and 84 mL of ethanol and stirred at ice bath temperature. To this solution, tetranitromethane (28 mL, 45.4 g, 0.232 mol) was added portion-wise over a period of ten minutes. The temperature of the reaction mixture was kept below 20 ºC. The ice bath was removed and the reaction mixture was allowed to warm to room temperature (20–25 ºC) and stirred for 20 min. After completion of the reaction,

the mixture was cooled to 0 ºC and the solid was filtered off and washed with 20 mL of ice-cold EtOH. Yield 91 %; 39.9 g; bright yellow crystals; mp 83 ºC (decomp.).

General Experimental Procedure for the Synthesis of 2-nitroarenofurans

Potassium trinitromethanide (1.14 g, 6 mmol) was added in three equal portions over a period of 20 minutes to a stirred solution of *o*-QM precursor (2 mmol) and triethylamine (0.84 mL, 6 mmol) in acetonitrile (20 mL) at reflux temperature under an Ar atmosphere. Afterwards, the mixture was refluxed for another 20 minutes and poured into 50 mL of saturated water solution of sodium chloride to yield a solid product, which was filtered, washed with water and dried. The crude product was purified by column chromatography over silica gel using dichloromethane as eluent, followed by recrystallization from ethanol.

5,6-Dimethyl-2-nitrobenzofuran (2a): yield 79%; 302 mg; yellow solid; mp 135–136 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.58 (s, 1H), 7.48 (s, 1H), 7.37 (s, 1H), 2.41 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.7 (C), 152.7 (C), 140.9 (C), 134.9 (C), 123.8 (C), 123.6 (CH), 112.8 (CH), 107.5 (CH), 21.2 (CH_3), 20.1 (CH_3); IR, ν_{max} (KBr): 729, 802, 864, 953, 1080, 1198, 1267, 1323, 1364 (NO_2), 1452, 1503 (NO_2), 1555, 1620, 2924, 3140 (CH Fu) cm^{-1}; MS (EI) m/z: 191 $[M]^+$ (51), 161 $[M - NO]^+$ (93), 133 $[M - CNO_2]^+$ (36), 117 (41), 115 (74), 105 $[C_8H_9]^+$ (22), 91 $[C_7H_7]^+$ (44), 46 $[NO_2]^+$ (100). Anal. Calcd (%) for $C_{10}H_9NO_3$: C, 62.82; H, 4.74; N, 7.33. Found (%): C, 62.90; H, 4.72; N, 7.27.

Methyl 2-nitrobenzofuran-6-carboxylate (2b): yield 51%; 225 mg; light yellow solid; mp 144–145 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.30 (d, ^{4}J = 1.3 Hz, 1H), 8.10 (dd, ^{3}J = 8.4, ^{4}J = 1.3 Hz, 1H), 7.83 (d, ^{3}J = 8.4 Hz, 1H), 7.69 (d, ^{5}J = 0.8 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.0 (C=O), 154.6 (C), 152.4 (C), 131.7 (C), 129.7 (C), 126.3 (CH), 124.0 (CH), 114.5 (CH), 106.7 (CH), 52.8 (CH_3); IR, ν_{max} (KBr): 729, 766, 814, 974, 1072, 1225, 1260, 1281, 1312, 1341 (NO_2), 1373, 1422, 1435, 1526 (NO_2), 1566, 1714 (C=O), 2854, 2924, 2959, 3138 (CH Fu) cm^{-1}. Anal. Calcd (%) for $C_{10}H_7NO_5$: C, 54.31; H, 3.19; N, 6.33. Found (%): C, 54.40; H, 3.24; N, 6.26.

5-Methoxy-2-nitrobenzofuran (2c): yield 59%; 228 mg; yellow solid; mp 127–128 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 (s, 1H), 7.50 (d, ^{3}J = 8.8 Hz, 1H), 7.19 (dd, ^{3}J = 8.8, ^{4}J = 1.8 Hz, 1H), 7.11 (d, ^{4}J = 1.8 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.6 (C), 153.5 (C), 148.5 (C), 126.5 (C), 120.6 (CH), 113.7 (CH), 107.4 (CH), 104.3 (CH), 56.0 (CH_3); IR, ν_{max} (KBr): 748, 818, 878, 1026, 1169, 1202, 1265, 1327 (NO_2), 1369, 1510 (NO_2), 1562, 2924, 3102 (CH Fu), 3126 cm^{-1}; MS (EI) m/z: 193 $[M]^+$ (84), 163 $[M - NO]^+$ (100), 135 $[M - CNO_2]^+$ (27), 119 (58), 107 $[C_7H_7O]^+$ (7). Anal. Calcd (%) for $C_9H_7NO_4$: C, 55.96; H, 3.65; N, 7.25. Found (%): C, 56.06; H, 3.60; N, 7.31.

5-*tert*-Butyl-2-nitrobenzofuran (2d): yield 36%; 158 mg; light yellow solid; mp 80–81 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.71 (d, ^{4}J = 2.1 Hz, 1H), 7.66 (dd, ^{3}J = 8.9, ^{4}J = 2.1 Hz, 1H), 7.63 (d, ^{5}J = 0.7 Hz, 1H), 7.54 (d, ^{3}J = 8.9 Hz, 1H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.3 (C), 151.8 (C), 148.8 (C), 128.6 (CH), 125.7 (C), 119.9 (CH), 112.2 (CH), 107.7 (CH), 35.1 (C), 31.6 ($3CH_3$); IR, ν_{max} (KBr): 731, 816, 841, 955, 1101, 1126, 1192, 1236, 1267, 1304, 1319, 1358 (NO_2), 1466, 1520 (NO_2), 1562, 2870 (CH_3), 2961, 3138 (CH Fu) cm^{-1}. Anal. Calcd (%) for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found (%): C, 65.82; H, 6.04; N, 6.36.

5-(1-Adamantyl)-2-nitrobenzofuran (2e): yield 61%; 362 mg; light yellow solid; mp 165–167 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.64–7.67 (m, 3H), 7.53 (d, ^{3}J = 8.7 Hz, 1H), 2.13 (br s, 3H), 1.92–1.97 (m, 6H), 1.75–1.84 (m, 6H); ^{13}C NMR (400 MHz, DMSO-d_6) δ: 153.3 (C), 151.9 (C), 149.1 (C), 128.2 (CH), 125.7 (C), 119.8 (CH), 112.2 (CH), 107.8 (CH), 43.5 ($3CH_2$), 36.7 ($3CH_2$), 36.6 (C), 29.0 (3CH); IR, ν_{max} (KBr): 729, 800, 831, 849, 876, 955, 1092, 1242, 1317, 1331, 1344, 1362 (NO_2), 1371, 1470, 1524 (NO_2), 1568, 2851, 2901, 3142 (CH Fu) cm^{-1}. Anal. Calcd (%) for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found (%): C, 72.80; H, 6.39; N, 4.66.

5-Benzyl-2-nitrobenzofuran (2f): yield 68%; 344 mg; yellow solid; mp 130–131 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (d, ^{5}J = 0.9 Hz, 1H), 7.51–7.53 (m, 2H), 7.43 (dd, ^{3}J = 8.7, ^{4}J = 1.8 Hz, 1H), 7.29–7.33 (m, 2H), 7.21–7.25 (m, 1H), 7.18–7.20 (m, 2H), 4.10 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.3 (C), 152.2 (C), 140.4 (C), 138.8 (C), 131.5 (CH), 129.0 (CH), 128.8

(CH), 126.6 (CH), 126.1 (C), 123.6 (CH), 112.7 (CH), 107.3 (CH), 41.7 (CH_2); IR, ν_{max} (KBr): 700, 737, 835, 957, 1099, 1250, 1335 (NO_2), 1373, 1433, 1468, 1506 (NO_2), 1560, 3136 (CH Fu) cm^{-1}. Anal. Calcd (%) for $C_{15}H_{11}NO_3$: C, 71.14; H, 4.38; N, 5.53. Found (%): C, 71.20; H, 4.31; N, 5.61.

5-Chloro-2-nitrobenzofuran (2g): yield 57%; 226 mg; light yellow solid; mp 118–120 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.75 (br s, 1H), 7.61 (s, 1H), 7.55–7.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.0 (C), 151.6 (C), 131.3 (C), 130.5 (CH), 127.1 (C), 123.4 (CH), 114.1 (CH), 106.5 (CH); IR, ν_{max} (KBr): 692, 729, 814, 835, 880, 957, 1101, 1190, 1244, 1314, 1360 (NO_2), 1435, 1449, 1506, 1524 (NO_2), 1562, 3136 (CH Fu) cm^{-1}; MS (EI) m/z: 197 $[M]^+$ (35), 167 $[M - NO]^+$ (51), 139 $[M - CNO_2]^+$ (30), 123 (57), 111 $[C_6H_4Cl]^+$ (22), 46 $[NO_2]^+$ (100). Anal. Calcd (%) for $C_8H_4ClNO_3$: C, 48.63; H, 2.04; N, 7.09. Found (%): C, 48.66; H, 1.97; N, 7.15.

Methyl 2-nitro-1-benzofuran-5-carboxylate (2h): yield 62%; 274 mg; light yellow solid; mp 145–147 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.51 (d, ^4J = 1.6 Hz, 1H), 8.28 (dd, ^3J = 8.7 Hz, ^4J = 1.6 Hz, 1H), 7.72 (s, 1H), 7.67 (d, ^3J = 8.7 Hz, 1H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.1 (C=O), 155.5 (C), 153.9 (C), 131.2 (CH), 127.9 (C), 126.6 (CH), 125.9 (C), 112.9 (CH), 107.4 (CH), 52.7 (CH_3); IR, ν_{max} (KBr): 746, 770, 839, 912, 1101, 1128, 1194, 1234, 1273, 1298, 1335 (NO_2), 1366, 1429, 1439, 1470, 1524 (NO_2), 1566, 1618, 1715 (C=O), 3109 (CH Fu), 3142 cm^{-1}. Anal. Calcd (%) for $C_{10}H_7NO_5$: C, 54.31; H, 3.19; N, 6.33. Found (%): C, 54.26; H, 3.24; N, 6.40.

5-Acetyl-2-nitrobenzofuran (2i): yield 68%; 279 mg; light yellow solid; mp 161–163 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.40 (d, ^4J = 1.6 Hz, 1H), 8.22 (dd, ^3J = 8.7, ^4J = 1.6 Hz, 1H), 7.74 (s, 1H), 7.69 (d, ^3J = 8.7 Hz, 1H), 2.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 196.4 (C=O), 155.5 (C), 153.9 (C), 134.9 (C), 130.0 (C), 125.9 (CH), 125.3 (CH), 113.0 (CH), 107.5 (CH), 26.8 (CH_3); IR, ν_{max} (KBr): 581, 621, 733, 827, 916, 953, 1055, 1099, 1130, 1184, 1223, 1263,

1335 (NO_2), 1364, 1435, 1470, 1522 (NO_2), 1568, 1612, 1676 (C=O), 3142 (CH Fu) cm^{-1}. Anal. Calcd (%) for $C_{10}H_7NO_4$: C, 58.54; H, 3.44; N, 6.83. Found (%): C, 58.62; H, 3.49; N, 6.77.

2,5-Dinitrobenzofuran (2j): yield 50%; 208 mg; yellow solid; mp 172–173 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.75 (d, ^4J = 2.3 Hz, 1H), 8.51 (dd, ^3J = 9.2, ^4J = 2.3 Hz, 1H), 7.81 (d, ^5J = 0.9 Hz, 1H), 7.79 (d, ^3J = 9.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.4 (C), 154.8 (C), 145.8 (C), 126.2 (C), 125.1 (CH), 120.7 (CH), 113.8 (CH), 107.3 (CH); IR, ν_{max} (KBr): 683, 739, 831, 905, 955, 1069, 1194, 1296, 1342 (NO_2), 1377, 1539 (NO_2), 1570, 1626, 3115 (CH Fu), 3144 cm^{-1}; MS (EI) m/z: 208 $[M]^+$ (42), 207 $[M - H]^+$ (27), 178 $[M - NO]^+$ (100), 162 $[M - NO_2]^+$ (8), 132 $[M - NO_2 - NO]^+$ (17), 120 $[M - CNO_2 - NO]^+$ (26), 104 (15), 88 (66), 76 (39), 62 (47). Anal. Calcd (%) for $C_8H_4N_2O_5$: C, 46.17; H, 1.94; N, 13.46. Found (%): C, 46.22; H, 2.01; N, 13.43.

5-*tert*-Butyl-2,7-dinitrobenzofuran (2k): yield 39%; 206 mg; light yellow solid; mp 152–153 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 and 8.48 (d, ^4J = 1.8 Hz, 2H), 7.74 (s, 1H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.4 (C) 149.9 (C), 143.3 (C), 134.0 (C), 129.1 (C), 127.0 (CH), 124.0 (CH), 106.8 (CH), 35.5 (C), 31.4 ($3CH_3$); IR, ν_{max} (KBr): 725, 791, 845, 899, 926, 949, 1111, 1192, 1242, 1323, 1358 (NO_2), 1481, 1531 (NO_2), 1574, 2878, 2936, 2974, 3121 (CH Fu) cm^{-1}. Anal. Calcd (%) for $C_{12}H_{12}N_2O_5$: C, 54.55; H, 4.58; N, 10.60. Found (%): C, 54.61; H, 4.56; N, 10.70.

7-(1-Adamantyl)-5-methyl-2-nitrobenzofuran (2l): yield 73%; 454 mg; colorless solid; mp 229–231 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.55 (s, 1H), 7.34 (s, 1H), 7.23 (s, 1H), 2.45 (s, 3H), 2.14–2.19 (m, 9H), 1.81–1.88 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.7 (C), 150.5 (C), 136.4 (C), 135.1 (C), 128.2 (CH), 126.8 (C), 120.9 (CH), 107.0 (CH), 41.3 (CH_2), 36.9 (CH_2), 36.5 (C), 28.8 (CH), 21.7 (CH_3); IR, ν_{max} (KBr): 731, 853, 962, 1252, 1275, 1331, 1344, 1358 (NO_2), 1402, 1454, 1524 (NO_2), 1570, 2851, 2905, 3152 (CH Fu) cm^{-1}. Anal. Calcd (%) for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found (%): C, 73.33; H, 6.77; N, 4.59.

7-Methoxy-2-nitrobenzofuran-5-carbaldehyde (2m): yield 59%; 261 mg; light yellow solid; mp 163–164 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 10.04 (s, 1H), 7.86 (d, ^{4}J = 1.1 Hz, 1H), 7.75 (s, 1H), 7.58 (d, ^{4}J = 1.1 Hz, 1H), 4.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 190.6 (CHO), 153.9 (C), 146.9 (C), 146.2 (C), 135.4 (C), 127.4 (C), 121.0 (CH), 108.5 (CH), 107.6 (CH), 56.6 (CH_3); IR, ν_{max} (KBr): 795, 988, 1098, 1144, 1215, 1277, 1325, 1356 (NO_2), 1479, 1537 (NO_2), 1570, 1599, 1616, 1697 (CO), 3115 (CH Fu), 3140 cm^{-1}. Anal. Calcd (%) for $C_{10}H_7NO_5$: C, 54.31; H, 3.19; N, 6.33. Found (%): C, 54.38; H, 3.25; N, 6.26.

Methyl 7-methoxy-2-nitro-1-benzofuran-5-carboxylate (2n): yield 60%; 301 mg; light yellow solid; mp 185–187 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08 (d, ^{4}J = 1.4 Hz, 1H), 7.72 (d, ^{4}J = 1.4 Hz, 1H), 7.69 (s, 1H), 4.08 (s, 3H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.2 (C=O), 153.8 (C), 145.8 (C), 145.3 (C), 128.7 (C), 127.0 (C), 118.2 (CH), 111.6 (CH), 107.7 (CH), 56.5 (CH_3), 52.7 (CH_3); IR, ν_{max} (KBr): 772, 841, 976, 1103, 1180, 1207, 1231, 1246, 1285, 1358 (NO_2), 1481, 1524 (NO_2), 1570, 1605, 1620, 1713 (C=O), 2955, 3117, 3144 (CH Fu) cm^{-1}. Anal. Calcd (%) for $C_{11}H_9NO_6$: C, 52.60; H, 3.61; N, 5.58. Found (%): C, 52.70; H, 3.55; N, 5.64.

2-Nitronaphtho[2,1-*b*]furan (2q): yield 56%; 239 mg; greenish yellow solid; mp 143–144 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.17 (d, ^{3}J = 8.2 Hz, 1H), 8.14 (d, ^{5}J = 0.7 Hz, 1H), 7.99–8.03 (m, 2H), 7.72 (td, ^{3}J = 7.1, ^{4}J = 1.2 Hz, 1H), 7.68 (d, ^{4}J = 8.9 Hz, 1H), 7.62 (ddd, ^{3}J = 8.2, ^{3}J = 7.1, ^{4}J =1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.6 (C), 152.0 (C), 132.1 (CH), 130.9 (C), 129.5 (CH), 128.4 (CH), 128.0 (C), 126.6 (CH), 123.4 (CH), 122.3 (C), 112.4 (CH), 106.8 (CH); IR, ν_{max} (KBr): 733, 758, 779, 806, 959, 1076, 1123, 1186, 1209, 1261, 1298, 1350 (NO_2), 1512 (NO_2), 1549, 1584, 3140 (CH Fu) cm^{-1}. Anal. Calcd (%) for $C_{12}H_7NO_3$: C, 67.61; H, 3.31; N, 6.57. Found (%): C, 67.62; H, 3.27; N, 6.64.

1-Acetyl-2-methyl-7-nitrobenzo[1,2-*b*:4,3-*b*']difuran (2r): yield 52%; 269 mg; yellow solid; mp 191–192 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.55 (s, 1H), 7.49 and 7.63 (d, ^{3}J = 9.0 Hz, 2H), 2.89 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.8 (C=O), 162.8 (C), 152.5 (C), 151.3 (C), 150.4 (C), 121.2 (C), 120.2 (C), 120.1 (C), 113.3 (CH), 110.8 (CH), 109.2 (CH), 30.6

(CH_3), 16.3 (CH_3); IR, ν_{max} (KBr): 844, 955, 1113, 1144, 1256, 1300, 1344 (NO_2), 1408, 1516, 1551 (NO_2), 1655 (C=O), 3169 (CH Fu) cm^{-1}. Anal. Calcd (%) for $C_{13}H_9NO_5$: C, 60.24; H, 3.50; N, 5.40. Found (%): C, 60.21; H, 3.41; N, 5.44.

Ethyl 6,7-dimethyl-2-nitro-6*H*-furo[3,2-*e*]indole-8-carboxylate (2s): yield 41%; 248 mg; bright yellow solid; mp 211–213 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.39 (s, 1H), 7.55 and 7.86 (d, ^3J = 9.2 Hz, 2H), 4.34 (q, ^3J = 7.1 Hz, 2H), 3.79 (s, 3H), 2.71 (s, 3H), 1.38 (t, ^3J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 164.9 (C=O), 151.8 (C), 151.1 (C), 146.4 (C), 133.1 (C), 120.0 (C), 118.1 (C), 115.0 (CH), 110.9 (CH), 106.6 (CH), 104.7 (C), 60.2 (CH_2), 31.0 (CH_3N), 14.9 (CH_3), 12.8 (CH_3); IR, ν_{max} (KBr): 860, 932, 1026, 1094, 1111, 1155, 1186, 1236, 1290, 1337 (NO_2), 1402, 1499, 1545 (NO_2), 1686 (C=O), 2924, 2988, 3090, 3175 (CH Fu) cm^{-1}. Anal. Calcd (%) for $C_{15}H_{14}N_2O_5$: C, 59.60; H, 4.67; N, 9.27. Found (%): C, 59.69; H, 4.61; N, 9.30.

2-Nitro-6,8,9,10-tetrahydro-7*H*-furo[3,2-*e*]pyrido[3,4-*b*]indol-7-one (2t): yield 39%; 211 mg; red solid; mp > 300 ºC (decomp.); ^{1}H NMR (400 MHz, DMSO-d_6) δ: 12.28 (s, 1H), 8.44 (d, ^5J = 0.7 Hz, 1H), 7.71 (s, 1H), 7.68 (d, ^3J = 9.2 Hz, 1H), 7.59 (dd, ^3J = 9.2, ^5J = 0.7 Hz, 1H), 3.53 (td, ^3J = 6.9, ^4J = 2.3 Hz, 2H), 3.16 (t, ^3J = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 161.7 (C=O), 152.7 (C), 150.1 (C), 134.1 (C), 129.1 (C), 119.0 (C), 118.9 (C), 118.1 (C), 117.5 (CH), 109.1 (CH), 108.7 (CH), 41.6 (CH_2), 21.5 (CH_2); IR, ν_{max} (KBr): 820, 920, 1088, 1128, 1209, 1240, 1271, 1302, 1319, 1352 (NO_2), 1400, 1445, 1499, 1543 (NO_2), 1676 (C=O), 2926, 3123 (CH Fu), 3231 (NH), 3375 (NH) cm^{-1}. Anal. Calcd (%) for $C_{13}H_9N_3O_4$: C, 57.57; H, 3.34; N, 15.49. Found (%): C, 57.62; H, 3.28; N, 15.56.

2-Nitrobenzofuran (2o)

Potassium trinitromethanide (1.14 g, 6 mmol) was added in three equal portions over a period of 20 minutes to a stirred solution of 2-(acetyloxy)benzyl acetate (0.42 g, 2 mmol) and triethylamine (0.84 mL, 6 mmol) in 60% aqueous ethanol (20 mL) at reflux temperature under an Ar atmosphere. Afterwards, the mixture was refluxed for another 20 minutes, poured into 50 mL

of saturated aqueous sodium chloride and extracted with dichloromethane (2x20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by column chromatography over silica gel using dichloromethane as eluent, followed by recrystallization from EtOH. Yield 150 mg (46%); light yellow solid; mp 134–135 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.76 (d, ^3J = 8.0 Hz, 1H), 7.68 (s, 1H), 7.57–7.63 (m, 2H), 7.39–7.44 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.4 (C), 153.2 (br s, C), 130.1 (CH), 125.9 (C), 125.4 (CH), 124.1 (CH), 112.8 (CH), 107.4 (CH); IR, ν_{max} (KBr): 729, 756, 833, 955, 1090, 1244, 1265, 1304, 1315, 1333, 1368 (NO_2), 1443, 1479, 1516, 1562 (NO_2), 1612, 2926, 3154 (CH Fu) cm^{-1}. Anal. Calcd (%) for $C_8H_5NO_3$: C, 58.90; H, 3.09; N, 8.59. Found (%): C, 59.01; H, 3.02; N, 8.64.

5-Bromo-2-nitrobenzofuran (2p) was prepared similarly to compound **2o** from 2-(acetyloxy)-5-bromobenzyl acetate **1p**. Yield 51%; 247 mg; light yellow solid; mp 168–169 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.92 (d, ^4J = 1.8 Hz, 1H), 7.69 (dd, ^3J = 9.2, ^4J = 1.8 Hz, 1H), 7.61 (s, 1H), 7.52 (d, ^3J = 9.2 Hz); ^{13}C NMR ($CDCl_3$) δ: 153.6 (C), 152.0 (C), 133.2 (CH), 127.6 (C), 126.6 (CH), 118.6 (C), 114.4 (CH), 106.3 (CH); IR, ν_{max} (KBr): 810, 837, 876, 957, 1099, 1188, 1238, 1312, 1373 (NO_2), 1439, 1528 (NO_2), 1562, 3140 (CH Fu) cm^{-1}. Anal. Calcd (%) for $C_8H_4BrNO_3$: C, 39.70; H, 1.67; N, 5.79. Found (%): C, 39.77; H, 1.59; N, 5.86.

6,7-Dimethyl-2-dimethylamino-4*H*-1,3-benzoxazine (3).

When using TMG instead of TEA only benzoxazine **3** was isolated under the conditions previously indicated. Yield 54%; 220 mg; white solid; mp 82–83 °C (from hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.77 (s, 1H), 6.68 (s, 1H), 4.43 (s, 2H), 2.93 (s, 6H), 2.20 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 151.2 (C), 148.1 (C), 135.8 (C), 132.0 (C), 126.6 (CH), 118.5 (C), 116.0 (CH), 44.7 (CH_2), 37.2 ($2CH_3$), 19.6 (CH_3), 19.1 (CH_3); IR υ_{max} (KBr): 866, 880, 959, 1099, 1175, 1202, 1254, 1269, 1373, 1389, 1450, 1462, 1487, 1504, 1674 (C=N), 2851 cm^{-1}; Anal. Calcd (%) for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90; N, 13.71. Found (%): C, 70.60; H, 7.92; N, 13.80.

4-Nitro-2-(2,2,2-trinitroethyl)phenol (4a)

A mixture of 2-(chloromethyl)-4-nitrophenol **1v** (1 g, 5.3 mmol) and potassium trinitromethanide (1.06 g, 5.6 mmol) in CH_3CN (20 mL) under an Ar atmosphere was stirred at room temperature for 4 h. Afterwards, the mixture was poured into 50 mL of saturated aqueous sodium chloride and extracted with dichloromethane (2x20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by recrystallization from ethanol. Yield 50%; 800 mg; light orange solid; mp 139–140 ºC (decomp.); ^{1}H NMR (DMSO-d_6) δ: 11.86 (1H, br s), 8.12-8.15 (2H, m), 6.99 (1H, d, ^3J = 9.1 Hz), 4.79 (s, 2H); ^{13}C NMR (DMSO-d_6): 163.6 (C), 140.1 (C), 129.1 (C), 128.5 (CH), 127.5 (CH), 116.1 (C), 116.0 (CH), 33.6 (CH_2); IR, ν_{max} (KBr): 638, 756, 812, 825, 839, 864, 920, 937, 1090, 1221, 1288, 1335 (NO_2), 1495, 1516 (NO_2), 1591 ($C(NO_2)_3$), 1609, 3500–3300 (OH) cm^{-1}. Anal. Calcd (%) for $C_8H_6N_4O_9$: C, 31.80; H, 2.00; N, 18.54. Found (%): C, 31.90; H, 1.96; N, 18.57.

1-[4-Hydroxy-3-(2,2,2-trinitroethyl)phenyl]ethanone (4b)

A mixture of 3-chloromethyl-4-hydroxyacetophenone **1w** (1 g, 5.4 mmol) and potassium trinitromethanide (1.06 g, 5.6 mmol) in CH_3CN (20 mL) under an Ar atmosphere was stirred at room temperature for 4 h. Afterwards, the mixture was poured into 50 mL of saturated aqueous sodium chloride to yield a solid product, which was filtered, washed with water and purified by recrystallization from ethanol. Yield 71%; 1.15 g; pink solid; mp 160–161 ºC (decomp.); ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.12 (1H, br s), 7.86 (dd, ^3J = 8.5, ^4J = 2.1 Hz, 1H), 7.79 (d, ^4J = 2.1 Hz, 1H), 6.91(d, ^3J = 8.5 Hz, 1H), 4.72 (s, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, CD_3CN): 196.0 (C=O), 160.3 (C), 132.1 (CH), 131.9 (CH), 130.4 (C), 128.7 (br s, C), 115.1 (CH), 114.6 (C), 33.8 (CH_2), 25.7 (CH_3); IR, ν_{max} (KBr): 814, 833, 864, 964, 1080, 1119, 1285, 1304, 1362, 1431, 1585, 1597 ($C(NO_2)_3$), 1667 (C=O), 3400–3100 (OH) cm^{-1}. Anal. Calcd (%) for $C_{10}H_9N_3O_8$: C, 40.14; H, 3.03; N, 14.04. Found (%): C, 40.22; H, 2.96; N, 14.13.

2,2,5-Trinitro-2,3-dihydrobenzofuran (5a)

4-Nitro-2-(2,2,2-trinitroethyl)phenol **4a** (0.3 g, 1 mmol) was dissolved in DMSO (2 mL) and the solution obtained was stored at room temperature for 5 h. The solution was poured into 15 mL of

saturated aqueous sodium chloride to yield a solid product, which was filtered, washed with water and dried. Yield 43%; 110 mg; light yellow solid; mp 92–94 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.32-8.33 (m, 1H), 8.29 (dd, ^{3}J = 8.9, ^{4}J = 2.3 Hz, 1H), 7.58 (d, ^{3}J = 8.9 Hz, 1H), 4.70 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): 160.7 (C), 145.1 (C), 130.1 (C), 126.7 (CH), 125.8 (C), 121.8 (CH), 111.8 (CH), 38.7 (CH_2); IR, ν_{max} (KBr): 745, 829, 903, 926, 1070, 1152, 1240, 1290, 1319, 1348 (NO_2), 1474, 1524 (NO_2), 1584 ($C(NO_2)_2$), 1603 cm^{-1}. Anal. Calcd (%) for $C_8H_5N_3O_7$: C, 37.66; H, 1.98; N, 16.47. Found (%): C, 37.71; H, 1.98; N, 16.58.

5-Acetyl-2,2-dinitro-2,3-dihydrobenzofuran (5b)

1-[4-Hydroxy-3-(2,2,2-trinitroethyl)phenyl]ethanone **4b** (0.3 g, 1 mmol) was dissolved in DMSO (2 mL) and the solution obtained was stored at room temperature for 5 days. The solution was poured into 15 mL of saturated aqueous sodium chloride, product extracted with CH_2Cl_2 and solvent was evaporated *in vacuo* at room temperature. The residue was crystallized from chloroform. Yield 40%; 101 mg; light yellow solid; mp 108–110 ºC (decomp.); ^{1}H NMR (DMSO-d_6) δ: 7.98-8.02 (m, 2H), 7.43 (d, 1H, J = 9.2 Hz), 4.66 (s, 2H), 2.54 (s, 3H); ^{13}C NMR (DMSO-d_6) δ: 196.9 (C=O), 159.6 (C), 134.6 (C), 131.2 (CH), 130.2 (C), 125.9 (CH), 124.2 (C), 111.0 (CH), 38.6 (CH_2), 27.2 (CH_3); IR, ν_{max} (KBr): 621, 1119, 1146, 1254, 1296, 1362, 1485, 1605($C(NO_2)_2$), 1670 (C=O) cm^{-1}. Anal. Calcd (%) for $C_{10}H_8N_2O_6$: C, 47.63; H, 3.20; N, 11.11. Found (%): C, 47.73; H, 3.27; N, 11.04.

Acknowlegement

This work was financially supported by the Russian Ministry of Education and Science within basic part of government assignment for scientific research with use of equipment of Multiple-Access Center “Investigation of the physicochemical properties of substances and materials” of Samara State Technical University.

ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all new synthesized compounds.

This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.

References

(1) (*a*) Tietze, L. F; Brasche, G.; Gericke, K. M., Eds. *Domino reactions in Organic Synthesis* Wiley-VCH: Weinheim, Gemany, **2006**, (*b*) Babaev, E. V. *Chem. Heterocycl. Comp.* **1993**, *29*, 796-817.

(2) For selected examples of the synthesis using ambiphilic building blocks, see: (*a*) Rofle, A.; Samarakoon, T. B.; Hanson, P. R. *Org. Lett.* **2010**, *12*, 1216-1219; (*b*) Dudnik, A. S.; Chernyak, N.; Huang, C.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2012**, *49*, 8729-8732; (*c*) Hili, R.; Rai, V.; Yudin, A. K. *J. Am. Chem. Soc.* **2010**, *132*, 2889-2891.

(3) For early reports on 1,1-ambiphiles, see: (*a*) Nakamura, Y.; Ukita, T. *Org. Lett.* **2002**, *4*, 2317-2320; (*b*) De Fusco, C.; Fuoco, T.; Croce, G.; Lattanzi, A. *Org. Lett.* **2012**, *14*, 4078-4081; (*c*) Katritzky, A. R.; Wang, X.; Xie, L.; Toader, D. *J. Org. Chem.* **1998**, *63*, 3445-3449; (*d*) Wasserman, H. H.; De Simone, R. W.; Ho, W.-B.; McCarthy, K. E. *Tetrahedron Lett.* **1992**, *33*, 7207-7210; (*e*) Trost, B. M.; Ghadiri, M. R. *J. Am. Chem. Soc.* **1984**, *106*, 7260-7261; (*f*) Wasserman, H. H.; Ho, W.-B. *J. Org. Chem.* **1994**, *59*, 4364-4366; (*g*) Trost, B. M.; Quayle, P. *J. Am. Chem. Soc.* **1984***, 106*, 2469-2471; (*h*) Katritzky, A. R.; Luo, Z.; Fang, Y.; Steel, P. J. *J. Org. Chem.* **2001**, *66*, 2858-2861; (*i*) Sato, T.; Okura, S.; Otera, J.; Nozaki, H. *Tetrahedron Lett.* **1987**, *28*, 6299-3602; (*j*) Trost, B. M.; Granja, J. R. *J. Am. Chem. Soc.* **1991***, 113*, 1044-1046.

(4) (*a*) Averina, E. A.; Kuznetsova, T. S.; Zefirov, N. S. *Synlett* **2009**, *10*, 1543-1557 (account); (*b*) Volkova, Yu. A.; Averina, E. B.; Grishin, Yu. K.; Bruheim, P.; Kuznetsova, T. S.; Zefirov, N. S. *J. Org. Chem.* **2010**, *75*, 3047-3052; (c) Averina, E. B.; Samoilichenko, Yu. V.; Volkova, Yu. A.; Grishin, Yu. K.; Rybakov, V. B.; Kutateladze, A. G.; Elyashberg, M. E.; Kuznetsova, T. S.; Zefirov, N. S. *Tetrahedron Lett.* **2012**, *53*, 1472-1475.

(5) Willis, N. J.; Bray, C. D. *Chem. Eur. J.* **2012**, *18*, 9160-9173.

(6) (*a*) De Water, R. W.; Pettus, T. R. R. *Tetrahedron* **2002**, *58*, 5367-5405. (*b*) Rokita, S. E., Ed. *Quinone methides*; Wiley: Hoboken, **2009**.

(7) (*a*) Samarakoon, T. B.; Hur, M. Y.; Kurtz, R. D.; Hanson, P. R. *Org. Lett.* **2010**, *12*, 2182-2185; (*b*) Osyanin, V. A.; Osipov, D. V.; Klimochkin, Yu. N. *J. Org. Chem.* **2013**, *78*, 5505-5520 and references therein.

(8) Bilger, C.; Demerseman, P.; Buisson, J.-P.; Royer, R.; Gayral, P.; Fourniat, J. *Eur. J. Med. Chem.*, **1987**, 22, 213-219.

(9) Cavier, R.; Buisson, J. P.; Royer, R. *Eur. J. Med. Chem.* **1982**, *17*, 91-92.

(10) Averbeck, D.; Bensasson, R. V.; Buisson, J. P.; Land, E. J.; Rene, L.; Royer, R.; Santus, R. *Int. J. Radiat. Biol.* **1982**, *42*, 457-468.

(11) Quillardet, P.; Touati, E.; Hofnung, M. *Mutation Research* **1996**, *358*, 113-122 and references therein.

(12) Guével, R.; Oger, F.; Lecorgne, A.; Dudasova, Z.; Chevance, S.; Bondon, A.; Barath, P.; Simonneaux, G.; Salbert, G. *Bioorg. Med. Chem.* **2009**, *17*, 7021-7030.

(13) Lin, S.-Y.; Chen, C.-L.; Lee, Y.-J. *J. Org. Chem.* **2003**, *68*, 2968-2971.

(14) Rosa, C. D. D.; Sanchez, J. P.; Kneeteman, M. N.; Mancini, P. M. E. *Tetrahedron Lett.* **2011**, *52*, 2316-2319.

(15) Gribble, G. W.; Pelkey, E. T.; Switzer, F. L. *Synlett* **1998**, 1061-1062.

(16) (a) Tromelin, A.; Demerseman, P.; Royer, R. *Synthesis* **1985**, 1074-1076 and references therein. (b) Yoshitaka, O.; Doi, Y.; Nakanishi, T. *Chem. Pharm. Bull.* **1988**, *36*, 1336-1342.

(17) (a) Bastian, G.; Royer, R.; Cavier, R. *Eur. J. Med. Chem.* **1983**, *18*, 365-367. (b) Kaluza, F.; Perold, G. *Chem. Ber*. **1955**, *88*, 597-601.

(18) Royer, R. *Ann. Pharm. Fr.* **1983**, *41*, 299-311.

(19) Einhorn, J.; Demerseman, P.; Royer, R. *Synthesis* **1984**, 978-980.

(20) Yadav, R. R.; Vishwakarma, R. A.; Bharate, S. B. *Tetrahedron Lett*. **2012**, *53*, 5958-5960.

(21) Hwu, J. R.; Chen, K.-L.; Ananthan, S. *J. Chem. Soc., Chem. Commun*. **1994**, 1425-1426.

(22) Lu, S.-C.; Zheng, P.-R.; Liu, G. *J. Org. Chem.* **2012**, *77*, 7711-7717.

(23) (a) Göbel, M.; Klapötke, T. M.; Mayer, P. Z. *Anorg. Allg. Chem.* **2006**, *632*, 1043-1050. (b) Altukhov, K. V.; Perekalin, V. V. *Russ. Chem. Rev.* **1976**, *45*, 1052.

(24) Further studies of this reaction are in progress.

(25) Bladé-Font, A.; Rocabayera, T. *J. Chem. Soc., Perkin Trans. 1* **1982**, 841-848.

(26) Weinert, E. E.; Dondi, R.; Colloredo-Melz, S.; Frankenfield, K. N.; Mitchel, C. H.; Freccero, M.; Rokita, S. E. *J. Am. Chem. Soc*. **2006**, *128*, 11940-11947.

(27) Tramontini, M. *Synthesis* **1973**, 703-775.

(28) Brode, W. R.; Littman, J. B. *J. Am. Chem. Soc*. **1931**, *53*, 1531-1532.

(29) Fanghänel, E.; Böckelmann, J.; Grossman, N.; Pfeifer, D. *J. Prakt. Chem.* **1986**, *328*, 724-728.