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Unusual Reactivity of Aryl Aldehydes with Triethyl Phosphite and Zinc Bromide: A Facile Preparation of Epoxides, Benzisoxazoles, and α-Hydroxy Phosphonate Esters

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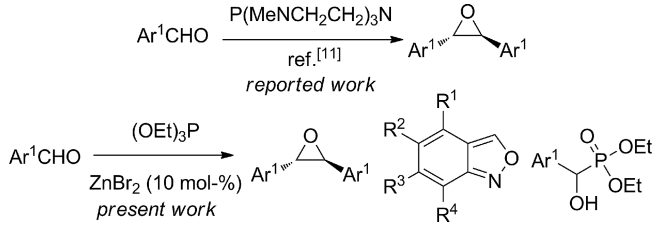
A facile preparation of *trans*-epoxides was achieved by a $(EtO)_3P$–$ZnBr_2$-mediated deoxygenation reaction of the corresponding 2-nitrobenzaldehydes. The sterically hindered analogues of 2-nitrobenzaldehyde underwent a reaction with triethyl phosphite in the presence of $ZnBr_2$ as the catalyst to form benzisoxazoles as the sole product. Under identical conditions, the reactions of electron-rich as well as moderately electron-deficient aryl aldehydes furnished the corresponding α-hydroxy phosphonate esters.

Introduction

Epoxides are traditionally prepared by oxidation of olefins with peracids. However, preparations of epoxides with sensitive structural features have recently been achieved by reactions of aldehydes with sulfur ylides,[1] ammonium ylides,[2] phosphorus ylides,[3] selenium ylides[4] and telluronium ylides,[5] respectively. Rearrangements, stereospecific nucleophilic ring-opening reactions, and other synthetic transformations that involve epoxides make them versatile reagents.[6] Despite the several known asymmetric epoxidation strategies that exist to date,[7] the stereoselective synthesis of epoxides from aldehydes has remained a challenging task.

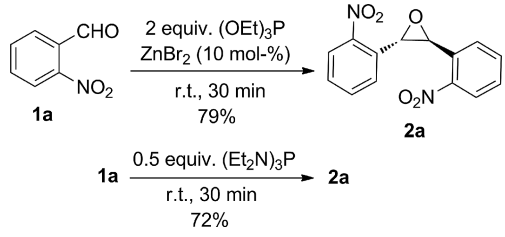
The transformation of aryl aldehydes into the corresponding epoxides by using tris(dimethylamino)phosphine was first observed by Mark to involve a reductive dimerization of two molecules of aryl aldehydes.[8] Subsequently, Ramirez and co-workers confirmed that the reaction of nitroaryl aldehydes with trialkyl phosphite led to the formation of a (trialkoxy)dioxaphospholane.[9,10] Recently, Liu and Verkade achieved the facile transformation of aryl aldehydes into their respective epoxides by using cyclic aminophosphine, $P(MeNCH_2CH_2)_3N$.[11] The efficient preparation of α-hydroxy phosphonates[12] were achieved by the reaction of aryl aldehydes and triethyl phosphite using a Brønsted acid as well as a Lewis acid as catalysts.[13] We have recently reported a $ZnBr_2$-mediated Arbuzov reaction of benzylic bromides and alcohols at room temperature.[14] As a continuation of this study, we herein report our results of the reaction of aryl aldehydes with triethyl phosphite in the presence of $ZnBr_2$ (Scheme 1).



Scheme 1. Reaction of aryl aldehydes with trivalent phosphorus.

Results and Discussion

As a representative case, the reaction of 2-nitrobenzaldehyde (**1a**) with 2 equiv. of $P(OEt)_3$ in the presence of 10 mol-% $ZnBr_2$ at room temperature for 30 min led to the formation of *trans*-epoxide **2a** as the sole product in 79% yield (Scheme 2). The epoxide formation was only successful in the presence of $ZnBr_2$. Indeed, when the reaction was



Scheme 2. Reaction of 2-nitrobenzaldehyde with triethyl phosphite–$ZnBr_2$ system and tris(diethylamino)phosphine.

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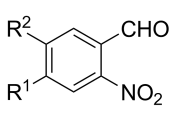
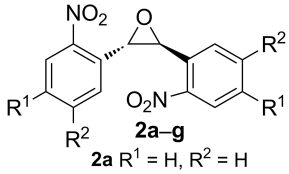
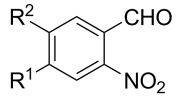
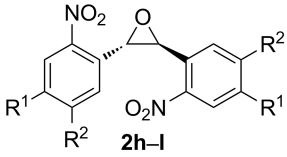
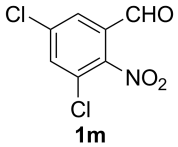
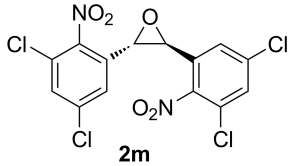
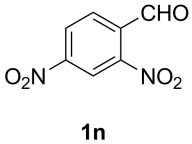
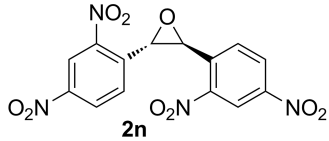
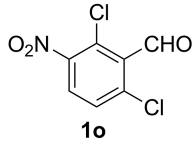
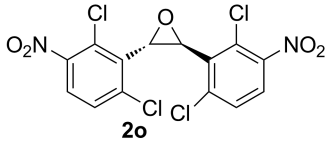
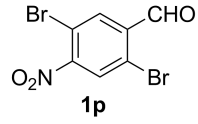
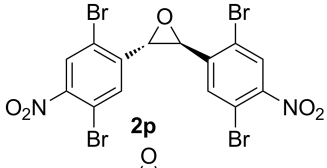
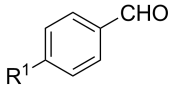
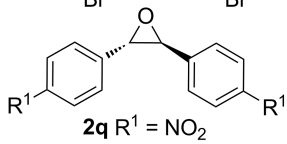
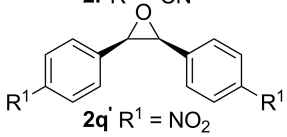
Table 1. Preparation of epoxides **2a**–**2r** by using the $(EtO)_3P$–$ZnBr_2$ system.

Entry	Substrate	Product[a]	Yield (%)[b]
1	 **1a–g**	 **2a–g**	
	1a R^1 = H, R^2 = H	**2a** R^1 = H, R^2 = H	79
	1b R^1 = Cl, R^2 = H	**2b** R^1 = Cl, R^2 = H	83
	1c R^1 = H, R^2 = Cl	**2c** R^1 = H, R^2 = Cl	82
	1d R^1 = F, R^2 = H	**2d** R^1 = F, R^2 = H	80
	1e R^1 = H, R^2 = F	**2e** R^1 = H, R^2 = F	88
	1f R^1 = H, R^2 = Br	**2f** R^1 = H, R^2 = Br	81
	1g R^1 = H, R^2 = OMe	**2g** R^1 = H, R^2 = OMe	81
2	 **1h–l**	 **2h–l**	
	1h R^1 = Cl, R^2 = Cl	**2h** R^1 = Cl, R^2 = Cl	89
	1i R^1 = Cl, R^2 = F	**2i** R^1 = Cl, R^2 = F	90
	1j R^1 = F, R^2 = Cl	**2j** R^1 = F, R^2 = Cl	92
	1k R^1 = F, R^2 = Br	**2k** R^1 = F, R^2 = Br	87
	1l R^1, R^2 = OCH_2O	**2l** R^1, R^2 = OCH_2O	79
3	 **1m**	 **2m**	75
4	 **1n**	 **2n**	85
5	 **1o**	 **2o**	73
6	 **1p**	 **2p**	84
7	 **1q** R^1 = NO_2 **1r** R^1 = CN	 **2q** R^1 = NO_2	53
		2r R^1 = CN	50
		 **2q'** R^1 = NO_2	32
		2r' R^1 = CN	30

[a] Reagents and conditions: aldehyde **1a**–**1r** (1 equiv.), $P(OEt)_3$ (2 equiv.), and $ZnBr_2$ (10 mol-%) at room temperature for 10–30 min. [b] Isolated yield.

performed without $ZnBr_2$, a complex mixture resulted. The deoxygenation of 2-nitrobenzaldehyde (**1a**) with 0.5 equiv. of relatively expensive tris(diethylamino)phosphine at room temperature also led to the formation of **2a** in an almost comparable yield. However, the facile transformation of 2-nitrobenzaldehyde (**1a**) into *trans*-epoxide **2a** by using the triethyl phosphite–$ZnBr_2$ system prompted us to explore the reaction with other 2-nitrobenzaldehyde analogues (Table 1).

To our delight, epoxide formation was successful with the wide variety of electron-deficient benzaldehydes **1a**–**1r** (Table 1). The presence of electron-withdrawing (F, Cl, Br, NO_2) or electron-donating groups (OMe, OCH_2O) on the 2-nitrobenzaldehydes had only a negligible influence on the reaction yields (Table 1, Entries 1–4). In all of these cases, the exclusive formation of the *trans* product was confirmed by ^1H NMR spectroscopic data. Although, 3-nitrobenzaldehyde is known to produce an α-hydroxy phosphonate ester,[14] 2,6-dichloro-3-nitrobenzaldehyde (**1o**) afforded *trans*-epoxide **2o** as the sole product (Table 1, Entry 5). The reaction of 2,5-dibromo-4-nitrobenzaldehyde (**1p**) with triethyl phosphite and $ZnBr_2$ as the catalyst furnished *trans*-epoxide **2p** in 84% yield (Table 1, Entry 6). However, the reactions of 4-nitrobenzaldehyde (**1q**) and 4-cyanobenzaldehyde (**1r**), respectively, with the $(EtO)_3P$–$ZnBr_2$ system led to a mixture of *cis*- and *trans*-epoxides (Table 1, Entry 7). The formation of the *cis*-epoxides **2q′** and **2r′** can occur as a result of the sterically less demanding natures of aldehydes **1q** and **1r**. As representative cases, the structures of *trans*-epoxide **2g** (Figure 1) and *cis*-epoxide **2q′** (Figure 2) were confirmed by single-crystal X-ray analysis.[15]

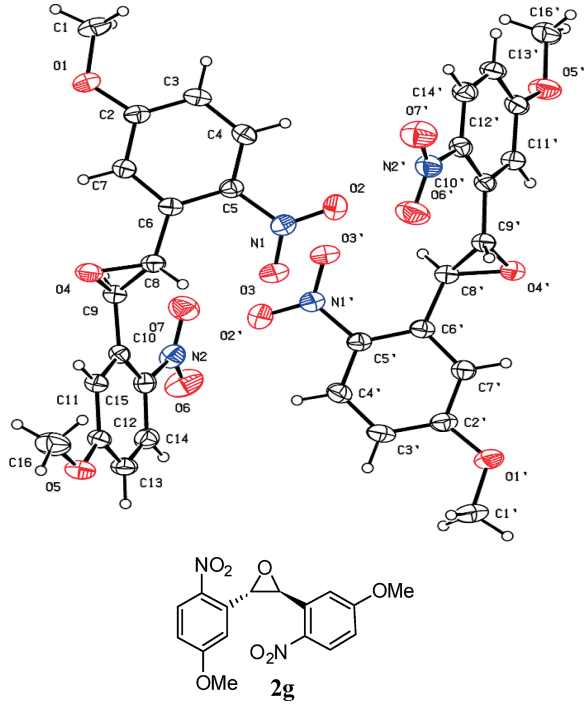


Figure 1. Single-crystal X-ray structure of **2g**.

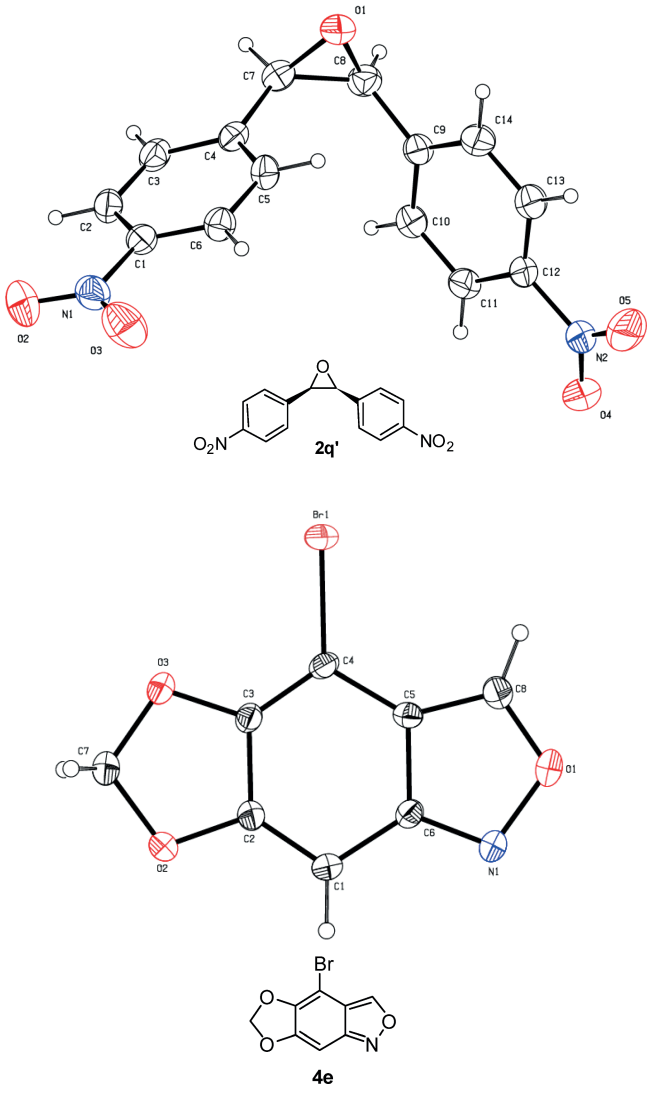


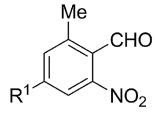
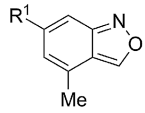
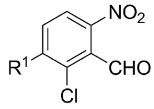
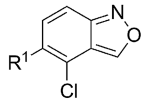
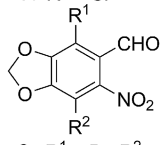
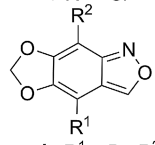
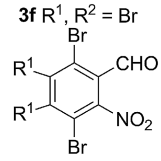
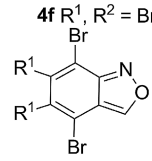
Figure 2. Single-crystal X-ray structures of **2q′** and **4e**.

To our surprise, 2-nitrobenzaldehydes **3a**–**3h** with a substituent at the 6-position was subjected to the reaction conditions and treated with 3 equiv. of triethyl phosphite and $ZnBr_2$ as the catalyst to form benzisoxazoles **4a**–**4h** in 75–90% yields (Table 2). Benzisoxazole **4e** was chosen as a representative product, and its structure was confirmed by a single-crystal X-ray analysis (Figure 2).[15]

Finally, the reaction of moderately electron-deficient/electron-rich aryl aldehydes **5a**–**5h** and the triethyl phosphite–$ZnBr_2$ system produced the corresponding α-hydroxy phosphonates **6a**–**6h** in good yields (Table 3). Although 4-chlorobenzaldehyde (**5a**) is known to give an epoxide[11] upon reaction with $P(MeNCH_2CH_2)_3N$, only α-hydroxy phosphonate ester **6a**[14] was obtained under the present conditions.

The presence of electron-withdrawing groups (Cl, CO_2Me, CF_3, and NO_2) on the benzaldehyde substrate led to the formation of the respective α-hydroxy phosphonate ester (Table 3, Entries 1–3). Upon reaction with

Table 2. Preparation of benzisoxazoles **4a**–**4h** by using $(EtO)_3P$–$ZnBr_2$ system.

Entry	Substrate	Product[a]	Yield (%)[b]
1			
	3a R^1 = H	**4a** R^1 = H	83
	3b R^1 = Br	**4b** R^1 = Br	80
2			
	3c R^1 = H	**4c** R^1 = H	80
	3d R^1 = Cl	**4d** R^1 = Cl	86
3			
	3e R^1 = Br, R^2 = H	**4e** R^1 = Br, R^2 = H	78
	3f R^1, R^2 = Br	**4f** R^1, R^2 = Br	75
4			
	3g R^1 = H	**4g** R^1 = H	90
	3h R^1 = OMe	**4h** R^1 = OMe	82

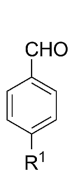
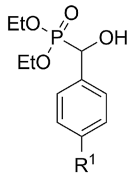
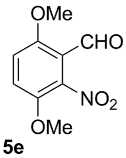
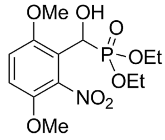
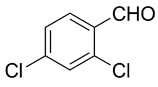
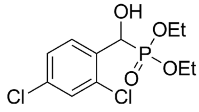
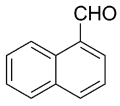
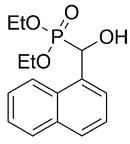
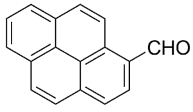
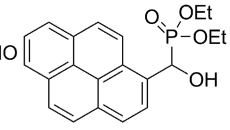
[a] Reagents and conditions: aldehyde **3a**–**3h** (1 equiv.), $P(OEt)_3$ (3 equiv.), and $ZnBr_2$ (10 mol-%) for 10–15 min. [b] Percent yield after column chromatography.

$P(MeNCH_2CH_2)_3N$, naphthalene-1-carbaldehyde (**5g**) and pyrene-1-carbaldehyde (**5h**) gave the respective epoxides[11]. However, only the corresponding α-hydroxy phosphonate esters **6g** and **6h** were obtained by using our triethyl phosphite–$ZnBr_2$ system.

A plausible mechanism for the formation of epoxide **2a**–**2l** from 2-nitrobenzaldehyde **1a**–**1l** (Scheme 3) begins with the attack of triethyl phosphite on the carbonyl oxygen atom followed by an intermolecular attack of the resulting carbanion with another molecule of the aldehyde to give intermediate **7**. Dioxaphospholane intermediate **7** can then undergo a $ZnBr_2$-mediated elimination of triethyl phosphate to afford *trans*-epoxide **2a**–**2p**. In the case of 4-nitrobenzaldehyde (**1q**), the reduced steric environment leads to the formation of a diastereomeric mixture of dioxaphospholane intermediate **8**, which affords a mixture of *cis*-epoxide **2q′** and *trans*-epoxide **2q**.

In the case of 2-nitrobenzaldehydes **3a**–**3h** that have substituents at the 6-position, the dioxaphospholane-type of adduct (i.e, **7**/**8**) cannot form because of steric effects. Hence, initially formed 1:1 adduct **9** undergoes an intramolecular cyclization followed by the elimination of triethyl phosphate to afford **11**. The oxygenated benzisoxazole **11** is reduced by treatment with triethyl phosphite to lead to products **4a**–**4h**. In the case of aryl aldehydes **5a**–**5h**, the

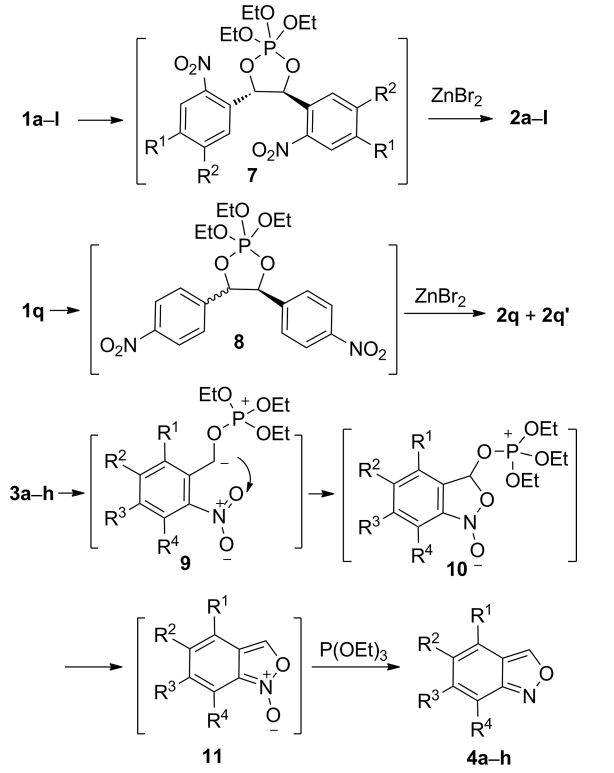
Table 3. Preparation of α-hydroxyphosphonates **6a–6h** by using triethyl phosphite–$ZnBr_2$ system.

Entry	Substrate	Product[a]	Yield (%)[b]
1			
	5a R^1 = Cl	**6a** R^1 = Cl	87
	5b R^1 = Br	**6b** R^1 = Br	85
	5c R^1 = CO_2Me	**6c** R^1 = CO_2Me	79
	5d R^1 = CF_3	**6d** R^1 = CF_3	68
2			
	5e	**6e**	79
3			
	5f	**6f**	91
4			
	5g	**6g**	81
5			
	5h	**6h**	83

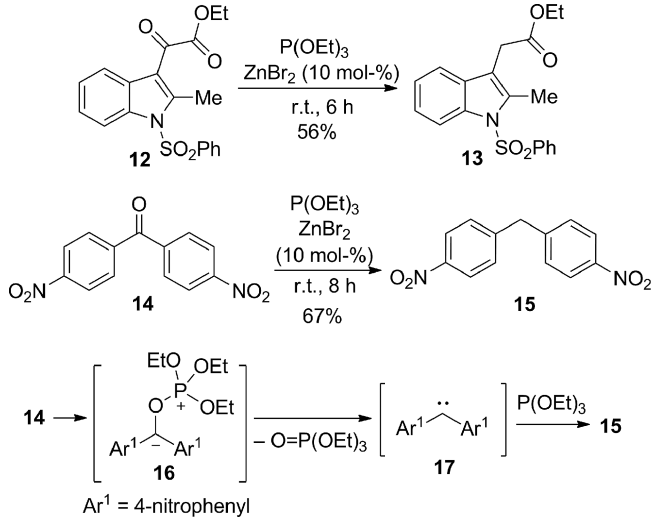
[a] Reagents and conditions: aldehyde **5a–5h** (1 equiv.), $P(OEt)_3$ (3 equiv.), and $ZnBr_2$ (10 mol-%) for 10–30 min. [b] Percent yield after column chromatography.

moderately electron-withdrawing substituents facilitate the attack of triethyl phosphite on the carbonyl carbon atom to afford α-hydroxy phosphonate esters **6a–6h**.

To further determine the mechanism for the deoxygenation, keto ester **12** was treated with 2.5 equiv. triethyl phosphite and $ZnBr_2$ (10 mol-%) at room temperature for 6 h. The usual workup followed by column chromatographic purification led to the isolation of reduction product **13** in 56% yield (Scheme 4). Under identical conditions, the reaction of bis(4-nitrophenyl)methanone (**14**)[16] with the $(EtO)_3$-P–$ZnBr_2$ system also led to the formation di(*p*-nitrophenyl)-methane (**15**) in 67% yield. As a representative case, the formation of reduction product **15** is proposed to occur through the formation of the carbene **17** intermediate, which upon reduction by a hydride transfer from triethyl phosphite followed by protonation during workup affords compound **15**.



Scheme 3. Plausible mechanism for deoxygenation of 2-nitrobenzaldehdyes.



Scheme 4. Deoxygenation of α-keto ester **12** and ketone **14** by using triethyl phosphite–$ZnBr_2$ system.

Conclusions

In summary, the reaction of aryl aldehydes with triethyl phosphite in the presence of $ZnBr_2$ as the catalyst led to the exclusive formation of *trans*-epoxides, benzisoxazoles, and α-hydroxy phosphonates, depending on the nature of the substituents on the starting aldehyde. Compared with the Liu and Verkade procedure[11] in which expensive $P(MeNCH_2CH_2)_3N$[17] was employed for the facile transformation of aryl aldehydes into *trans*-epoxides, the (EtO)

$_3$P–$ZnBr_2$ system reported herein is more advantageous. For the preparation of benzisoxazoles, the present procedure involves a double deoxygenation protocol and is more facile than literature methods.[18] The $(EtO)_3P$–$ZnBr_2$ mediated deoxygenation procedure that was reported herein for aryl aldehydes may find application in other systems[19] as well.

Experimental Section

General Methods: All the experiments were carried out under nitrogen, unless otherwise stated. The progress of all reactions was monitored by TLC analysis (ethyl acetate/hexanes). Column chromatography was carried out on silica gel (230–400 mesh, Merck) by increasing the polarity of the eluent. The ^{1}H, ^{13}C, and DEPT 135 NMR spectroscopic data were recorded at room temperature in $CDCl_3$ or [D_6]DMSO with a Bruker 300 MHz spectrometer. TMS was used as the internal standard. Chemical shift values are reported in parts per million (ppm), and coupling constants are reported in Hertz (Hz). Elemental analysis data was recorded on an Elementar Vario Series Analyzer instrument. HRMS was recorded on a JEOL GC Mate II (EI).

(A) General Procedures for the Preparation of Epoxides

I. Preparation of *trans*-Epoxide: To a mixture of the 2-nitro-substituted aryl aldehyde (1 equiv.) and triethyl phosphite (2 equiv.) was added $ZnBr_2$ (10 mol-%) at room temperature, and the resulting mixture was stirred at room temperature for 10–30 min (slightly exothermic). Upon the consumption of the starting material (monitored by TLC), the reaction mass was poured over crushed ice (50 g), and the resulting mixture was extracted with ethyl acetate (2× 15 mL). The combined organic extracts were washed with brine solution (2× 20 mL) and dried with Na_2SO_4. Removal of the solvent followed by trituration from methanol afforded the *trans*-epoxide.

II. Preparation of *cis*- and *trans*-Epoxide: To a mixture of the 4-substituted benzaldehyde (1 equiv.) and triethyl phosphite (2 equiv.) was added $ZnBr_2$ (10 mol-%) at room temperature, and the resulting mixture was stirred at room temperature for 30 min (slightly exothermic). Upon the consumption of the starting material (monitored by TLC), the reaction mass was poured over crushed ice (50 g), and the resulting mixture was extracted with ethyl acetate (2× 15 mL). The combined organic extracts were washed with brine solution (2× 20 mL) and dried with Na_2SO_4. Removal of the solvent followed by column chromatographic separation [5% ethyl acetate (EA) in hexane] afforded the *trans*-epoxide. Further elution of the column (10% ethyl acetate in hexane) furnished the *cis*-epoxide.

(2*S,3*S**)-2,3-Bis(2-nitrophenyl)oxirane (2a):** The reaction of 2-nitrobenzaldehyde (**1a**, 0.5 g, 3.30 mmol) with triethyl phosphite (1.09 g, 6.61 mmol) in the presence of $ZnBr_2$ (0.075 g, 0.330 mmol) at room temperature for 10 min followed by workup using general procedure I afforded *trans*-epoxide **2a** (0.38 g, 79%) as a colorless solid; m.p. 168–170 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.19 (d, J = 8.1 Hz, 2 H, ArH), 7.77–7.70 (m, 4 H, ArH), 7.56–7.51 (m, 2 H, ArH), 4.49 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 147.8, 134.4, 132.9, 129.0, 126.9, 125.0, 59.6 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 134.4, 129.0, 126.9, 125.0, 59.6 ppm. HRMS (EI): calcd. for $C_{14}H_{10}N_2O_5$ $[M]^+$ 286.0590; found 286.0590.

(2*S,3*S**)-2,3-Bis(4-chloro-2-nitrophenyl)oxirane (2b):** The reaction of 4-chloro-2-nitrobenzaldehyde (**1b**,[20] 0.5 g, 2.69 mmol) with triethyl phosphite (0.89 g, 5.39 mmol) in the presence of $ZnBr_2$ (0.06 g, 0.27 mmol) at room temperature for 10 min followed by workup using general procedure I afforded *trans*-epoxide **2b** (0.4 g, 83%) as a colorless solid; m.p. 160–162 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.24 (s, 2 H, ArH), 7.70 (s, 4 H, ArH), 4.44 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 148.1, 135.1, 134.5, 131.2, 128.2, 125.2, 59.2 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 134.5, 128.2, 125.2, 59.2 ppm. HRMS (EI): calcd. for $C_{14}H_8Cl_2N_2O_5$ $[M]^+$ 353.9810; found 353.9800.

(2*S,3*S**)-2,3-Bis(5-chloro-2-nitrophenyl)oxirane (2c):** The reaction of 5-chloro-2-nitrobenzaldehyde (**1c**,[21] 0.5 g, 2.69 mmol) with triethyl phosphite (0.89 g, 5.39 mmol) in the presence of $ZnBr_2$ (0.06 g, 0.269 mmol) at room temperature for 10 min followed by workup using general procedure I afforded *trans*-epoxide **2c** (0.38 g, 82%) as a colorless solid; m.p. 206–208 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.23 (d, J = 8.7 Hz, 2 H, ArH), 7.76 (d, J = 2.4 Hz, 2 H, ArH), 7.62–7.58 (m, 2 H, ArH), 4.54 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 144.9, 140.1, 133.6, 128.4, 126.0, 125.7, 58.0 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 128.3, 125.9, 125.6, 57.9 ppm. HRMS (EI): calcd. for $C_{14}H_8Cl_2N_2O_5$ $[M]^+$ 353.9810; found 353.9800.

(2*S,3*S**)-2,3-Bis(4-fluoro-2-nitrophenyl)oxirane (2d):** The reaction of 4-fluoro-2-nitrobenzaldehyde (**1d**,[20] 0.5 g, 2.95 mmol) with triethyl phosphite (0.98 g, 5.91 mmol) in the presence of $ZnBr_2$ (0.07 g, 0.29 mmol) at room temperature for 15 min followed by workup using general procedure I afforded *trans*-epoxide **2d** (0.38 g, 80%) as a colorless solid; m.p. 158–160 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96–7.93 (m, 2 H, ArH), 7.79–7.74 (m, 2 H, ArH), 7.49–7.43 (m, 2 H, ArH), 4.44 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 163.5, 160.2, 148.5, 128.9 (d, J = 7.5 Hz), 121.6 (d, J = 21.1 Hz), 112.7 (d, J = 27.1 Hz), 59.2 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 128.9 (d, J = 7.5 Hz), 121.6 (d, J = 21.1 Hz), 112.7 (d, J = 27.1 Hz), 59.2 ppm. HRMS (EI): calcd. for $C_{14}H_8F_2N_2O_5$ $[M]^+$ 322.0401; found 322.0400.

(2*S,3*S**)-2,3-Bis(5-fluoro-2-nitrophenyl)oxirane (2e):** The reaction of 5-fluoro-2-nitrobenzaldehyde (**1e**,[20] 0.5 g, 2.95 mmol) with triethyl phosphite (0.98 g, 5.91 mmol) in the presence of $ZnBr_2$ (0.07 g, 0.29 mmol) at room temperature for 20 min followed by workup using general procedure I afforded *trans*-epoxide **2e** (0.42 g, 88%) as a colorless solid; m.p. 158–160 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.32–8.27 (m, 2 H, ArH), 7.46–7.42 (m, 2 H, ArH), 7.27–7.19 (m, 2 H, ArH), 4.53 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 167.7, 164.3, 143.8, 136.5 (d, J = 9.0 Hz), 128.3 (d, J = 9.8 Hz), 116.2 (d, J = 24.1 Hz), 114.6 (d, J = 26.3 Hz), 59.4 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 128.3 (d, J = 9.8 Hz), 116.2 (d, J = 23.3 Hz), 114.6 (d, J = 25.6 Hz), 59.4 ppm. HRMS (EI): calcd. for $C_{14}H_8F_2N_2O_5$ $[M]^+$ 322.0401; found 322.0400.

(2*S,3*S**)-2,3-Bis(5-bromo-2-nitrophenyl)oxirane (2f):** The reaction of 5-bromo-2-nitrobenzaldehyde (**1f**,[22] 0.5 g, 2.17 mmol) with triethyl phosphite (0.72 g, 4.34 mmol) in the presence of $ZnBr_2$ (0.05 g, 0.21 mmol) at room temperature for 10 min followed by workup using general procedure I afforded *trans*-epoxide **2f** (0.39 g, 81%) as a colorless solid; m.p. 212–214 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (d, J = 9.0 Hz, 2 H, ArH), 7.89 (s, 2 H, ArH), 7.70–7.67 (m, 2 H, ArH), 4.50 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 146.5, 134.5, 132.4, 130.1, 129.9, 126.6, 59.1 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 132.4, 130.1, 126.6, 59.1 ppm. HRMS (EI): calcd. for $C_{14}H_8Br_2N_2O_5$ $[M]^+$ 441.8800; found 441.8800.

(2*S,3*S**)-2,3-Bis(5-methoxy-2-nitrophenyl)oxirane (2g):** The reaction of 5-methoxy-2-nitrobenzaldehyde (**1g**,[23] 0.5 g, 2.76 mmol)

with triethyl phosphite (0.91 g, 5.52 mmol) in the presence of $ZnBr_2$ (0.07 g, 0.27 mmol) at room temperature for 30 min followed by workup using general procedure I afforded *trans*-epoxide **2g** (0.39 g, 81%) as a colorless solid; m.p. 168–170 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.23 (d, J = 9.0 Hz, 2 H, ArH), 7.26–7.21 (m, 2 H, ArH), 6.97–6.94 (m, 2 H, ArH), 4.55 (s, 2 H, CH), 3.94 (s, 6 H, OCH_3) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 164.3, 140.7, 135.9, 127.7, 113.9, 111.2, 59.9, 55.9 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 127.8, 114.0, 111.3, 60.0, 56.1 ppm. HRMS (EI): calcd. for $C_{16}H_{14}N_2O_7$ $[M]^+$ 346.0801; found 346.0800. For single-crystal X-ray analysis of **2g**, all calculations were performed by using the SHELXL-97 program.[15] Crystal data of **2g**: $C_{16}H_{14}N_2O_7$, MW = 346.29 g mol^{-1}, triclinic crystal system, space group $P\bar{1}$, Z = 4, a = 8.3888(2) Å, b = 10.3595(2) Å, c = 18.7561(4) Å, α = 78.077(1)°, β = 86.902(1)°, γ = 78.219(1)°, V = 1561.10(6) Å^3, and $D_{calcd.}$ = 1.473 Mg m^{-3}. In total, 22756 independent reflections were collected, of which 4964 were considered as observed [$I > 2\sigma(I)$]. The structure was solved by direct methods and refined by full-matrix least-squares procedures to give a final R-value of 4.10%.

CCDC-1051703 (for **2g**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(2*S,3*S**)-2,3-Bis(4,5-dichloro-2-nitrophenyl)oxirane (2h):** The reaction of 4,5-dichloro-2-nitrobenzaldehyde (**1h**,[24] 0.5 g, 2.27 mmol) with triethyl phosphite (0.75 g, 4.54 mmol) in the presence of $ZnBr_2$ (0.05 g, 0.22 mmol) at room temperature for 10 min followed by workup using general procedure I afforded *trans*-epoxide **2h** (0.43 g, 89%) as a colorless solid; m.p. 193–195 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.36 (s, 2 H, ArH), 7.83 (s, 2 H, ArH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 145.8, 139.9, 133.8, 132.2, 128.7, 127.2, 58.9 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 128.7, 127.2, 58.9 ppm. HRMS (EI): calcd. for $C_{14}H_6Cl_4N_2O_5$ $[M]^+$ 421.9031; found 421.9000.

(2*S,3*S**)-2,3-Bis(4-chloro-5-fluoro-2-nitrophenyl)oxirane (2i):** The reaction of 4-chloro-5-fluoro-2-nitrobenzaldehyde (**1i**,[25] 0.5 g, 2.45 mmol) with triethyl phosphite (0.81 g, 4.91 mmol) in the presence of $ZnBr_2$ (0.06 g, 0.24 mmol) at room temperature for 10 min followed by workup using general procedure I afforded *trans*-epoxide **2i** (0.43 g, 90%) as a colorless solid; m.p. 158–160 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.37 (d, J = 6.6 Hz, 2 H, ArH), 7.52 (d, J = 9.0 Hz, 2 H, ArH), 4.45 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 163.4, 159.9, 143.5, 134.2 (d, J = 8.2 Hz), 128.5, 122.3 (d, J = 19.6 Hz), 115.1 (d, J = 24.8 Hz), 59.1 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 128.5, 115.1 (d, J = 24.8 Hz), 59.1 ppm. HRMS (EI): calcd. for $C_{14}H_6Cl_2F_2N_2O_5$ $[M]^+$ 389.9622; found 389.9600.

(2*S,3*S**)-2,3-Bis(5-chloro-4-fluoro-2-nitrophenyl)oxirane (2j):** The reaction of 5-chloro-4-fluoro-2-nitrobenzaldehyde (**1j**,[25] 0.5 g, 2.45 mmol) with triethyl phosphite (0.81 g, 4.91 mmol) in the presence of $ZnBr_2$ (0.06 g, 0.24 mmol) at room temperature for 10 min followed by workup using general procedure I afforded *trans*-epoxide **2j** (0.44 g, 92%) as a colorless solid; m.p. 175–177 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07 (d, J = 8.1 Hz, 2 H, ArH), 7.82 (d, J = 7.2 Hz, 2 H, ArH), 4.47 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 159.0, 155.6, 146.1 (d, J = 7.5 Hz), 129.7 (d, J = 3.4 Hz), 129.2, 128.8 (d, J = 17.8 Hz), 114.0 (d, J = 26.4 Hz), 58.9 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 129.2, 114.0 (d, J = 26.4 Hz), 58.9 ppm. HRMS (EI): calcd. for $C_{14}H_6Cl_2F_2N_2O_5$ $[M]^+$ 389.9622; found 389.9600.

(2*S,3*S**)-2,3-Bis(5-bromo-4-fluoro-2-nitrophenyl)oxirane (2k):** The reaction of 5-bromo-4-fluoro-2-nitrobenzaldehyde (**1k**,[26] 0.5 g, 2.01 mmol) with triethyl phosphite (0.67 g, 4.03 mmol) in the presence of $ZnBr_2$ (0.05 g, 0.20 mmol) at room temperature for 10 min followed by workup using general procedure I afforded *trans*-epoxide **2k** (0.42 g, 87%) as a colorless solid; m.p. 178–180 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02–7.96 (m, 4 H, ArH), 4.46 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 160.2, 156.8, 146.9 (d, J = 7.1 Hz), 132.1, 129.7 (d, J = 4.70 Hz), 117.2 (d, J = 21.1 Hz), 113.6 (d, J = 27.6 Hz), 58.8 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 132.1, 113.6 (d, J = 27.9 Hz), 58.8 ppm. HRMS (EI): calcd. for $C_{14}H_6Br_2F_2N_2O_5$ $[M]^+$ 477.8612; found 477.8600.

(2*S,3*S**)-2,3-Bis(6-nitrobenzo[*d*][1,3]dioxol-5-yl)oxirane (2l):** The reaction of 6-nitrobenzo[*d*][1,3]dioxole-5-carbaldehyde (**1l**,[27] 0.5 g, 2.56 mmol) with triethyl phosphite (0.85 g, 5.12 mmol) in the presence of $ZnBr_2$ (0.06 g, 0.25 mmol) at room temperature for 25 min followed by workup using general procedure I afforded *trans*-epoxide **2l** (0.38 g, 79%) as a colorless solid; m.p. 172–174 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69 (s, 1 H, ArH), 7.13 (s, 1 H, ArH), 6.16 (s, 2 H, -OCH_2O-), 4.45 (s, 1 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 152.9, 147.8, 130.4, 105.8, 105.7, 103.2, 59.8 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 105.8, 105.7, 103.2, 59.9 ppm. HRMS (EI): calcd. for $C_{16}H_{10}N_2O_9$ $[M]^+$ 374.0386; found 374.0380.

(2*S,3*S**)-2,3-Bis(3,5-dichloro-2-nitrophenyl)oxirane (2m):** The reaction of 3,5-dichloro-2-nitrobenzaldehyde (**1m**,[28] 0.5 g, 2.27 mmol) with triethyl phosphite (0.75 g, 4.54 mmol) in the presence of $ZnBr_2$ (0.05 g, 0.22 mmol) at room temperature for 10 min followed by workup using general procedure I gave *trans*-epoxide **2m** (0.36 g, 75%) as a colorless solid; m.p. 228–230 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55 (d, J = 2.1 Hz, 2 H, ArH), 7.37 (d, J = 2.1 Hz, 2 H, ArH), 3.90 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 144.8, 135.9, 130.5, 129.2, 125.1, 124.0, 55.6 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 131.0, 124.7, 57.5 ppm. HRMS (EI): calcd. for $C_{14}H_6Cl_4N_2O_5$ $[M]^+$ 421.9031; found 421.9000.

(2*S,3*S**)-2,3-Bis(2,4-dinitrophenyl)oxirane (2n):** The reaction of 2,4-dinitrobenzaldehyde (**1n**, 0.5 g, 2.54 mmol) with triethyl phosphite (0.84 g, 5.09 mmol) in the presence of $ZnBr_2$ (0.06 g, 0.25 mmol) at room temperature for 10 min followed by workup using general procedure I gave *trans*-epoxide **2n** (0.41 g, 85%) as a colorless solid; m.p. 160–162 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.91 (s, 2 H, ArH), 8.69 (d, J = 7.2 Hz, 2 H, ArH), 7.99 (d, J = 7.8 Hz, 2 H, ArH), 4.77 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 145.8, 145.5, 136.5, 127.0, 126.8, 118.3, 57.1 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 127.0, 126.8, 118.3, 57.1 ppm. HRMS (EI): calcd. for $C_{14}H_8N_4O_9$ $[M]^+$ 376.0291; found 376.0290.

(2*S,3*S**)-2,3-Bis(2,6-dichloro-3-nitrophenyl)oxirane (2o):** The reaction of 2,6-dichloro-3-nitrobenzaldehyde (**1o**,[29] 0.5 g, 2.27 mmol) with triethyl phosphite (0.75 g, 4.54 mmol) in the presence of $ZnBr_2$ (0.05 g, 0.22 mmol) at room temperature for 30 min followed by workup using general procedure I gave *trans*-epoxide **2o** (0.35 g, 73%) as a colorless solid; m.p. 175–177 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.79 (d, J = 8.4 Hz, 2 H, ArH), 7.55 (d, J = 8.4 Hz, 2 H, ArH), 4.76 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 148.0, 139.6, 134.1, 129.4, 129.0, 125.7, 58.2 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 129.4, 125.7, 58.2 ppm. HRMS (EI): calcd. for $C_{14}H_6Cl_4N_2O_5$ $[M]^+$ 421.9031; found 421.9031.

2,5-Dibromo-4-nitrobenzaldehyde (1p): To a solution of 4-nitrobenzaldehyde (0.5 g, 3.30 mmol) in concentrated H_2SO_4 (10 mL) was added *N*-bromosuccinimide (NBS, 1.90 g, 6.61 mmol) at 0 °C for 10 min, and the reaction mixture was warmed to room temperature and stirred for 3 h. Upon consumption of the starting material

(monitored by TLC), the reaction mass was poured over crushed ice (50 g), and the resulting mixture was extracted with ethyl acetate (2× 15 mL). The combined organic extracts were washed with brine solution (2× 20 mL) and dried with Na_2SO_4. Removal of the solvent followed by column chromatographic purification afforded 2,5-dibromo-4-nitrobenzaldehyde (**1p**, 0.98 g, 96%) as a yellow solid; m.p. 100–102 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.30 (s, 1 H, CHO), 8.20 (s, 1 H, ArH), 8.09 (s, 1 H, ArH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 188.5, 152.6, 135.9, 130.4, 124.9, 113.9 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 188.5, 135.9, 130.4 ppm. $C_7H_3Br_2NO_3$ (308.91): calcd. C 27.22, H 0.98, N 4.53; found C 27.45, H 1.23, N 4.78.

(2*S,3*S**)-2,3-Bis(2,5-dibromo-4-nitrophenyl)oxirane (2p):** The reaction of 2,5-dibromo-4-nitrobenzaldehyde (**1p**, 0.5 g, 1.61 mmol) with triethyl phosphite (0.53 g, 3.23 mmol) in the presence of $ZnBr_2$ (0.04 g, 0.16 mmol) at room temperature for 10 min followed by workup using general procedure I afforded *trans*-epoxide **2p** (0.41 g, 84%) as a colorless solid; m.p. 242–244 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.21 (s, 2 H, ArH), 7.75 (s, 2 H, ArH), 4.17 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 154.4, 145.8, 137.0, 134.1, 126.1, 118.5, 65.4 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 131.7, 128.9, 60.2 ppm. HRMS (EI): calcd. for $C_{14}H_6Br_4N_2O_5$ $[M]^+$ 597.7010; found 597.7010.

(2*S,3*S**)-2,3-Bis(4-nitrophenyl)oxirane (2q):** The reaction of 4-nitrobenzaldehyde (**1q**, 0.5 g, 3.30 mmol) with triethyl phosphite (1.09 g, 6.61 mmol) in the presence of $ZnBr_2$ (0.08 g, 0.33 mmol) at room temperature for 30 min followed by workup using general procedure II afforded of *trans*-epoxide **2q** (0.25 g, 53%) as a colorless solid; m.p. 214–216 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, J = 7.2 Hz, 4 H, ArH), 7.37 (d, J = 7.2 Hz, 4 H, ArH), 4.53 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 147.6, 140.7, 127.5, 123.4, 59.0 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 127.5, 123.4, 59.0 ppm. HRMS (EI): calcd. for $C_{14}H_{10}N_2O_5[M]^+$ 286.0590; found 286.0580.

(2*S,3*R**)-2,3-Bis(4-nitrophenyl)oxirane (2q′):** The reaction of 4-nitrobenzaldehyde (**1q**, 0.5 g, 3.30 mmol) with triethyl phosphite (1.09 g, 6.61 mmol) in the presence of $ZnBr_2$ (0.08 g, 0.33 mmol) at room temperature for 30 min followed by workup using general procedure II afforded *cis*-epoxide **2q′** (0.15 g, 32%) as a colorless solid; m.p. 172–174 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.26 (d, J = 8.4 Hz, 4 H, ArH), 7.53 (d, J = 8.4 Hz, 4 H, ArH), 3.97 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 148.2, 143.2, 126.4, 124.0, 62.0 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 126.3, 124.0, 62.0 ppm. $C_{14}H_{10}N_2O_5$ (286.24): calcd. C 58.74, H 3.52, N 9.79; found C 59.01, H 3.75, N 9.51. For single-crystal X-ray analysis of **2q′**, all calculations were performed by using the SHELXL-97 program.[15] Crystal data of **2q′**: $C_{14}H_{10}N_2O_5$, MW = 286.24 g mol^{-1}, monoclinic crystal system, space group $P21/c$, Z = 4, a = 7.600(5) Å, b = 21.916(5) Å, c = 7.771(5) Å, α = 90(5)°, β = 98.829(5)°, γ = 90(5)°, V = 1279.0(12) Å^3, and $D_{calcd.}$ = 1.487 Mg m^{-3}. In total, 12043 independent reflections were collected, of which 2211 were considered as observed [$I > 2\sigma(I)$]. The structure was solved by direct methods and refined by full-matrix least-squares procedures to give a final R value of 4.3%.

CCDC-1051697 (for **2q′**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

4,4′-[(2*S,3*S**)-Oxirane-2,3-diyl]dibenzonitrile (2r):** The reaction of 4-formylbenzonitrile (**1r**, 0.5 g, 3.81 mmol) with triethyl phosphite (1.2 g, 7.62 mmol) in the presence of $ZnBr_2$ (0.08 g, 0.38 mmol) at room temperature for 30 min followed by workup using general procedure II gave *trans*-epoxide **2r** (0.23 g, 50%) as a colorless solid; m.p. 178–180 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50 (d, J = 7.8 Hz, 4 H, ArH), 7.27 (d, J = 8.1 Hz, 4 H, ArH), 4.45 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 138.8, 131.9, 127.3, 118.3, 112.0, 59.1 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 131.9, 127.3, 59.1 ppm. HRMS (EI): calcd. for $C_{16}H_{10}N_2O$ $[M]^+$ 246.0793; found 246.0790.

4,4′-[(2*S,3*R**)-Oxirane-2,3-diyl]dibenzonitrile (2r′):** The reaction of 4-formylbenzonitrile (**1r**, 0.5 g, 3.81 mmol) with triethyl phosphite (1.2 g, 7.62 mmol) in the presence of $ZnBr_2$ (0.08 g, 0.38 mmol) at room temperature for 30 min followed by workup using general procedure II afforded *cis*-epoxide **2r′** (0.14 g, 30%) as a colorless solid; m.p. 178–180 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70 (d, J = 7.8 Hz, 4 H, ArH), 7.45 (d, J = 8.1 Hz, 4 H, ArH), 3.89 (s, 2 H, CH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 141.4, 132.5, 126.2, 118.4, 112.5, 62.2 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 132.6, 126.2, 62.2 ppm. $C_{16}H_{10}N_2O$ (246.26): calcd. C 78.03, H 4.09, N 11.38; found C 77.81, H 3.87, N 11.61.

(B) General Procedure for the Preparation of Benzisoxazoles and Hydroxy Phosphonate Esters: To a mixture of the 4-substituted benzaldehyde (1 equiv.) and triethyl phosphite (3 equiv.) was added $ZnBr_2$ (10 mol-%) at room temperature. The reaction mixture was stirred at room temperature for 10–15 min (slightly exothermic). Upon the consumption of the starting material (monitored by TLC), the reaction mass was poured over crushed ice (50 g), and the resulting mixture was extracted with ethyl acetate (2× 15 mL). The combined organic extracts were washed with brine solution (2× 20 mL) and dried with Na_2SO_4. Removal of the solvent followed by column chromatographic purification (for benzisoxazole, 5% EA in hexane; for hydroxy phosphonate ester, 30% EA in hexane) afforded the respective product in the reported yield.

4-Methylbenzo[*c*]isoxazole (4a): The reaction of 2-methyl-6-nitrobenzaldehyde (**3a**,[30] 0.5 g, 3.02 mmol) with triethyl phosphite (1.5 g, 9.08 mmol) in the presence of $ZnBr_2$ (0.07 g, 0.30 mmol) at room temperature for 10 min followed by workup using general procedure B afforded 4-methylbenzo[*c*]isoxazole (**4a**, 0.33 g, 83%) as a thick liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.11 (s, 1 H, ArH), 7.45 (d, J = 9.0 Hz, 1 H, ArH), 7.22–7.19 (m, 1 H, ArH), 6.75 (d, J = 6.3 Hz, 1 H, ArH), 2.50 (s, 3 H, Me) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 156.4, 153.5, 131.3, 130.2, 122.9, 120.2, 112.3, 19.2 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 153.5, 131.3, 122.9, 112.3, 19.2 ppm. HRMS (EI): calcd. for C_8H_7NO $[M]^+$ 133.0528; found 133.0528.

4-Bromo-2-methyl-6-nitrobenzaldehyde (3b): To a solution of 1,2-dimethyl-3-nitrobenzene (2 g, 13.26 mmol) in concentrated H_2SO_4 (10 mL) was added NBS (2.60 g, 14.55 mmol) at 0 °C for 10 min, and the reaction mixture was warmed to room temperature and stirred for 3 h. Upon consumption of the starting material (monitored by TLC), the reaction mass was poured over crushed ice (50 g), and the resulting mixture was extracted with ethyl acetate (2× 15 mL). The combined organic extracts were washed with brine solution (2× 20 mL) and dried with Na_2SO_4. Removal of the solvent afforded 5-bromo-1,2-dimethyl-3-nitrobenzene (2.0 g, 67%). The crude product was used in the next step without any further characterization. To a stirred solution of 5-bromo-1,2-dimethyl-3-nitrobenzene (2.0 g, 8.7 0 mmol) in *N*,*N*-dimethylformamide (DMF, 8 mL) was added *N*,*N*-dimethylformamide dimethyl acetal (DMF·DMA, 3.10 g, 26.1 mmol). The reaction mixture was stirred at 100 °C for 12 h. The dark reaction mixture was then cooled to room temperature and added quickly to a rapidly stirred solution of $NaIO_4$ (7.5 g, 34.79 mmol) in H_2O (10 mL) and DMF (10 mL) at 0 °C. The reaction flask was rinsed with DMF (5 mL)

at 0 °C, and the resulting solution was added to the $NaIO_4$ mixture. The reaction mixture was stirred at room temp. for 5 h followed by filtration and rinsing with toluene (60 mL). The filtrate was then washed with H_2O (3 × 25 mL) and brine solution (3 × 25 mL). The extract was dried with Na_2SO_4 and then concentrated. Purification by flash chromatography (silica gel, 5–10% ethyl acetate/hexanes) led to the isolation of 4-bromo-2-methyl-6-nitrobenzaldehyde (**3b**, 1.5 g, 70% for two steps) as a brown solid; m.p. 88–90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.19 (s, 1 H, CHO), 8.01 (s, 1 H, ArH), 7.66 (s, 1 H, ArH), 2.41 (s, 3 H, Me) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 189.1, 149.5, 141.3, 139.5, 134.9, 130.5, 125.1, 19.6 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 189.2, 139.5, 125.1, 19.6 ppm. $C_8H_6BrNO_3$ (244.04): calcd. C 39.37, H 2.48, N 5.74; found C 39.57, H 2.62, N 5.92.

6-Bromo-4-methylbenzo[*c*]isoxazole (4b): The reaction of 4-bromo-2-methyl-6-nitrobenzaldehyde (**3b**, 0.5 g, 2.05 mmol) with triethyl phosphite (1.0 g, 6.14 mmol) in the presence of $ZnBr_2$ (0.05 g, 0.20 mmol) at room temperature for 10 min followed by workup using general procedure B gave 6-bromo-4-methylbenzo[*c*]isoxazole (**4b**, 0.33 g, 80%) as a brown solid; m.p. 55–57 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.0 (s, 1 H, ArH), 7.59 (s, 1 H, ArH), 6.78 (s, 1 H, ArH), 2.41 (s, 3 H, Me) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 156.7, 154.3, 127.1, 126.1, 118.9, 118.4, 114.4, 18.9 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 154.3, 127.1, 114.4, 18.9 ppm. HRMS (EI): calcd. for C_8H_6BrNO $[M]^+$ 210.9633; found 210.9633.

4-Chlorobenzo[*c*]isoxazole (4c): The reaction of 2-chloro-6-nitrobenzaldehyde (**3c**,[31] 0.5 g, 2.70 mmol) with triethyl phosphite (1.3 g, 8.08 mmol) in the presence of $ZnBr_2$ (0.06 g, 0.27 mmol) at room temperature for 10 min followed by workup using general procedure B afforded 4-chlorobenzo[*c*]isoxazole (**4c**, 0.33 g, 80%) as a thick liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.19 (s, 1 H, ArH), 7.52 (d, J = 9.0 Hz, 1 H, ArH), 7.21 (t, J = 7.9 Hz, 1 H, ArH), 6.98 (d, J = 7.2 Hz, 1 H, ArH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 156.4, 154.7, 130.9, 125.1, 123.1, 119.2, 113.6 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 154.8, 131.1, 123.2, 113.7 ppm. HRMS (EI): calcd. for C_7H_4ClNO $[M]^+$ 152.9981; found 152.9981.

4,5-Dichlorobenzo[*c*]isoxazole (4d): The reaction of 2,3-dichloro-6-nitrobenzaldehyde (**3d**,[31] 0.5 g, 2.20 mmol) with triethyl phosphite (1.13 g, 6.82 mmol) in the presence of $ZnBr_2$ (0.05 g, 0.22 mmol) at room temperature for 10 min followed by workup using general procedure B gave 4,5-dichlorobenzo[*c*]isoxazole (**4d**, 0.37 g, 86%) as a colorless solid; m.p. 98–100 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.17 (s, 1 H, ArH), 7.51 (d, J = 9.3 Hz, 1 H, ArH), 7.29 (d, J = 9.3 Hz, 1 H, ArH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 155.1, 154.8, 133.4, 127.8, 122.2, 119.8, 115.0 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 154.8, 133.4, 115.0 ppm. HRMS (EI): calcd. for $C_7H_3Cl_2NO$ $[M]^+$ 186.9592; found 186.9592.

Bromoaldehyde 3e and Dibromoaldehyde 3f: To a solution of 6-nitrobenzo[*d*][1,3]dioxole-5-carbaldehyde (1 g, 5.12 mmol) in concentrated H_2SO_4 (8 mL) was added NBS (1.82 g, 10.25 mmol) at 0 °C for 10 min, and the reaction mixture was warmed to room temperature and stirred for 3 h. Upon consumption of the starting material (monitored by TLC), the reaction mass was poured over crushed ice (100 g), and the resulting mixture was extracted with ethyl acetate (2 × 15 mL). The combined organic extracts were washed with brine solution (2 × 30 mL) and dried with Na_2SO_4. Removal of the solvent in vacuo afforded a mixture of bromoaldehyde **3e** and dibromoaldehyde **3f**. The crude residue was triturated from hot methanol, and the resulting mixture was filtered to separate the insoluble bromoaldehyde **3e** as a brown solid (0.56 g, 40%). The filtrate, which contained dibromoaldehyde **3f**, was concentrated and dried. Crude dibromoaldehyde **3f** (0.54 g, 30%) was used without any further characterization in the epoxidation reaction. Data for bromoaldehyde **3e**: m.p. 128–130 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.04 (s, 1 H, CHO), 7.42 (s, 1 H, ArH), 6.21 (s, 2 H, -OCH_2O) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 187.0, 151.4, 149.09, 143.8, 129.3, 104.1, 103.9, 99.8 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 187.0, 104.1, 103.9 ppm. $C_8H_4BrNO_5$ (274.02): calcd. C 35.06, H 1.47, N 5.11; found C 35.25, H 1.65, N 5.30.

4-Bromo-5,6-methylenedioxybenzo[*c*]isoxazole (4e): The reaction of 4-bromo-6-nitrobenzo[*d*][1,3]dioxole-5-carbaldehyde (**3e**, 0.5 g, 1.82 mmol) with triethyl phosphite (0.9 g, 5.47 mmol) in the presence of $ZnBr_2$ (0.04 g, 0.18 mmol) at room temperature for 10 min followed by workup using the general procedure B afforded 4-bromo-5,6-methylenedioxybenzo[*c*]isoxazole (**4e**, 0.35 g, 78%) as a brown solid; m.p. 150–152 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.83 (s, 1 H, ArH), 6.79 (s, 1 H, ArH), 6.09 (s, 2 H, -OCH_2O-) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 154.8, 153.3, 152.8, 145.7, 117.9, 102.2, 89.1, 84.2 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 513.3, 102.2, 89.1 ppm. HRMS (EI): calcd. for $C_8H_4BrNO_3$ $[M]^+$ 240.9375; found 240.9375. For single-crystal X-ray analysis of **4e**, all calculations were performed by using the SHELXL-97 program.[15] Crystal data of **4e**: $C_8H_4BrNO_3$, MW = 242.03 g mol^{-1}, triclinic crystal system, space group $P\bar{1}$, Z = 2, a = 7.3213(3) Å, b = 8.1203(3) Å, c = 8.1385(3) Å, α = 101.875(2)°, β = 116.393(2)°, γ = 101.106(2)°, V = 401.23(3) Å^3, and $D_{calcd.}$ = 2.003 Mg m^{-3}. In total, 5431 independent reflections were collected, of which 1309 were considered as observed [$I > 2\sigma(I)$]. The structure was solved by direct methods and refined by full-matrix least-squares procedures to give a final R-value of 6.10%.

CCDC-1051260 (for **4e**) contains the supplementary crystallographic data this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

4,7-Dibromo-5,6-methylenedioxybenzo[*c*]isoxazole (4f): The reaction of 4,7-dibromo-6-nitrobenzo[*d*][1,3]dioxole-5-carbaldehyde (**3f**, 0.5 g, 1.41 mmol) with triethyl phosphite (0.7 g, 4.25 mmol) in the presence of $ZnBr_2$ (0.03 g, 0.14 mmol) at room temperature for 15 min followed by workup using general procedure B afforded 4,7-dibromo-5,6-methylenedioxybenzo[*c*]isoxazole (**4f**, 0.34 g, 75%) as a brown solid; m.p. 206–208 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.86 (s, 1 H, ArH), 6.09 (s, 2 H, -OCH_2O-) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 154.9, 154.0, 150.7, 145.4, 117.9, 102.7, 83.8, 81.8 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 154.9, 102.8 ppm. HRMS (EI): calcd. for $C_8H_3Br_2NO_3$ $[M]^+$ 318.8480; found 318.8480.

4,7-Dibromobenzo[*c*]isoxazole (4g): The reaction of 3,6-dibromo-2-nitrobenzaldehyde (**3g**,[32] 0.5 g, 1.61 mmol) with triethyl phosphite (0.80 g, 4.85 mmol) in the presence of $ZnBr_2$ (0.04 g, 0.16 mmol) at room temperature for 15 min followed by workup using general procedure B afforded 4,7-dibromobenzo[*c*]isoxazole (**4g**, 0.41 g, 90%) as a colorless solid; m.p. 140–142 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.28 (s, 1 H, ArH), 7.42 (d, J = 7.5 Hz, 1 H, ArH), 7.09 (d, J = 7.5 Hz, 1 H, ArH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 157.8, 155.3, 133.9, 127.4, 121.3, 111.9, 108.1 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 157.8, 133.9, 127.4 ppm. HRMS (EI): calcd. for $C_7H_3Br_2NO$ $[M]^+$ 274.8581; found 274.8581.

4,7-Dibromo-5,6-dimethoxybenzo[*c*]isoxazole (4h): The reaction of 2,5-dibromo-3,4-dimethoxy-6-nitrobenzaldehyde (**3h**,[33] 0.5 g, 1.35 mmol) with triethyl phosphite (0.67 g, 4.06 mmol) in the presence of $ZnBr_2$ (0.03 g, 0.14 mmol) at room temperature for 10 min followed by workup using general procedure B afforded 4,7-di-

bromo-5,6-dimethoxybenzo[*c*]isoxazole (**4h**, 0.37 g, 82%) as a colorless solid; m.p. 84–86 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.06 (s, 1 H, ArH), 3.92 (s, 3 H, -OCH_3), 3.83 (s, 3 H, -OCH_3) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 157.0, 155.6, 153.5, 149.9, 118.2, 102.9, 99.9, 61.4 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 157.0, 61.4 ppm. HRMS (EI): calcd. for $C_9H_7Br_2NO_3$ $[M]^+$ 334.8793; found 334.8793.

Methyl 4-[(Diethoxyphosphoryl)(hydroxy)methyl]benzoate (6c): The reaction of methyl 4-formylbenzoate (**5c**, 0.5 g, 3.04 mmol) with triethyl phosphite (1.5 g, 9.14 mmol) in the presence of $ZnBr_2$ (0.07 g, 0.30 mmol) at room temperature for 20 min followed by workup using general procedure B afforded methyl 4-[(diethoxyphosphoryl)(hydroxy)methyl]benzoate (**6c**, 0.72 g, 79%) as a colorless solid; m.p. 106–108 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.01 (d, J = 7.8 Hz, 2 H, ArH), 7.56 (d, J = 7.8 Hz, 2 H, ArH), 5.10 (d, J = 12.6 Hz, 1 H, CH), 4.04 (q, J = 6.7 Hz, 4 H, -OCH_2), 3.91 (s, 3 H, OCH_3), 1.27–1.20 (m, 6 H, CH_3) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 166.8, 142.1 (d, J = 3.7 Hz), 129.4, 129.2, 126.8 (d, J = 5.2 Hz), 70.3 (d, J = 149.3 Hz), 63.4 (d, J = 7.5 Hz), 63.0 (d, J = 7.5 Hz), 51.9, 51.9, 16.2 (d, J = 6.0 Hz) ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 129.5, 126.8 (d, J = 5.2 Hz), 70.27 (d, J = 159.0 Hz), 63.48 (d, J = 7.5 Hz), 63.0 (d, J = 7.5 Hz), 51.9, 16.2 (d, J = 6.0 Hz) ppm. HRMS (EI): calcd. for $C_{13}H_{19}O_6P$ $[M]^+$ 302.0919; found 302.0910.

Diethyl Hydroxy[4-(trifluoromethyl)phenyl]methylphosphonate (6d): The reaction of 4-(trifluoromethyl)benzaldehyde (**5d**, 0.5 g, 2.87 mmol) with triethyl phosphite (1.4 g, 8.61 mmol) in the presence of $ZnBr_2$ (0.07 g, 0.28 mmol) at room temperature for 20 min followed by workup using general procedure B afforded diethyl hydroxy[4-(trifluoromethyl)phenyl]methylphosphonate (**6d**, 0.60 g, 68%) as a colorless solid; m.p. 150–152 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.59 (s, 4 H, ArH), 5.11 (d, J = 12 Hz, 1 H, CH), 4.97 (s, 1 H, OH), 4.06–4.05 (m, 4 H, -OCH_2), 1.27–1.20 (m, 6 H, -CH_3) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 141.0, 129.9 (d, J = 35.4 Hz), 127.3 (d, J = 5.2 Hz), 125.9, 124.9 (d, J = 3.0 Hz), 122.2, 70.0 (d, J = 159.8 Hz), 63.5 (q, J = 7.1 Hz), 16.3 (d, J = 4.5 Hz) ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 127.3 (d, J = 5.2 Hz), 125.0, 124.9 (d, J = 3.0 Hz), 70.0 (d, J = 159.8 Hz), 63.5 (q, J = 7.1 Hz), 16.3 (d, J = 4.5 Hz) ppm. $C_{12}H_{16}F_3O_4P$ (312.22): calcd. C 46.16, H 5.17; found C 46.39, H 4.95.

Diethyl (3,6-Dimethoxy-2-nitrophenyl)(hydroxy)methylphosphonate (6e): The reaction of 3,6-dimethoxy-2-nitrobenzaldehyde (**5e**,[34] 0.5 g, 2.36 mmol) with triethyl phosphite (1.2 g, 7.10 mmol) in the presence of $ZnBr_2$ (0.05 g, 0.23 mmol) at room temperature for 10 min followed by workup using general procedure B gave diethyl (3,6-dimethoxy-2-nitrophenyl)(hydroxy)methylphosphonate (**6e**, 0.65 g, 79%) as a colorless solid; m.p. 172–174 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.99 (s, 2 H, ArH), 5.14 (d, J = 17.1 Hz, 1 H, CH), 4.40 (s, 1 H, OH), 4.45–3.97 (m, 4 H, -OCH_2), 3.91 (s, 3 H, -OMe), 3.83 (s, 3 H, -OMe), 1.32 (t, J = 7.05 Hz, 3 H, CH_3), 1.20 (t, J = 7.05 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 151.6 (d, J = 3.77 Hz), 145.1, 140.9, 119.2, 113.6, 113.0, 66.4 (d, J = 161.3 Hz), 63.1 (t, J = 6.78 Hz), 56.9 (d, J = 3.77 Hz), 16.3 (q, J = 6.0 Hz) ppm. DEPT-135 (75 MHz, $CDCl_3$): δ = 113.6, 113.0, 66.4 (d, J = 161.3 Hz), 63.1 (t, J = 6.78 Hz), 56.9 (d, J = 3.77 Hz), 16.3 (q, J = 6.0 Hz) ppm. HRMS (EI): calcd. for $C_{13}H_{20}NO_8P$ $[M]^+$ 349.0927; found 349.0920.

Diethyl Hydroxy(naphthalen-1-yl)methylphosphonate (6g): The reaction of 1-naphthaldehyde (**5g**, 0.5 g, 3.20 mmol) with triethyl phosphite (1.6 g, 9.60 mmol) in the presence of $ZnBr_2$ (0.07 g, 0.32 mmol) at room temperature for 30 min followed by workup using general procedure B afforded diethyl hydroxy(naphthalen-1-yl)methylphosphonate (**6g**, 0.77 g, 81%) as a colorless solid; m.p. 108–110 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07–8.04 (m, 1 H, ArH), 7.90–7.77 (m, 3 H, ArH), 7.50–7.45 (m, 3 H, ArH), 5.85 (d, J = 9.6 Hz, 1 H, CH), 4.95 (s, 1 H, OH), 4.04–3.73 (m, 4 H, -OCH_2), 1.14 (t, J = 7.05 Hz, 3 H, CH_3), 1.02 (t, J = 7.05 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 133.5, 133.0 (d, J = 1.43 Hz), 130.8 (d, J = 6.0 Hz), 128.5, 128.4, 125.8, 125.5, 125.4, 125.2 (d, J = 3.3 Hz), 123.7, 67.1 (d, J = 161.3 Hz), 63.2 (q, J = 7.54 Hz), 16.2 (q, J = 5.65 Hz) ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 128.5, 128.4, 125.8, 125.6, 125.5, 125.4, 125.3, 125.2, 123.7, 67.1 (d, J = 161.3 Hz), 63.2 (q, J = 7.54 Hz), 16.2 (q, J = 5.65 Hz) ppm. HRMS (EI): calcd. for $C_{15}H_{19}O_4P$ $[M]^+$ 294.1021; found 294.1020.

Diethyl (3a1,8-Dihydropyren-1-yl)(hydroxy)methylphosphonate (6h): The reaction of pyrene-1-carbaldehyde (**5h**, 0.5 g, 2.17 mmol) with triethyl phosphite (1.1 g, 6.51 mmol) in the presence of $ZnBr_2$ (0.05 g, 0.22 mmol) at room temperature for 30 min followed by workup using general procedure B afforded diethyl hydroxy(pyren-1-yl)methylphosphonate **6h** (0.68 g, 83%) as a colorless solid; m.p. 168–170 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.39 (dd, J_1 = 8.1 Hz, J_2 = 8.1 Hz, 1 H, ArH), 8.24 (d, J = 9.3 Hz, 1 H, ArH), 8.18–8.12 (m, 3 H, ArH), 8.05–7.95 (m, 3 H, ArH), 6.13 (d, J = 11.4 Hz, 1 H, CH), 4.73 (s, 1 H, -OH), 4.06–3.78 (m, 4 H, -OCH_2), 1.15 (t, J = 7.05 Hz, 3 H, CH_3), 1.03 (t, J = 7.05 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 131.3, 131.1 (d, J = 3.0 Hz), 130.6, 130.3 (d, J = 0.45 Hz), 128.3 (d, J = 6.9 Hz), 128.5, 127.5, 127.5, 127.4, 125.9, 125.3, 125.2, 125.1, 124.9 (d, J = 3.1 Hz), 124.6, 123.0, 67.7 (d, J = 161.2 Hz), 63.3 (q, J = 7.54 Hz), 16.3 (t, J = 5.65 Hz) ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 127.5 (d, J = 6.9 Hz), 125.9, 125.3, 125.2, 125.1, 124.9 (d, J = 3.1 Hz), 124.6, 123.0, 67.7 (d, J = 161.2 Hz), 63.3 (q, J = 7.54 Hz), 16.3 (t, J = 5.65 Hz) ppm. HRMS (EI): calcd. for $C_{21}H_{21}O_4P$ $[M]^+$ 368.1177; found 368.1170.

Ethyl 2-[2-Methyl-1-(phenylsulfonyl)-1*H*-indol-3-yl]-2-oxoacetate (12): To a solution of 2-methylindole (2 g, 15.2 mmol) in dry diethyl ether (10 mL) was slowly added oxalyl dichloride (3.9 g, 30.53 mmol) at 0 °C, and the resulting mixture was stirred for 1 h. Dry ethanol (10 mL) was slowly added, and the mixture was stirred for an additional 1 h. The resulting reaction mixture was poured over crushed ice (200 g), the resulting solid was filtered off and dried with $CaCl_2$ in a desiccator to give ethyl 2-(2-methyl-1*H*-indol-3-yl)-2-oxoacetate (2.65 g, 80%) as a brown solid; m.p. 158–160 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.95 (s, 1 H, NH), 7.98 (d, J = 6.9 Hz, 1 H, ArH), 7.33 (d, J = 6.9 Hz, 1 H, ArH), 7.30–7.21 (m, 3 H, ArH), 4.41 (q, J = 6.9 Hz, 2 H, -OCH_2), 2.62 (s, 3 H, CH_3), 1.36 (t, J = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 182.3, 166.5, 148.0, 135.1, 126.7, 123.5, 123.0, 120.4, 111.5, 109.8, 62.2, 14.4, 14.0 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 123.5, 123.0, 120.4, 111.5, 62.2, 14.4, 14.0 ppm. To a solution of crude ethyl 2-(2-methyl-1*H*-indol-3-yl)-2-oxoacetate (2 g, 8.65 mmol) in dry dichloromethane (DCM, 25 mL) were added Et_3N (1.76 g, 17.3 mmol) and 4-(*N*,*N*-dimethylamino)pyridine (DMAP, 105 mg, 0.87), and the resulting mixture was stirred for 15 min. Benzenesulfonyl chloride (2.0 g, 11.24 mmol) in dry DCM (10 mL) was then added, and the reaction was stirred for an additional 6 h. The reaction mixture was then poured over 2% aqueous HCl (10 mL) and brine (10 mL). The organic layer was separated and then dried with Na_2SO_4. Removal of solvent followed by column chromatographic purification (10% EA in hexane) afforded ethyl 2-[2-methyl-1-(phenylsulfonyl)-1*H*-indol-3-yl]-2-oxoacetate (**12**, 2.8 g, 87%) as a light brown solid; m.p. 98–100 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.25 (d, J = 9.0 Hz, 1 H, ArH), 7.88–7.80 (m, 3 H, ArH), 7.63–7.59 (m, 1 H, ArH), 7.49 (t, J = 7.5 Hz, 2 H,

ArH), 7.40–7.32 (m, 2 H, ArH), 4.43 (q, J = 7.2 Hz, 2 H, -OCH_2), 2.85 (s, 3 H, CH_3), 1.39 (t, J = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 183.5, 164.6, 146.3, 138.5, 135.9, 134.7, 129.7, 126.7, 125.5, 124.9, 120.5, 115.7, 114.3, 62.5, 14.1, 13.9 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 134.7, 129.7, 126.6, 125.5, 124.9, 120.5, 114.3, 62.5, 14.2, 13.9 ppm. $C_{19}H_{17}NO_5S$ (371.40): calcd. C 61.44, H 4.61, N 3.77; found C 61.71, H 4.39, N 4.01.

Ethyl 2-[2-Methyl-1-(phenylsulfonyl)-1*H*-indol-3-yl]acetate (13): A mixture of ethyl 2-[2-methyl-1-(phenylsulfonyl)-1*H*-indol-3-yl]-2-oxoacetate (**12**, 0.5 g, 1.34 mmol) with triethyl phosphite (0.67 g, 4.03 mmol) in the presence of $ZnBr_2$ (0.03 g, 0.13 mmol) was stirred at room temperature for 6 h. Upon consumption of the starting material (monitored by TLC), the reaction mass was poured over crushed ice (50 g), and the resulting mixture was extracted with ethyl acetate (2× 15 mL). The combined organic extracts were washed with brine solution (2× 20 mL) and dried with Na_2SO_4. Removal of the solvent followed by column chromatographic purification (5% EA/hexane) afforded ethyl 2-[2-methyl-1-(phenylsulfonyl)-1*H*-indol-3-yl]acetate (**13**, 0.27 g, 56%) as a thick liquid. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.18 (d, J = 8.1 Hz, 1 H, ArH), 7.74 (d, J = 7.8 Hz, 2 H, ArH), 7.51–7.37 (m, 4 H, ArH), 7.28–7.24 (m, 2 H, ArH), 4.09 (q, J = 7.2 Hz, 2 H, -OCH_2), 3.59 (s, 2 H, CH_2), 2.57 (s, 3 H, CH_3), 1.16 (t, J = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 170.5, 139.2, 136.2, 134.6, 133.6, 130.0, 129.2, 126.2, 124.2, 123.5, 118.4, 114.5, 113.6, 60.9, 30.4, 14.1, 12.9 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 133.6, 129.2, 126.2, 124.2, 123.5, 118.4, 114.5, 60.9, 30.4, 14.1, 12.9 ppm. $C_{19}H_{19}NO_4S$ (357.42): calcd. C 63.85, H 5.36, N 3.92; found C 64.09, H 5.17, N 4.16.

Bis(4-nitrophenyl)methane (15): A mixture of bis(4-nitrophenyl) methanone (**14**,[16] 0.5 g, 1.83 mmol) with triethyl phosphite (0.91 g, 5.51 mmol) in the presence of $ZnBr_2$ (0.04 g, 0.18 mmol) was stirred at room temperature for 8 h. Upon consumption of the starting material (monitored by TLC), the reaction mass was poured over crushed ice (50 g), and the resulting mixture was extracted with ethyl acetate (2× 15 mL). The combined organic extracts were washed with brine solution (2× 20 mL) and dried with Na_2SO_4. Removal of the solvent followed by column chromatographic purification (5% EA/hexane) afforded bis(4-nitrophenyl) methane (**15**, 0.32 g, 67%) as a colorless solid; m.p. 180–185 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.11 (d, J = 8.1 Hz, 4 H, ArH), 7.27 (d, J = 8.4 Hz, 4 H, ArH), 4.12 (s, 2 H, CH_2) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 146.9, 146.6, 129.7, 124.0, 41.3 ppm. DEPT-135 (75.4 MHz, $CDCl_3$): δ = 129.2, 124.0, 41.3 ppm.

Supporting Information (see footnote on the first page of this article): Copies of ^1H NMR, ^{13}C NMR, and DEPT-135 NMR spectra of prepared compounds as well as X-ray crystal structures of **2g**, **2q′**, and **4e**.

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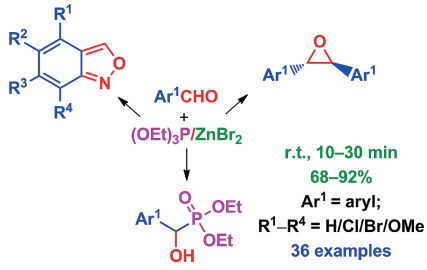
A $(EtO)_3P$–$ZnBr_2$-mediated deoxygenation reaction of 2-nitrobenzaldehydes was developed for the facile preparation of *trans*-epoxides. When sterically hindered 2-nitrobenzaldehydes were treated with triethyl phosphite and $ZnBr_2$, benzisoxazoles were formed as the sole product. Electron-rich and moderately electron-deficient aryl aldehydes gave α-hydroxy phosphonate esters under identical conditions.



Keywords: Synthetic methods / Oxygen heterocycles / Phosphorus / Aldehydes / Epoxidation / Diastereoselectivity

