JOC The Journal of Organic Chemistry

pubs.acs.org/joc Article

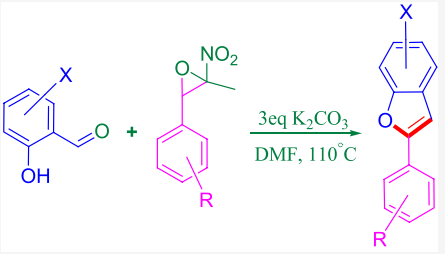
Catalyst-Free Synthesis of Benzofuran Derivatives from Cascade Reactions between Nitroepoxides and Salicylaldehydes

Mohammad A. Ranjbari and Hossein Tavakol*

Cite This: J. Org. Chem. 2021, 86, 4756−4762 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: Different benzofuran derivatives are synthesized via a catalyst-free reaction between nitroepoxides and salicylaldehydes. In the employed methodology, K_2CO_3 and DMF have been used at 110 °C, and the reactions were completed after 12 h in 33−84% yields. The highest yields were obtained using 3-nitrosalicylaldehyde. Finally, a plausible mechanism was proposed for the reaction, and some evidence was provided for this mechanism such as the detection of released acetate anion (using FTIR) and isolation and structure determination of the critical intermediate.



1. INTRODUCTION

The synthesis and chemistry of α-nitroepoxides were first developed by Newman and Angier in 1970.[1] They could be easily prepared by the oxidation of β-nitrostyrenes using different reagents.[2] However, until the 21st century, the development of their chemistry and reactions was limited to a few reports including their photochemical reactions.[3] During the first three decades, the most essential aspects of these structures were their reactions in some carbohydrate derivatives.[4] Nevertheless, during the past decade, their reactions and chemistry have been of wide interest. α-Nitroepoxides could be rearranged to α-nitroketones[5] and α-hydroxy ketones[6] or reduced to β-nitrobenzylamine derivatives as the precursors for pseudoephedrines.[1] Moreover, several useful syntheses could be started from β-nitrostyrenes to produce structures of interest.[7−10]

The most interesting transformation is the ring-opening reaction by the attack of a nucleophile followed by the release of the nitro group. In line with this, different nucleophiles such as dithiocarbamates,[11] various amines,[12,13] and fluoride and phenoxy anions[1] have been used to perform the ring-opening reaction. This bifunctional capability of these structures makes them the right choice for performing complex multicomponent reactions.[14] Noticeably, the use of bifunctional nucleophiles in the reaction with α-nitroepoxides has been employed for the synthesis of critical heterocyclic structures.[15−20] In agreement with this, the syntheses of pyrroles, cyclic thioureas, thiazoles, and quinoxalines have been successfully performed starting from α-nitroepoxides.

Despite the synthesis of different nitrogen- and sulfur-containing heterocycles from α-nitroepoxides, the synthesis of oxygen-containing heterocycles such as furan or benzofurans has not been reported using α-nitroepoxides yet. Benzofurans are an important class of organic compounds with promising bioactive properties and medicinal significance.[21] Their derivatives have antitumor,[22] cytotoxic,[23] antifungal,[24] and anti-inflammatory[25] abilities. Because of the biological and medicinal importance of benzofuran derivatives, many methodologies have been developed to synthesize them. They have been prepared using C−C coupling reactions,[26] oxidative annulation,[27] olefination of phenols,[28] Fujiwara−Moritani arylations,[29] cycloaddition of benzoquinones with stilbene oxides,[30] and many other reactions.[31−33] However, the research on the synthesis of benzofuran derivatives using new starting materials is still open. In this way, the use of mild conditions, simple methodology, and available materials is highly desirable.

Herein, in continuation of the recent focus of this research group on the development of new catalyst-free methodologies using simple and green media,[34,35] the synthesis of benzofuran derivatives from α-nitroepoxides has been investigated. The reaction has been designed between salicylaldehyde derivatives and different α-nitroepoxides. Salicylaldehydes are available materials, and α-nitroepoxides can be easily prepared from the condensation of aldehydes with nitroalkanes (both are available), followed by the epoxidation of the produced C=C double bond.

2. RESULTS AND DISCUSSION

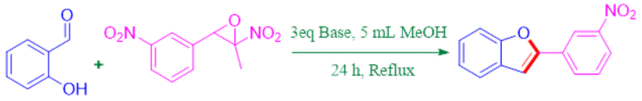
Most of the reported synthetic methodologies for benzofurans consist of coupling reactions involving expensive (and in many cases toxic) transition metals. More importantly, there is not

Received: January 19, 2021
Published: March 3, 2021

https://dx.doi.org/10.1021/acs.joc.1c00143
J. Org. Chem. 2021, 86, 4756−4762

any report on the synthesis of these compounds from α-nitroepoxides and salicylaldehydes. In this report, the suggested reaction has been performed successfully in catalyst-free conditions using a small amount of solvent. For the optimization of the reaction conditions, since the presence of base is vital, various common bases have been examined to find the best choice. It should be noticed that, because of the moderate acidity of the salicylaldehyde derivatives ($pK_a \approx 8$), the examined bases should have sufficient basicity (pK_a of their conjugate acids should be higher than 9). For this purpose, the model reaction consists of 2-methyl-2-nitro-3-(3-nitrophenyl) oxirane (1 mmol), salicylaldehydes (1 mmol), and 3 mmol of each base in 5 mL of methanol at reflux. The reaction was followed by TLC, and after 24 h, the product was isolated and weighed. The results of these experiments are listed in Table 1.

Table 1. Results of the Optimizations of the Selection of Base[a]



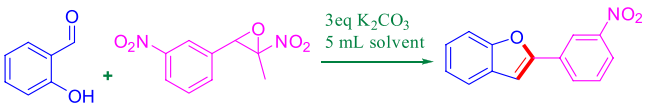
entry	base	time (h)	yield (%)
1	urea	24	
2	pyridine	24	
3	Et_3N	24	
4	NaOH	24	
5	KOH	24	
6	K_2CO_3	24	30
7	KO^{t}Bu	24	

[a]Reaction conditions: 1 mmol of salicylaldehyde, 1 mmol of nitroepoxide, and 3 mmol of base with reflux in 5 mL of methanol.

These reactions showed that, among seven examined organic and inorganic bases, only potassium carbonate afforded the product (in 30% yield). Therefore, this base was selected for the next optimization and reactions.

The next optimization attempts were made for the selection of the best solvent, temperature, and reaction time. The results of these optimizations are shown in Table 2. For the selection

Table 2. Results of the Optimization of the Solvent and Reaction Temperature[a]



entry	solvent	temp. (°C)	time (h)	yield (%)
1	THF	80	24	
2	toluene	80	24	
3	acetonitrile	80	12	32
4	water	80	12	trace
5	DMSO[b]	80	12	54
6	solvent-free	80	12	48
7	DMF[b]	80	12	62
9	DMF[b]	100	12	70
10	DMF[b]	110	12	81
11	DMF[b]	120	12	80

[a]Reaction conditions: 1 mmol of salicylaldehyde, 1 mmol of nitroepoxide, and 3 mmol of base with reflux in 5 mL of solvent. [b]1 mL of solvent was used.

of the best solvent, in addition to methanol (which was examined in the previous experiments) and solvent-free conditions, THF, toluene, acetonitrile, water, DMSO, and DMF (1 mL for the last two solvents and 5 mL for others) were examined for the model reaction at 80 °C for 12 and 24 h (entries 1−7). The yields of all reactions were not increased after 12 h. However, for the first two solvents (and also for methanol), the reaction was allowed to be continued for 24 h to ensure this. The highest yield (62%) was obtained using DMF (entry 7). Then, to increase the yield of the reaction, higher reaction temperatures were examined using the previously optimized conditions (K_2CO_3 as the base and DMF as the solvent for 12 h) for the model reaction. Among the three assayed temperatures (entries 8−11), 110 °C (entry 10) gave the highest yield.

After the optimization of the reaction parameters, a series of new reactions was designed to prepare various benzofuran derivatives. All of these new reactions were performed at 1 mL of DMF and using 3 mmol of K_2CO_3 at 110 °C for 12 h (the optimized conditions). First, 5-bromo, 5-chloro, 3-methoyxy, 4-(*N*,*N*-diethylamino), and 5-fluoro salicylaldehyde derivatives were reacted with simple and substituted (4-chloro, 4-nitro, and 3-nitro) nitroepoxides, and 20 different benzofurans were obtained, as shown in Scheme 1. The yields were between 33% and 84%, and in general, 3-nitro derivatives of nitroepoxides gave the highest yields (**3e** and **3f**); the smallest yields are, respectively, related to the methyl-containing nitroepoxides (**3p** and **3q** with 33−35% yield), naphthalene nitroepoxides (**3n** and **3o** with 42−45% yield), and reactions involving 4-(*N*,*N*-diethylamino)salicylaldehyde (**3l** and **3m** with 52−56% yield). The differences between the yields of the other derivatives are not meaningful.

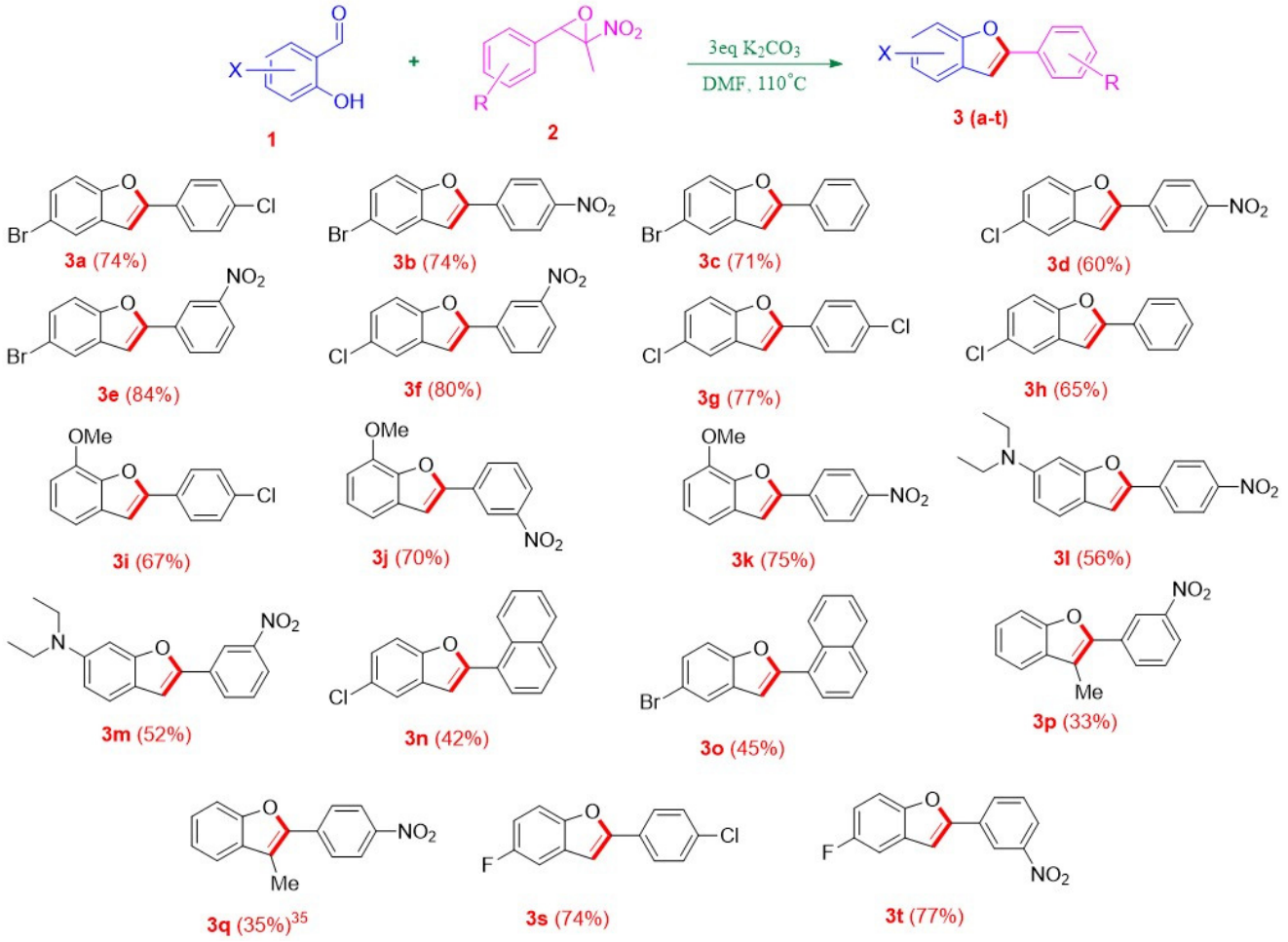
After the successful preparation of the mentioned derivatives, some nitroepoxides were reacted with simple salicylaldehyde (**1c**) to prepare three new benzofuran derivatives (**3u**−**3x**), and the results are depicted in Scheme 2. The yields of these new reactions (64−81%) were comparable with the previous derivatives, and interestingly, the product of the reaction with the 3-nitro derivative of nitroepoxide showed the highest yield.

It seems that proposing the plausible mechanism for this reaction could be interesting. It is more interesting when one takes a deep look at the reaction and perceives that, in addition to the release of the nitro group, the product has two carbons and two oxygens less than the reactants. These atoms could belong to the acetate group, and when the reaction was monitored, the release of the acetate ion was detected (by recording FTIR of the reaction mixture and observing acetate ion bands at 1570 and 1650 cm^{-1}). A plausible mechanism based on this foundation is depicted in Scheme 3. According to this mechanism, after the deprotonation of the phenolic hydroxy by the base, it (**I1**) attacks the benzylic position of the epoxy for ring-opening. The return of the anionic charge of the oxyanion leads to the release of the nitro group and the formation of carbonyl (**I2**). Then, the hydrogen between carbonyl and phenolic oxygen is removed by the base, and the carbanion (**I3**) attacks the carbonyl group to produce **I4**.

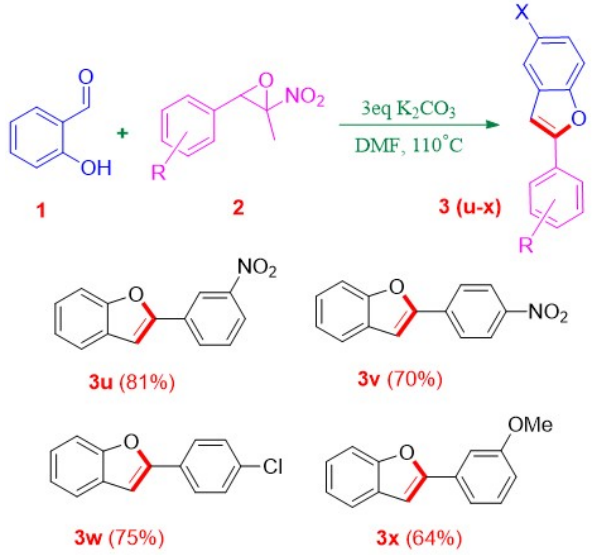
Then, the oxyanion of **I4** takes a proton from the conjugated acid, and the produced intermediate (**I5**) is attacked by the hydroxy group to produce **I6**. Finally, the shown rearrangement in **I6** leads to the product (**3**). The intermediates **I4**, **I5**, and **I6** have two asymmetric centers and have been produced in both cis and trans diastereomers. However, by following the

https://dx.doi.org/10.1021/acs.joc.1c00143
J. Org. Chem. 2021, 86, 4756−4762

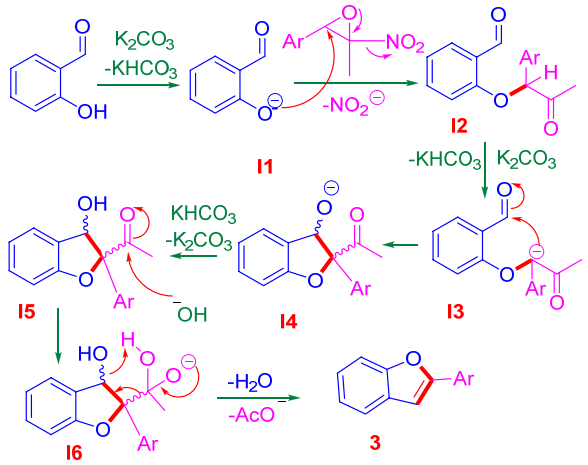
Scheme 1. Reaction of Various Nitroepoxides with Salicylaldehyde Derivatives



Scheme 2. Reaction of Nitroepoxides with Salicylaldehyde



Scheme 3. Plausible Mechanism for the Studied Reaction



reaction with TLC, it was found that both of these stereoisomers convert to the product (only at different rates).

To provide more evidence for this mechanism, in the reaction producing **3i**, the intermediate **I5** was isolated and its structure was identified by ^{1}H and ^{13}C NMR. The characterization data and real spectra of this intermediate (Supporting Information) completely confirm the formation of this intermediate and could be considered proof for the proposed mechanism.

3. CONCLUSION

In summary, a mild and efficient procedure for the catalyst-free conversion of nitroepoxides and salicylaldehydes to benzofuran derivatives was studied. The optimized condition consisted of

https://dx.doi.org/10.1021/acs.joc.1c00143
J. Org. Chem. 2021, 86, 4756−4762

3 mmol of K_2CO_3 as the base, 1 mL of DMF as the solvent, 110 °C temperature, and 12 h. Three different salicylaldehyde derivatives, including its 5-bromo and 5-chloro derivatives, and four nitroepoxide derivatives (simple, 3-nitro, 4-nitro, and 4-chloro) were used, and the yields were between 33% and 84%. The highest yields were obtained by using the 3-nitro derivative of nitroepoxide. The plausible mechanism for the reaction was proposed and confirmed by some evidence such as finding the released acetate anion and isolating the critical intermediate, followed by its analysis by ^1H and ^{13}C NMR. The major defects of this work are poor atom economy and using DMF as a nonenvironmentally friendly solvent. However, since many other reports for the preparation of benzofurans involve the use of heavy metals or have fewer atom economies, this work seems better in some aspects.

4. EXPERIMENTAL DETAILS

4.1. Materials and Instruments. The employed solvents and other materials have been bought from Sigma-Aldrich, Dae-Jung, Merck, and Fluka companies in high purities (>0.99%, reagent grade), and most of them were used without further purification. Melting points were obtained using the Gallen Kamp apparatus. FT-IR spectra have been recorded using KBr pellets by the JASCO FT-IR instrument. All ^1H NMR and ^{13}C NMR spectra were recorded using a Bruker Ultrashield 300 MHz NMR instrument with $CDCl_3$ or DMSO-d_6 as solvents. Elemental analyses were performed using a CHNS Vario EL III analyzer.

4.2. General Procedure for the Synthesis of Nitroepoxide Derivatives. To a 5 mL round-bottom flask with a magnet, 38 mL of methanol and 12 mL of nitroalkene were added. The flask was placed in a 0 °C ice−water bath, and 2.5 mL of hydrogen peroxide solution (50 v/v%) was added. Then, 3.9 mL of a 2 M solution of NaOH was added, and the mixture was stirred for 10 min at 0 °C. After this, 10 mL of cold water (5−10 °C) was added to the mixture, and the organic products were extracted 2× with 30 mL of diethyl ether. The organic layer was dried using sodium sulfate, and the solvent was evaporated. The crude product was purified using column chromatography on silica and a hexane−ethyl acetate (1:10) mixture as eluent (for all derivatives). All of these products are known, and their structures were confirmed by comparison of their melting points with the reports.[36−43]

4.3. General Procedure for the Synthesis of Benzofuran Derivatives. To a 10 mL round-bottom flask with a magnet over a heater−stirrer, one mL of DMF, 3 mmol of K_2CO_3, and 1 mmol of salicylaldehyde were added, and the reaction was stirred at room temperature. After 10 min, 1 mmol of nitroepoxide was added to the solution, and the temperature was increased to 110 °C using an oil bath. The reaction progress was followed by TLC (1:10 mixture of hexane−ethyl acetate) until completion (12 h). Then, the solvent (DMF) was removed by vacuum distillation, and 5 mL of water was added. The organic compounds were extracted from the mixture using 15 mL of ethyl acetate (2×). The organic layer was washed with 15 mL of brine (3×) and dried over sodium sulfate, and its solvent was evaporated. Before the purification of the product, the mixture was analyzed with FTIR (in some reactions) to find some evidence for the mechanism of the reaction (as it will be said later, the acetate ion band has been observed at this step). Then, the crude product was purified using column chromatography on silica and the hexane−ethyl acetate (1:10) mixture as eluent (for all derivatives). Among the 23 synthesized products, 19 compounds were characterized using FT-IR, ^1H NMR, ^{13}C NMR, and melting points (as described in the next sections), and their structures were confirmed by the comparison of their melting points and spectra with the reports. For the unknown products, in addition to the above analyses, elemental analyses were recorded to confirm their structures.

4.4. Spectral and Physical Data for All Synthesized Compounds. *4.4.1. 5-Bromo-2-(4-chlorophenyl) Benzofuran (**3a**).* White solid (228 mg, 74% yield), mp 176−178 °C; T-IR ν_{max} (KBr): 2924, 1486, 1439, 1384, 1094, 792; ^1H NMR (400 MHz, chloroform-*d*) δ 7.82−7.80 (m, 1H), 7.79−7.77 (m, 1H), 7.73−7.72 (t, J = 1.2 Hz, 1H), 7.47−7.45 (m, 1H), 7.44−7.42 (m, 1H), 7.40 (d, J = 1.2 Hz, 2H), 6.97 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 156.1, 153.6, 134.9, 131.0, 129.2, 128.4, 127.4, 126.3, 123.6, 116.2, 112.7, 101.1; known compound.[29]

*4.4.2. 5-Bromo-2-(4-nitrophenyl) Benzofuran (**3b**).* Yellow solid (232 mg, 74% yield), mp 191−193 °C; FT-IR ν_{max} (KBr): 3105, 1599, 1517, 1343, 1106, 851; ^1H NMR (400 MHz, chloroform-*d*) δ 8.40−8.30 (m, 2H), 8.06−7.97 (m, 2H), 7.80−7.78 (m, 1H), 7.50−7.43 (m, 2H), 7.20 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDzCl_3$) δ 154.5, 154.1, 147.5, 135.7, 130.6, 128.7, 125.5, 124.4, 124.2, 116.6, 113.0, 104.3; known compound.[30]

*4.4.3. 5-Bromo-2-phenyl Benzofuran (**3c**).* White solid (194 mg, 71% yield), mp 157−158 °C; FT-IR ν_{max} (KBr): 3100, 1450, 1439, 807, 762, 688; ^1H NMR (400 MHz, chloroform-*d*) δ 7.90−7.85 (m, 2H), 7.73 (dd, J = 1.8, 0.7 Hz, 1H), 7.51−7.46 (m, 2H), 7.44−7.37 (m, 3H), 6.99 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 157.2, 153.6, 131.2, 129.9, 129.0, 128.9, 127.1, 125.1, 123.5, 116.0, 112.6, 100.6; known compound.[26]

*4.4.4. 5-Chloro-2-(4-nitrophenyl) Benzofuran (**3d**).* Yellow solid (164 mg, 60% yield), mp 194−195 °C; FT-IR ν_{max} (KBr): 3106, 1597, 1508, 1382, 1345, 1325, 851; ^1H NMR (400 MHz, chloroform-*d*) δ 8.36−8.31 (m, 2H), 8.03−7.99 (m, 2H), 7.63 (d, J = 1.8 Hz, 1H), 7.50 (d, J = 8.8 Hz, 1H), 7.34 (dd, J = 8.7, 2.1 Hz, 1H), 7.20 (d, J = 0.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 154.6, 153.8, 147.5, 135.7, 130.0, 129.1, 126.0, 125.4, 124.4, 121.1, 112.5, 104.5; known compound.[39]

*4.4.5. 5-Bromo-2-(3-nitrophenyl) Benzofuran (**3e**).* Pale yellow solid (267 mg, 84% yield), mp 176−178 °C; FT-IR ν_{max} (KBr): 3102, 1525, 1432, 1351, 1050, 809, 798; ^1H NMR (300 MHz, DMSO-d_6) δ 8.69 (t, J = 1.9 Hz, 1H), 8.40 (d, J = 8.0 Hz, 1H), 8.29 (dd, J = 8.2, 1.5 Hz, 1H), 7.97 (d, J = 2.0 Hz, 1H), 7.84 (t, J = 8.0 Hz, 1H), 7.75 (s, 1H), 7.72 (d, J = 8.9 Hz, 1H), 7.55 (dd, J = 8.7, 2.1 Hz, 1H). $^{13}C\{^1H\}$ NMR (76 MHz, DMSO) δ 154.6, 153.8, 149.0, 131.5, 131.4, 131.3, 131.2, 128.6, 124.5, 124.1, 119.6, 116.4, 114.0, 104.5, 40.8, 40.6, 40.3, 40.0, 39.7, 39.4, 39.2; Anal. Calcd (%) for $C_{14}H_8BrNO_3$: C, 52.86; H, 2.53; N, 4.40. Found: C, 53.52; H, 2.68; N, 4.61.

*4.4.6. 5-Chloro-2-(3-nitrophenyl) Benzofuran (**3f**).* Pale yellow solid (219 mg, 80% yield), mp 182−184 °C; ^1H NMR (300 MHz, DMSO-d_6) δ 8.72−8.66 (m, 1H), 8.40 (ddd, J = 7.8, 1.6, 0.9 Hz, 1H), 8.29 (ddd, J = 8.2, 2.3, 0.9 Hz, 1H), 7.89−7.73 (m, 4H), 7.43 (dd, J = 8.9, 2.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (76 MHz, DMSO) δ 154.8, 153.4, 148.9, 131.5, 131.3, 131.3, 130.6, 128.4, 125.9, 124.1, 121.5, 119.6, 113.5, 104.6; Anal. Calcd (%) for $C_{14}H_8ClNO_3$: C, 61.44; H, 2.95; N, 5.12. Found: C, 62.31; H, 2.34; N, 4.78.

*4.4.7. 5-Chloro-2-(4-chlorophenyl) Benzofuran (**3g**).* White solid (203 mg, 77% yield), mp 154−155 °C; FT-IR ν_{max} (KBr): 3084, 1730, 1484, 1442, 1090, 811, 800; ^1H NMR (300 MHz, DMSO-d_6) δ 8.01−7.92 (m, 2H), 7.77 (d, J = 2.2 Hz, 1H), 7.69 (d, J = 8.7 Hz, 1H), 7.64−7.57 (m, 2H), 7.50 (d, J = 0.9 Hz, 1H), 7.38 (dd, J = 8.7, 2.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (76 MHz, DMSO) δ 156.1, 153.3, 134.3, 130.9, 129.7, 128.6, 128.2, 127.1, 125.2, 121.2, 113.2, 102.9; known compound.[40]

*4.4.8. 5-Chloro-2-phenyl Benzofuran (**3h**).* White solid (149 mg, 65% yield), mp 152−153 °C; FT-IR ν_{max} (KBr): 2913, 1606, 1432, 1345, 879; ^1H NMR (300 MHz, DMSO-d_6) δ 7.99−7.91 (m, 2H), 7.75 (d, J = 2.2 Hz, 1H), 7.69 (d, J = 8.7 Hz, 1H), 7.59−7.51 (m, 2H), 7.50−7.42 (m, 2H), 7.36 (dd, J = 8.7, 2.3 Hz, 1H). $^{13}C\{^1H\}$ NMR (76 MHz, DMSO) δ 157.3, 153.2, 131.0, 129.8, 129.7, 129.6, 128.1, 125.4, 125.0, 121.0, 113.2, 102.2; known compound.[40]

*4.4.9. 2-(4-Chlorophenyl)-7-Methoxybenzofuran (**3i**).* White solid (173 mg, 67% yield), mp 73−74 °C; FT-IR ν_{max} (KBr): 2947, 1591, 1487, 1093, 800, 727; ^1H NMR (300 MHz, DMSO-d_6) δ 7.94 (d, J = 8.6 Hz, 2H), 7.58 (d, J = 8.6 Hz, 2H), 7.49 (s, 1H), 7.27−7.16 (m, 2H), 6.98 (dd, J = 7.3, 1.7 Hz, 1H), 3.99 (s, 3H). $^{13}C\{^1H\}$ NMR (76 MHz, DMSO) δ 154.4, 145.4, 143.9, 133.7, 130.7, 129.6, 129.1, 126.8, 124.6, 113.8, 107.9, 103.5, 56.3; known compound.[45]

*4.4.10. 7-Methoxy-2-(3-nitrophenyl) Benzofuran (**3j**).* Yellow solid (188 mg, 70% yield), mp 144−143 °C; FT-IR ν_{max} (KBr):

https://dx.doi.org/10.1021/acs.joc.1c00143
J. Org. Chem. 2021, 86, 4756−4762

1521, 1494, 1344, 1101, 727; ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.74 (t, *J* = 1.9 Hz, 1H), 8.28−8.17 (m, 2H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.29−7.17 (m, 3H), 6.90 (dd, *J* = 6.8, 2.1 Hz, 1H), 4.10 (s, 3H). ^{13}C{^{1}H} NMR (76 MHz, $CDCl_3$) δ 153.3, 148.8, 145.5, 144.5, 132.1, 130.5, 130.4, 129.8, 124.1, 122.9, 119.8, 113.7, 107.4, 103.9, 77.5, 77.0, 76.6, 56.1. Anal. Calcd (%) for $C_{15}H_{11}NO_4$: C, 66.91; H, 4.12; N, 5.20. Found: C, 66.08; H, 4.21; N, 5.40.

*4.4.11. 7-Methoxy-2-(4-nitrophenyl) Benzofuran (**3k**).* Yellow solid (201 mg, 75% yield), mp 171−172 °C; FT-IR ν_{max} (KBr): 2925, 1595, 1514, 1332, 1272, 852, 730; ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.33 (d, *J* = 8.9 Hz, 2H), 8.05 (d, *J* = 8.9 Hz, 2H), 7.31−7.18 (m, 3H), 6.91 (dd, *J* = 6.8, 2.1 Hz, 1H), 4.10 (s, 3H). ^{13}C{^{1}H} NMR (76 MHz, $CDCl_3$) δ 153.4, 147.3, 145.5, 144.9, 136.1, 130.3, 125.3, 124.3, 113.8, 107.7, 105.4, 77.5, 77.0, 76.6, 56.1; known compound.[44]

*4.4.12. N,N-Diethyl-2-(4-nitrophenyl) Benzofuran-6-amine (**3l**).* Red crystal (173 mg, 56% yield), mp 155−157 °C; FT-IR ν_{max} (KBr): 1602, 1521, 1344, 1282, 1112, 862; ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.29 (d, *J* = 9.0 Hz, 2H), 7.91 (d, *J* = 9.0 Hz, 2H), 7.45 (d, *J* = 8.7 Hz, 1H), 7.15 (s, 1H), 6.81 (s, 1H), 6.76 (dd, *J* = 8.7, 2.3 Hz, 1H), 3.48 (q, *J* = 7.0 Hz, 4H), 1.26 (t, *J* = 7.1 Hz, 6H). ^{13}C{^{1}H} NMR (76 MHz, $CDCl_3$) δ 158.2, 150.6, 147.6, 146.1, 137.0, 124.4, 123.9, 121.9, 117.9, 110.3, 105.7, 93.4, 77.4, 77.0, 76.6, 45.0, 12.6; known compound (PubChem ID: 16460625).

*4.4.13. N,N-Diethyl-2-(3-nitrophenyl) Benzofuran-6-amine (**3m**).* Red crystal (161 mg, 52% yield), mp 98−99 °C; FT-IR ν_{max} (KBr): 2966, 1631, 1625, 1525, 1506, 1357, 1344, 1118, 794, 734; ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.63 (t, *J* = 2.0 Hz, 1H), 8.16−8.01 (m, 2H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 8.7 Hz, 1H), 7.08 (s, 1H), 6.85 (s, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 3.47 (q, *J* = 7.1 Hz, 4H), 1.26 (t, *J* = 7.0 Hz, 6H). ^{13}C{^{1}H} NMR (76 MHz, $CDCl_3$) δ 157.7, 148.8, 147.2, 132.8, 131.9, 129.6, 129.3, 121.6, 121.5, 120.9, 118.7, 110.2, 103.7, 93.8, 77.5, 77.0, 76.6, 45.0, 12.6. Anal. Calcd (%) for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03. Found: C, 68.94; H, 5.58; N, 9.20.

*4.4.14. 5-Chloro-2-(naphthalen-1-yl) Benzofuran (**3n**).* Pale yellow solid (117 mg, 42% yield), mp 74−75 °C; FT-IR ν_{max} (KBr): 3053, 1689, 1444, 1261, 798, 773; ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.53−8.42 (m, 1H), 8.04−7.86 (m, 3H), 7.75−7.52 (m, 5H), 7.34 (dd, *J* = 8.7, 2.2 Hz, 1H), 7.07 (s, 1H). ^{13}C{^{1}H} NMR (76 MHz, $CDCl_3$) δ 157.2, 153.4, 133.9, 130.6, 130.4, 129.9, 128.7, 128.5, 127.8, 127.5, 127.1, 126.2, 125.3, 125.3, 124.5, 120.5, 112.3, 105.4, 77.5, 77.0, 76.6; known compound (PubChem ID: 91689946).

*4.4.15. 5-Bromo-2-(naphthalen-1-yl) Benzofuran (**3o**).* Pale yellow solid (145 mg, 45% yield), mp 72−73 °C; FT-IR ν_{max} (KBr): 3037, 1703, 1651, 1444, 1259, 1176, 790, 763; ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.52−8.41 (m, 1H), 8.02−7.95 (m, 2H), 7.92 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.83 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.71−7.56 (m, 3H), 7.56−7.42 (m, 2H), 7.07 (s, 1H). ^{13}C{^{1}H} NMR (76 MHz, $CDCl_3$) δ 157.0, 153.7, 133.9, 131.0, 130.6, 129.9, 128.7, 127.7, 127.5, 127.2, 127.1, 126.2, 125.3, 125.3, 123.6, 116.0, 112.7, 105.3, 77.4, 77.0, 76.6; known compound (PubChem ID: 91689945).

*4.4.16. 3-Methyl-2-(3-nitrophenyl) Benzofuran (**3p**).* Yellow solid (83 mg, 33% yield), mp 77−79 °C; FT-IR ν_{max} (KBr): 2923, 1525, 1348, 808, 750, 734, 676; ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.72 (t, *J* = 2.0 Hz, 1H), 8.23 (ddd, *J* = 8.2, 2.3, 1.0 Hz, 1H), 8.18 (dt, *J* = 7.9, 1.4 Hz, 1H), 7.69 (t, *J* = 8.1 Hz, 1H), 7.65−7.53 (m, 2H), 7.45−7.30 (m, 2H), 2.60 (s, 3H). ^{13}C{^{1}H} NMR (76 MHz, $CDCl_3$) δ 153.9, 148.6, 148.0, 133.1, 131.9, 130.7, 129.7, 125.4, 122.8, 122.2, 121.2, 119.8, 113.8, 111.2, 9.6; known compound.[42]

*4.4.17. 3-Methyl-2-(4-nitrophenyl) Benzofuran (**3q**).* Yellow solid (88 mg, 35% yield), mp 133−134 °C; FT-IR ν_{max} (KBr): 1597, 1510, 1338, 1097, 854, 738; ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.38 (d, *J* = 9.0 Hz, 2H), 8.03 (d, *J* = 9.0 Hz, 2H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.42 (td, *J* = 8.2, 7.7, 1.4 Hz, 1H), 7.34 (td, *J* = 7.5, 1.1 Hz, 1H), 2.61 (s, 3H). ^{13}C{^{1}H} NMR (76 MHz, $CDCl_3$) δ 154.2, 148.2, 146.6, 137.5, 130.7, 126.6, 125.9, 124.1, 122.9, 119.9, 115.4, 111.3, 77.5, 77.0, 76.6, 9.9; known compound.[42]

*4.4.18. 2-(4-Chlorophenyl)-5-Fluorobenzofuran (**3s**).* White solid (182 mg, 74% yield), mp 123−124 °C; FT-IR ν_{max} (KBr): 2925, 1720, 1458, 1176, 954, 802; ^{1}H NMR (300 MHz, chloroform-*d*) δ 7.81 (d, *J* = 8.6 Hz, 2H), 7.46 (d, *J* = 8.6 Hz, 3H), 7.27 (dd, *J* = 8.5, 2.6 Hz, 1H), 7.09−6.99 (m, 2H). ^{13}C{^{1}H} NMR (76 MHz, chloroform-*d*) δ 159.4 (d, *J* = 238.4 Hz), 156.6, 151.2, 134.75, 129.9 (d, *J* = 10.9 Hz), 129.1, 128.6, 126.2, 112.2 (d, *J* = 26.5 Hz), 111.8 (d, *J* = 9.7 Hz), 106.4 (d, *J* = 25.1 Hz), 101.9 (d, *J* = 4.1 Hz); known compound.[46]

*4.4.19. 5-Fluoro-2-(3-nitrophenyl) Benzofuran (**3t**).* Yellow solid (187 mg, 77% yield), mp 124−125 °C; FT-IR ν_{max} (KBr): 1525, 1471, 1452, 1352, 1186, 1130, 792, 732; ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.72 (t, *J* = 2.0 Hz, 1H), 8.24 (ddd, *J* = 8.2, 2.3, 1.0 Hz, 1H), 8.18 (dt, *J* = 7.9, 1.3 Hz, 1H), 7.67 (t, *J* = 8.0 Hz, 1H), 7.52 (dd, *J* = 9.0, 4.1 Hz, 1H), 7.35−7.30 (m, 1H), 7.19 (s, 1H), 7.11 (td, *J* = 9.1, 2.6 Hz, 1H). ^{13}C{^{1}H} NMR (76 MHz, chloroform-*d*) δ 159.5 (d, *J* = 239.3 Hz), 154.9, 151.38, 148.8, 131.8, 130.4, 129.9, 129.5 (d, *J* = 11.1 Hz), 123.2, 119.8, 113.2 (d, *J* = 26.5 Hz), 112.1 (d, *J* = 9.6 Hz), 106.8 (d, *J* = 25.1 Hz), 103.7 (d, *J* = 4.1 Hz); known compound (CAS Registry Number: 1238315-03-1).

*4.4.20. 2-(3-Nitrophenyl) Benzofuran (**3u**).* Pale yellow solid (194 mg, 81% yield), mp 134−135 °C; FT-IR ν_{max} (KBr): 3084, 1527, 1449, 1348, 800, 762; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.68 (t, *J* = 1.9 Hz, 1H), 8.39 (d, *J* = 7.9 Hz, 1H), 8.26 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.83 (t, *J* = 8.0 Hz, 1H), 7.77 (s, 1H), 7.76−7.68 (m, 2H), 7.45−7.37 (m, 1H), 7.37−7.28 (m, 1H). ^{13}C{^{1}H} NMR (76 MHz, DMSO) δ 155.0, 153.2, 149.0, 131.8, 131.3, 131.3, 1289.0, 126.0, 124.1, 123.6, 122.2, 119.3, 111.9, 105.0; known compound.[41]

*4.4.21. 2-(4-Nitrophenyl) Benzofuran (**3v**).* Yellow solid (167 mg, 70% yield), mp 182−184 °C; FT-IR ν_{max} (KBr): 3085, 1600, 1517, 1344, 1110, 852, 752; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.43−8.33 (m, 2H), 8.26−8.16 (m, 2H), 7.85−7.66 (m, 3H), 7.44 (td, *J* = 8.4, 7.8, 1.4 Hz, 1H), 7.34 (td, *J* = 7.5, 0.9 Hz, 1H). ^{13}C{^{1}H} NMR (76 MHz, DMSO) δ 155.3, 153.4, 147.4, 136.1, 128.9, 126.5, 126.0, 124.9, 124.2, 122.4, 111.9, 106.6; known compound.[37]

*4.4.22. 2-(4-Chlorophenyl) Benzofuran (**3w**).* White solid (172 mg, 75% yield), mp 147−148 °C; FT-IR ν_{max} (KBr): 3055, 1486, 1449, 1384, 1093, 804, 749, 585; ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.85−7.79 (m, 2H), 7.63−7.59 (m, 1H), 7.57−7.52 (m, 1H), 7.47−7.41 (m, 2H), 7.36−7.30 (m, 1H), 7.30−7.24 (m, 1H), 7.04 (d, *J* = 0.9 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.9, 154.8, 134.3, 129.1, 129.0, 126.1, 124.6, 123.1, 121.0, 111.2, 101.8; known compound.[38]

*4.4.23. 2-(3-Methoxyphenyl) Benzofuran (**3x**).* White oil (143 mg, 64% yield), mp; FT-IR ν_{max} (KBr): 2923, 1571, 1488, 1454, 1238, 779, 750; ^{1}H NMR (300 MHz, chloroform-*d*) δ 7.67−7.57 (m, 2H), 7.53 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.49 (dd, *J* = 2.6, 1.5 Hz, 1H), 7.45−7.26 (m, 3H), 7.08 (s, 1H), 6.97 (ddd, *J* = 8.2, 2.6, 1.0 Hz, 1H), 3.95 (s, 3H). ^{13}C{^{1}H} NMR (76 MHz, $CDCl_3$) δ 160.0, 155.8, 154.9, 131.8, 129.9, 129.2, 124.4, 123.0, 120.9, 117.6, 114.5, 111.2, 110.2, 101.7, 77.5, 77.1, 76.7, 55.4; known compound.[43]

*4.4.24. 1-(3-Hydroxy-2-(3-nitrophenyl)-2,3-Dihydrobenzofuran-2-yl) Ethane-1-one (Intermediate **I5**).* ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.56 (t, *J* = 2.1 Hz, 1H), 8.18 (ddd, *J* = 8.2, 2.3, 1.0 Hz, 1H), 8.05 (ddd, *J* = 7.9, 1.9, 1.1 Hz, 1H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.41−7.35 (m, 2H), 7.20 (d, *J* = 8.1 Hz, 1H), 7.04 (td, *J* = 7.5, 1.0 Hz, 1H), 5.48 (s, 1H), 3.31 (d, *J* = 3.9 Hz, 1H), 2.44 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 207.0, 158.6, 148.3, 139.6, 132.1, 131.6, 129.6, 126.3, 125.6, 123.6, 122.8, 121.1, 111.0, 81.4, 28.2.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00143.

NMR spectra for all reported compounds (PDF)

FAIR data, including the primary NMR FID files, for compounds **3a**−**x** as well as IR spectra (ZIP)

https://dx.doi.org/10.1021/acs.joc.1c00143
J. Org. Chem. 2021, 86, 4756−4762

AUTHOR INFORMATION

Corresponding Author

Hossein Tavakol − *Department of Chemistry, Isfahan University of Technology, Isfahan 84156-83111, Iran;* orcid.org/0000-0002-3296-9575; Email: h_tavakol@iut.ac.ir

Author

Mohammad A. Ranjbari − *Department of Chemistry, Isfahan University of Technology, Isfahan 84156-83111, Iran*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.1c00143

Funding

The authors clearly state that no funding has been used in this work.

Notes

The authors declare no competing financial interest.

REFERENCES

(1) Newman, H.; Angier, R. B. The Preparation and Chemistry of α-Nitroepoxides. *Tetrahedron* **1970**, *26*, 825−836.

(2) Vidal-Albalat, A.; Świderek, K.; Izquierdo, J.; Rodríguez, S.; Moliner, V.; González, F. V. Catalytic Enantioselective Epoxidation of Nitroalkenes. *Chem. Commun.* **2016**, *52*, 10060−10063.

(3) Saito, I.; Takami, M.; Konoike, T.; Matsuura, T. Photoinduced Reactions. LXII. Photochemical Reaction of α-Nitroepoxides. *Tetrahedron Lett.* **1972**, *13*, 2689−2692.

(4) Nakagawa, T.; Sakakibara, T.; Kumazawa, S.; Hoshijima, Y.; Sudoh, R. Denitration of Carbohydrate α-Nitroepoxides by Nucleophiles. *Carbohydr. Res.* **1987**, *163*, 227−237.

(5) Martínez, R.; Velasco, M.; Martínez, I.; Menconi, I.; Ramfrez, A.; Angeles, E.; Regla, I.; López, R. Clay Catalized Rearrangement of Phenyloxiranes. *J. Heterocycl. Chem.* **1997**, *34*, 1865−1866.

(6) Chakraborty, R.; Das, A. R.; Ranu, B. C. Ion Exchange Resin-Mediated Hydrolytic Cleavage of α-Nitroepoxides. Simple One-Pot Synthesis of α-Hydroxyketones. *Synth. Commun.* **1992**, *22*, 1523−1528.

(7) Guan, Z. R.; Liu, Z. M.; Wan, Q.; Ding, M. W. One-pot four-component synthesis of polysubstituted thiazoles via cascade Ugi/Wittig cyclization starting from odorless Isocyano (triphenylphosphoranylidene)-acetates. *Tetrahedron* **2020**, *76*, 131101.

(8) Hubbell, A. K.; Coates, G. W. Nucleophilic Transformations of Lewis Acid-Activated Disubstituted Epoxides with Catalyst-Controlled Regioselectivity. *J. Org. Chem.* **2020**, *85*, 13391−13414.

(9) Zhu, Y.; Chen, W.; Zhao, D.; Zhang, G.; Yu, Y. One-Pot Three-Component Strategy for Polysubstituted 2-Aminothiazoles via Ring Opening of α-Nitro Epoxides. *Synthesis* **2019**, *51*, 2023−2029.

(10) Badali, E.; Rahimzadeh, H.; Sharifi, A.; Habibi, A.; Halimehjani, A. Z. Nitroepoxide ring opening with thionucleophiles in water: synthesis of α-xanthyl ketones, β-keto sulfones and β-keto sulfonic acids. *Org. Biomol. Chem.* **2020**, *18*, 4983−4987.

(11) Ziyaei-Halimehjani, A.; Lotfi-Nosood, Y. Synthesis of N, S-Heterocycles and Dithiocarbamates by the Reaction of Dithiocarbamic Acids and S-Alkyl Dithiocarbamates with Nitroepoxides. *Org. Lett.* **2017**, *19*, 6748−6751.

(12) Zhao, D.; Zhu, Y.; Guo, S.; Chen, W.; Zhang, G.; Yu, Y. A Three-Component One-Pot Synthesis of Penta-Substituted Pyrroles via Ring Opening of α-Nitroepoxides. *Tetrahedron* **2017**, *73*, 2872−2877.

(13) Capobianco, A.; Meninno, S.; Lattanzi, A. Unravelling the Mechanism of the Organocatalyzed Aminolytic Kinetic Resolution of α-Nitroepoxides: A Theoretical Study. *Catal. Sci. Technol.* **2020**, *10*, 1422−1430.

(14) Liu, X.; Nie, Z.; Shao, J.; Chen, W.; Yu, Y. A Multi-Component Synthesis of N -Substituted 2-Amino-3-Cyano Pyrroles via Ring-Opening of Nitroepoxides. *New J. Chem.* **2018**, *42*, 2368−2371.

(15) Nosood, Y. L.; Ziyaei Halimehjani, A.; González, F. V. Regioselective Opening of Nitroepoxides with Unsymmetrical Diamines. *J. Org. Chem.* **2018**, *83*, 1252−1258.

(16) Agut, J.; Vidal, A.; Rodríguez, S.; González, F. V. Dynamic Kinetic Asymmetric Ring-Opening/Reductive Amination Sequence of Racemic Nitroepoxides with Chiral Amines: Enantioselective Synthesis of Chiral Vicinal Diamines. *J. Org. Chem.* **2013**, *78*, 5717−5722.

(17) Zhu, Y.; Wang, Q.; Luo, H.; Zhang, G.; Yu, Y. Efficient and Facile Strategy to Substituted 2-Aminothiazoles via Ring Opening of α-Nitroepoxides. *Tetrahedron* **2018**, *74*, 7143−7147.

(18) Capel, E.; Vidal-Albalat, A.; Rodríguez, S.; González, F. Preparation of Morpholines and Benzoxazines Starting from Nitroepoxides. *Synthesis* **2016**, *48*, 2572−2580.

(19) Vidal-Albalat, A.; Rodríguez, S.; González, F. V. Nitroepoxides as Versatile Precursors to 1,4-Diamino Heterocycles. *Org. Lett.* **2014**, *16*, 1752−1755.

(20) Guo, X.; Chen, W.; Chen, B.; Huang, W.; Qi, W.; Zhang, G.; Yu, Y. One-Pot Three-Component Strategy for Functionalized 2-Aminoimidazoles via Ring Opening of α-Nitro Epoxides. *Org. Lett.* **2015**, *17*, 1157−1159.

(21) Khanam, H.; Shamsuzzaman. Bioactive Benzofuran Derivatives: A Review. *Eur. J. Med. Chem.* **2015**, *97*, 483−504.

(22) Ibrahim, M. M.; Grau, D.; Hampel, F.; Tsogoeva, S. B. α-Nitro Epoxides in Organic Synthesis: Development of a One-Pot Organocatalytic Strategy for the Synthesis of Quinoxalines. *Eur. J. Org.* **2014**, *2014*, 1401−1405.

(23) Banskota, A. H.; Tezuka, Y.; Midorikawa, K.; Matsushige, K.; Kadota, S. Two Novel Cytotoxic Benzofuran Derivatives from Brazilian Propolis. *J. Nat. Prod.* **2000**, *63* (9), 1277−1279.

(24) Aslam, S. N.; Stevenson, P. C.; Phythian, S. J.; Veitch, N. C.; Hall, D. R. Synthesis of Cicerfuran, an Antifungal Benzofuran, and Some Related Analogues. *Tetrahedron* **2006**, *62*, 4214−4226.

(25) Dawood, K. M.; Abdel-Gawad, H.; Rageb, E. A.; Ellithey, M.; Mohamed, H. A. Synthesis, Anticonvulsant, and Anti-Inflammatory Evaluation of Some New Benzotriazole and Benzofuran-Based Heterocycles. *Bioorg. Med. Chem.* **2006**, *14*, 3672−3680.

(26) Nagamochi, M.; Fang, Y.-Q.; Lautens, M. A General and Practical Method of Alkynyl Indole and Benzofuran Synthesis via Tandem Cu- and Pd-Catalyzed Cross-Couplings. *Org. Lett.* **2007**, *9*, 2955−2958.

(27) Zhu, R.; Wei, J.; Shi, Z. Benzofuran Synthesis via Copper-Mediated Oxidative Annulation of Phenols and Unactivated Internal Alkynes. *Chem. Sci.* **2013**, *4*, 3706.

(28) Agasti, S.; Sharma, U.; Naveen, T.; Maiti, D. Orthogonal Selectivity with Cinnamic Acids in 3-Substituted Benzofuran Synthesis through C−H Olefination of Phenols. *Chem. Commun.* **2015**, *51*, 5375−5378.

(29) Zhang, H.; Ferreira, E. M.; Stoltz, B. M. Direct Oxidative Heck Cyclizations: Intramolecular Fujiwara-Moritani Arylations for the Synthesis of Functionalized Benzofurans and Dihydrobenzofurans. *Angew. Chem., Int. Ed.* **2004**, *43*, 6144−6148.

(30) Kokubo, K.; Harada, K.; Mochizuki, E.; Oshima, T. A New Approach to Benzofuran Synthesis: Lewis Acid Mediated Cycloaddition of Benzoquinones with Stilbene Oxides. *Tetrahedron Lett.* **2010**, *51*, 955−958.

(31) Lamaa, D.; Hauguel, C.; Lin, H. P.; Messe, E.; Gandon, V.; Alami, M.; Hamze, A. Sequential One-Pot Synthesis of 3-Arylbenzofurans from N-Tosylhydrazones and Bromophenol Derivatives. *J. Org. Chem.* **2020**, *85*, 13664−13673.

(32) Li, M.; Wang, T.; An, Z.; Yan, R. B(C6F5)-3-Catalyzed cyclization of alkynes: direct synthesis of 3-silyl heterocyclic compounds. *Chem. Commun.* **2020**, *56*, 11953−11956.

(33) Kondoh, A.; Ma, C.; Terada, M. Synthesis of diarylalkanes through an intramolecular/intermolecular addition sequence by auto-tandem catalysis with strong Brønsted base. *Chem. Commun.* **2020**, *56*, 10894−10897.

(34) Tavakol, H.; Mahmoudi, A.; Ranjbari, M.-A. Synthesis Of Di- and Tri-Substituted Thiourea Derivatives in Water Using Choline Chloride−Urea Catalyst. *J. Sulfur Chem.* **2019**, *40*, 113−123.

(35) Jafari-Chermahini, M. T.; Tavakol, H. Immobilized Gelatin-λ-Carrageenan on Magnetite Nanoparticles as an Efficient Organocatalyst for Enantioselective Biginelli Reaction. *ChemistrySelect* **2019**, *4*, 1895−1902.
(36) Sharma, U.; Naveen, T.; Maji, A.; Manna, S.; Maiti, D. Palladium-Catalyzed Synthesis of Benzofurans and Coumarins from Phenols and Olefins. *Angew. Chem., Int. Ed.* **2013**, *52*, 12669−12673.
(37) Csékei, M.; Novák, Z.; Kotschy, A. Development of a One-Pot Sequential Sonogashira Coupling for the Synthesis of Benzofurans. *Tetrahedron* **2008**, *64*, 8992−8996.
(38) Rao, M. L. N.; Awasthi, D. K.; Talode, J. B. Palladium-Catalyzed Cross-Couplings of Functionalized 2-Bromobenzofurans for Atom-Economic Synthesis of 2-Arylbenzofurans Using Triarylbismuth Reagents. *Tetrahedron Lett.* **2012**, *53*, 2662−2666.
(39) Pu, W.; Yuan, Y.; Lu, D.; Wang, X.; Liu, H.; Wang, C.; Wang, F.; Zhang, G. 2-Phenylbenzo[b]Furans: Synthesis and Promoting Activity on Estrogen Biosynthesis. *Bioorg. Med. Chem. Lett.* **2016**, *26*, 5497−5500.
(40) Bates, C. G.; Saejueng, P.; Murphy, J. M.; Venkataraman, D. Synthesis of 2-Arylbenzo[b]Furans via Copper(I)-Catalyzed Coupling of o -Iodophenols and Aryl Acetylenes. *Org. Lett.* **2002**, *4*, 4727−4729.
(41) Miyata, O.; Takeda, N.; Naito, T. Highly Effective Synthetic Methods for Substituted 2-Arylbenzofurans Using [3,3]-Sigmatropic Rearrangement: Short Syntheses of Stemofuran A and Eupomatenoid 6. *Org. Lett.* **2004**, *6*, 1761−1763.
(42) Quibell, J. M.; Duan, G.; Perry, G. J. P.; Larrosa, I. Decarboxylative Suzuki−Miyaura Coupling of (Hetero)Aromatic Carboxylic Acids Using Iodine as the Terminal Oxidant. *Chem. Commun.* **2019**, *55*, 6445−6448.
(43) Yin, S.-C.; Zhou, Q.; Zhao, X.-Y.; Shao, L.-X. N-Heterocyclic Carbene-Palladium(II)-1-Methylimidazole Complex Catalyzed Direct C−H Bond Arylation of Benzo[b]Furans with Aryl Chlorides. *J. Org. Chem.* **2015**, *80*, 8916−8921.
(44) Pu, W.-C.; Mu, G.-M.; Zhang, G.-L.; Wang, C. Copper-Catalyzed Decarboxylative Intramolecular C−O Coupling: Synthesis of 2-Arylbenzofuran from 3-Arylcoumarin. *RSC Adv.* **2014**, *4*, 903−906.
(45) Wang, X.; Liu, M.; Xu, L.; Wang, Q.; Chen, J.; Ding, J.; Wu, H. Palladium-catalyzed addition of potassium aryltrifluoroborates to aliphatic nitriles: Synthesis of alkyl aryl ketones, diketone compounds, and 2-arylbenzo [b] furans. *J. Org. Chem.* **2013**, *78*, 5273−5281.
(46) Rao, M. L.; Jadhav, D. N.; Dasgupta, P. Pd-Catalyzed Tandem Chemoselective Synthesis of 2-Arylbenzofurans using Threefold Arylating Triarylbismuth Reagents. *Eur. J. Org. Chem.* **2013**, *2013*, 781−788.

https://dx.doi.org/10.1021/acs.joc.1c00143
J. Org. Chem. 2021, 86, 4756−4762