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Corey–Chaykovsky Reactions of Nitro Styrenes Enable *cis*-Configured Trifluoromethyl Cyclopropanes

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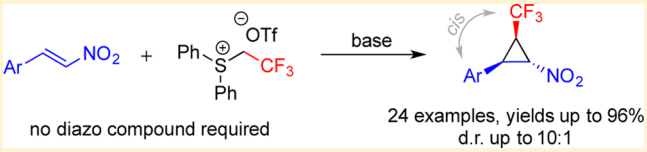
Supporting Information

ABSTRACT: Trifluoromethyl-substituted cyclopropanes are an attractive family of building blocks for the construction of pharmaceutical and agrochemical agents. This work demonstrated the utilization of fluorinated sulfur ylides as versatile reagents for Corey–Chaykovsky cyclopropanation reactions of nitro styrenes. This protocol favored the synthesis of *cis*-configured trifluoromethyl cyclopropanes for a broad range of substrates with excellent yields and good diastereoselectivities.

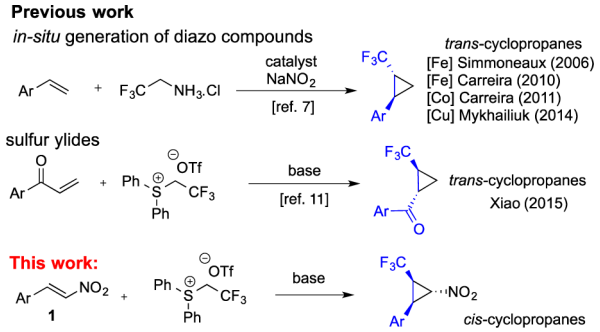


Cyclopropanes are a small and fascinating class of building blocks that possess unique and highly desirable properties for organic synthesis.[1] Because of their unique structure, they allow precise spatial arrangement of functional groups, and hence, unsurprisingly, cyclopropanes have found widespread application in pharmaceutical or agrochemical research.[1a,2] Of particular interest are fluorinated cyclopropane moieties where the introduction of one or more fluorine atoms[3] can significantly alter the chemical, biological, and physiological properties of the molecules.[4] The construction of trifluoromethyl-substituted cyclopropanes is important in the design of new bioactive molecules, as they are often considered the fluorinated bioisostere of the *tert*-butyl group.[5]

Recently, there have been numerous innovative developments in the synthesis of trifluoromethyl cyclopropanes ranging from the ring-contraction reaction to the ring-closure of acyclic precursors or the [2 + 1] cycloaddition reaction between alkenes and carbenes.[5a,6] Of the latest strategy, trifluoro diazoethane as CF_3-bearing carbene precursor has found its way into the standard organic synthesis repertoire.[7] However, handling this small and reactive molecule is not favorable and still poses serious safety hazards even with modern technological solutions.[8] Encouraged by our own experience in the field,[8] we set out to develop a new convenient and efficient synthetic approach for the trifluoromethylation reaction of alkenes using sulfur ylides (Scheme 1).

Sulfur-ylides are a well-known class of reagents and have been extensively studied over the past years as stoichiometric reagents[9,10] or catalysts.[11] Fluorinated sulfur-ylides, however, were only introduced recently as reagents for organic synthesis.[5a] In particular, trifluoroethyl diphenylsulfonium salts offer attractive and reliable alternatives to trifluoro diazoethane.[12] This sulfonium salt was recently demonstrated to be a versatile trifluoromethyl carbene source for iron-catalyzed cyclopropanation reactions of alkenes[12b] and Corey–Chaykovsky cyclopropanation reactions of terminal vinyl ketones.[12a] In line with our current research interests in the chemistry of diazo compounds[8] and electron-rich alkenes with ylide character,[13] we were intrigued to utilize fluorinated diphenylsulfonium ylides in the cyclopropanation reaction of nitro styrenes. To our knowledge, there have been only a limited number of examples in the literature describing cyclopropanation reactions of nitro styrene derivatives with sulfur ylides; however, little was known about their substrate scope and applicability.[14] Herein, we report our development of the first general example of Corey–Chaykovsky cyclopropanation reactions of nitro olefins, which enable access to a family of synthetically useful trifluoromethyl- and nitrogen-substituted cyclopropanes with unusual *cis* configurations.

Scheme 1. Synthesis of Trifluoromethyl Cyclopropanes



We started our investigations toward the Corey–Chaykovsky cyclopropanation of nitro styrenes using trifluoroethyl diphenylsulfonium triflate as the ylide precursor. As the base plays a key role in the deprotonation of the sulfonium salt, we

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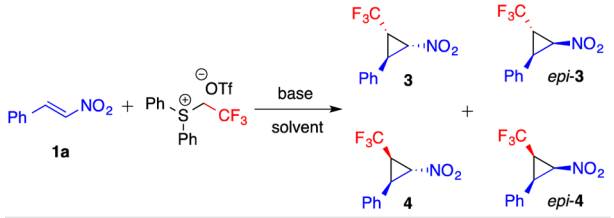
first investigated different bases and were delighted to observe that tetrabutyl ammonium difluoro triphenyl silicate (TBAT) provided the desired cyclopropane in excellent total yield (Table 1, entry 1). However, the reaction proceeded only with

Table 1. Optimization of Reaction Conditions



#[a]	base	solvent	yield[b] 3	yield[b] 4 and epi-3
1	TBAT	toluene	56%	37%
2	TBAT	$CHCl_3$	n.d.	43%
3	K_2CO_3	$CHCl_3$		7% (n.d.)
4	CsF	$CHCl_3$		2% (n.d.)
5	NaH	$CHCl_3$		no reaction
6	Cs_2CO_3	DMF		no reaction
7	Cs_2CO_3	DMAc	n.d.	67% (1:1)
8	Cs_2CO_3	THF	n.d.	60% (1:1)
9[c]	Cs_2CO_3	$CHCl_3$	9%	85% (10:1)

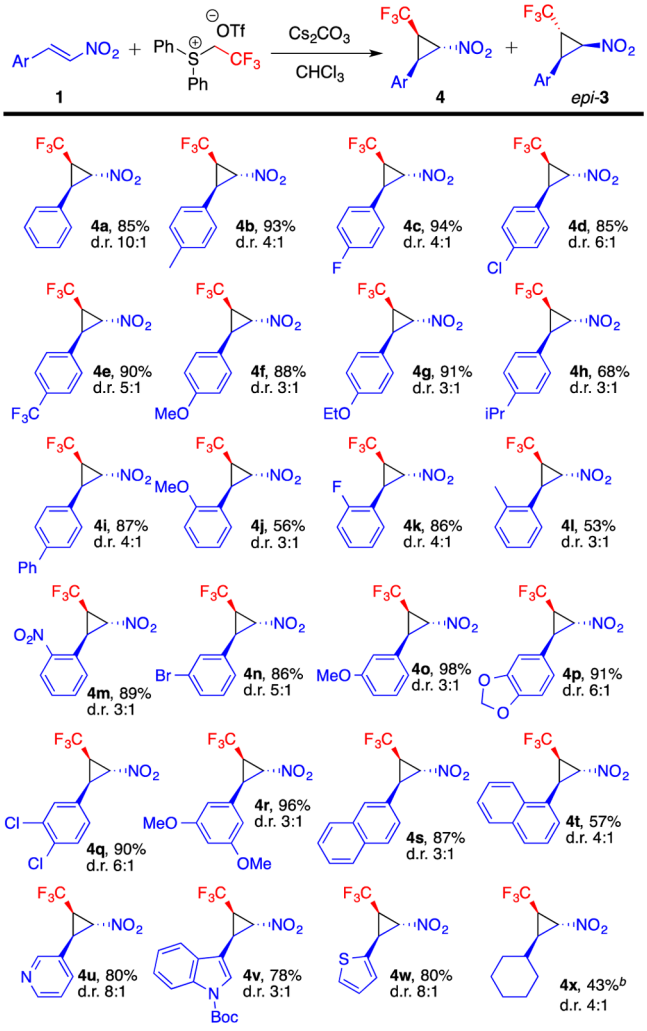
[a]Nitro styrene **1a** (0.2 mmol), sulfonium salt (2.0 equiv, 0.4 mmol), base (2.0 equiv, 0.4 mmol), and 80 mg of 4 Å molecular sieves were suspended in the indicated solvent and stirred at room temperature for 4 h. [b]Yields were reported for isolated products; n.d. = not determined. [c]Reaction time of 24 h.

little diastereoselectivity, and **3** and **4** could be isolated with 56 and 37% yield, respectively. Different solvents were investigated, and interestingly, a switch from toluene to chloroform proved highly effective, and a 20:1 mixture of isomers **4** and **3** was obtained, yet with significantly diminished yield (43%). Interestingly, *epi*-**3** was not formed under these reaction conditions (Table 1, entry 2).

Further investigations thus concentrated on different bases using chloroform as solvent. Potassium carbonate, cesium fluoride, and sodium hydride led to sluggish reactions, and little or no product could be isolated.[15] We hypothesized that hydrogen bonding catalysts might be beneficial for the activation of nitro olefin; however, application of Schreiner's catalyst provided no reaction product in the absence of base.[15] Surprisingly, cesium carbonate was very effective, and the desired product was obtained after 24 h of reaction time in 85% yield as a 10:1 mixture of **4** and *epi*-**3** (Table 1, entry 9). Again, different solvents were investigated, though only in THF and dimethylacetamide could the desired cyclopropane be isolated in acceptable yield and only as a 1:1 mixture of **4** and *epi*-**3**. In a further test, we probed this transformation in the absence of base, and no product was observed.[15]

With the optimal conditions (Table 1, entry 9) in hand, we subsequently investigated the substrate scope of this transformation. We investigated a range of different substituted nitro styrenes. Different halogens, electron-donating and -withdrawing substituents in the para position are well-tolerated, and the desired *cis*-trifluoromethyl cyclopropanes were isolated in moderate-to-excellent yields and moderate-to-good diastereomeric excess. Further investigations concentrated on ortho- and meta-substituted nitro styrene. Although a substantial decrease in reaction yield was observed for *o*-methyl or *o*-methoxy nitro styrenes (Table 2, entry **4j** and **4l**), the more electron-deficient fluorinated or nitro-substituted analogues

Table 2. Substrate Scope[a]



[a]Nitro styrene **1** (0.2 mmol), sulfonium salt **2** (2.0 equiv, 0.4 mmol), Cs_2CO_3 (2.0 equiv, 0.4 mmol), and 80 mg of 4 Å molecular sieves were suspended in $CHCl_3$ and stirred at room temperature for 24 h. Yields were reported for isolated products; d.r. refers to the ratio of **4** and *epi*-**3**. [b]Yield by NMR spectroscopy.

(Table 2, entry **4k** and **4m**) reacted smoothly, and the trifluoromethyl cyclopropanes were isolated in excellent yields. Notably, the mesityl-substituted nitro olefin did not convert to the desired cyclopropane, probably due to the bulkiness of the 2,4,6-trisubstituted aromatic system. Halogens or electron-donating groups are well-tolerated in the meta position; similarly disubstituted nitro styrenes smoothly converted to the cyclopropane product.

Further studies concentrated on different carbo- and heterocyclic-substituted nitro styrene derivatives. In all cases, the desired *cis*-configured cyclopropanes were obtained in good-to-excellent yields with diastereomeric ratios ranging from 3:1 to 8:1. Notably, heteroaromatic systems such as pyridine, Boc-protected indole, and thiophene provided the desired cyclopropanes in 78−80% isolated yield. The Boc group proved to be compatible under the reaction conditions as no cleavage was observed. Aliphatic nitroalkenes were investigated, though

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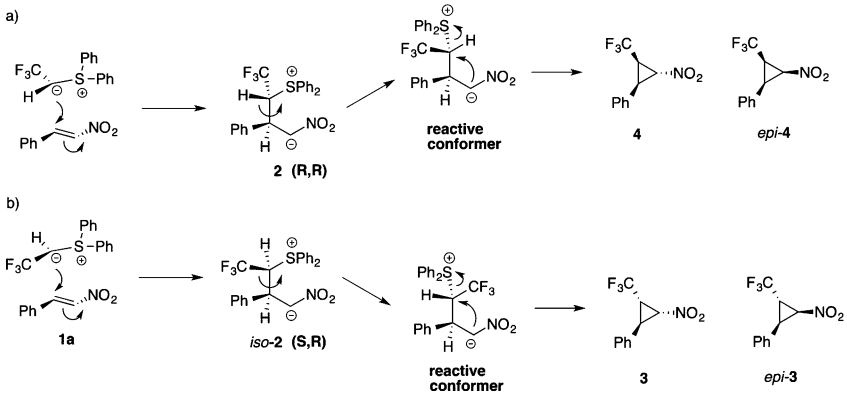
Scheme 2. Proposed Mechanism of the Reaction



the desired product (Table 2, entry **4x**) was obtained only in significantly reduced yield, as determined by NMR spectroscopy. It should be noted that α-methyl-nitro styrene did not react under the present reaction conditions.

Theoretical calculations (see Computational Methods)[15,16] were carried out to investigate the proposed two-step mechanism (Scheme 2), where the sulfur ylide first adds to the nitro olefin to form a zwitterionic intermediate followed by cyclization to form the cyclopropane products. There are two possible pathways involving Michael addition to either face of the nitro olefin that will form one of the two diastereomeric intermediates **2** and *iso*-**2**.

Considering first the pathway involving diastereomer **2** that leads to the formation of *cis*-configured trifluoromethyl cyclopropane **4** (Scheme 2a). Figure 1 shows the free energy

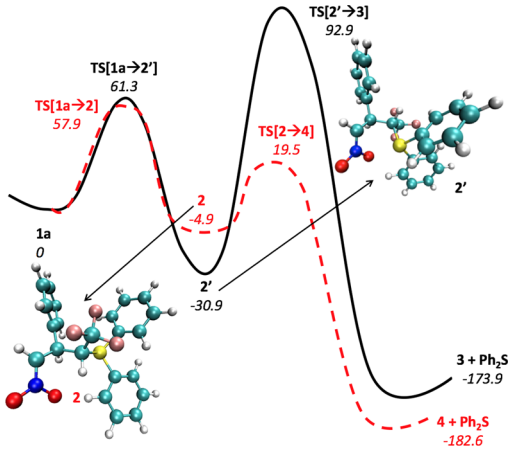


Figure 1. Free energy profiles involving reactive (red dashed) and nonreactive conformations for pathways involving diastereomer **2** and formation of **4** (RIMP2/aug-cc-pVTZ//M062*X*/6-31+G(d) and SMD implicit solvent model (chloroform)).

profiles based on two different conformers (see Computational Methods and SI). Although the **2′** conformer is the global minimum structure, the subsequent cyclization to form **3** involves a significantly higher barrier of ∼92.9 kJ mol^{-1} due to poor alignment between the carbanion lone-pair (HOMO) and the C−S antibonding σ^* molecular orbital (LUMO). By comparison, formation of higher energy intermediate **2** proceeds via a similar addition barrier (∼58 kJ mol^{-1}), but the subsequent cyclization to form **4** has a significantly lower barrier (19.5 kJ mol^{-1}). As such, cyclization of **2** (a reactive conformer) is likely to proceed very rapidly. It is also noted that there may be sufficient time for **2** to equilibrate into the global minimum **2′** conformer (the C−C rotational barrier from **2** to **2′** is ∼10 kJ mol^{-1}). Analogous free energy profiles for reactive conformers resulting in the formation of *epi*-**4** display significantly higher barriers due to steric effects (see Supporting Information). These results suggest that addition of sulfur ylide to **1a** to form **2** would lead to cyclopropane **4** as the dominant kinetic product.

Considering next the pathway involving the *iso*-**2** diastereomer (Scheme 2b), the free energy profiles involving the reactive conformers *iso*-**2** and *iso*-**2′** that will lead to products **3** and *epi*-**3**, respectively, are shown in Figure 2. The latter

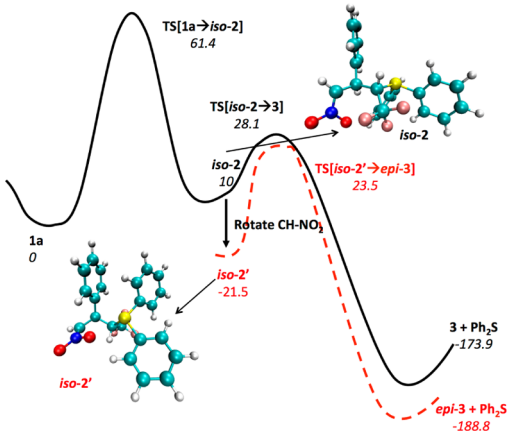


Figure 2. Free energy profiles (kJ mol^{-1}) of two competing reactive conformations involving the *iso*-**2** diastereomer and formation of **3** and *epi*-**3** (RIMP2/aug-cc-pVTZ//M062*X*/6-31+G(d) and SMD implicit solvent model (chloroform)).

conformer is not likely to be formed in the Michael addition step because it would require the nitro olefin to be in the *cis* configuration. Most likely, formation of *iso*-**2** takes place first and can interconvert with the *iso*-**2′** conformer through rotation of the −CH-NO$_2$ group. Consistent with expectations, the cyclization barrier of the reactive conformers is significantly lower compared to the Michael addition step. The cyclization of *iso*-**2** (to form **3**) is approximately 28 kJ mol^{-1}, whereas the corresponding barrier for *iso*-**2′** (to form *epi*-**3**) is slightly lower around 23.5 kJ mol^{-1}. We have computed the barrier for rotation of −CH-NO$_2$ group *iso*-**2** → *iso*-**2′** (39 kJ mol^{-1}) and found that it is higher than the barrier for cyclization, which suggests that **3** is the favored product.

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To reconcile with the experimental observation that *epi*-**3** is formed when a strong base (Cs_2CO_3) is used, we hypothesize that **3**, which is formed first, can readily undergo epimerization to form the thermodynamic product *epi*-**3** (see entry 9 in Table 1 and SI page S2 for thermodynamic product ratios predicted computationally and SI page S9 for the experimentally oberseved isomerization).

These calculations indicate that **4** is the kinetic product arising from Michael addition of the sulfur ylide to one face of the nitro olefin. In support of these calculations, which predict that the Michael addition step is rate-limiting, simple kinetic studies have shown that the rate-limiting step is likely to follow second-order kinetics.[15] On the basis of the most favorable pathways for the formation of **4** and **3**, we note that the barriers for the rate-limiting step in each case are around 57.9 kJ mol^{-1} (**1a** + ylide → **2**) and 61.4 kJ mol^{-1} (**1a** + ylide → *iso*-**2**), respectively, because the latter transition state has a configuration in which the CF_3 and NO_2 groups are slightly eclipsed. Naively, the difference in these barriers are actually in accordance with the observed **4**:**3** product ratios. These mechanistic insights will facilitate in silico screening of more effective reagents and further optimization of this synthetic procedure.

In conclusion, we have developed a new convenient and efficient synthetic approach for the sulfonium ylide-mediated trifluoromethylation reactions of nitroalkenes to afford a family of *cis*-trifluoromethyl cyclopropanes. These cyclopropanes are important synthetic building blocks that possess unique and highly desirable configurational properties for the construction of pharmaceutical and agrochemical agents.

EXPERIMENTAL SECTION

Unless otherwise noted, all commercially available compounds were used as provided without further purification. Chemicals used in this manuscript were purchased from Sigma-Aldrich and Alfa Aesar.

Solvents used in the reactions were p.A. grade. Solvents for chromatography were technical grade and distilled prior to use. Analytical thin-layer chromatography (TLC) was performed on Macherey−Nagel silica-gel aluminum plates with F-254 indicator visualized by irradiation under UV light. Column chromatography was performed using silica-gel Merck 60 (0.063−0.2 mm particle size). Solvent mixtures are understood as volume/volume.

^1H, ^{19}F, and ^{13}C NMR were recorded on a Varian AV600 or AV400 spectrometer in $CDCl_3$. Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated as br (broadened singlet), s (singlet), d (doublet), t (triplet), q (quartet), p (pentelet), m (multiplet); and coupling constants (J) are in hertz (Hz). EI MS data were recorded on a Shimadzu GCMS sytem (QP 2010 SE and GC2010plus, CP-Sil-8-MS column, 30 m, 0.25 μm ID, method: 60 °C for 5 min, 20 K/min to 300 °C and kept for 20 min). HRMS data were recorded on a Finnigan MAT 95 using EI ionization at 70 eV or on a ThermoFisher Scientific LTQ Orbitrap XL using ESI ionization. CI MS data were recorded on a Finnigan SSQ 7000 using CI Ionization at 100 eV (methane). IR spectra were recorded on a PerkinElmer-100 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Elemental analysis was performed on an Elementar VarioEL instrument.

Synthesis of Diphenyl(2,2,2-trifluoroethyl)sulfonium Trifluoromethanesulfonate. In a tightly capped vial, 4 mL of diphenyl (5 equiv) sulfide and 1 g of trifluoroethane trifluoromethylsulfonate (1 equiv) was added. The resulting mixture was heated to 150 °C for 30 h and then slowly cooled to room temperature. A white solid precipitated during cooling. To the reaction mixture was added 20 mL of diethyl ether, and the resulting mixture was filtered to afford the title compound as a colorless solid (1.51 g, 84%). ^1H NMR (400 MHz, acetone-d_6) δ 8.38−8.37 (m, 4H), 7.98−7.90 (m, 2H), 7.89−7.83 (m, 4H), 5.75 (q, J = 8.8 Hz, 2H); ^{19}F NMR (376 acetone-d_6) δ −61.29 (t, J = 8.8 Hz), −78.95; MS (CI) m/z (%) 269 ([M + H], 100%), 214.2 ([M − OH], 53%), 185.2 ([M − NO_2], 59%); HRMS (ESI): m/z calcd for [$C_{14}H_{12}F_3S^+$] [M − OTf]$^+$ 269.06063, found 269.06003; IR (KBr) 3066, 299, 2935, 1449, 1339, 1241, 1157, 1093, 1020, 749, 685 cm^{-1}. The analytical data is in correspondence with the literature.[12a]

General Procedure for the Corey−Chaykovsky Cyclopropanation Reactions. Nitrostyrene (1eq, 0.2 mmol) was added to diphenyl(2,2,2-trifluoroethyl)sulfonium trifluoromethanesulfonate (2 equiv), Cs_2CO_3 (1.5 equiv), and a 4 Å molecular sieve (80 mg). Then, 0.5 mL of chloroform was added under argon atmosphere, and the resulting mixture was stirred for 24 h at rt. DCM and silica-gel were added, and the solvent was evaporated under reduced pressure to run a dry loaded column to afford the desired product.

((1R,2R*,3R*)-2-Nitro-3-(trifluoromethyl)cyclopropyl)benzene (**4a**).* Compound **4a** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 50:1) as a colorless liquid in 85% yield (39 mg, 10:1 dr). ^1H NMR (600 MHz, $CDCl_3$) δ 7.41−7.29 (m, 5H), 4.99 (dd, J = 4.7, 3.7 Hz) and 4.85 (dd, J = 9.2, 3.7 Hz, 1H), 3.70−3.49 and 3.46−3.33 (m, 1H), 3.28−3.19 and 3.15−3.04 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 129.5, 128.8, 128.58, 128.54, 123.0 (q, J = 273.7 Hz), 59.4, 31.5, 30.3 (q, J = 37.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −60.86 (d, J = 7.0 Hz), −66.26 (d, J = 6.3 Hz); Anal. calcd for $C_{10}H_8F_3NO_2$ C 51.96, H 3.49, N 6.06; Found C 51.87, H 3.75, N 6.68; MS (CI) m/z (%) 232.2 ([M + H], 100%), 214.2 ([M − OH], 53%), 185.2 ([M − NO_2], 59%); IR (KBr) 3061, 2902, 2323, 2116, 1555, 1439, 1363, 1269, 1139, 742, 697 cm^{-1}; HPLC t_R (major) = 5.3 min, t_R (minor) = 6.5 min.

1-Methyl-4-((1R,2R*,3R*)-2-nitro-3-(trifluoromethyl)-cyclopropyl)benzene (**4b**).* Compound **4b** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 50:1) as a yellowish liquid in 93% yield (46 mg, 4:1 dr). ^1H NMR (600 MHz, $CDCl_3$) δ 7.21−7.15 (m, 4H), 4.96 (dd, J = 4.7, 3.7 Hz) and 4.83 (dd, J = 9.2, 3.7 Hz, 1H), 3.65−3.54 and 3.43−3.32 (m, 1H), 3.25−3.17 and 3.13−3.02 (m, 1H), 2.35 (s) and 2.34 (s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.8, 138.4, 129.6, 129.5, 128.48, 128.41, 126.4, 126.0, 123.0 (q, J = 273.8 Hz), 60.8, 59.5, 31.3 (q, J = 37.0 Hz), 21.1; ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.79 (d, J = 7.4 Hz), −66.24 (d, J = 6.5 Hz); HRMS (EI) m/z calcd for [$C_{11}H_{10}F_3NO_2$] 245.06582, found 245.06683; IR (KBr) 3094, 3056, 2105, 1555, 1441, 1366, 1269, 1141, 1036, 813, 733, 675 cm^{-1}.

1-Fluoro-4-((1R,2R*,3R*)-2-nitro-3-(trifluoromethyl)cyclopropyl)benzene (**4c**).* Compound **4c** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 50:1) as a yellowish liquid in 94% yield (47 mg, 4:1 dr). ^1H NMR (600 MHz, $CDCl_3$) δ 7.33−7.27 (m, 2H), 7.10−7.01 (m, 2H), 4.95 (dd, J = 4.7, 3.7 Hz) and 4.84 (dd, J = 9.1, 3.6 Hz, 1H), 3.68−3.51 and 3.42−3.25 (m, 1H), 3.24−3.16 and 3.14−3.03 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.4, 161.7, 130.4, 130.3, 122.9 (q, J = 273.9 Hz), 116.1, 116.09, 116.02, 115.9, 60.7, 59.5, 30.7, 30.2 (q, J = 37.3 Hz), 29.2; ^{19}F NMR (564 MHz, Chloroform-d) δ −60.81 (d, J = 7.3 Hz), −66.24 (d, J = 6.4 Hz), −111.98 − −112.26 (m), −112.55 − −112.76 (m); HRMS (EI) m/z calcd for [$C_{10}H_7F_4NO_2$] 249.04074, found 249.04162; IR (KBr) 3066, 2914, 2667, 2332, 2093, 1890, 1755, 1548, 1366, 1246, 1142, 832, 737 cm^{-1}.

1-Chloro-4-((1R,2R*,3R*)-2-nitro-3-(trifluoromethyl)cyclopropyl)benzene (**4d**).* Compound **4d** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 50:1) as a colorless liquid in 85% yield (45 mg, 6:1 dr). ^1H NMR (600 MHz, $CDCl_3$) δ 7.42−7.27 (m, 2H), 7.28−7.19 (m, 2H), 4.95 (dd, J = 4.7, 3.7 Hz) and 4.85 (dd, J = 9.1, 3.6 Hz, 1H), 3.65−3.47 and 3.39−3.30 (m, 1H), 3.23−3.17 and 3.16−3.03 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 135.0, 134.6, 129.99, 129.96, 129.2, 129.1, 128.0, 122.8 (q, J = 274.0 Hz), 60.6, 59.3, 30.7, 30.2 (q, J = 37.4 Hz), 29.3, 27.5 (q, J = 38.9 Hz); ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.83 (d, J = 7.0 Hz), −66.24 (d, J = 6.2 Hz); HRMS (EI) m/z calcd for [$C_{10}H_7ClF_3NO_2$] 265.01119, found

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265.01132; IR (KBr) 3092, 2919, 2313, 1556, 1365, 1267, 1144, 1096, 1018, 925, 824, 735 cm^{-1}.

1-((1R,2R*,3R*)-2-Nitro-3-(trifluoromethyl)cyclopropyl)-4-(trifluoromethyl)benzene (**4e**).* Compound **4e** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 50:1) as a colorless liquid in 90% yield (54 mg, 5:1 dr). ^1H NMR (600 MHz, $CDCl_3$) δ 7.64 (m, 2H), 7.50−7.36 (m, 2H), 5.01 (dd, J = 4.8, 3.7 Hz) and 4.90 (dd, J = 9.1, 3.7 Hz, 1H), 3.76−3.61 and 3.47−3.34 (m, 1H), 3.32−3.22 and 3.22−3.08 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 133.5, 130.9 (q, J = 33.0 Hz), 129.17, 129.12, 126.2−125.3 (m), 123.6 (q, J = 272.5 Hz), 122.79 (q, J = 274.1 Hz), 60.5, 59.1, 30.7, 30.2 (q, J = 37.5 Hz), 29.3, 27.5 (d, J = 38.9 Hz); ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.90 (d, J = 6.9 Hz), −62.88, −62.91, −66.25 (d, J = 6.1 Hz); Anal. Calcd for $C_{11}H_7F_6NO_2$ C 44.16, H 2.36, N 4.68; Found: C 44.31, H 3.23, N 5.17; MS (CI) m/z (%) 300.2 ([M + H], 100%), 282.2 ([M − OH], 55%), 280.1 ([M − F], 94%), 253.2 ([M − NO_2], 38%); IR (KBr) 3090, 2922, 1558, 1368, 1323, 1269, 1130, 837, 727 cm^{-1}.

1-Methoxy-4-((1R,2R*,3R*)-2-nitro-3-(trifluoromethyl)cyclopropyl)benzene (**4f**).* Compound **4f** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 20:1) as a colorless liquid in 88% yield (46 mg, 3:1 dr). ^1H NMR (600 MHz, $CDCl_3$) δ 7.24−7.16 (m, 2H), 6.92−6.84 (m, 2H), 4.94 (dd, J = 4.7, 3.7 Hz, and 4.81 (dd, J = 9.1, 3.7 Hz, 1H), 3.81 (s) and 3.80 (s, 1H), 3.64−3.47 and 3.40−3.29 (m, 1H), 3.23−3.15 and 3.12−2.92 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.6, 129.8, 129.7, 122.6 (q, J = 400.1 Hz), 114.3, 114.2, 59.7, 55.2, 31.0, 30.4 (q, J = 37.2 Hz), 29.6, 27.5 (q, J = 38.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −60.73 (d, J = 7.1 Hz), −66.23 (d, J = 6.4 Hz); HRMS (EI) m/z calcd for [$C_{11}H_{10}F_3NO_3$] 261.06073, found 261.06067; IR (KBr) 3056, 2940, 2112, 1613, 1554, 1517, 1442, 1365, 1251, 1140, 1030, 830, 734 cm^{-1}.

1-Ethoxy-4-((1R,2R*,3R*)-2-nitro-3-(trifluoromethyl)cyclopropyl)benzene (**4g**).* Compound **4g** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 20:1) as a yellowish liquid in 91% yield (50 mg, 3:1 dr). ^1H NMR (600 MHz, $CDCl_3$) δ 7.24−7.13 (m, 2H), 6.90−6.81 (m, 2H), 4.93 (dd, J = 4.7, 3.7 Hz) and 4.81 (dd, J = 9.1, 3.7 Hz, 1H), 4.10−3.90 (m, 3H), 3.61−3.50 and 3.38−3.30 (m, 1H), 3.22−3.15 and 3.11−2.96 (m, 1H), 1.45−1.36 (m, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.3, 159.0, 129.8, 129.7, 123.0 (q, J = 274.0 Hz), 121.1, 114.8, 114.7, 63.4, 59.7, 31.1, 30.4 (q, J = 37.0 Hz), 29.7, 14.7; ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.73 (d, J = 7.3 Hz), −66.23 (d, J = 6.5 Hz); HRMS (EI) m/z calcd for [$C_{12}H_{12}F_3NO_3$] 275.07638, found 275.0766; IR (KBr) 2922, 2330, 2092, 1890, 1747, 1547, 1366, 1255, 1141, 829 cm^{-1}.

1-Isopropyl-4-((1R,2R*,3R*)-2-nitro-3-(trifluoromethyl)cyclopropyl)benzene (**4h**).* Compound **4h** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 50:1) as a yellowish liquid in 68% yield (37 mg, 3:1 dr). ^1H NMR (600 MHz, $CDCl_3$) δ 7.24−7.17 (m, 4H), 4.96 (dd, J = 4.8, 3.7 Hz) and 4.83 (dd, J = 9.2, 3.7 Hz, 1H), 3.65−3.54 and 3.46−3.34 (m, 1H), 3.25−3.16 and 3.15−3.02 (m, 1H), 2.90 (hept, J = 6.8 Hz, 1H), 1.27−1.21 (m, 6fH); ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.7, 149.3, 128.59, 128.50, 127.0, 126.9, 126.7, 123.0 (q, J = 273.8 Hz), 60.9, 59.6, 33.7, 33.7, 31.4, 30.4 (q, J = 37.1 Hz), 29.9, 27.4 (q, J = 38.7 Hz), 23.8, 23.7; ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.75 (d, J = 7.2 Hz), −66.26 (d, J = 6.4 Hz); HRMS (EI) m/z calcd for [$C_{13}H_{14}F_3NO_2$] 273.09712, found 273.09748; IR (KBr) 2959, 2321, 2097, 1905, 1739, 1552, 1364, 12669, 1143, 837, 733 cm^{-1}.

4-((1R,2R*,3R*)-2-Nitro-3-(trifluoromethyl)cyclopropyl)-1,1′-biphenyl (**4i**).* Compound **4i** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 50:1) as a yellowish solid in 87% yield (43 mg, 4:1 dr). ^1H NMR (600 MHz, $CDCl_3$) δ 7.65−7.54 (m, 4H), 7.51−7.41 (m, 2H), 7.41−7.33 (m, 3H), 5.03 (dd, J = 4.8, 3.7 Hz) and 4.88 (dd, J = 9.2, 3.7 Hz, 1H), 3.78−3.64 and 3.54−3.37 (m, 1H), 3.34−3.24 and 3.20−3.07 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 141.8, 141.4, 140.0, 129.08, 129.01, 128.8, 128.4, 127.9, 127.7, 127.6, 127.5, 127.08, 127.04, 123.0 (q, J = 274.0 Hz), 60.9, 59.5, 31.2, 30.4 (q, J = 37.3 Hz), 29.8, 27.5 (q, J = 38.8 Hz); ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.72 (d, J = 7.1 Hz), −66.20 (d, J = 6.2 Hz); HRMS (EI) m/z calcd for [$C_{16}H_{12}F_3NO_2$] 307.08147, found 307.08117; mp 106−111 °C; IR (KBr) 3063, 2922, 1553, 1441, 1363, 1266, 1140, 1032, 838, 762, 693 cm^{-1}.

1-Methoxy-2-((1R,2R*,3R*)-2-nitro-3-(trifluoromethyl)cyclopropyl)benzene (**4j**).* Compound **4j** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 20:1) as a colorless liquid in 56% yield (29 mg, 3:1 dr). ^1H NMR (600 MHz, $CDCl_3$) δ 7.32 (m, 1H), 7.26−7.16 (m, 1H), 7.03−6.81 (m, 2H), 4.92 (dd, J = 5.0, 3.8 Hz) and 4.89 (dd, J = 9.0, 3.7 Hz, 1H) 3.87 (s) and 3.79 (s, 1H), 3.52−3.46 and 3.32−3.22 (m, 1H), 3.17−3.02 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.3, 158.1, 130.1, 129.9, 129.8, 128.7, 123.2 (d, J = 274.0 Hz), 120.6, 120.3, 118.1, 110.5, 110.4, 60.3, 59.6, 55.4, 30.2 (q, J = 37.2 Hz), 28.0, 26.7; ^{19}F NMR (564 MHz, $CDCl_3$) δ −61.43 (d, J = 7.4 Hz), −66.25 (d, J = 6.5 Hz); HRMS (EI) m/z calcd for [$C_{11}H_{10}F_3NO_3$] 261.06073, found 261.06111; IR (KBr) 2933, 2334, 2092, 1895, 1747, 1551, 1461, 1362, 1261, 1141, 752 cm^{-1}.

1-Fluoro-2-((1R,2R*,3R*)-2-nitro-3-(trifluoromethyl)cyclopropyl)benzene (**4k**).* Compound **4k** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 50:1) as a yellowish liquid in 86% yield (43 mg, 4:1 dr). ^1H NMR (600 MHz, $CDCl_3$) δ 7.40−7.32 (m, 1H), 7.30−7.22 (m, 1H), 7.20−7.03 (m, 2H), 5.02 (dd, J = 4.9, 3.8 Hz) and 4.91 (dd, J = 8.9, 3.7 Hz, 1H), 3.59−3.52 and 3.41−3.34 (m, 1H), 3.21−3.09 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.6 (d, J = 249.1 Hz), 130.7 (d, J = 8.3 Hz), 130.5 (d, J = 8.4 Hz), 130.2, 129.6, 124.4 (d, J = 3.7 Hz), 124.3 (d, J = 3.8 Hz), 122.8 (q, J = 273.9 Hz), 117.1 (d, J = 14.4 Hz), 115.9 (d, J = 21.1 Hz), 115.7, 59.9, 58.8, 29.8 (q, J = 37.5 Hz), 25.9, 24.7; ^{19}F NMR (564 MHz, $CDCl_3$) δ −61.69 (dd, J = 7.1, 3.4 Hz), −66.37 (d, J = 6.2 Hz), −114.87 − −115.31 (m), −115.64 − −116.00 (m); HRMS (EI) m/z calcd for [$C_{10}H_7F_4NO_2$] 249.04074, found 249.04156; IR (KBr) 3067, 2921, 2678, 2334, 2094, 1747, 1553, 1457, 1367, 1258, 1146, 756 cm^{-1}.

1-Methyl-2-((1R,2R*,3R*)-2-nitro-3-(trifluoromethyl)cyclopropyl)benzene (**4l**).* Compound **4l** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 50:1) as a yellowish liquid in 53% yield (26 mg, 3:1 dr). ^1H NMR (600 MHz, $CDCl_3$) δ 7.25−7.21 (m, 1H), 7.17−7.04 (m, 3H), 4.97 (dd, J = 4.7, 3.7 Hz) and 4.83 (dd, J = 9.2, 3.7 Hz, 1H), 3.66−3.56 and 3.44−3.29 (m, 1H), 2.36 (s) and 2.35 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 138.6, 129.6, 129.4, 129.29, 129.22, 128.8, 128.7, 125.6, 125.5, 123.0 (q, J = 273.8 Hz), 60.8, 59.5, 31.5, 30.3 (q, J = 37.0 Hz), 21.3; ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.83 (d, J = 7.1 Hz), −66.25 (d, J = 6.2 Hz); HRMS (EI) m/z calcd for [$C_{11}H_{10}F_3NO_2$] 245.06582, found 245.06612; IR (KBr) 3051, 2920, 2675, 2328, 2092, 1746, 1553, 1454, 1364, 1264, 1141, 929, 778, 700 cm^{-1}.

1-Nitro-2-((1R,2R*,3R*)-2-nitro-3-(trifluoromethyl)cyclopropyl)-benzene (**4m**).* Compound **4m** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 10:1) as a yellowish solid in 89% yield (49 mg, 3:1 dr). ^1H NMR (600 MHz, $CDCl_3$) δ 8.34−8.08 (m, 1H), 7.83−7.66 (m, 1H), 7.64−7.48 (m, 2H), 5.04 (dd, J = 9.0, 3.7 Hz) and 4.99 (dd, J = 5.2, 3.7 Hz, 1H), 4.26−4.09 and 3.70−3.57 (m, 1H), 3.48−3.36 and 3.35−3.21 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.1, 134.0, 133.99, 131.91, 130.7, 130.2, 130.0, 125.8, 125.65, 125.61, 124.5 (q, J = 263.0 Hz), 60.8, 59.8, 30.4, 30.0 (q, J = 37.2 Hz), 29.3, 28.9 (m); ^{19}F NMR (564 MHz, $CDCl_3$) δ −62.08 (d, J = 7.1 Hz), −66.06 (d, J = 6.1 Hz); Anal. Calcd for $C_{10}H_7F_3N_2O_4$ C 43.49, H 2.55, N 10.14; Found C 43.55, H 2.62, N 10.06; MS (CI) m/z (%) 230.2 ([M − NO_2], 9%), 186.2 ([M − 2(NO_2)], 16%), 166.1 ([M − 2(NO_2)F], 90%), 117.1 ([M − 2(NO_2)CF_3], 32%); mp 66−69 °C; IR (KBr) 3068, 2922, 1527, 1439, 1350, 1262, 1139,1031, 955, 835, 792, 737 cm^{-1}.

1-Bromo-3-((1R,2R*,3R*)-2-nitro-3-(trifluoromethyl)cyclopropyl)benzene (**4n**).* Compound **4n** was prepared according to the general procedure and was obtained after column chromatography (*n*-

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pentane → *n*-pentane:diethyl ether 50:1) as a yellowish liquid in 86% yield (53 mg, 5:1 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53−7.42 (m, 2H), 7.29−7.18 (m, 2H), 4.96 (dd, J = 4.8, 3.7 Hz) and 4.85 (dd, J = 9.1, 3.7 Hz, 1H), 3.79−3.54 and 3.47−3.33 (m, 1H), 3.33−3.17 and 3.19−2.97 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 132.1, 131.8, 131.7, 131.6, 130.4, 127.29, 127.22, 122.84, 122.83 (q, J = 274.0 Hz), 60.6, 59.1, 30.6, 30.2 (q, J = 37.5 Hz); ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.85 (d, J = 7.1 Hz), −66.24 (d, J = 6.4 Hz); HRMS (EI) m/z calcd for $[C_{10}H_7BrF_3NO_2]$ 308.96068, found 308.96081; IR (KBr) 3086, 2325, 1556, 1439, 1363, 1266, 1145, 1088, 890, 784, 675 cm^{-1}.

1-Methoxy-3-((1R,2R*,3R*)-2-nitro-3-(trifluoromethyl)cyclopropyl)benzene (**4o**).* Compound **4o** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 20:1) as a colorless liquid in 98% yield (51 mg, 3:1 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35−7.25 (m, 1H), 6.97−6.76 (m, 3H), 4.96 (dd, J = 4.8, 3.7 Hz, and 4.84 (dd, J = 9.2, 3.7 Hz, 1H), 3.81 (s) and 3.80 (s, 1H), 3.65−3.60 and 3.48−3.33 (m, 1H), 3.32−3.18 and 3.18−3.03 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.8, 130.9, 130.0, 129.9, 123.0 (q, J = 273.7 Hz), 114.5, 114.1, 113.8, 59.5, 55.2, 31.4, 30.3 (q, J = 37.3 Hz); ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.87 (d, J = 7.0 Hz), −66.26 (d, J = 6.4 Hz); HRMS (EI) m/z calcd for $[C_{11}H_{10}F_3NO_3]$ 261.06073, found 261.06070; IR (KBr) 3057, 2936, 2326, 2093, 1744, 1561, 1455, 1363, 1263, 1145, 1047, 778, 692 cm^{-1}.

5-((1R,2R*,3R*)-2-Nitro-3-(trifluoromethyl)cyclopropyl)benzo[d][1,3]dioxole (**4p**).* Compound **4p** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 20:1) as a yellowish liquid in 91% yield (50 mg, 6:1 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.81−6.69 (m, 3H), 6.10−5.93 (m, 2H), 4.90 (dd, J = 4.6, 3.7 Hz) and 4.80 (dd, J = 9.1, 3.7 Hz, 1H), 3.70−3.52 and 3.44−3.26 (m, 1H), 3.27−3.12 and 3.10−2.94 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.0, 147.8, 123.0 (q, J = 274.3 Hz), 122.9, 122.3, 122.0, 108.9, 108.8, 108.6, 108.5, 101.4, 60.8, 59.7, 31.3, 30.3 (q, J = 37.1 Hz), 29.8, 27.7 (q, J = 38.7 Hz); ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.77 (d, J = 7.4 Hz), −66.25 (d, J = 6.4 Hz); HRMS (EI) m/z calcd for $[C_{11}H_8F_3NO_4]$ 275.03999, found 275.04036; IR (KBr) 3061, 2909, 2311, 2083, 1744, 1553, 1467, 1364, 1244, 1138, 1036, 931, 820, 736 cm^{-1}.

1,2-Dichloro-4-((1R,2R*,3R*)-2-nitro-3-(trifluoromethyl)cyclopropyl)benzene (**4q**).* Compound **4q** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 50:1) as a yellowish liquid in 90% yield (54 mg, 6:1 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49−7.37 (m, 2H), 7.20−7.06 (m, 1H), 4.94 (dd, J = 4.8, 3.7 Hz) and 4.85 (dd, J = 9.1, 3.7 Hz, 1H), 3.74−3.49 and 3.47−3.29 (m, 1H), 3.24−2.97 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 133.2, 133.1, 130.9, 130.7, 130.6, 129.6, 127.9, 127.8, 122.7 (q, J = 274.2 Hz), 59.1, 30.4 (q, J = 37.4 Hz), 30.0; ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.82 (d, J = 7.0 Hz), −66.23 (d, J = 6.1 Hz); HRMS (EI) m/z calcd for $[C_{10}H_6Cl_2F_3NO_2]$ 298.97222, found 298.97362; IR (KBr) 3094, 2918, 1556, 1444, 1363, 1266, 1139, 1034, 819, 737, 679 cm^{-1}.

1,3-Dimethoxy-5-((1R,2R*,3R*)-2-nitro-3-(trifluoromethyl)-cyclopropyl)benzene (**4r**).* Compound **4r** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 20:1) as a colorless liquid in 96% yield (56 mg, 3:1 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.58−6.34 (m, 3H), 4.93 (dd, J = 4.7, 3.7 Hz) and 4.82 (dd, J = 9.2, 3.6 Hz, 1H), 3.79 (s) and 3.78 (s, 3H), 3.62−3.56 and 3.40−3.31 (m, 1H), 3.23−3.15 and 3.14−3.00 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.07, 161.03, 131.6, 131.3, 123.2 (q, J = 272.7 Hz), 123.0 (q, J = 273.8 Hz), 106.8, 106.7, 100.5, 100.2, 60.7, 59.4, 55.39, 55.37, 31.6, 30.3 (q, J = 37.5 Hz), 30.0, 27.5 (q, J = 38.9 Hz); ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.91 (d, J = 7.1 Hz), −66.28 (d, J = 6.2 Hz); HRMS (EI) m/z calcd for $[C_{12}H_{12}F_3NO_4]$ 291.07129, found 291.07112; IR (KBr) 29053, 2314, 2093, 1742, 1573, 1442, 1364, 1258, 1152, 944, 840, 689 cm^{-1}.

2-((1R,2R*,3R*)-2-Nitro-3-(trifluoromethyl)cyclopropyl)-naphthalene (**4s**).* Compound **4s** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 50:1) as a colorless solid in 87% yield (49 mg, 3:1 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88−7.74 (m, 4H), 7.57−7.49 (m, 2H), 7.44−7.33 (m, 1H), 5.12 (dd, J = 4.8, 3.7 Hz) and 4.93 (dd, J = 9.1, 3.6 Hz, 1H), 3.94−3.77 and 3.58−3.51 (m, 1H), 3.45−3.36 and 3.38−3.00 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 133.0, 132.9, 128.9, 128.8, 128.1, 127.8, 127.7 (q, J = 2.4 Hz), 126.9, 126.7 (d, J = 5.8 Hz), 125.9, 125.7, 123.0 (d, J = 273.7 Hz), 60.9, 59.6, 31.7, 30.5 (q, J = 37.4 Hz), 27.6 (q, J = 38.8 Hz); ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.73 (d, J = 7.1 Hz), −66.14 (d, J = 6.4 Hz); HRMS (EI) m/z calcd for $[C_{14}H_{10}F_3NO_2]$ 281.06582, found 281.06609; mp 91−92°; IR (KBr) 3098, 3061, 2300, 1552, 1437, 1363, 1270, 1136, 1035, 967, 947, 821, 750 cm^{-1}.

1-((1R,2R*,3R*)-2-Nitro-3-(trifluoromethyl)cyclopropyl)-naphthalene (**4t**).* Compound **4t** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 50:1) as a colorless solid in 57% yield (32 mg, 4:1 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11−8.05 (m, 1H), 7.93−7.85 (m, 2H), 5.18 (dd, J = 4.9, 3.6 Hz) and 5.14 (dd, J = 8.6, 3.9 Hz, 1H), 3.95 (dd, J = 11.1, 4.9 Hz) and 3.62−3.54 (m) and 3.36 (dqd, J = 10.8, 7.1, 3.7 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 133.6, 131.9, 129.6, 129.4, 128.8, 126.8, 126.4, 125.6, 125.1, 125.0, 123.2, 59.3, 30.6 (m); ^{19}F NMR (564 MHz, CDCl3) δ −61.22 (d, J = 7.0 Hz), −65.93 (d, J = 6.0 Hz); HRMS (EI) m/z calcd for $[C_{14}H_{10}F_3NO_2]$ 281.06582, found 281.06603; mp 104−107 °C; IR (KBr) 3109, 3044, 1551, 1435, 1364, 1262, 1142, 1105, 1029, 949, 865, 783, 749, 687 cm^{-1}.

3-((1R,2R*,3R*)-2-Nitro-3-(trifluoromethyl)cyclopropyl)pyridine (**4u**).* Compound **4u** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 10:1) as a yellowish liquid in 80% yield (37 mg, 8:1 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.78−8.53 (m, 2H), 7.68−7.56 (m, 1H), 7.39−7.30 (m, 1H), 5.02 (dd, J = 4.7, 3.7 Hz) and 4.90 (dd, J = 9.0, 3.7 Hz, 1H), 3.74−3.59 and 3.47−3.39 (m, 1H), 3.26−3.09 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.83, 149.82, 136.1, 123.5, 122.7 (q, J = 275.1 Hz) 58.7, 29.9 (q, J = 37.4 Hz), 28.6; ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.83 (d, J = 7.0 Hz), −66.22 (d, J = 6.1 Hz); HRMS (EI) m/z calcd for $[C_9H_7F_3N_2O_2]$ 232.04541, found 232.04644; IR (KBr) 3441, 3036, 2324, 2097, 1741, 1556, 1370, 1265, 1142, 710 cm^{-1}.

tert-Butyl 3-((1R,2R*,3R*)-2-Nitro-3-(trifluoromethyl)cyclopropyl)-1H-indole-1-carboxylate (**4v**).* Compound **4v** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 10:1) as a yellowish liquid in 78% yield (58 mg, 3:1 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23−8.03 (m, 1H), 7.68−7.51 (m, 2H), 7.42−7.27 (m, 2H), 5.01−4.94 (m, 1H), 3.53−3.46 and 3.45−3.33 (m, 1H), 3.27−3.14 (m, 1H), 1.68 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.2, 135.2, 129.4, 125.3, 125.2, 124.5, 123.0 (q, J = 273.6 Hz), 123.1, 118.5, 118.1, 115.6, 115.5, 109.6, 109.2, 84.5, 60.2, 59.3, 29.7 (q, J = 37.7 Hz), 28.1, 27.4 (q, J = 38.7 Hz), 23.2, 21.8; ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.86 (d, J = 7.0 Hz), −66.16 (d, J = 6.3 Hz); HRMS (EI) m/z calcd for $[C_{17}H_{17}F_3N_2O_4]$ 370.11349, found 370.11520; IR (KBr) 3065, 2982, 1733, 1556, 1454, 1370, 1258, 1145, 914, 847, 741 cm^{-1}.

2-((1R,2R*,3R*)-2-Nitro-3-(trifluoromethyl)cyclopropyl)-thiophene (**4w**).* Compound **4w** was prepared according to the general procedure and was obtained after column chromatography (*n*-pentane → *n*-pentane:diethyl ether 50:1) as a yellowish liquid in 80% yield (38 mg, 8:1 dr). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35−7.27 (m, 1H), 7.07−6.95 (m, 2H), 4.98 (t, J = 4.2 Hz) and 4.83 (dd, J = 8.8, 3.9 Hz, 1H), 3.72−3.59 and 3.49−3.39 (m, 1H), 3.34−3.23 and 3.19−3.03 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 131.4, 127.7, 127.1, 126.4, 122.7 (q, J = 273.7 Hz), 60.6, 30.8 (q, J = 37.5 Hz), 26.2; ^{19}F NMR (564 MHz, $CDCl_3$) δ −60.94 (d, J = 7.0 Hz), −66.36 (d, J = 6.5 Hz); Anal. Calcd for $C_8H_6F_3NO_4S$ C 40.51, H 2.00, N 5.79; Found C 39.93, H 2.00, N 6.02; MS (CI) m/z (%) 238.1 ([M], 41%), 221.1 ([M − O], 24%), 220.1 ([M − OH], 84%), 191.1 ([M − NO_2], 100%); IR (KBr) 3060, 2672, 2330, 2093, 1743, 1553, 1366, 1256, 1145, 848, 707 cm^{-1}.

COMPUTATIONAL METHODS

All electronic structure calculations were carried in the Gaussian09 (revision E01)[17] and Q-Chem programs.[18] All

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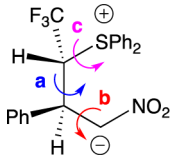
molecular geometries were optimized at the M06-2X/6-31+G(d) level of theory in the gas phase and in conjunction with the SMD implicit solvation model to simulate the solvent (chloroform).[19] Systematic conformational searches were carried out by scanning each rotatable bond (a, b, and c) at 120° or 180° resolution (see below).



Solvation free energies were computed from the difference between the SCF energy of the solution and gas phase optimized geometries so that the effect of geometrical relaxation is included. Vibrational analyses confirmed that all reactants and products have zero imaginary frequencies and that transition states are true first-order saddle points on the potential energy surface. Intrinsic reaction coordinate (IRC) calculations were also carried out to confirm that these are the correct transition states connecting the reactants and products. All thermal corrections (at 298 K) to the gas phase Gibbs free energy were computed using the ideal gas molecular partition function and the rigid-rotor harmonic oscillator approximation (RRHO). RIMP2/aug-cc-pVTZ single point calculations were performed on the gas-phase optimized geometries. The solution phase free energies were obtained as the sum of the gas phase free energy and solvation free energy plus a standard state correction ($\Delta nRT\ln(RT/P)$) so that they correspond to a reference state of 1 mol L^{-1} (see Scheme S1). Unless stated otherwise, all reported free energies are relative to the starting reagents (**1a** and **ylide**) and correspond to RIMP2/aug-cc-pVTZ gas phase energies plus SMD solvation free energies.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00951.

Stereochemical assignment, isomerization and reaction kinetics data, reaction optimization data, computational details, and copies of NMR spectra and M06-2X/6-31+G(d) Cartesian coordinates (PDF)

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Notes

The authors declare no competing financial interest.

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