3,5-Bis-(trifluoromethyl)phenyl sulfones in the synthesis of 3,5-disubstituted cyclopent-2-enones

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Dedicated to Professor Lutz F. Tietze

Abstract

3,5-Bis-(trifluoromethyl)phenyl sulfones (BTFP sulfones) **1a**–**e**, easily synthesized from 3,5-bis-(trifluoromethyl)benzenethiol, react under PTC with (*Z*)-1,4-dichloro-2-butene to afford the cyclopentenyl sulfones **3**, which suffer further diastereoselective alkene epoxidation with MCPBA giving BTFP sulfonyl cyclopentene oxides **5** and **6** in good yields. These epoxides are convenient precursors of 3,5-disubstituted cyclopent-2-enones, which are given after epoxide ring-opening with different nucleophiles and final successive oxidation–BTFP sulfinate elimination.

Keywords: Sulfones, cyclopentenones, epoxides, dialkylation, oxidation, elimination

Introduction

The cyclopentenone structure occurs in a wide variety of biologically active compounds such as prostaglandins, pyrethroids, and steroids. Cyclopentenones are also often used as building blocks for the synthesis of other biologically active compounds owing to their suitability for further functionalization via nucleophilic 1,4-addition and reaction with electrophiles at the 2- and 5-positions (Figure 1). For all these reasons, numerous synthetic methods have been developed for their preparation. Among them we can mention classical routes such as the base-catalyzed intramolecular aldol condensation of 1,4-dicarbonyl compounds,[1] the intramolecular Wittig- type reactions,[2] intramolecular 1,5-C-H insertions,[3] and the Nazarov[4] cyclization. Moreover, different transition metal-mediated approaches[5] such as the Pauson–Khand reaction,[6] and the Rautenstrauch rearrangement,[7] have become very popular for the synthesis of this type of compounds.

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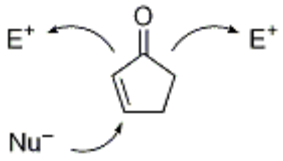


Figure 1. Cyclopentene functionalization.

We have recently shown that the 3,5-bis-(trifluoromethyl)phenyl (BTFP) group is a strong electron-withdrawing group, and that the corresponding BTFP sulfonyl group is an excellent nucleofuge in base-promoted β-elimination processes used in the stereoselective synthesis of *E*-aconitates by dialkylation under phase-transfer-catalyzed conditions followed by concomitant elimination[8] (Figure 2). 2-BTFP-sulfonyl-ethanol is an efficient protective group for carboxylic acids, which is easily removed with aqueous $NaHCO_3$ (Figure 2). [9] Also, alkyl BTFP sulfones can be used in the stereoselective synthesis of di-, tri-, and tetra-substituted olefins through the Julia–Kocienski olefination[10] of aliphatic and aromatic aldehydes and ketones under very simple and mild reaction conditions by using KOH and phosphazenes as bases[11] (Figure 2).

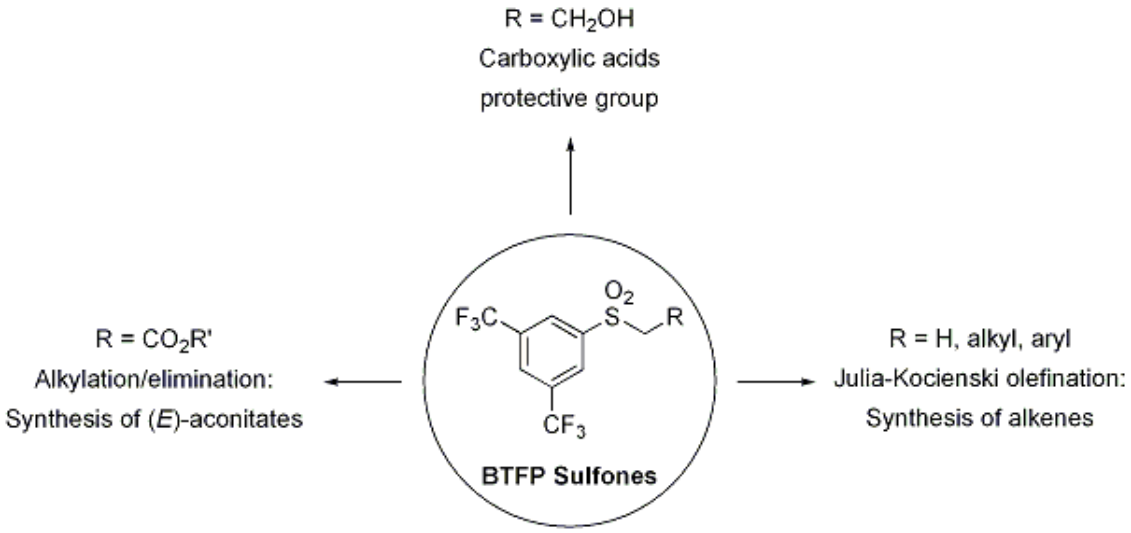
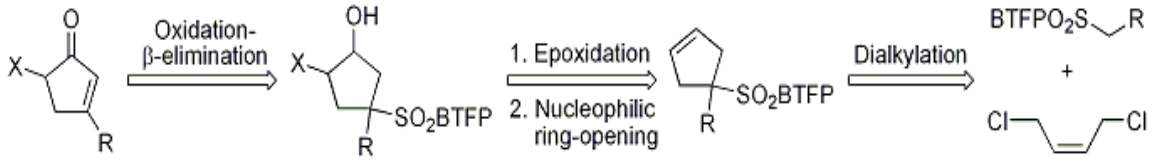


Figure 2. BTFP sulfones in organic synthesis.

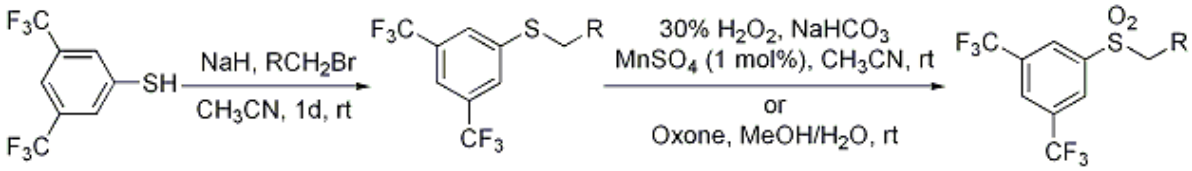
Recently, functionalized 3,5-disubstituted cyclopent-2-enones have been prepared via a solid-phase sulfone-linker strategy employing a phenylsulfonyl- functionalized polystyrene/ divinylbenzene resin.[12] In the present study, we report on the synthesis of 3,5-disubstituted cyclopentenones, employing functionalized alkyl BTFP sulfones in a four-step synthetic strategy as depicted in the retrosynthetic Scheme 1. We assume that the dialkylation step should be easily performed under PTC[8] and the final oxidation and β-elimination of BTFP sulfinic acid should take readily place in an *in situ* process.



Scheme 1. Retrosynthesis of 3,5-disubstituted cyclopentenones from BTFP sulfones.

Results and Discussion

For the preparation of alkyl BTFP sulfones **1**, a previously described two-step procedure was used (Scheme 2).[8] The alkylation reaction of 3,5-bis-(trifluoromethyl)benzenethiol[13] with alkyl bromides using NaH as base in CH_3CN at RT afforded the corresponding sulfides **2**, which were oxidized without further purification. The oxidation was performed with 30% H_2O_2 in the presence of sub-stoichiometric amounts of $MnSO_4.H_2O$ (1 mol %) and a buffer solution of $NaHCO_3$[14] for sulfides **1a**–**c**, or Oxone® in $MeOH/H_2O$ at RT for the synthesis of sulfones **1d**–**e** (Scheme 2). The overall yields obtained ranged from 60% for the phosphonate derivative **1e** to 93% for the benzyl sulfone **1a** (Scheme 2).



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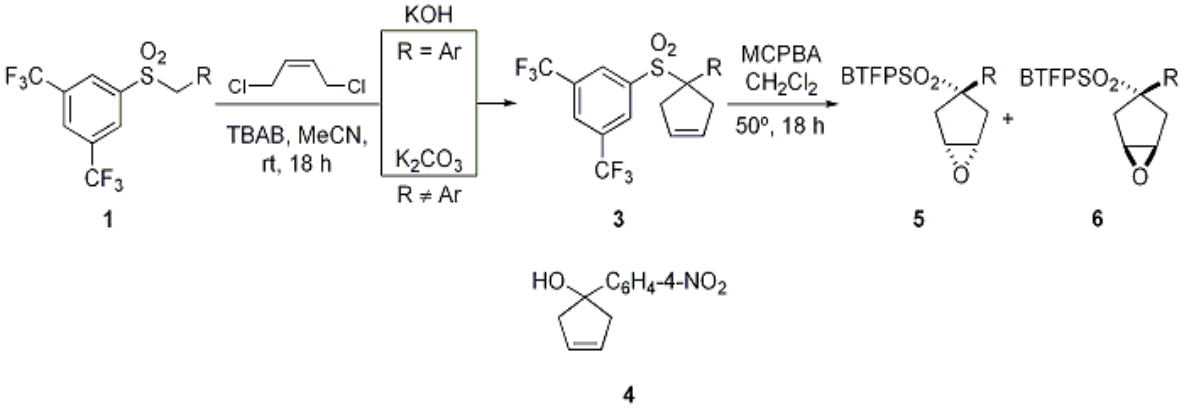
1a, R = Ph (93%)
1b, R = 4–$NO_2C_6H_4$ (64%)
1c, R = CO_2Pr^i (82%)
1d, R = CN (77%)
1e, R = $PO(OEt)_2$ (60%)

Scheme 2. Synthesis of the BTFP sulfones **1a**–**e**.

The cyclopentenes **3a–e** were prepared in good yields under very mild PTC conditions by α,α-dialkylation reaction of the sulfone with (*Z*)-1,4-dichlorobut-2-ene (Scheme 3, Table 1). The benzylic sulfones **1a** and **1b** were submitted to the dialkylation process employing KOH as base to give the cyclopentene derivatives **3a** and **3b** in 76 and 58% yield, respectively (Table 1, entries 1 and 2). In the α,α-dialkylation of BTFP sulfone **1b** a 28% yield of the cyclopentenol **4** was also obtained as a consequence of a nucleophilic substitution of the sulfonyl group by the base. On the other hand, K_2CO_3 was the base which gave the best yields for the α,α-dialkylation reaction of the more acidic sulfones **1c–e**, affording the corresponding adducts **3c**–**e** in yields between 60 and 76% (Table 1, entries 3–5). It is worth mentioning that non-activated benzyl sulfones require much stronger bases, such as *n*-BuLi at 0ºC, to perform this α,α-dialkylation process with (*Z*)-1,4-dichlorobut-2-ene.[12]

Epoxidation of the sulfonyl cyclopentenes **3** with MCPBA in CH_2Cl_2 at 50ºC for 18 h delivered diastereoselectively the corresponding oxiranes **5**–**6** which were easily separated by column

chromatography (Scheme 3, Table 1). We initially assumed that the observed major diastereomer in the epoxidation reaction corresponded to the product with the relative stereochemistry depicted in **6**, since these isomers were the only products obtained in similar epoxidations performed with (phenylsulfonyl)cyclopentene derivatives.[12,15a] The formation of the major diastereomer **6** can be probably be due to steric reasons.



Scheme 3. Synthesis of BTFP sulfonyl cyclopentenes **3** and oxiranes **5** and **6**.

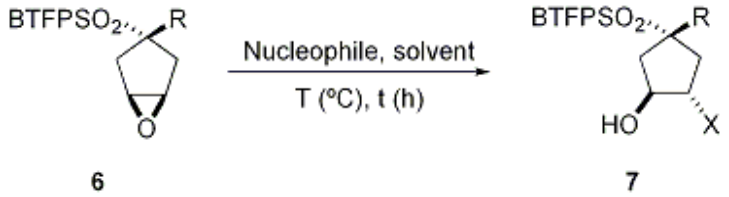
Table 1. Synthesis of BTFP sulfonylcyclopentenes **3** and oxiranes **5** and **6**

	BTFP sulfones			Cyclopentyl sulfones		BTFP sulfonyl oxiranes	
Entry	No.	R	Base	No.	Yield (%)[a]	**5** Yield (%)[b]	**6** Yield (%)[b]
1	**1a**	Ph	KOH	**3a**	76	**5a** (9)	**6a** (76)
2	**1b**	4-$NO_2C_6H_4$	KOH	**3b**	58[c]	**5b** (2)	**6b** (43)
3	**1c**	CO_2Pr^i	K_2CO_3	**3c**	60	**5c** (3)	**6c** (69)
4	**1d**	CN	K_2CO_3	**3d**	64	**5d** (6)	**6d** (39)
5	**1e**	$PO(OEt)_2$	K_2CO_3	**3e**	76	**5e** (20)	**6e** (47)

[a] Isolated yield after flash chromatography, based on the starting sulfones **1**. [b] Isolated yield after flash chromatography, based on the cyclopentenes **3**. [c] A 28% yield of **4** was also obtained.

The next step towards the synthesis of 2-cyclopentenones consisted in the nucleophilic ring opening of the sulfonyl epoxides with various nucleophiles (Scheme 4, Table 2). This study was carried out with the major epoxide diastereomers **6** in order to prepare diastereomerically pure products **7**. A preliminary screening of the reaction was performed with epoxide **6a**, employing different nucleophiles. Nucleophilic ring-opening of the epoxide moiety in **6a** with sodium azide in DMF at 100ºC afforded the cyclopentanol **7aa** in a 54% yield (Table 2, entry 1). A higher yield (66%) was obtained when the reaction was performed employing an excess of lithium azide (20% aqueous solution) (Table 2, entry 2). When employing amines as nucleophiles, it was necessary to use a larger excess of the reagent, longer reaction times, and solventless conditions, as depicted for benzylamine in Table 2 entries 3 and 4. With the purpose of reducing the reaction time, the ring opening was performed under microwave irradiation (200W) and solventless conditions, but no improvement of the yield of **7ab** was observed (Table 2, entry 5). When using *n*-butylamine as

nucleophile, the best yield of the corresponding sulfonyl β-amino alcohol **7ac** was observed under solventless conditions at 78ºC (Table 2, compare entries 5 and 6). No ring-opening reaction was observed with carbon nucleophiles such as sodium alkylmalonates, sodium cyanide, or trimethylsilyl cyanide under different conditions, only starting material being recovered from the reaction. Very recently, a highly regioselective ring opening of epoxides and aziridines using (bromodimethyl)sulfonium bromide has been reported.[16] The ring opening of **6a** with this reagent in MeCN at RT, led to the corresponding bromohydrin **7ad** in a 69% yield (Table 2, entry 7).



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Scheme 4. Nucleophilic epoxide opening reactions.

At this point, the relative stereochemistry of epoxides **5** and **6** was confirmed by carrying out NOE studies on the ring-opening adducts **7** and **8**. For this purpose, the diastereomeric epoxide **5a** was also submitted to nucleophilic ring opening with LiN_3 and Me_2SBr_2, to afford the alcohols **8aa** and **8ad** in a 62 and 67% yield, respectively (Scheme 5, Table 1, entries 8 and 9). As depicted in Figure 3, the relative stereochemistry assigned to compounds **5** and **6** was corroborated by using the NOEs observed for the corresponding β-azido- alcohol compounds **7aa** and **8aa** as well as the bromohydrins **7ad** and **8ad**.

The BTFP sulfonyl epoxides **6b**–**e** were also submitted to ring opening with some of the previously studied nucleophiles (Table 1, entries 10–16). The use of (bromodimethyl)sulfonium bromide led to the β-bromo alcohols **7bd**, **7cd**, **7dd**, and **7ed** with yields ranging from 54 to 87% (Table 1, entries 10–13). The BTFP sulfone **6d** reacted in a very low isolated yield with benzylamine under solventless conditions at 80ºC to give the functionalized sulfone **7db** (Table 2, entry 14). Only a 34% yield of compound **7ca** was obtained when BTFP-sulfone **6c** reacted with LiN_3 in DMF at 80ºC for 24 h (Table 1, entry 15). This was due in part to the formation of compound **9** in a 31% yield as a consequence of the hydrolysis and thermal decarboxylation of the isopropyl ester moiety (Figure 4). In order to avoid the hydrolysis of the ester group, the reaction was carried out in anhydrous conditions using NaN_3 as nucleophile (Table 1, entry 16). However, under these conditions the carbonate **10** was isolated in a 52% yield as a result of the intramolecular nucleophilic attack of the alkoxide on the ester group (Figure 4).

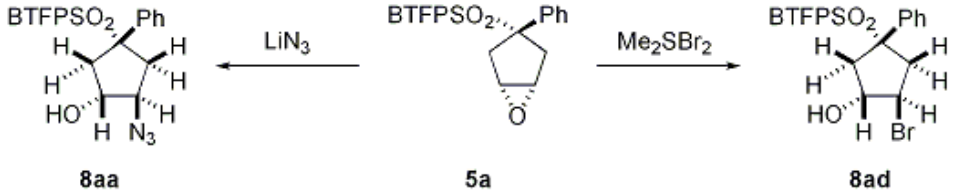
Table 2. Nucleophilic epoxide-opening reactions

	Epoxide						Product		
Entry	**No.**	R	Nu (equiv.)	Solvent	T (ºC)	t (h)	**No.**	X	Yield %[a]
1	**6a**	Ph	NaN_3 (10)	DMF	100	24	**7aa**	N_3	54
2	**6a**	Ph	LiN_3 (10)	DMF	80	24	**7aa**	N_3	66
3	**6a**	Ph	$BnNH_2$ (20)	DMF	100	24	**7ab**	BnNH	20
4	**6a**	Ph	$BnNH_2$ (30)	–	80	70	**7ab**	BnNH	72

Table 2. Continued

	Epoxide						Product		
Entry	**No.**	R	Nu (equiv.)	Solvent	T (ºC)	t (h)	**No.**	X	Yield %[a]
5	**6a**	Ph	$BnNH_2$ (5)	–	95[b]	0.5	**7ab**	BnNH	40
6	**6a**	Ph	$BuNH_2$ (30)	–	78	38	**7ac**	BuNH	63
7	**6a**	Ph	Me_2SBr_2 (5)	MeCN	RT	13	**7ad**	Br	69
8	**5a**	Ph	LiN_3 (10)	DMF	80	24	**8aa**	N_3	62
9	**5a**	Ph	Me_2SBr_2 (5)	MeCN	RT	13	**8ad**	Br	67
10	**6b**	4-$NO_2C_6H_4$	Me_2SBr_2 (5)	MeCN	RT	13	**7bd**	Br	87
11	**6c**	CO_2Pr^i	Me_2SBr_2 (5)	MeCN	RT	13	**7cd**	Br	66
12	**6d**	CN	Me_2SBr_2 (5)	MeCN	RT	13	**7dd**	Br	73
13	**6e**	$PO(OEt)_2$	Me_2SBr_2 (5)	MeCN	RT	13	**7ed**	Br	54
14	**6d**	CN	$BnNH_2$ (30)	–	80	70	**7db**	BnNH	15
15	**6c**	CO_2Pr^i	LiN_3 (10)	DMF	80	24	**7ca**	N_3	34[c]
16	**6c**	CO_2Pr^i	NaN_3 (10)	DMF	80	48	**10**	N_3	52

[a] Isolated yield after flash chromatography, based on starting epoxides. [b] The reaction was performed under 200W microwave irradiation. [c] A 31% yield of **9** was also obtained.



Scheme 5. Nucleophilic ring opening of epoxide **5a**.

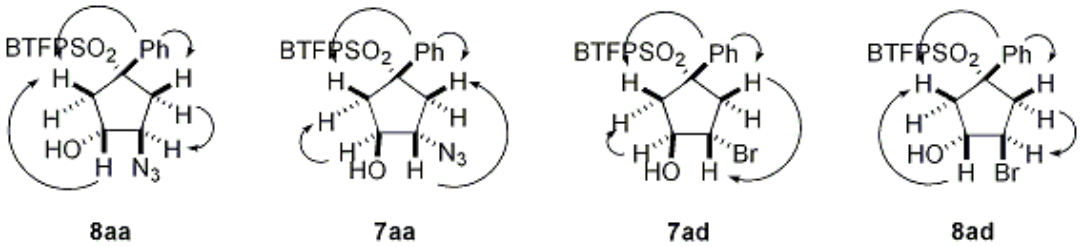


Figure 3. Determination of relative stereochemistry of compounds **7** and **8**.

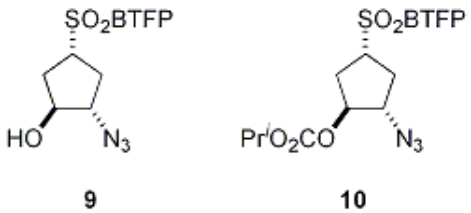
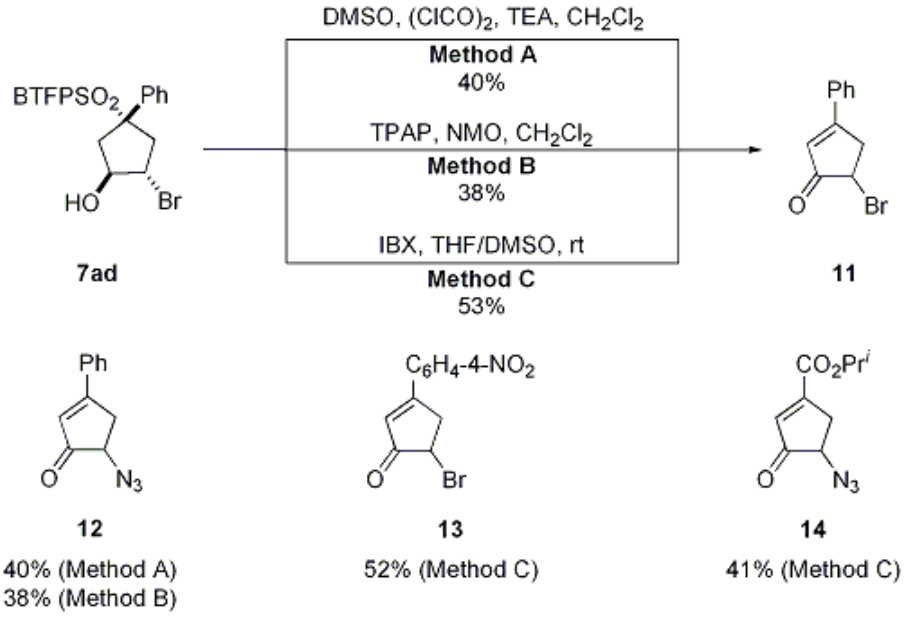


Figure 4. Azide ring opening reactions of **6c**.

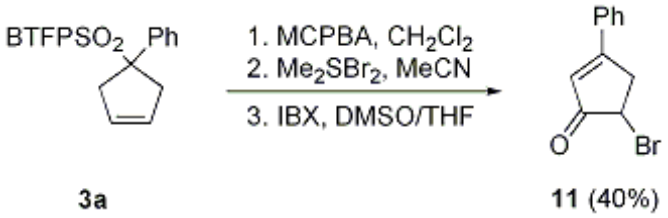
The last step of the synthesis of the 3,5-disubstituted cyclopentenones consisted of the oxidation and subsequent BTFP-sulfinic acid elimination from the cyclopentanols **7**. The bromohydrin **7ad** was chosen as a model substrate to perform an optimization of the reaction conditions since the obtained 5-bromocyclopentenone is a suitable substrate for further modification of the cyclopentene structure. As illustrated in Scheme 6, oxidation of the bromo cyclopentanol **7ad** under Swern conditions (Method A) led, after *in situ* triethylamine (TEA)-catalyzed sulfinate elimination, to the corresponding 5-bromo-3-phenylcyclopent-2-enone (**11**) in 40% yield. A similar result was obtained when the oxidation was carried out employing the system tetra-*n*-propylammonium perruthenate/*N*-methylmorpholine-*N*-oxide (TPAP/NMO)[17,18] where the *in situ*- generated *N*-methylmorpholine performed the elimination of the BTFP sulfinate (Method B, Scheme 6). A better (53%) yield was obtained when the oxidation was carried out employing 2-iodoxybenzoic acid (IBX)[19] under base-free conditions (Method C). The low to moderate yields obtained in the final step of the cyclopentenone synthesis were probably associated with the isolation process, owing to the high volatility of the cyclopentenone **11**, since the conversions in the oxidation reactions were in all cases very high. A similar study of reaction conditions was performed with the BTFP sulfones **7aa**, **7bd**, and **7ca**, the best results being those depicted in Scheme 6. Methods A or B gave the best results for the oxidation–elimination sequence of the 2-azidocyclopentanol **7aa** which afforded the cyclopent-2-enone **12** in a moderate 40% yield. On the other hand, the cyclopentenones **13** and **14** were obtained after oxidation with IBX of **7bd** and **7ca** in 52 and 41% yields, respectively (Scheme 5). The amino- alcohol derivatives such as **7ab** and **7ac** were also submitted to the oxidation–elimination sequence under the studied conditions, but unfortunately only decomposition products were detected in the crude reaction mixtures.



Scheme 6. Synthesis of 3,5-disubstituted cyclopentenones.

Finally, it is worth mentioning that the isolated total yield from the cyclopentenone synthesis can be improved if the synthetic sequence is performed without any purification and/or isolation of

the corresponding intermediates. For example, the cyclopentenone **11** was obtained in a 40% isolated overall yield from BTFP sulfonyl cyclopentene **3a** without any purification and/or separation of the intermediates **5a**/**6a** and **7ad** (Scheme 7). This result represents an increase of nearly 10% in yield compared to the previously described procedures.



Scheme 7. Synthesis of cyclopentenone **11** without intermediate purifications.

In conclusion, this work further demonstrates the chemical versatility of BTFP sulfones, which can be used for the synthesis of highly functionalized 3,5-disubstituted cyclopent-2-enones. Owing to the strongly electron-withdrawing character of the BTFP sulfonyl group the dialkylation can be performed under milder conditions than previously reported (BuLi) for phenyl sulfones employing non-metallic bases such as KOH or K_2CO_3 under PTC conditions. The last oxidation–elimination step has been performed with different oxidants, such as Swern conditions, TPAP/NMO, and IBX. It can be concluded that IBX is the best reagent to perform this tandem process under very mild reaction conditions. The excellent nucleofugal properties of the BTFP sulfonyl group also facilitates the final elimination step. Consequently, the methodology described here makes use of readily available starting materials, mild reaction conditions, and very simple procedures, and is especially useful for the synthesis of new 5-bromocyclopentenone substrates, which allows future further functionalization.

Experimental Section

General Procedures. Melting points were obtained with a Reichert Thermovar apparatus and were not corrected. IR data were collected on a FTIR apparatus, Nicolet Impact 400D, and peaks are reported in cm^{-1}. Only the structurally most important IR peaks have been listed. NMR spectra were recorded on a Bruker AC-300 (300 MHz for ^{1}H- NMR and 75 MHz for ^{13}C NMR) using $CDCl_3$ as solvent and TMS as internal standard unless otherwise noted; chemical shifts are given in δ (ppm) and coupling constants (*J*) in Hz. Low-resolution electron impact (EI) mass spectra were obtained at 70 eV on a Shimadzu QP-5000 and Agilent 5973 spectrometers, and fragment ions have *m/z* with relative intensities (*%*) in parentheses. HRMS were performed on a Finnigan MAT 95S spectrometer. Analytical TLC was visualized with UV light at 254 nm or with $KMnO_4$. Thin layer chromatography was carried out on TLC aluminum sheets with silica gel 60 F_{254} (Merck). For flash chromatography, silica gel 60 (0.040–0.063 mm) was employed. Microwave reactions were performed with a CEM Discover Synthesis Unit in glass vessels (10 mL) sealed with a septum under magnetic stirring. Reactions under inert atmosphere (argon) were performed in oven-dried

glassware, sealed with a rubber septum, using anhydrous MeCN, THF or DMF. RT denotes room temperature.
Compounds **1a**,[11c] **1b**,[11c] **1c**,[8a,8b] **2a**,[11c] **2b**,[11c] **2c**,[8a,8b] **12**[12] have been described previously.

General procedure for the synthesis of 3,5-bis-(trifluoromethyl)phenyl sulfanes 2a–e. To a room temperature solution NaH (95%, 303 mg, 12 mmol) in MeCN (60 mL) under argon atmosphere, 3,5-bis-(trifluoromethyl)benzenethiol (1.7 mL, 10 mmol) was added dropwise. After 20 min, the corresponding alkyl bromide (11 mmol) was added and the reaction mixture was stirred at the same temperature for 1 day. After quenching with H_2O (70 mL), the mixture was extracted with EtOAc (2 x 50 mL). The combined organic layers were dried ($MgSO_4$) and evaporated to afford the corresponding pure crude 3,5-bis-(trifluoromethyl)phenyl sulfanes **2a–e**, which were used in the next oxidation step without further purification.
Cyanomethyl 3,5-bis-(trifluoromethyl)phenyl sulfane (2d). ^{1}H NMR δ 7.95 (s, 2H, ArH), 7.87 (s, 1H, ArH), 3.71 (s, 2H, CH_2S); ^{13}C NMR δ 135.3 (ArC), 132.9 (q, $J_{C\text{-}F}$ = 33.7, 2 x *C*CF_3), 131.2 (ArCH), 122.6 (q, $J_{C\text{-}F}$ = 272.5, 2 x CF_3), 122.5 (ArCH), 115.2 (CN), 20.5 (CH_2); MS *m/z* 286 (M^+ + 1, 11), 285 (M^+, 91), 266 (21), 245 (100), 225 (46), 176 (14), 132 (10).
(Diethylphosphoryl)methyl 3,5-bis-(trifluoromethyl)phenyl sulfane (2e). ^{1}H NMR δ 7.84 (s, 2H, ArH), 7.69 (s, 1H, ArH), 4.17 (m, 4H, OCH_2), 3.25 (d, J = 13.6, 2H, CH_2S), 1.31 (t, J = 7.1, 6H, 2 x CH_3); ^{13}C NMR δ 139.3 (ArC), 132.2 (q, $J_{C\text{-}F}$ = 34.0, 2 x *C*CF_3), 128.3 (ArCH), 122.9 (q, $J_{C\text{-}F}$ = 273.3, 2 x CF_3), 120.1 (ArCH), 63.0 (d, $J_{C\text{-}P}$ = 6.6, 2 x OCH_2), 27.5 (d, $J_{C\text{-}P}$ = 150.4, 2 x CH_2S), 16.2 (d, $J_{C\text{-}P}$ = 6.0, 2 x CH_3); MS *m/z* 397 (M^+ + 1, 10), 396 (M^+, 65), 377 (14), 368 (18), 340 (18), 320 (19), 260 (23), 259 (100), 239 (46), 195 (13), 138 (13), 109 (25), 81 (14).
General procedure for the synthesis of 3,5-bis-(trifluoromethyl)phenyl sulfones 1a–c. To a RT stirred solution of the corresponding sulfide **2a–c** (1 mmol) and $MnSO_4$ monohydrate (2 mg, 1 mol %) in MeCN (23 mL), was slowly added a previously prepared at 0 ºC aqueous mixture comprised by 30% H_2O_2 (5 mmol, 515 µL) and a 0.2 *M* buffer solution of $NaHCO_3$ (17 mL). After stirring for 1 d the reaction was quenched with a saturated aqueous solution of NaCl (30 mL), extracted with EtOAc (2 × 20 mL) and dried with anhydrous Na_2SO_4. Filtration and evaporation of the solvents afforded the corresponding pure crude sulfones **1a–c** which were recrystallized in hexane.
General procedure for the synthesis of 3,5-bis-(trifluoromethyl)phenyl sulfones 1d–e. To a stirred solution of the corresponding sulfide **2d–e** (10 mmol) in a 1/1 mixture of MeOH/H_2O (88 mL) at 0 ºC, was slowly added Oxone® (100 mmol, 62 g) and the resulting mixture was stirred at RT for 1 d. Then, MeOH was evaporated, the residue was dissolved in CH_2Cl_2 (100 mL) and filtered through Celite. To the resulting solution water was added and the mixture was extracted with CH_2Cl_2 (2 x 50 mL), was washed with a saturated solution of NaCl (3 x 100 mL), and dried ($MgSO_4$). Filtration and evaporation of the solvent afforded the corresponding pure crude sulfones **1d–e** which were recrystallized in ether/hexane or purified by flash chromatography (hexane/EtOAc).
Cyanomethyl 3,5-bis-(trifluoromethyl)phenyl sulfone (1d). Beige solid; R_f (hexane/EtOAc: 4/1) 0.41; mp 114–116 ºC; IR ν 3103, 3090, 2989, 2930, 2270, 1874, 1851, 1633, 1610, 1364, 1291, 1137; ^{1}H NMR δ 8.49 (s, 2H, ArH), 8.29 (s, 1H, ArH), 4.18 (s, 2H, CH_2S); ^{13}C NMR (100 MHz) δ 139.1 (ArC), 136.9 (q, $J_{C\text{-}F}$ = 35.0, 2 x *C*CF_3), 129.4, 129.1 (ArCH), 122.0 (q, $J_{C\text{-}F}$ = 273.5, 2 x CF_3), 109.5 (CN), 45.7 (CH_2); MS *m/z* 317 (M^+, 0.5), 298 (11), 277 (44), 213 (100), 163 (14); HRMS Calcd for $C_{10}H_5F_6NO_2S$ (M^+) 316.9945, found: 316.9902.

(Diethylphosphoryl)methyl 3,5-bis-(trifluoromethyl)phenyl sulfone (1e). White solid; R_f (hexane/EtOAc: 2/1) 0.17; mp 78–80 ºC; IR ν 3090, 2985, 2908, 1633, 1337, 1278, 1159, 1137, 1014; ^{1}H NMR δ 8.48 (s, 2H, ArH), 8.17 (s, 1H, ArH), 4.17 (sept., J = 7.4, 4H, 2 x OCH_2), 3.84 (d, J = 16.7, 2H, CH_2S), 1.29 (t, J = 7.1, 6H, 2 x CH_3); ^{13}C NMR δ 142.1 (ArC), 132.8 (q, $J_{C\text{-}F}$ = 35.0, 2 x CCF_3), 129.3, 127.6 (ArCH), 122.3 (q, $J_{C\text{-}F}$ = 273.5, 2 x CF_3), 63.6 (d, $J_{C\text{-}P}$ = 6.7, 2 x OCH_2), 53.9 (d, $J_{C\text{-}P}$ = 137.4, 2 x CH_2S), 16.1 (d, $J_{C\text{-}P}$ = 5.4, 2 x CH_3); MS *m/z* 428 (M^+, 1), 409 (29), 401 (66), 383 (33), 373 (46), 355 (39), 354 (11), 353 (94), 337 (21), 336 (30), 309 (38), 308 (47), 293 (12), 292 (43), 290 (18), 277 (29), 261 (44), 257 (12), 230 (43), 227 (100), 213 (95), 208 (28), 194 (28), 163 (28), 144 (23), 143 (15), 125 (30), 124 (22), 123 (24), 109 (38), 108 (43), 107 (29), 97 (78), 96 (29), 95 (37), 93 (33), 81 (28), 80 (41), 79 (47), 78 (24), 65 (44), 45 (13), 43 (13); HRMS Calcd for $C_{13}H_{15}F_6O_5PS$ (M^+), 428.0282, found: 428.0281.

General procedure for the synthesis of [3,5-bis-(trifluoromethyl)phenylsulfonyl]-cyclopentenes, 3. To a CH_3CN (40 mL) solution of TBAB (65 mg, 0.2 mmol) and the corresponding sulfone (2 mmol) at RT, was added KOH (1.08 g, 18 mmol, for sulfone **1a–b**) or K_2CO_3 (1.656 g, 18 mmol, for sulfones **1c–e**). The mixture was stirred for 30 min and *cis*-1,4-dichloro-2-butene (240 μL, 2.2 mmol) was added. The reaction mixture was stirred overnight and quenched with a saturated solution of NH_4Cl (50 mL), extracted with EtOAc (2 x 50 mL), and the organic phase was dried ($MgSO_4$). Filtration and solvent evaporation afforded the corresponding crude cyclopentenes, which were purified by flash chromatography (hexane/EtOAc) to afford pure compounds **3**.

1-[3,5-Bis-(trifluoromethyl)phenylsulfonyl]-1-phenyl-3-cyclopentene (3a). White solid; R_f (hexane/EtOAc: 2/1) 0.68; mp 95–96 ºC; IR ν 3073, 3042, 2914, 2853, 1629, 1607, 1453, 1352, 1282, 1150; ^{1}H NMR δ 8.02 (s, 1H, ArH), 7.75 (s, 2H, ArH), 739–7.27 (m, 3H, ArH), 7.19 (d, J = 7.0, 2H, ArH), 5.75 (s, 2H, CH=CH), 3.62 (d, J = 16.4, 2H, CH_2), 3.15 (d, J = 16.7, 2H, CH_2); ^{13}C NMR δ 138.2, 136.6 (ArC), 132.0 (q, $J_{C\text{-}F}$ = 34.4, 2 x CCF_3), 130.3, 129.9 129.1, 128.4, 126.8 (ArCH), 128.3 (CH=CH), 122.2 (q, $J_{C\text{-}F}$ = 274.3, 2 x CF_3), 77.6 (CS), 40.9 (2 x CH_2); MS *m/z* 401 (M^+ - F, 0.4), 144 (17), 143 (100), 142 (14), 141 (21), 128 (60), 115 (20); HRMS Calcd for $C_{19}H_{14}F_6O_2S$ (M^+) 420.0619, (M^+ - F) 401.0635, found: 401.0681.

1-[3,5-Bis-(trifluoromethyl)phenylsulfonyl]-1-(4-nitrophenyl)-3-cyclopentene (3b). Yellow solid; R_f (hexane/EtOAc: 2/1) 0.63; mp 202–204 ºC; IR ν 3080, 2951, 2856, 1607, 1513, 1354, 1283, 1142; ^{1}H NMR δ 8.21, 7.50 (2d, J = 8.9, 4H, ArH), 8.10 (s, 1H, ArH), 7.95 (s, 2H, ArH), 5.61 (s, 2H, CH=CH), 3.63 (d, J = 16.5, 2H, CH_2), 3.16 (d, J = 16.7, 2H, CH_2); ^{13}C NMR δ 148.0, 143.0, 138.3 (ArC), 132.6 (q, $J_{C\text{-}F}$ = 35.1, 2 x CCF_3), 131.32, 130.3 128.3, 123.3 (CH=CH, ArCH), 122.1 (q, $J_{C\text{-}F}$ = 274.3, 2 x CF_3), 77.7 (CS), 41.2 (2 x CH_2); MS *m/z* 188 (M^+ - $BTFPSO_2$, 100), 142 (49), 141 (49), 139 (10), 128 (11), 115 (34); HRMS Calcd for $C_{19}H_{13}F_6NO_4S$ (M^+) 465.0469, (M^+ - F) 446.0485, found: 446.0488.

Isopropyl 1-[3,5-bis-(trifluoromethyl)phenylsulfonyl]-3-cyclopentenecarboxylate (3c). White solid; R_f (hexane/EtOAc: 9/1) 0.55; mp 90–92 ºC; IR ν 3107, 2980, 2932, 1718, 1447, 1363, 1333, 1297, 1141; ^{1}H NMR δ 8.33 (s, 2H, ArH), 8.16, (s, 1H, ArH), 5.67 (s, 2H, CH=CH), 4.98 (sept., J = 6.2, 1H, OCH), 3.21 (2d, J = 16.4, 4H, 2 x CH_2), 1.23 (d, J = 6.2, 6H, 2 x CH_3); ^{13}C NMR δ 167.4 (CO_2Et), 139.7 (ArC), 132.5 (q, $J_{C\text{-}F}$ = 34.0, 2 x CCF_3), 130.4, 127.5 (ArCH), 127.4 (CH=CH), 122.3 (q, $J_{C\text{-}F}$ = 273.5, 2 x CF_3), 78.1 (CS), 71.4 (OCH), 38.9 (2 x CH_2), 21.2 (2 x CH_3); MS *m/z* 430 (M^+, 0.3), 257 (16), 239 (11), 239 (177), 150 (13), 149 (100), 129 (12), 125 (11), 111 (26), 105 (14), 99 (10), 98 (11), 97 (26), 95 (12), 93 (12), 85 (26), 84 (14), 83 (25), 82 (11), 81 (16), 73 (17),

71 (37), 69 (28), 67 (14), 60 (18), 57 (57), 56 (34), 55 (36), 44 (15), 43 (52), 41 (35); HRMS Calcd for $C_{17}H_{16}F_6O_4S$ (M^+) 430.0673, (M^+-OPr^i) 371.0177, found: 371.0197.

1-[3,5-Bis-(trifluoromethyl)phenylsulfonyl]-1-cyanocyclopent-3-ene (3d). White solid; R_f (hexane/EtOAc: 4/1) 0.54; mp 146–148 ºC; IR ν 3080, 2926, 2862, 2238, 1628, 1442, 1364, 1332, 1282, 1200, 1132; ^{1}H NMR δ 8.50 (s, 2H, ArH), 8.27 (s, 1H, ArH), 5.76 (s, 2H, CH=CH), 3.39 (d, J = 15.2, 2H, CH_2), 3.02 (d, J = 15.6, 2H, CH_2); ^{13}C NMR (100 MHz) δ 137.5 (ArC), 133.5 (q, $J_{C\text{-}F}$ = 35.0, 2 x CCF_3), 130.6, 128.8 (ArCH), 127.0 (CH=CH), 122.1 (q, $J_{C\text{-}F}$ = 274.8, 2 x CF_3), 118.1 (CN), 64.7 (CCN), 41.0 (2 x CH_2); MS *m/z* 369 (M^+, 0.1), 312 (11), 257 (38), 239 (19), 213 (15), 177 (13), 167 (15), 150 (13), 149 (100), 129 (15), 111 (11), 97 (16), 92 (36), 91 (45), 85 (15), 83 (18), 81 (12), 73 (18), 71 (27), 70 (14), 69 (22), 65 (16), 60 (11), 57 (45), 56 (44), 55 (28), 43 (46), 41 (26); HRMS Calcd for $C_{14}H_9F_6NO_2S$ (M^+) 369.0258, (M^+-F) 350.0274, found: 350.0262.

Diethyl 1-[3,5-bis-(trifluoromethyl)phenylsulfonyl]-3-cyclopentenylphosphonate (3e). White solid; R_f (hexane/EtOAc: 4/1) 0.13; mp 71–73 ºC; IR ν 3076, 2994, 2930, 2857, 1360, 1287, 1260, 1150, 1023; ^{1}H NMR δ 8.47 (s, 2H, ArH), 8.14 (s, 1H, ArH), 5.63 (s, 2H, CH=CH), 4.21–4.12 (m, 4H, 2 x OCH_2), 3.34–3.07 (m, 4H, 2 x =CHCH_2), 1.27 (t, J = 7.0, 6H, 2 x CH_3); ^{13}C NMR δ 140.3 (ArC), 132.2 (q, $J_{C\text{-}F}$ = 34.0, 2 x CCF_3), 131.5 (CH=CH), 127.6, 127.5 (ArCH), 122.4 (q, $J_{C\text{-}F}$ = 273.3, 2 x CF_3), 70.3 (d, $J_{C\text{-}P}$ = 143.8, CP), 63.8 (d, $J_{C\text{-}P}$ = 6.6, 2 x OCH_2), 38.7 (2 x CH=CH_2), 16.1 (d, $J_{C\text{-}P}$ = 5.5, 2 x CH_3); MS *m/z* 480 (M^+, 0.01), 204 (10), 203 (100), 202 (23), 175 (19), 149 (33), 147 (61), 146 (18), 129 (20), 92 (10), 81 (13), 66 (25), 65 (21); HRMS Calcd for $C_{17}H_{19}F_6O_5PS$ (M^+) 480.0595, (M^+ - $C_{13}H_9F_6O_2S$) 137.0368, found: 137.0378.

1-(4-Nitrophenyl)-3-cyclopentenol (4). Yellow oil; R_f (hexane/EtOAc: 4/1) 0.15; IR ν 3424, 3073, 2923, 2853, 1601, 1521, 1335; ^{1}H NMR δ 8.17, 7.62 (2d, J = 8.9, 2H, ArH), 5.83 (s, 2H, CH=CH), 2.94, 2.77 (2d, J = 16.2, 2H, CH_2); ^{13}C NMR δ 154.6, 146.6 (ArC), 128.2, 125.7, 123.3 (ArCH, CH=CH), 81.7 (COH), 51.0 (2 x CH_2); MS *m/z* 205 (M^+, 10), 151 (11), 150 (100), 104 (12); HRMS Calcd for $C_{11}H_{11}NO_3$ (M^+) 205.0739, found: 205.0719.

General procedure for the synthesis of [3,5-bis-(trifluoromethyl)phenyl]sulfonyl oxiranes, 5 and 6. To a solution of [3,5-bis-(trifluoromethyl)phenylsulfonyl]cyclopentene, **3** (5 mmol), in CH_2Cl_2 (100 mL) at RT, MCPBA (6.75 g, 30 mmol) was added and the mixture was heated at 50 ºC for 18 h. The reaction mixture was then quenched with a saturated solution of $NaHCO_3$ (100 mL), and extracted with CH_2Cl_2 (2 x 80 mL). The organic phase was further washed with a saturated solution of Na_2SO_3 (3 x 50mL) and $NaHCO_3$ (2 x 50 mL). The organic phase was dried ($MgSO_4$), and after solvent evaporation the corresponding crude oxiranes were obtained as a mixture of diastereomers (see Scheme 3), which were purified by flash chromatography (hexane/EtOAc) to afford pure compounds **5** and **6**.

(1*R,3*s*,5*S**)-3-[3,5-Bis-(trifluoromethyl)phenylsulfonyl]-3-phenyl-6-oxabicyclo[3.1.0]hexane (6a).** White solid; R_f (hexane/EtOAc: 2/1) 0.64; mp 153–155 ºC; IR ν 3076, 3038, 2940, 1623, 1443, 1355, 1290, 1132; ^{1}H NMR δ 8.00 (s, 1H, ArH), 7.54 (s, 2H, ArH), 7.32–7.20 (m, 3H, ArH), 7.10 (d, J = 7.6, 2H, ArH), 3.72 (s, 2H, 2 x OCH), 3.04, 2.82 (2d, J = 15, 4H, 2 x CH_2); ^{13}C NMR δ 138.0, 136.0 (ArC), 131.9 (q, $J_{C\text{-}F}$ = 35.0, 2 x CCF_3), 129.9, 128.8, 128.6, 128.2, 126.9 (ArCH), 122.1 (q, $J_{C\text{-}F}$ = 273.5, 2 x CF_3), 76.8 (CS), 56.9 (2 x OCH), 35.3 (2 x CH_2); MS *m/z* (M^+ - $BTFPSO_2$, 100), 144 (15), 141 (22), 131 (35), 129 (30), 128 (17), 116 (17), 115 (53), 103 (12), 91 (74), 77 (14), 43 (11); HRMS Calcd for $C_{19}H_{14}F_6O_3S$ (M^+) 436.0568, (M^+-F) 417.0584, found: 417.0597.

(1*R,3*r*,5*S**)-3-[3,5-Bis-(trifluoromethyl)phenylsulfonyl]-3-phenyl-6-oxabicyclo[3.1.0]hexane (5a).** White solid; R_f (hexane/EtOAc: 2/1) 0.26; mp 168–170 ºC; IR ν 3089, 3064, 3050, 2937, 1626, 1361, 1272, 1125; ^{1}H NMR δ 7.95 (s, 1H, ArH), 7.83 (s, 2H, ArH), 7.28–7.20 (m, 3H, ArH), 7.14 (d, J = 7.5, 2H, ArH), 3.62 (s, 2H, 2 x OCH), 3.40, 2.65 (2d, J = 16, 4H, 2 x CH_2); ^{13}C NMR (100 MHz) δ 140.6, 138.1 (ArC), 131.9 (q, $J_{C\text{-}F}$ = 34.1, 2 x *C*CF_3), 129.9, 129.5, 129.0, 128.4, 126.4 (ArCH), 122.3 (q, $J_{C\text{-}F}$ = 273.3, 2 x CF_3), 78.7 (CS), 56.2 (2 x OCH), 37.2 (2 x CH_2); MS *m/z* 436 (M^+, 0.01), 160 (11), 159 (100), 144 (10), 141 (14), 131 (22), 129 (18), 128 (11), 116 (11), 115 (32), 91 (42); HRMS Calcd for $C_{19}H_{14}F_6O_3S$ (M^+) 436.0568, (M^+-F) 417.0584, found: 417.0566.

(1*R,3*s*,5*S**)-3-[3,5-Bis-(trifluoromethyl)phenylsulfonyl]-3-(4-nitrophenyl)-6-oxabicyclo–[3.1.0]hexane (6b).** White solid; R_f (pentane/EtOAc: 6/1) 0.15; mp 225–227 ºC; IR ν 3089, 3035, 2937, 1596, 1523, 1351, 1277, 1149; ^{1}H NMR δ 8.12, 7.37 (2d, J = 8.9, 4H, ArH), 8.05 (s, 1H, ArH), 7.59 (s, 2H, ArH), 3.75 (s, 2H, 2 x OCH), 3.09, 2.89 (2d, J = 14.8, 2H, CH_2); ^{13}C NMR δ 147.7, 143.3, 137.8 (ArC), 132.7 (q, J = 35.0, 2 x *C*CF_3), 129.6, 127.5, 123.2 (ArH), 122.5 (q, $J_{C\text{-}F}$ = 273.3, 2 x CF_3), 75.0 (CS), 56.0 (2 x OCH), 35.5 (2 x CH_2); MS *m/z* 481 (M^+, 0.09), 398 (12), 213 (18), 205 (26), 204 (100), 187 (16), 160 (13), 158 (45), 157 (14), 136 (32), 131 (10), 130 (29), 129 (53), 128 (51), 127 (19), 116 (14), 115 (39), 102 (12); HRMS Calcd for $C_{19}H_{13}F_6NO_5S$ (M^+) 481.0419, found: 481.0425.

(1*R,3*s*,5*S**)-Isopropyl 3-[3,5-bis-(trifluoromethyl)phenylsulfonyl]-6-oxabicyclo-[3.1.0]-hexane 3-carboxylate (6c).** White solid; R_f (hexane/EtOAc: 2/1) 0.21; mp 115–117 ºC; IR ν 3091, 3055, 2983, 1729, 1611, 1363, 1275, 1131; ^{1}H NMR δ 8.21 (s, 2H, ArH), 8.18 (s, 1H, ArH), 4.89 [sept., J = 6.2, 1H, C*H*$(CH_3)_2$], 3.62 (s, 2H, 2 x OCH), 3.02, 2.54 (2d, J = 14, 4H, 2 x CH_2), 1.19 (d, J = 6.2, 6H, 2 x CH_3); ^{13}C NMR δ 166.3 (CO), 139.4 (ArC), 132.8 (q, $J_{C\text{-}F}$ = 35.1, 2 x *C*CF_3), 130.0, 127.8 (ArCH), 122.3 (q, $J_{C\text{-}F}$ = 273.3, 2 x CF_3), 74.3 (CS), 71.3 [O*C*H$(CH_3)_2$], 54.7 (2 x OCH), 33.6 (2 x CH_2), 21.1 (2 x CH_3); MS *m/z* 446 (M^+, 0.05), 261 (16), 177 (24), 150 (12), 149 (100), 127 (11), 126 (36), 125 (17), 99 (11), 97 (13), 83 (10), 81 (15), 43 (28), 41 (11); HRMS Calcd for $C_{17}H_{16}F_6O_5S$ (M^+) 446.0623, (M^+ - F) 427.0639, found: 427.0667.

(1*R,3*s*,5*S**)-3-[3,5-Bis-(trifluoromethyl)phenylsulfonyl]-3-cyano-6-oxabicyclo[3.1.0]hexane (6d).** White solid; R_f (hexane/EtOAc: 2/1) 0.45; mp 164–166 ºC; IR ν 3113, 3059, 3025, 2956, 2244, 1631, 1351, 1282, 1140; ^{1}H NMR δ 8.43 (s, 2H, ArH), 8.28 (s, 1H, ArH), 3.78 (s, 2H, 2 x OCH), 2.72 (d, J = 14.4, 2H, CH_2), 2.64 (d, J = 14.3, 2H, CH_2); ^{13}C NMR (100 MHz) δ 137.5 (ArC), 133.6 (q, $J_{C\text{-}F}$ = 35.0, 2 x *C*CF_3), 130.5, 129.0 (ArCH), 122.0 (q, $J_{C\text{-}F}$ = 273.5, 2 x CF_3), 117.5 (CN), 61.9 (CS), 55.3 (2 x OCH), 35.3 (2 x CH_2); MS *m/z* 385 (M^+, 044), 366 (45), 276 (19), 262 (10), 261 (25), 214 (16), 213 (95), 195 (13), 194 (30), 163 (25), 144 (23), 143 (13), 108 (44), 107 (100), 106 (46), 91 (91), 81 (21), 80 (37), 79 (18), 53 (50), 52 (17); HRMS Calcd for $C_{14}H_9F_6NO_3S$ (M^+) 385.0207, (M^+ - F) 366.0223, found: 366.0229.

(1*R,3*r*,5*S**)-3-[3,5-Bis-(trifluoromethyl)phenylsulfonyl]-3-cyano-6-oxabicyclo[3.1.0]hexane (5d).** White solid; R_f (hexane/EtOAc: 2/1) 0.45; ^{1}H NMR δ 8.43 (s, 2H, ArH), 8.27 (s, 1H, ArH), 3.70 (s, 2H, 2 x OCH), 2.99 (d, J = 16.0, 2H, CH_2), 2.61 (d, J = 15.1, 2H, CH_2); ^{13}C NMR δ 137.5 (ArC), 133.4 (q, $J_{C\text{-}F}$ = 35.0, 2 x *C*CF_3), 130.8, 128.7 (ArCH), 122.1 (q, $J_{C\text{-}F}$ = 274.8, 2 x CF_3), 117.9 (CN), 61.5 (CS), 57.2 (2 x OCH), 36.8 (2 x CH_2).

(1*R,3*s*,5*S**)-Diethyl 3-[3,5-bis-(trifluoromethyl)phenylsulfonyl]-6-oxabicyclo[3.1.0] phosphonate (6e).** White solid; R_f (hexane/EtOAc: 2/1) 0.13; mp 98–100 ºC; IR ν 3106, 2982, 1601, 1368, 1288, 1126; ^{1}H NMR δ 8.45 (s, 2H, ArH), 8.15 (s, 1H, ArH), 4.18–4.08 (m, 4H, 2 x OCH_2), 3.75 (s, 2H, 2 x OCH), 2.84–2.58 (m, 4H, 2 x CH_2), 1.26 (t, J = 7.0, 6H, 2 x CH_3); ^{13}C

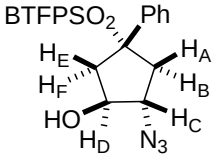
NMR δ 139.9 (d, $J_{C\text{-}P}$ = 2.2, ArC), 132.2 (q, $J_{C\text{-}F}$ = 34.0, 2 x *C*CF_3), 131.3, 127.6 (ArCH), 122.4 (q, $J_{C\text{-}F}$ = 273.3, 2 x CF_3), 74.2 (d, $J_{C\text{-}P}$ = 147.1, CP), 64.1 (d, $J_{C\text{-}P}$ = 6.6, 2 x OCH_2), 59.2 (d, $J_{C\text{-}P}$ = 4.4, 2 x OCH), 33.6 (d, $J_{C\text{-}P}$ = 2.2, 2 x CCH_2), 16.1 (d, $J_{C\text{-}P}$ = 5.6, 2 x CH_3); MS *m/z* 496 (M^+, 0.04), 261 (14), 219 (33), 218 (139), 213 (13), 189 (18), 163 (22), 161 (11), 149 (11), 83 (11), 82 (14), 81 (100), 65 (10), 53 (11); HRMS Calcd for $C_{17}H_{19}F_6O_6SP$ (M^+) 496.0544, (M^+ - F) 477.0560, found: 477.0551.

(1*R,3*r*,5*S**)-Diethyl 3-[3,5-bis-(trifluoromethyl)phenylsulfonyl]-6-oxabicyclo[3.1.0] phosphonate (5e).** White solid; R_f (hexane/EtOAc: 1/1) 0.12; mp 94–96 ºC; IR ν 3072, 2916, 1701, 1573, 1411, 1288, 1155; ^{1}H NMR δ 8.39 (s, 2H, ArH), 8.13 (s, 1H, ArH), 4.26–4.17 (m, 4H, 2 x OCH_2), 3.55 (s, 2H, 2 x OCH), 2.83–2.61 (m, 4H, 2 x CCH_2), 1.32 (t, *J* = 6.9, 6H, 2 x CH_3); ^{13}C NMR δ 141.0 (d, $J_{C\text{-}P}$ = 2.2, ArC), 132.2 (q, $J_{C\text{-}F}$ = 34.0, 2 x *C*CF_3), 131.1, 127.4 (ArCH), 122.8 (q, $J_{C\text{-}F}$ = 273.3, 2 x CF_3), 73.7 (d, $J_{C\text{-}P}$ = 136.1, CP), 64.3 (d, $J_{C\text{-}P}$ = 6.7, 2 x OCH_2), 58.2 (d, $J_{C\text{-}P}$ = 6.7, 2 x OCH), 34.0 (d, $J_{C\text{-}P}$ = 1.5, 2 x CH_2), 16.2 (d, $J_{C\text{-}P}$ = 5.4, 2 x CH_3); MS *m/z* 496 (M^+, 0.69), 432 (14), 261 (26), 219 (82), 218 (27), 213 (23), 194 (10), 191 (17), 190 (17), 189 (38), 163 (57), 162 (14), 161 (23), 145 (29), 135 (23), 133 (16), 109 (17), 83 (15), 82 (20), 81 (100), 65 (14), 53 (17); HRMS Calcd for $C_{17}H_{19}F_6O_6SP$ (M^+) 496.0544, found: 496.0537.

General procedure for epoxide opening with azide. To a DMF (5 mL) solution of the corresponding epoxide (0.5 mmol), an aqueous 20% v/v solution of LiN_3 (1.2 mL, 5 mmol) or NaN_3 (325 mg, 5 mmol) was added. The mixture was heated at 80 ºC for 24–48 h. The reaction was quenched with a saturated solution of NH_4Cl (15 mL), extracted with EtOAc (2 x 15 mL), the organic phase was washed with H_2O (2 x 15 mL) and dried ($MgSO_4$). Filtration and solvent evaporation afforded the corresponding crude azido alcohols, which were purified by flash chromatography (hexane/EtOAc) to afford pure compounds.

(1*R,2*R**,4*R**)-2-Azido-4-[3,5-bis-(trifluoromethyl)phenylsulfonyl]-4-phenylcyclopentanol (7aa).** Beige solid; R_f (hexane/EtOAc: 2/1) 0.44; mp 61–63 ºC; IR ν 3467, 3082, 2926, 2109, 1616, 1598, 1459, 1351, 1279, 1147; ^{1}H NMR δ 8.0 (s, 1H, ArH), 7.56 (s, 2H, ArH), 7.38–7.25 (m, 3H, ArH), 7.11 (d, *J* = 7.5, 2H, ArH), 4.65–4.59 (m, 1H, C*H*OH), 3.77–3.70 (m, 1H, CHN_3), 3.03 (dd, *J* = 14.5, 7.1, 1H x C*H*$_2$CHOH), 2.87 (d, *J* = 9.1, 2H, C*H*$_2$$CHN_3$), 2.35 (dd, *J* = 14.3, 9.3, 1H x C*H*$_2$CHOH); ^{13}C NMR δ 137.1, 136.2 (ArC), 132.1 (q, $J_{C\text{-}F}$ = 35.0, 2 x *C*CF_3), 130.1, 129.5, 128.7, 128.4, 127.2 (ArCH), 122.1 (q, $J_{C\text{-}F}$ = 273.5, 2 x CF_3), 75.5 (CHOH), 72.8 (CS), 65.7 (CHN_3), 39.6 (*C*H_2CHOH), 35.2 (*C*$H_2$$CHN_3$); MS *m/z* 202 ($M^+$ - $BTFPSO_2$, 72), 159 (79), 156 (21), 145 (22), 144 (579), 141 (15), 131 (24), 130 (25), 129 (54), 128 (259), 119 (39), 118 (22), 117 (34), 116 (17), 115 (56), 105 (11), 104 (30), 91 (100), 79 (13), 78 (16), 77 (45), 51 (12), 43 (12), 41 (16); HRMS Calcd for $C_{19}H_{15}F_6N_3O_3S$ (M^+) 479.0738, (M^+-H_2O-N_2) 433.0577, found: 433.0571.

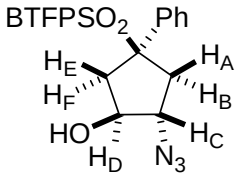
COSY summary: the following crossing peaks are observed: H_A and H_C; H_B and H_C; H_C and H_D; H_D and H_E, H_F; H_E and H_F.



(1*R,2*R**,4*S**)-2-Azido-4-[3,5-bis-(trifluoromethyl)phenylsulfonyl]-4-phenylcyclopentanol (8aa).** Beige solid; R_f (hexane/EtOAc: 4/1) 0.25; mp 79–80 ºC; IR ν 3442, 3082, 2929, 2115, 1629, 1279, 1137; ^{1}H NMR δ 8.02 (s, 1H, ArH), 7.55 (s, 2H, ArH), 739–7.26 (m, 3H, ArH), 7.07 (d, *J* =

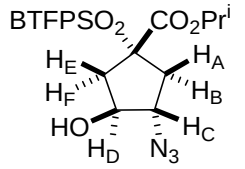
7.5, 2H, ArH), 4.34–4.30 (m, 1H, CHN_3), 4.21 (bs, 1H, C*H*OH), 3.22 (dd, *J* = 15.0, 6.6, 1H x CH_2CHN_3), 2.87 (d, *J* = 6.2, 2H, CH_2CHOH), 2.44 (dd, *J* = 15.0, 6.4, 1H x CH_2CHN_3); ^{13}C NMR δ 136.9, 136.2 (ArC), 132.3 (q, $J_{C\text{-}F}$ = 35.0, 2 x *C*CF_3), 130.2, 129.6, 128.8, 128.6, 127.4 (ArCH), 122.0 (q, $J_{C\text{-}F}$ = 273.5, 2 x CF_3), 76.1 (CHOH), 75.9 (CS), 67.8 (CHN_3), 40.1 (*C*H_2CHOH), 37.1 (*C*H_2CHN_3); MS *m/z* 213 (M^+-$C_{11}H_{12}N_3O_3S$, 21), 203 (12), 202 (100), 145 (23), 144 (60), 129 (44), 119 (43), 115 (40), 103 (48), 91 (80), 77 (34); HRMS Calcd for $C_{19}H_{15}F_6N_3O_3S$ (M^+) 479.0738, (M^+ - H_2O - F) 442.0649, found: 442.0692.

COSY summary: the following crossing peaks are observed: H_A and H_C; H_B and H_C; H_D and H_E, H_F.



(1*R,3*R**,4*R**)-Isopropyl 3-azido-1-[3,5-bis-(trifluoromethyl)phenylsulfonyl]-4-hydroxy–cyclopentanecarboxylate (7ca).** White solid; R_f (hexane/EtOAc: 2/1) 0.41; mp 90–93 ºC; IR ν 3410, 3075, 2994, 2964, 2944, 2152, 1736, 1629, 1355, 1340, 1320, 1274, 1132; ^{1}H NMR δ 8.29 (s, 2H, ArCH), 8.18 (s, 1H, ArCH), 4.96 (sept., *J* = 6.3, 1H, OCH), 4.31–4.27 (m, 1H, C*H*OH), 3.91–2.99 (m, 1H, CHN_3), 2.96 (dd, *J* = 14.8, 7.1, 1H x CH_2CHN_3), 2.75 (dd, *J* = 14.3, 5.8, 1H x CH_2CHOH), 2.51–2.40 (m, 2H, 1 x CH_2CHN_3, 1 x CH_2CHOH), 1.22 (d, *J* = 6.2, 6H, 2 x CH_3); ^{13}C NMR δ 167.1 (CO), 139.2 (ArC), 132.8 (q, $J_{C\text{-}F}$ = 35.0, 2 x *C*CF_3), 130.3, 127.8 (ArCH), 122.2 (q, $J_{C\text{-}F}$ = 273.5, 2 x CF_3), 76.4 (CS), 76.0 (CHOH), 71.9 (OCH), 66.4 (CHN_3), 38.2 (*C*H_2CHOH), 34.2 (*C*H_2CHN_3), 21.2, 21.1 (CH_3); MS *m/z* 430 (M^+ - H_2O - N_2, 7), 261 (32), 213 (44), 194 (16), 163 (10), 144 (10), 143 (10), 142 (92), 127 (11), 125 (13), 124 (62), 115 (13), 114 (48), 98 (10), 97 (100), 96 (74), 69 (32), 68 (19), 53 (11), 43 (52), 41 (37); HRMS Calcd for $C_{17}H_{17}F_6N_3O_5S$ (M^+) 489.0793, (M^+-$C_9H_{14}N_3O_3$) 276.9758, found: 276.9757.

COSY summary: the following crossing peaks are observed: H_A and H_C; H_B and H_C, H_C and H_D, H_D and H_E, H_F.



(1*R,2*R**,4*S**)-2-Azido-4-[3,5-bis-(trifluoromethyl)phenylsulfonyl]cyclopentanol (9).** White solid; R_f (hexane/EtOAc: 2/1) 0.30; mp 96–98 ºC; IR ν 3410, 3086, 2944, 2132, 2111, 1731, 1619, 1371, 1295, 1137; ^{1}H NMR δ 8.36 (s, 2H, ArH), 8.17 (s, 1H, ArH), 4.38–4.26 (m, 1H, C*H*OH), 3.36–3.45 (m 2H, CHS, CHN_3), 2.47–2.37 (m, 2H, CH_2CHOH), 2.18–2.11, 1.98–1.92 (2m, 2H, CH_2CHN_3); ^{13}C NMR δ 141.1 (ArC), 133.4 (q, $J_{C\text{-}F}$ = 35.0, 2 x *C*CF_3), 128.8, 127.6 (ArCH), 122.2 (q, $J_{C\text{-}F}$ = 273.5, 2 x CF_3), 75.9 (CHOH), 66.6 (CHN_3), 60.3 (CHS), 32.9 (*C*H_2CHOH), 29.5 (*C*H_2CHN_3); MS *m/z* 277 (M^+-$C_5H_8N_3O$, 5), 261 (36), 214 (18), 213 (66), 195 (13), 194 (28), 163 (26), 149 (20), 144 (21), 143 (13), 98 (100), 97 (18), 96 (12), 83 (45), 71 (77), 70 (33), 69 (23), 68 (21), 55 (13), 53 (13), 43 (75), 42 (13), 41 (41); HRMS Calcd for $C_{13}H_{11}F_6N_3O_3S$ (M^+) 403.0425, (M^+-$C_5H_8N_3O$) 276.9758, found: 276.9761.

(1*R,2*R**,4*R**)-2-Azido-4-[3,5-bis-(trifluoromethyl)phenylsulfonyl]cyclopentyl isopropyl carbonate (10).** Colorless oil; R_f (pentane/EtOAc: 6/1) 0.53; IR ν 3085, 2989, 2934, 2112, 1744, 1618, 1285, 1149; ^{1}H NMR (mixture of rotamers) δ 8.35 (s, 2H, ArH), 8.18 (s, 1H, ArH), 5.00–4.82 [m, 2H, OCH, OC*H*$(CH_3)_2$], 4.21–4.08 (m, 1H, CHN_3), 3.81–3.7 (m, 1H, CHS), 2.59–2.41, 2.30–1.99 (2m, 2H, CH_2), 1.30, 1.26 (2d, J = 4.9, 3H, CH_3); ^{13}C NMR (mixture of rotamers) δ 153.4, 153.1 (CO), 141.0, 140.7 (ArC), 133.4 (q, $J_{C\text{-}F}$ = 33.1, 2 x *C*CF_3), 128.9, 127.7 (ArCH), 122.2 (q, $J_{C\text{-}F}$ = 273.3, 2 x CF_3), 80.6, 79.5 (CHO), 73.17, 73.05 [O*C*H$(CH_3)_2$], 64.7, 64.4 (CHN_3), 61.1, 60.5 (CHS), 31.3, 30.59, 30.55, 30.3 (CH_2), 21.6, 21.5 (CH_3); MS *m/z* 473 (M^+, 0.06), 279 (17), 277 (45), 262 (21), 261 (40), 214 (12), 213 (79), 194 (16), 163 (11), 98 (21), 97 (16), 96 (17), 81 (11), 80 (100), 71 (13), 69 (13), 68 (17), 53 (17), 43 (100), 41 (26); HRMS Calcd for $C_{17}H_{17}F_6N_3O_4S$ (M^+) 473.0844, (M^+-Pr^i) 430.0296, found: 430.0282.

General procedure for epoxide opening with benzylamine. Benzylamine (1.1 mL, 10 mmol) was added to a DMF (5 mL) solution of epoxide **6a** (0.5 mmol) and the reaction mixture was heated at 100 ºC for 24 h. The reaction was quenched with a saturated solution of NH_4Cl (10 mL), extracted with EtOAc (2 x 10 mL), and the organic phase dried ($MgSO_4$). Solvent evaporation afforded the corresponding crude alcohol amine, which was purified by flash chromatography to afford pure compound **7ab**.

General procedure for epoxide opening with amines under solventless conditions. A mixture of the corresponding epoxide **6a** or **6d** (0.3 mmol) and benzyl or butyl amine (1 mL) was heated at 80 ºC for 38 h. The reaction was quenched with a saturated solution of NH_4Cl (10 mL), extracted with EtOAc (2 x 10 mL), and the organic phase was dried ($MgSO_4$). Solvent evaporation afforded the corresponding crude alcohol amine, which was purified by flash chromatography (hexane/EtOAc) to afford pure compounds **7ab**, **7ac** and **7db**.

Experimental procedure for synthesis of compound 7ab under microwave irradiation. A 10 mL glass tube was charged with epoxide **6a** (0.3 mmol) and benzyl amine (1 mL), sealed with a septum and heated at 95 ºC (200W) for 0.5 h with air stream cooling. The reaction mixture was cooled at room temperature and quenched with a saturated solution of NH_4Cl (10 mL). The mixture was extracted with EtOAc (2 x 10 mL) and the organic phase was dried ($MgSO_4$). Filtration and solvent evaporation afforded the corresponding crude alcohol amine, which was purified by flash chromatography (hexane/EtOAc) to afford pure compound **7ab**.

(1*R,2*R**,4*R**)-2-(Benzylamino)-4-[3,5-bis-(trifluoromethyl)phenylsulfonyl]-4-phenyl–cyclopentanol (7ab).** White solid; R_f (hexane/EtOAc: 1/1) 0.12; mp 168–169 ºC; IR ν 3300, 3074, 2927, 2873, 2814, 1626, 1444, 1365, 1287, 1140; ^{1}H NMR δ 7.98 (s, 1H, ArH), 7.53 (s, 2H, ArH), 7.35–7.23 (m, 10H, ArH), 7.08 (d, J = 8.0, 2H, ArH), 4.49–4.43 (m, 1H, C*H*OH), 3.94, 3.85 (2d, J = 14.0, 2H, CH_2Ph), 3.05–2.94 (m, 2H, CHN, 1 x C*H*$_2$CHOH), 2.80–2.66 (m, 2H, C*H*$_2$CHN), 2.29 (dd, J = 14.2, 8.7, 1H x C*H*$_2$CHOH); ^{13}C NMR δ 139.6, 137.5, 136.9 (ArC), 132.0 (q, $J_{C\text{-}F}$ = 35.0, 2 x *C*CF_3), 130.1, 129.3, 128.9, 128.6, 128.4, 128.2, 127.3, 127.0 (ArCH), 122.1 (q, $J_{C\text{-}F}$ = 273.5, 2 x CF_3), 76.1 (CHOH), 73.9 (CS), 64.4 (CHN), 52.4 (CH_2Ph), 40.0 (*C*H_2CHOH), 37.1 (*C*H_2CHN); MS *m/z* 543 (M^+, 0.09), 266 (44), 248 (18), 222 (19), 120 (15), 106 (44), 91 (100); HRMS Calcd for $C_{26}H_{23}F_6NO_3S$ (M^+) 543.1303, (M^+-BTFPSO$_2$) 266.1545, found: 266.1512.

(1*R,3*R**,4*R**)-3-(Benzylamino)-1-[3,5-bis-(trifluoromethyl)phenylsulfonyl]-4-hydroxy-1–cyanocyclopentane (7db).** White solid. R_f (hexane/EtOAc: 1/1) 0.43; mp 162–163 ºC; IR ν 3446, 3258, 3086, 2918, 2842, 1624, 1604, 1467, 1345, 1284, 1137; ^{1}H NMR δ 8.45 (s, 2H, ArH), 8.26 (s, 1H, ArH), 7.37–7.27 (m, 5H, ArH), 4.27–4.22 (m, 1H, C*H*OH), 3.87, 381 (2d, J = 13.3, 2H,

CH_2Ph), 3.31 (m, 1H, CHN), 2.82 (dd, J =14.3, 6.0, 1H x CH_2CHOH), 2.61, 2.35 (2dd, J =14.3, 6.6, 2H, CH_2CHN), 2.19 (dd, J =14.2, 4.5, 1H x CH_2CHOH); ^{13}C NMR δ 139.3, 137.3 (ArC), 134.0 (q, $J_{C\text{-}F}$ = 34.0, 2 x CCF$_3$), 130.6, 128.7, 128.0, 127.5 (ArCH), 122.1 (q, $J_{C\text{-}F}$ = 273.3, 2 x CF$_3$), 118.1 (CN), 76.1 (CHOH), 64.8 (CS), 63.7 (CHN), 52.3 (CH_2Ph), 39.6 (CH$_2$CHOH), 37.7 (CH$_2$CHN); MS *m/z* 492 (M^+, 0.01), 215 (26), 171 (24), 91 (10); HRMS Calcd for $C_{21}H_{18}F_6N_2O_3S$ (M^+) 492.0942, found: 492.0948.

(1*R,2*R**,4*R**)-4-[3,5-Bis-(trifluoromethyl)phenylsulfonyl]-2-(butylamino)-4-phenyl–cyclopentanol (7ac).** Beige solid; R_f (hexane/EtOAc: 1/4) 0.23; mp 173–174 ºC; IR ν 3291, 2959, 2919, 2847, 1451, 1357, 1308, 1276, 1133; ^{1}H NMR δ 7.98 (s, 1H, ArH), 7.55 (s, 2H, ArH), 7.35 (m, 3H, ArH), 7.13 (d, J = 7.6, 2H, ArH), 4.48–4.40 (m, 1H, CHOH), 2.99–2.28 (m, 7H, CHN, CH_2CHOH, CH_2CHN, NCH_2CH$_2$), 1.58–1.33 (m, 4H, 2 x CH$_2$), 0.94 (t, J = 7.3, 3H, CH$_3$); ^{13}C NMR δ 137.5, 137.1 (ArC), 132.0 (q, $J_{C\text{-}F}$ = 34.0, 2 x CCF$_3$), 130.2, 129.2, 129.0, 128.4, 126.9 (ArCH), 122.2 (q, $J_{C\text{-}F}$ = 273.3, 2 x CF$_3$), 75.7 (CHOH), 74.0 (CS), 64.9 (CHN), 48.0, 40.2, 37.2, 32.4, 20.4 (CH$_2$), 13.9 (CH$_3$); MS *m/z* 509 (M^+, 0.81), 466 (19), 233 (17), 232 (100), 214 (36), 213 (12), 202 (10), 189 (10), 188 (63), 177 (14), 170 (41), 159 (14), 158 (11), 149 (55), 144 (21), 141 (14), 129 (13), 115 (19), 111 (12), 105 (13), 97 (16), 95 (11), 91 (22), 86 (30), 85 (15), 84 (12), 83 (15), 77 (11), 72 (17), 71 (15), 69 (15), 57 (38), 55 (19), 44 (14), 43 (19), 41 (15); HRMS Calcd for $C_{23}H_{25}F_6NO_3S$ (M^+) 509.1459, found: 509.1484.

General procedure for epoxide ring opening with bromodimethylsulfonium bromide. To a solution of the corresponding epoxide (0.1 mmol) in CH_3CN (0.8 mL) stirred at RT bromodimethylsulfonium[16] (71 mg, 0.5 mmol) was added portionwise. After stirring at RT for 16 h the mixture was quenched with H_2O (2 mL), extracted with EtOAc (2 x 2 mL), and the organic phase dried ($MgSO_4$). Solvent evaporation afforded the corresponding crude bromo alcohols, which were purified by flash chromatography (hexane/EtOAc) to afford pure compounds.

(1*R,2*R**,4*R**)-4-[3,5-bis-(trifluoromethyl)phenylsulfonyl]-2-bromo-4-phenylcyclopentanol (7ad)**. White solid; R_f (hexane/EtOAc: 4/1) 0.28; mp 125–127 ºC; IR ν 3540, 3083, 1620, 1597, 1352, 1282, 1126; ^{1}H NMR δ 8.00 (s, 1H, ArH), 7.56 (s, 2H, ArH), 7.40–7.25 (m, 3H, ArH), 7.12 (d, J = 7.7, 2H, ArH), 4.80–4.70 (m, 1H, CHOH), 3.93–3.84 (m, 1H, CHBr), 3.26 (dd, J = 14.6, 10.8, 1H x CH_2CHBr), 3.11 (dd, J = 14.7, 8.1, 1H x CH_2CHBr), 3.03 (dd, J = 14.4, 7.4, 1H x CH_2CHOH), 2.50 (d, J = 3.9, 1H, OH), 2.33 (dd, J = 14.5, 9.2, 1H x CH_2CHOH); ^{13}C NMR δ 137.1, 135.8 (ArC), 132.2 (q, $J_{C\text{-}F}$ = 34.6, 2 x CCF$_3$), 130.2, 129.6, 128.8, 128.6, 127.2 (ArCH), 122.1 (q, $J_{C\text{-}F}$ = 273.9, 2 x CF$_3$), 78.2 (CHOH), 73.7 (CS), 50.8 (CHBr), 39.8 (CH$_2$CHBr), 39.5 (CH$_2$CHOH); MS *m/z* 241 (M^++2 - BTFPSO$_2$, 100), 239 (M^+-BTFPSO$_2$, 100), 223 (100), 221 (100), 213 (32), 163 (13), 160 (24), 159 (100), 144 (24), 143 (32), 142 (100), 141 (64), 131 (100), 129 (33), 115 (81), 105 (20), 103 (34), 91 (64), 77 (26); HRMS Calcd for $C_{19}H_{15}BrF_6O_3S$ (M^+) 515.9829, (M^+-BTFPSO$_2$) 239.0072 found: 239.0072.

(1*R,3*R**,4*S**)-4-[3,5-bis-(trifluoromethyl)phenylsulfonyl]-2-bromo-4-phenylcyclopentanol (8ad)**. White solid; R_f (hexane/EtOAc: 2/1) 0.51; mp 153–155 ºC; IR ν 3537, 3050, 1629, 1609, 1361, 1279, 1188, 1142; ^{1}H NMR δ 8.03 (s, 1H, ArH), 7.55 (s, 2H, ArH), 7.40–7.26 (m, 3H, ArH), 7.10 (d, J = 7.8, 2H, ArH), 4.54–4.42 (m, 2H, CHOH, CHBr), 3.56 (dd, J = 15.5, 6.5, 1H x CH_2CHBr), 3.51 (d, J = 7.8, 1H, OH), 3.08 (dd, J = 15.5, 6.8, 1H x CH_2CHBr), 2.92–2.83 (m, 2H, 1 x CH_2CHBr, 1 x CH_2CHOH); ^{13}C NMR (100MHz, C_6D_6) δ 137.7, 137.0 (ArC), 132.0 (q, $J_{C\text{-}F}$ = 34.0, 2 x CCF$_3$), 130.3, 129.19, 129.12, 128.3, 126.9 (ArCH), 122.5 (q, $J_{C\text{-}F}$ = 273.3, 2 x CF$_3$), 78.9 (CHOH), 76.3 (CS), 53.3 (CHBr), 41.5 (CH$_2$CHBr), 39.7 (CH$_2$CHOH); MS *m/z* 241 (M^++2 -

BTFPSO$_2$, 62), 239 (M$^+$-BTFPSO$_2$, 62), 223 (46), 221 (45), 213 (15), 159 (99), 144 (17), 142 (100), 141 (37), 131 (62), 129 (27), 115 (55), 105 (14), 103 (19), 91 (45), 77 (19), 43 (13); HRMS Calcd for $C_{19}H_{15}BrF_6O_3S$ (M$^+$) 515.9829, found: 515.98.38.

(1*R,2*R**,4*R**)-4-[3,5-Bis-(trifluoromethyl)phenylsulfonyl]-2-bromo-4-(4-nitrophenyl)-cyclopentanol (7bd)**. White solid; R$_f$ (hexane/EtOAc: 7/3) 0.47; mp 249–250 ºC; IR ν 3507, 3081, 2969, 2918, 2842, 1731, 1609, 1513, 1361, 1274, 1142; ^{1}H NMR (CD_3COCD_3) δ 8.41 (s, 1H, ArH), 8.15 (d, *J* = 8.9, 2H, ArH), 7.76 (s, 2H, ArH), 7.83 (d, *J* = 8.8, 2H, ArH), 4.91 (d, *J* = 5.4, 1H, OH) 4.70–4.65 (m, 1H, C*H*OH), 4.13–4.07 (m, 1H, CHBr), 3.38 (dd, *J* = 15.1, 8.1, 1H x CH_2CHBr), 3.25–3.17 (m, 2H, 1 x CH_2CHBr, 1 x CH_2CHOH), 2.45 (dd, *J* = 14.4, 8.4, 1H x CH_2CHOH); ^{13}C NMR (100MHz, CD_3COCD_3) δ 148.9, 144.7, 138.1 (ArC), 132.9 (q, $J_{C\text{-}F}$ = 35.0, 2 x *C*CF$_3$), 131.8, 131.2, 129.1, 123.8 (ArCH), 123.4 (q, $J_{C\text{-}F}$ = 272.1, 2 x CF$_3$), 79.0 (CHOH), 75.4 (CS), 52.2 (CHBr), 41.1 (*C*H$_2$CHBr), 40.9 (*C*H$_2$CHOH); MS *m/z* 563 (M$^+$+2, 0.23), 561 (M$^+$, 0.22), 286 (32), 284 (36), 268 (55), 266 (54), 214 (15), 213 (25), 205 (26), 204 (100), 195 (14), 188 (35), 187 (94), 176 (20), 163 (18), 158 (54), 150 (12), 145 (14), 144 (15), 141 (25), 139 (14), 131 (19), 130 (53), 129 (51), 128 (57), 127 (22), 116 (479, 115 (82), 103 (16), 102 (21), 91 (16), 89 (14), 77 (15), 63 (13), 58 (17), 43 (13); HRMS Calcd for $C_{19}H_{14}BrF_6NO_5S$ (M$^+$) 560.9680, found: 560.9674.

(1*R,3*R**,4*R**)-Isopropyl 1-[3,5-bis-(trifluoromethyl)phenylsulfonyl]-3-bromo-4-hydroxy-cyclopentanecarboxylate (7cd).** Yellow oil; R$_f$ (hexane/EtOAc: 4/1) 0.28; IR ν 3478, 3086, 2983, 2921, 1724, 1631, 1358, 1275, 1152; ^{1}H NMR δ 8.30 (s, 2H, ArH), 8.18 (s, 1H, ArH), 4.95 (sept., *J* = 6.2, 1H, OCH), 4.53–4.49 (m, 1H, C*H*OH), 4.04–3.99 (m, 1H, CHBr), 3.25 (dd, *J* = 15.1, 7.5, 1H x CH_2CHBr), 2.94 (dd, *J* = 14.3, 6.2, 1H x CH_2CHOH), 2.86 (dd, *J* = 15.0, 7.7, 1H x CH_2CHBr), 2.45 (dd, *J* = 14.4, 5.0, 1H x CH_2CHOH), 2.25 (s, 1H, OH), 1.21 (d, *J* = 6.7, 6H, 2 x CH$_3$); ^{13}C NMR δ 166.9 (CO), 139.2 (ArC), 132.8 (q, $J_{C\text{-}F}$ = 35.0, 2 x *C*CF$_3$), 130.4, 127.9 (ArCH), 122.2 (q, $J_{C\text{-}F}$ = 273.5, 2 x CF$_3$), 78.9 (CHOH), 76.8 (CS), 71.9 (OCH), 50.5 (CHBr), 38.8 (*C*H$_2$CHBr), 37.6 (*C*H$_2$CHOH), 21.2, 21.1 (CH$_3$); MS *m/z* 467 (M$^+$-OPr^i, 4.5), 422 (11), 420 (14), 391 (10), 378 (53), 350 (13), 349 (66), 331 (39), 279 (13), 261 (50), 213 (42), 209 (27), 207 (30), 194 (18), 191 (74); 189 (77), 169 (23), 168 (27), 163 (23), 161 (13), 157 (12), 147 (15), 145 (19), 144 (12), 127 (53), 126 (47), 125 (23); 115 (12); 111 (28), 110 (12), 109 (33), 99 (16), 97 (18), 83 (35), 82 (23), 81 (39), 65 (14), 55 (19), 53 (34), 43 (100), 41 (23); HRMS Calcd for $C_{17}H_{17}BrF_6O_5S$ (M$^+$) 525.9884, (M$^+$-OH) 508.9857 found: 508.9852.

(1*R,3*R**,4*R**)-1-[3,5-Bis-(trifluoromethyl)phenylsulfonyl]-3-bromo-4-hydroxy-1-cyano-cyclopentane (7dd).** White solid; R$_f$ (hexane/EtOAc: 2/1) 0.46; mp 120–122 ºC; IR ν 3481, 3082, 2934, 2863, 2257, 1623, 1607, 1279, 1148; ^{1}H NMR δ 8.48 (s, 2H, ArH), 8.28 (s, 1H, ArH), 4.58–4.56 (m, 1H, CHOH), 4.22–4.16 (m, 1H, CHBr), 3.10–2.90 (m, 3H, CH_2CHBr, 1 x CH_2CHOH), 2.60 (s, 1H, OH), 2.29 (dd, *J* = 14.3, 4.7, 1H, 1 x CH_2CHOH); ^{13}C NMR δ 137.0 (ArC), 133.7 (q, $J_{C\text{-}F}$ = 35.1 2 x *C*CF$_3$), 130.7, 129.1 (ArCH), 122.0 (q, $J_{C\text{-}F}$ = 274.2, 2 x CF$_3$), 117.5 (CN), 78.8 (CS), 64.1 (CHOH), 49.0 (CHBr), 40.6 (*C*H$_2$CHBr), 39.1 (*C*H$_2$CHOH); MS *m/z* 467 (M$^+$+2, 1.3), 465 (M$^+$,1.4), 448 (11), 446 (10), 310 (26), 279 (22), 277 (29), 261 (23), 214 (10), 213 (100), 195 (11), 194 (34); 190 (76); 188 (78), 172 (40); 170 (39); 163 (28), 149 (14), 144 (25), 143 (13), 109 (20); 108 (48), 107 (38), 106 (11), 92 (18), 91 (29), 81 (21), 80 (66), 53 (48), 52 (10), 43 (15); HRMS Calcd for $C_{14}H_{10}BrNF_6O_3S$ (M$^+$) 464.9469, found: 464.9467.

(1*R,3*R**,4*R**)-Diethyl 1-[3,5-bis-(trifluoromethyl)phenylsulfonyl]-3-bromo-4-hydroxy-cyclopentylphosphonate (7ed).** Yellow oil; R$_f$ (hexane/EtOAc: 1/1) 0.48; IR ν 3396, 3107, 2988, 2937, 1626, 1446, 1358, 1270, 1146, 1028; ^{1}H NMR δ 8.44 (s, 2H, ArH), 8.18 (s, 1H, ArH), 4.52–

4.43 (m, 1H, C*H*OH), 4.24–3.97 (m, 5H, CHBr, 2 x OCH_2), 3.35 (d, *J* = 6.2, 1H, OH), 2.99–2.74 (m, 3H, 1 x C*H*$_2$CHOH, C*H*$_2$CHBr), 2.33–2.19 (m, 1H x C*H*$_2$CHOH), 1.27, 1.17 (2t, *J* = 7.0, 6H, 2 x CH_3); ^{13}C NMR δ 139.9 (d, $J_{C\text{-}P}$ = 2.2, ArC), 132.5 (q, $J_{C\text{-}F}$ = 33.7, 2 x *C*CF_3), 131.1, 127.7 (ArCH), 122.3 (q, $J_{C\text{-}F}$ = 273.5, 2 x CF_3), 78.5 (d, $J_{C\text{-}P}$ = 5.4, CHOH), 69.2 (d, $J_{C\text{-}P}$ = 144.2, CS), 64.8, 64.1 (2d, $J_{C\text{-}P}$ = 6.7, 2 x OCH_2), 50.9 (d, $J_{C\text{-}P}$ = 6.7, CHBr), 37.4 (*C*H_2CHBr), 35.9 (*C*H_2CHOH), 16.1, 15.9 (2d, $J_{C\text{-}P}$ = 6.7, 2 x CH_3); MS *m/z* 577 (M^+, 0.24), 442 (13), 441 (83), 433 (25), 413 (13), 385 (19), 365 (38), 301(96), 299 (100), 283 (33), 281 (34), 273 (10), 271 (11), 261 (29), 255 (12), 253 (11), 243 (10), 227 (35), 225 (35), 219 (78), 218 (11), 213 (31), 207 (64), 194 (14), 191 (24), 187 (11), 163 (64), 161 (19), 155 (38), 147 (16), 146 (25), 145 (36), 135 (23), 133 (13), 127 (18), 109 (24), 99 (19), 83 (19), 82 (17), 81 (39), 65 (23), 53 (18); HRMS Calcd for $C_{17}H_{20}BrNF_6O_6PS$ (M^+) 575.9806, found: 575.9821.

General procedure for preparation of cyclopentenones 11–14. **Method A (Swern oxidation).** A mixture of CH_2Cl_2 (725 µL) and DMSO (246 µL, 3.2 mmol) was added within 5 min to a stirred solution of oxalyl chloride (145 µL, 1.6 mmol) in CH_2Cl_2 (3.6 mL) at -60 ºC. The reaction mixture was stirred for 15 min and then the alcohol **7** (1.45 mmol) was added within 5 min; stirring was continued for an additional 15 min. TEA (1 mL, 7.2 mmol) was then added, and the reaction mixture was stirred overnight and allowed to warm to room temperature. Water (10 mL) was then added and the aqueous layer was extracted with additional CH_2Cl_2 (2 x 10 mL). The organic layers were combined, washed with saturated NaCl solution (20 mL), and dried ($MgSO_4$). Solvent evaporation afforded the corresponding crude cyclopentenones, which were purified by flash chromatography (pentane/Et_2O).

Method B (TPAP/NMO). TPAP (27 mg, 0.075 mmol) was added to a stirred mixture of alcohol **7ad** (273 mg, 0.5 mmol) and NMO (180 mg, 1.5 mmol) in CH_2Cl_2 (2 mL) at RT. After stirred for 24 h at the same temperature, the reaction mixture was filtered through a pad of Celite, which was washed with Et_2O. Solvent evaporation afforded the corresponding crude cyclopentenone, which was purified by flash chromatography (pentane/Et_2O).

Method C (IBX). To a solution of corresponding alcohol (0.5 mmol) in THF (3 mL) and DMSO (3 mL, for compound **7ad**), or DMSO (6 mL, for **7bd** and **7ca**), was added IBX[20] (418 mg, 1.5 mmol), and the mixture was stirred at RT for 48 h. The mixture was diluted with H_2O (4 mL), and stirred at 0 ºC for 10 min. The resulting suspension was filtered through a Celite pad, which was washed with EtOAc. The filtrated was diluted with brine (5 mL), followed by extraction with Et_2O (3 x 15 ml) and dried ($MgSO_4$). Solvent evaporation afforded the corresponding crude cyclopentenones, which were purified by flash chromatography (pentane/Et_2O).

5-Bromo-3-phenyl-2-cyclopentenone (11). White solid; R_f (pentane/Et_2O: 6/1) 0.23; mp 58–60 ºC; IR ν 2919, 2850, 1691, 1598, 1441; ^{1}H NMR δ 7.65 (d, *J* = 7.0, 2H, ArH), 7.52–7.46 (m, 3H, ArH), 6.65 (bs, 1H, CH=C), 4.56 (dd, *J* = 6.8, 2.2, 1H, CHBr), 3.77–3.71 (m, 1H x CH_2), 3.36 (dd, *J* = 18.8, 1.6, 1H x CH_2); ^{13}C NMR δ 201.9 (CO), 171.0, 169.7 (ArC, CH=*C*), 132.1, 129.0, 127.0, 124.2 (ArCH, *C*H=C), 42.1 (CHBr), 40.2 (CH_2); MS *m/z* 238 (M^++2, 16), 236 (M^+, 17), 158 (14), 157 (100), 130 (38), 128 (62), 127 (24), 102 (20), 64 (11), 51 (12); HRMS Calcd for $C_{11}H_9BrO$ (M^+) 235.9837, found: 235.9835

5-Bromo-3-(4-nitrophenyl)-2-cyclopentenone (13). White solid; R_f (pentane/Et_2O: 2/1) 0.13; mp 158–160 ºC; IR ν 2912, 2844, 1719, 1587, 1464; ^{1}H NMR δ 8.34, 7.80 (2d, *J* = 8.9, 2H, ArH), 6.76 (s, 1H, CH=C), 4.56 (dd, *J* = 6.8, 2.2, 1H, CHBr), 3.82–3.73, 3.41–3.34 (2m, 2H, CH_2); ^{13}C NMR δ 201.0 (CO), 167.4 (CH=*C*), 138.7, 127.6 (ArC), 127.8, 124.3 (ArCH, *C*H=C), 40.2 (CHBr), 29.6

(CH_2); MS *m/z* 281 (M^++1, 1.70), 204 (M^++2 - Br, 10), 203 (M^++1 - Br, 83), 202 (M^+ - Br, 10), 187 (12), 186 (60), 157 (19), 156 (77), 129 (32), 128 (100), 127 (37), 115 (26), 102 (17), 101 (15), 89 (14), 77 (13), 75 (19), 63 (16), 51 (19); HRMS Calcd for $C_{11}H_8BrNO_3$ (M^+) 280.9681, 202.0599 (M^+-Br) found: 202.0499.

Isopropyl 4-azido-3-oxo-1-cyclopentenecarboxylate (14). Colorless oil; R_f (pentane/Et_2O: 4/1) 0.31; IR ν 2986, 2931, 2253, 2116, 1731, 1231, 1107, 910, 732; ^{1}H NMR δ 6.75 (s, 1H, CH=C), 5.17 (sept., J = 6.2, 1H, OCH), 4.14 (dd, J = 7.3, 3.1, 1H, CHN_3), 3.23–3.14, 2.63–2.55 (2m, 2H, CH_2), 1.33 (d, J = 6.2, 6H, 2 x CH_3); ^{13}C NMR δ 204.2 (CO), 168.8, 168.4 (CO_2Pr^i, CH=*C*), 135.1 (*C*H=C), 70.0 (OCH), 60.6 (CHN_3), 33.8 (CH_2), 21.6 (2 x CH_3); MS *m/z* 209 (M^+, 0.86), 167 (32), 150 (11), 149 (100), 71 (15), 70 (14), 57 (23); HRMS Calcd for $C_9H_{11}N_3O_3$ (M^+) 209.0800, (M^+-N_2) 181.0739, found: 181.0746

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