ORIGINAL SCIENTIFIC PAPER

Croat. Chem. Acta **2026**, *99*(2)
Published online: May 21, 2026
DOI: 10.5562/cca4248

Exploiting the Reactivity of 2-Diazo-1,1,3,3,3-Pentafluoropropyl Phosphonate in [2,3]-Sigmatropic Rearrangement Reactions

Ita Hajdin,[1,2,*] Romana Pajkert,[1] Antonija Mravak,[2] Jianlin Han,[3] Gerd-Volker Röschenthaler[1]

[1] School of Science, Constructor University Bremen gGmbH, 28759 Bremen, Germany
[2] Faculty of Chemistry and Technology, University of Split, Ruđera Boškovića 35, 21000 Split, Croatia
[3] Jiangsu Co-Innovation Centre of Efficient Processing and Utilization of Forest Resources, International Innovation Center for Forest Chemicals and Materials, College of Chemical Engineering, Nanjing Forestry University, Nanjing 210037, China
* Corresponding author's e-mail address: ihajdin@ktf-split.hr

RECEIVED: January 18, 2026 ★ REVISED: March 02, 2026 ★ ACCEPTED: March 03, 2026

Abstract: The Cu(II)-catalysed [2,3]-sigmatropic rearrangement of allyl and propargyl sulfides with the fluorinated diazo compound, 2-diazo-1,1,3,3,3-pentafluoropropyl phosphonate, has been investigated experimentally and computationally. The corresponding products 2 and 3a–d were obtained in yields of up to 79 %. Kinetic studies and DFT calculations indicate that Cu(I), generated in situ by reduction of Cu(II) with the diazo substrate, is the catalytically active species. The reaction proceeds via formation of a copper carbene and sulfonium ylide, which undergoes a facile [2,3]-sigmatropic rearrangement. These results expand the synthetic utility of fluorinated diazo compounds and provide mechanistic insight into the Doyle-Kirmse reaction under copper catalysis.

Keywords: diazo compound, [2,3]–sigmatropic rearrangement, DFT calculations, propargyl sulfide, allyl sulfide.

INTRODUCTION

THE [2,3]-sigmatropic rearrangement of sulfonium ylides generated from carbene species is known as the Doyle-Kirmse reaction.[1] This transformation was first reported by Kirmse et al. in 1968[2] and subsequently rediscovered 13 years later by Doyle et al.[3] It represents one of the distinctive methods for constructing C–S bonds. In this reaction, thioethers typically include allylic, propargylic, and allenic derivatives.[4] Catalysts commonly employed in the Doyle-Kirmse reaction are rhodium and copper complexes, however, other metals, such as palladium, gold, and iron, have also been shown to be effective.[5]

Fluorine is well established as a key element in the design of bioactive molecules, and the difluoromethylene group is among the most important fluorine-containing functional motifs.[6–8] In this context, fluorinated diazo compounds have emerged as attractive starting materials for [2,3]-sigmatropic rearrangement reactions. Although, to the best of our knowledge, reactions involving diazo compounds bearing a trifluoromethyl and difluoromethyl phosphonate moiety have not yet been reported, numerous examples of [2,3]-sigmatropic rearrangement reactions employing fluorinated diazo substrates are known. For instance, Ramirez et al.[9] described the copper(I)–catalysed gem–aminoalkynylation of fluorinated diazo compounds, demonstrating the feasibility of carbene-mediated transformations of such substrates. Hock et al.[10] reported the transient in situ generation of fluorinated diazo compounds under on-water conditions, followed by direct carbene formation and subsequent sigmatropic rearrangement. Furthermore, Vorobyeva et al.[11] presented a Cu(II)-catalysed [2,3]-sigmatropic rearrangement of propargyl- and/or allyl-substituted sulfur and nitrogen ylides, providing access to a range of fluorinated enynes, diolefins, and allenyne derivatives.

In the past, we presented the synthesis of the fluorinated diazo compound 2–diazo–1,1,3,3,3-pentafluoropropyl phosphonate and demonstrated its synthetic utility in cyclopropanation[12], 1,3–dipolar cycloaddition[13] and O–H insertion reactions.[14] Building upon these studies, we aimed to further explore the reactivity of this diazo compound and to extend its application to [2,3]-sigmatropic rearrangement reactions, thereby advancing the investigation of its carbene-mediated transformations (Figure 1). In this study, we report a Cu(II) catalysed [2,3]-sigmatropic rearrangement of propargyl and allyl sulfides with 2-diazo-1,1,3,3,3-pentafluoropropyl phosphonate (1), providing access to previously unexplored fluorinated sulfur-containing products.

EXPERIMENTAL

Materials and Methods

All reactions were carried out under anhydrous conditions and under an argon atmosphere. Toluene was freshly distilled from benzophenone ketyl before use. All reagents were purchased from commercial sources and used without further purification. 2–diazo–1,1,3,3,3–pentafluoropropyl phosphonate (1) was prepared according to the previously published procedure.[12] The products were purified by column chromatography over silica gel 60 (230–400 mesh ASTM). Analytical TLCs were performed with silica gel 60 F254 plates. Visualisation was accomplished using UV light or by spraying with $Ce(SO_4)_2$ solution in 5 % H_2SO_4. NMR spectra were recorded on a JEOL ECX400 instrument, and the frequencies for ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR are 400, 100, 376 and 161 MHz, respectively. ^{31}P NMR spectra were broadband decoupled from hydrogen nuclei. All measurements were carried out in the solution in $CDCl_3$. Chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. High-resolution mass spectra (HRMS) were recorded on an ESI-Qq-TOF mass spectrometer.

DFT-Calculations

All structures were optimised at B3LYP[15–17] level of theory with LANL2DZ[18–20] basis set. Solvent effects of toluene were included by polarizable continuum model (PCM)[21] using the integral equation formalism variant (IEFPCM). Minima and transition states were confirmed by the presence of zero and one imaginary frequency, respectively. Reported energies are relative Gibbs free energies at 384 K. All calculations were performed using Gaussian 16 software.[22] All reported energies in Figure 2. and Table 2. are Gibbs free energies calculated at 384 K.

Synthesis

General procedure for the Doyle-Kirmse reactions of propargyl and allyl sulfides with diazo compound (1):

To a solution of propargyl or allyl sulfide (1.01 mmol) and $Cu(F_3acac)_2$ (0.034 mmol) in dry toluene under argon atmosphere, 1 (1.01 mmol) was added. The reaction mixture was stirred under reflux. After the time indicated, the solvent was evaporated under reduced pressure, and the crude product was purified via flash chromatography on silica gel using DCM : EtOAc (10 : 1 ratio) as eluent.

Diethyl (1,1-difluoro-2-(phenylthio)-2-(trifluoromethyl)penta-3,4-dien-1-yl)phosphonate (2) was prepared from 0.3 g (1.01 mmol) of 1, 0.012 g (0.05 mmol) of $Cu(F_3acac)_2$, 0.09 mL (1.01 mmol) of phenyl propargyl sulfide and 5 mL of dry toluene. The reaction mixture was refluxed for 3 h to give compound 2 in 63 % yield as orange oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, $^3J_{HH}$ = 8.0 Hz, 2H), 7.33 (tt, $^3J_{HH}$ = 8.0 Hz, $^3J_{HH}$ = 4.0 Hz, 1H), 7.25 (tt, $^3J_{HH}$ = 8.0 Hz, $^3J_{HH}$ = 4.0 Hz, 2H), 5.36 (t, $^4J_{HH}$ = 8.0 Hz, 1H), 4.63 (ddd, $^2J_{HH}$ = 96.0 Hz, $^4J_{HH}$ = 12.0 Hz, $^4J_{HH}$ = 4.0 Hz, 2H), 4.37–4.15 (m, 4H), 1.32 (dt, $^2J_{HH}$ = 13.8 Hz, $^3J_{HH}$ = 6.9 Hz, $^3J_{HH}$ = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.9, 139.0, 130.4,

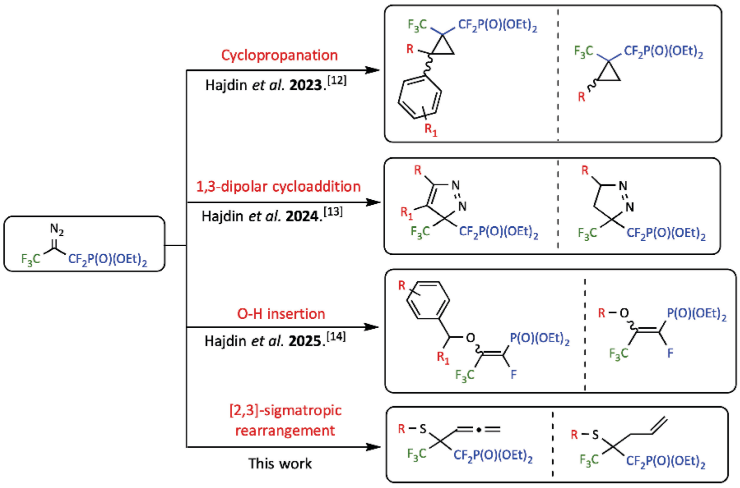


Figure 1. Summary of our previous research with the 2–diazo–1,1,3,3,3–pentafluoropropyl phosphonate.

128.7, 128.2, 125.3 (qdd, $^{1}J_{\mathrm{CF}}$ = 283.0 Hz, $^{3}J_{\mathrm{CF}}$ = 8.0 Hz, $^{3}J_{\mathrm{CP}}$ = 3.0 Hz), 118.9 (ddd, $^{1}J_{\mathrm{CF}}$ = 276.0 Hz, $^{1}J_{\mathrm{CP}}$ = 273.0 Hz, $^{2}J_{\mathrm{CS}}$ = 211.0 Hz), 83.6 (tt, $^{2}J_{\mathrm{CS}}$ = 4.0 Hz, $^{3}J_{\mathrm{CF}}$ = 1.0 Hz), 78.8, 65.3 (ddd, $^{2}J_{\mathrm{CP}}$ = 22.0 Hz, $^{4}J_{\mathrm{CF}}$ = 8.0 Hz, $^{4}J_{\mathrm{CF}}$ = 2.0 Hz), 63.2-62.2 (m), 16.3 (dd, $^{3}J_{\mathrm{CP}}$ = 8.0 Hz, $^{5}J_{\mathrm{CF}}$ = 6.0 Hz); ^{19}F NMR (376 MHz, $\mathrm{CDCl_3}$): δ -64.6 (td, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, $^{4}J_{\mathrm{FF}}$ = 3.8 Hz, 3F), -102.5 (ddq, $^{2}J_{\mathrm{FF}}$ = 308.3 Hz, $^{2}J_{\mathrm{FP}}$ = 101.5 Hz, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 1F), -108.2 (ddq, $^{2}J_{\mathrm{FF}}$ = 308.3 Hz, $^{2}J_{\mathrm{FP}}$ = 97.8 Hz, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 1F); ^{31}P {^{1}H} NMR (161 MHz, $\mathrm{CDCl_3}$): δ 4.2 (tq, $^{2}J_{\mathrm{PF}}$ = 99.8 Hz, $^{4}J_{\mathrm{PF}}$ = 3.0 Hz, 1P). HRMS (ESI) calcd. for $\mathrm{C_{16}H_{18}F_5NaO_3PS}$ [M + Na]$^+$ 439.0532, found 439.0533.

Diethyl (1,1-difluoro-2-(phenylthio)-2-(trifluoromethyl)pent-4-en-1-yl)phosphonate (3a) was prepared from 0.3 g (1.01 mmol) of 1, 0.019 g (0.05 mmol) of Cu($\mathrm{F_3}$acac)$_2$, 0.15 mL (1.01 mmol) of allyl phenyl sulfide and 5 mL of dry toluene. The reaction mixture was refluxed for 3h to give compound 3a in 72 % yield as blue oil. ^{1}H NMR (400 MHz, $\mathrm{CDCl_3}$): δ 7.66 (s, 2H), 7.33–7.23 (m, 3H), 5.80 (s, 1H), 5.00 (t, $^{3}J_{\mathrm{HH}}$ = 12.0 Hz, 2H), 4.26 (d, $^{3}J_{\mathrm{HH}}$ = 44.0 Hz, 4H), 3.07 (s, 1H), 2.61 (s, 1H), 1.29 (d, $^{3}J_{\mathrm{HH}}$ = 24.0 Hz 6H); ^{13}C NMR (100 MHz, $\mathrm{CDCl_3}$): δ = 138.6, 131.0, 130.4, 128.8, 127.9, 124.9 (qdd, $^{1}J_{\mathrm{CF}}$ = 285.0 Hz, $^{3}J_{\mathrm{CF}}$ = 4.0 Hz, $^{3}J_{\mathrm{CP}}$ = 2.0 Hz), 119.9 (ddd, $^{1}J_{\mathrm{CF}}$ = 277.0 Hz, $^{1}J_{\mathrm{CP}}$ = 271.0 Hz, $^{2}J_{\mathrm{CS}}$ = 210.0 Hz), 119.3, 65.2 (dd, $^{2}J_{\mathrm{CP}}$ = 30.0 Hz, $^{4}J_{\mathrm{CF}}$ = 6.0 Hz), 62.7-61.8 (m), 35.8, 16.3 (dd, $^{3}J_{\mathrm{CP}}$ = 16.0 Hz, $^{5}J_{\mathrm{CF}}$ = 5.0 Hz); ^{19}F NMR (376 MHz, $\mathrm{CDCl_3}$): δ -62.6 (t, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 3F), -99.9 (ddq, $^{2}J_{\mathrm{FF}}$ = 312.1 Hz, $^{2}J_{\mathrm{FP}}$ = 97.8 Hz, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 1F), -105.8 (ddq, $^{2}J_{\mathrm{FF}}$ = 312.1 Hz, $^{2}J_{\mathrm{FP}}$ = 101.5 Hz, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 1F); ^{31}P {^{1}H} NMR (161 MHz, $\mathrm{CDCl_3}$): δ 2.7 (s, 1P). HRMS (ESI) calcd. for $\mathrm{C_{16}H_{20}F_5NaO_3PS}$ [M + Na]$^+$ 441.0689, found 441.0685.

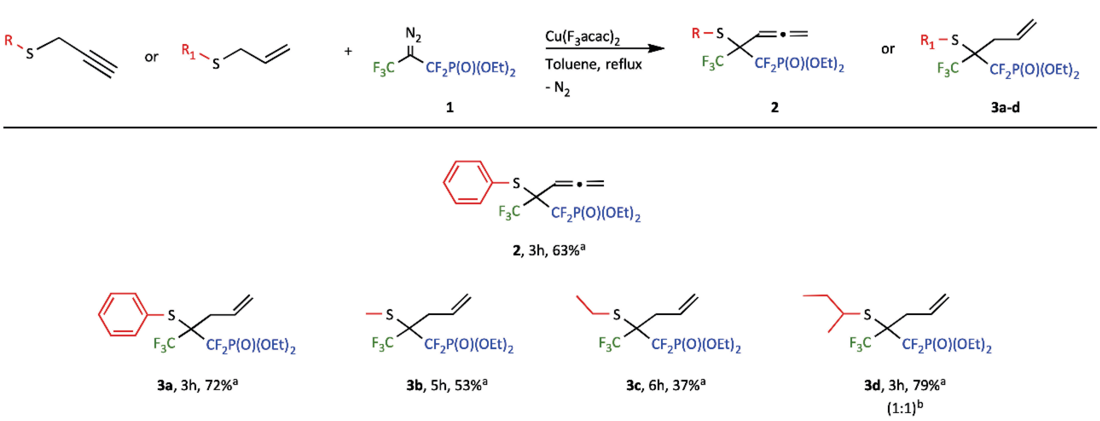
Diethyl (1,1-difluoro-2-(methylthio)-2-(trifluoromethyl)pent-4-en-1-yl)phosphonate (3b) was prepared from 0.3 g (1.01 mmol) of 1, 0.019 g (0.05 mmol) of Cu($\mathrm{F_3}$acac)$_2$, 0.11 mL (1.01 mmol) of allyl methyl sulfide and 5 mL of dry toluene. The reaction mixture was refluxed for 5 h to give compound 3b in 53 % yield as blue oil. ^{1}H NMR (400 MHz, $\mathrm{CDCl_3}$): δ 5.85–5.77 (m, 1H), 5.14-5.05 (m, 2H), 4.34–4.19 (m, 4H), 2.93 (tq, $^{3}J_{\mathrm{HH}}$ = 15.0 Hz, $^{3}J_{\mathrm{HP}}$ = 7.0 Hz, 2H), 2.26 (s, 3H), 1.33 (q, $^{3}J_{\mathrm{HH}}$ = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $\mathrm{CDCl_3}$): δ = 130.6, 125.4 (qdd, $^{1}J_{\mathrm{CF}}$ = 287.0 Hz, $^{3}J_{\mathrm{CF}}$ = 10.0 Hz, $^{3}J_{\mathrm{CP}}$ = 2.0 Hz), 120.9 (ddd, $^{1}J_{\mathrm{CF}}$ = 277.0 Hz, $^{1}J_{\mathrm{CP}}$ = 272.0 Hz, $^{2}J_{\mathrm{CS}}$ = 212.0 Hz), 119.6, 65.1 (t, $^{4}J_{\mathrm{CF}}$ = 7.0 Hz), 58.6–57.6 (m), 35.3, 16.3 (dd, $^{3}J_{\mathrm{CP}}$ = 5.0 Hz, $^{5}J_{\mathrm{CF}}$ = 4.0 Hz); ^{19}F NMR (376 MHz, $\mathrm{CDCl_3}$): δ –62.7 (t, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 3F), -99.6 (ddq, $^{2}J_{\mathrm{FF}}$ = 315.8 Hz, $^{2}J_{\mathrm{FP}}$ = 101.5 Hz, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 1F), -106.6 (ddq, $^{2}J_{\mathrm{FF}}$ = 315.8 Hz, $^{2}J_{\mathrm{FP}}$ = 101.5 Hz, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 1F); ^{31}P {^{1}H} NMR (161 MHz, $\mathrm{CDCl_3}$): δ 3.9 (t, $^{2}J_{\mathrm{PF}}$ = 96.6 Hz, 1P). HRMS (ESI) calcd. for $\mathrm{C_{11}H_{18}F_5NaO_3PS}$ [M + Na]$^+$ 379.0532, found 379.0533.

Diethyl (2-(ethylthio)-1,1-difluoro-2-(trifluoromethyl)pent-4-en-1-yl)phosphonate (3c) was prepared from 0.3 g (1.01 mmol) of 1, 0.019 g (0.05 mmol) of Cu($\mathrm{F_3}$acac)$_2$, 0.12 mL (1.01 mmol) of allyl ethyl sulfide and 5 mL of dry toluene. The reaction mixture was refluxed for 5 h to give compound 3c in 37 % yield as blue oil. ^{1}H NMR (400 MHz, $\mathrm{CDCl_3}$): δ 5.95–5.85 (m, 1H), 5.21–5.13 (m, 2H), 4.38–4.29 (m, 4H), 3.06–2.85 (m, 4H), 1.40 (q, $^{3}J_{\mathrm{HH}}$ = 4.0 Hz, 6H), 1.21 (t, $^{3}J_{\mathrm{HH}}$ = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $\mathrm{CDCl_3}$): δ = 130.7, 125.3 (qdd, $^{1}J_{\mathrm{CF}}$ = 286.0 Hz, $^{3}J_{\mathrm{CF}}$ = 8.0 Hz, $^{3}J_{\mathrm{CP}}$ = 2.0 Hz), 120.8 (ddd, $^{1}J_{\mathrm{CF}}$ = 276.0 Hz, $^{1}J_{\mathrm{CP}}$ = 271.0 Hz, $^{2}J_{\mathrm{CS}}$ = 211.0 Hz), 119.6, 65.2 (t, $^{4}J_{\mathrm{CF}}$ = 6.0 Hz), 59.4–58.7 (m), 35.5, 25.1, 16.3 (t, $^{3}J_{\mathrm{CP}}$ = 6.0 Hz), 13.3; ^{19}F NMR (376 MHz, $\mathrm{CDCl_3}$): δ –62.7 (t, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 3F), –99.9 (ddq, $^{2}J_{\mathrm{FF}}$ = 312.1 Hz, $^{2}J_{\mathrm{FP}}$ = 105.3 Hz, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 1F), –106.5 (ddq, $^{2}J_{\mathrm{FF}}$ = 312.1 Hz, $^{2}J_{\mathrm{FP}}$ = 101.5 Hz, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 1F); ^{31}P {^{1}H} NMR (161 MHz, $\mathrm{CDCl_3}$): δ 4.2 (t, $^{2}J_{\mathrm{PF}}$ = 103.0 Hz, 1P). HRMS (ESI) calcd. for $\mathrm{C_{12}H_{20}F_5NaO_3PS}$ [M + Na]$^+$ 393.0689, found 393.0686.

Diethyl (2-(sec-butylthio)-1,1-difluoro-2-(trifluoromethyl)pent-4-en-1-yl)phosphonate (3d) was prepared from 0.3 g (1.01 mmol) of 1, 0.019 g (0.05 mmol) of Cu($\mathrm{F_3}$acac)$_2$, 0.16 mL (1.01 mmol) of allyl sec-butyl sulfide and 5 mL of dry toluene. Reaction mixture was refluxed for 3 h to give compound 3d as a mixture of two stereoisomers in a 1 : 1 ratio in 79 % yield as blue oil. One stereoisomer: ^{1}H NMR (400 MHz, $\mathrm{CDCl_3}$): δ 5.83 (s, 1H), 5.09 (d, $^{3}J_{\mathrm{HH}}$ = 16.0 Hz, 2H), 4.33–4.18 (m, 4H), 3.23 (dh, $^{3}J_{\mathrm{HH}}$ = 12.0 Hz, $^{3}J_{\mathrm{HH}}$ = 8.0 Hz, 1H), 3.05–2.97 (m, 2H), 1.63 (ddt, $^{3}J_{\mathrm{HS}}$ = 20.0 Hz, $^{4}J_{\mathrm{HF}}$ = 12.0 Hz, $^{3}J_{\mathrm{HH}}$ = 8.0 Hz, 1H), 1.32 (q, $^{3}J_{\mathrm{HH}}$ = 8.0 Hz, 6H), 1.26 (t, $^{3}J_{\mathrm{HS}}$ = 8.0 Hz, 3H), 0.91 (q, $^{3}J_{\mathrm{HH}}$ = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $\mathrm{CDCl_3}$): δ = 130.9, 125.1 (qdd, $^{1}J_{\mathrm{CF}}$ = 283.0 Hz, $^{3}J_{\mathrm{CF}}$ = 5.0 Hz, $^{3}J_{\mathrm{CP}}$ = 3.0 Hz), 119.8 (ddd, $^{1}J_{\mathrm{CF}}$ = 274.0 Hz, $^{1}J_{\mathrm{CP}}$ = 267.0 Hz, $^{2}J_{\mathrm{CS}}$ = 207.0 Hz), 119.2 (d, $^{2}J_{\mathrm{CS}}$ = 2.0 Hz), 65.1 (dd, $^{2}J_{\mathrm{CP}}$ = 20.0 Hz, $^{4}J_{\mathrm{CF}}$ = 7.0 Hz), 61.2–60.3 (m), 42.0 (d, $^{3}J_{\mathrm{CS}}$ = 10.0 Hz), 36.1, 31.4 (d, $^{4}J_{\mathrm{CS}}$ = 3.0 Hz), 22.2 (d, $^{3}J_{\mathrm{CS}}$ = 12.0 Hz), 16.3 (dd, $^{3}J_{\mathrm{CP}}$ = 16.0 Hz, $^{5}J_{\mathrm{CF}}$ = 5.0 Hz) 11.2 (d, $^{3}J_{\mathrm{CP}}$ = 11.0 Hz); ^{19}F NMR (376 MHz, $\mathrm{CDCl_3}$): δ –62.2 (q, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 3F), –102.3 (ddq, $^{2}J_{\mathrm{FF}}$ = 315.8 Hz, $^{2}J_{\mathrm{FP}}$ = 97.8 Hz, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 1F), -106.4 (ddq, $^{2}J_{\mathrm{FF}}$ = 312.1 Hz, $^{2}J_{\mathrm{FP}}$ = 105.3 Hz, $^{3}J_{\mathrm{FS}}$ = 7.5 Hz, 1F); ^{31}P {^{1}H} NMR (161 MHz, $\mathrm{CDCl_3}$): δ 4.1 (t, $^{2}J_{\mathrm{PF}}$ = 99.8 Hz, 1P). Second stereoisomer: ^{1}H NMR (400 MHz, $\mathrm{CDCl_3}$): δ 5.83 (s, 1H), 5.05 (d, $^{3}J_{\mathrm{HH}}$ = 12.0 Hz, 2H), 4.33–4.18 (m, 4H), 3.23 (dh, $^{3}J_{\mathrm{HH}}$ = 12.0 Hz, $^{3}J_{\mathrm{HH}}$ = 8.0 Hz, 1H), 2.85–2.77 (m, 2H), 1.49 (dtd, $^{3}J_{\mathrm{HS}}$ = 16.0 Hz, $^{4}J_{\mathrm{HF}}$ = 8.0 Hz, $^{3}J_{\mathrm{HH}}$ = 4.0 Hz, 1H), 1.32 (q, $^{3}J_{\mathrm{HH}}$ = 8.0 Hz, 6H), 1.26 (t, $^{3}J_{\mathrm{HS}}$ = 8.0 Hz, 3H), 0.91 (q, $^{3}J_{\mathrm{HH}}$ = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $\mathrm{CDCl_3}$): δ = 130.9, 125.1 (qdd, $^{1}J_{\mathrm{CF}}$ = 283.0 Hz, $^{3}J_{\mathrm{CF}}$ = 5.0 Hz, $^{3}J_{\mathrm{CP}}$ = 3.0 Hz), 119.8 (ddd, $^{1}J_{\mathrm{CF}}$ = 274.0 Hz, $^{1}J_{\mathrm{CP}}$ = 267.0 Hz, $^{2}J_{\mathrm{CS}}$ = 207.0 Hz), 119.2 (d, $^{2}J_{\mathrm{CS}}$ = 2.0 Hz), 65.1 (dd, $^{2}J_{\mathrm{CP}}$ = 20.0 Hz, $^{4}J_{\mathrm{CF}}$ = 7.0 Hz), 61.2–60.3 (m), 42.0 (d, $^{3}J_{\mathrm{CS}}$ = 10.0 Hz), 36.1, 31.4 (d, $^{4}J_{\mathrm{CS}}$ = 3.0 Hz), 22.2 (d, $^{3}J_{\mathrm{CS}}$ = 12.0 Hz), 16.3 (dd, $^{3}J_{\mathrm{CP}}$ = 16.0 Hz, $^{5}J_{\mathrm{CF}}$ = 5.0 Hz) 11.2 (d, $^{3}J_{\mathrm{CP}}$ = 11.0 Hz); ^{19}F NMR (376 MHz, $\mathrm{CDCl_3}$): δ –62.2 (q, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 3F), –101.9 (ddq, $^{2}J_{\mathrm{FF}}$ = 315.8 Hz, $^{2}J_{\mathrm{FP}}$ = 97.8 Hz, $^{3}J_{\mathrm{FS}}$ = 11.3 Hz, 1F), –107.0 (ddq, $^{2}J_{\mathrm{FF}}$ = 315.8 Hz, $^{2}J_{\mathrm{FP}}$ = 105.3 Hz, $^{3}J_{\mathrm{FS}}$ = 7.5 Hz, 1F); ^{31}P {^{1}H} NMR (161 MHz, $\mathrm{CDCl_3}$): δ 4.1 (t, $^{2}J_{\mathrm{PF}}$ = 99.8 Hz, 1P). HRMS (ESI) calcd. for $\mathrm{C_{12}H_{20}F_5NaO_3PS}$ [M + Na]$^+$ 393.0689, found 393.0686.

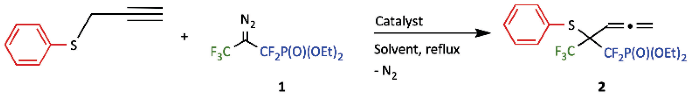
RESULTS AND DISCUSSION

The synthetic utility of the diazo compound 1 was examined in Doyle-Kirmse reactions with selected propargyl and allyl sulfides. As a result, five new rearrangement products that contain both the trifluoromethyl and the difluoromethylphosphonate moiety were synthesised (Scheme 1). To determine optimal reaction conditions, the Doyle-Kirmse reaction between phenyl propargyl sulfide and diazo reagent 1 was used as the model reaction. The results are summarised in Table 1. In the first two attempts, $Rh_2(OAc)_4$ was used as a catalyst in pentane at –30°C and RT, but the diazo compound 1 failed to react. Using CuI as a catalyst at RT in pentane resulted in the same way (entry 3). Furthermore, the diazo compound decomposed in the reaction without a catalyst using boiling DCM and under Blue LEDs (entry 4). The same result occurred in the reaction with the photocatalyst $Ru(bpy)_3(PF_6)_2$ in boiling DCM and under Blue LEDs (entry 5). The first conversion rates of the diazo compound 1 into



Scheme 1. Scope of the Doyle-Kirmse reaction. Reaction conditions: sulfide (1.01 mmol), diazo compound **1** (0.1 mmol), $Cu(F_3acac)_2$ (5 mol%), dry toluene, 111 °C, Ar atmosphere. [a] Yields refer to isolated products. [b] A mixture of 2 diastereoisomers in a 1:1 ratio was isolated.

Table 1. Optimisation of the reaction conditions.(a)



Entry	Sulfide (equviv)	Catalyst	Catalyst / mol %	*t* / h	*T* / °C	Solvent	Conversion rate(b) / %
1	1.2	$Rh_2(OAc)_4$	0.5	3	–30	Pentane	n.r.
2	1.2	$Rh_2(OAc)_4$	0.5	12	RT	Pentane	n.r.
3	1.2	CuI	5	12	RT	Pentane	n.r.
4(c)	5	–	–	12	40	DCM	–
5(c)	5	$Ru(bpy)_3(PF_6)_2$	1	12	40	DCM	–
6	1.5	$Rh_2(OAc)_4$	5	48	80	Benzene	5
7	1	$Rh_2(OAc)_4$	5	3	111	Toluene	8
8	1	CuI	5	3	111	Toluene	63
9	1	$Cu(CF_3SO_3)_2$	5	3	111	Toluene	74
10	1	$Cu(F_3acac)_2$	5	3	111	Toluene	100(d)

(a) Reaction conditions: phenyl propargyl sulfide, diazo reagent **1** (1.01 mmol), catalyst, dry solvent (5 mL), Ar atmosphere.

(b) Determined with ^{19}F NMR spectroscopy.

(c) Under the Blue LEDs. [n.r.] No reaction. [–] Decomposition of the diazo compound.

(d) Isolated yield was 79 %.

2, measuring 5 % and 8 %, were observed in the reactions with $Rh_2(OAc)_4$ as a catalyst in boiling benzene and toluene, respectively. Moderate conversion rates were observed in reactions with CuI and $Cu(CF_3SO_3)_2$ in boiling toluene (entries 8 and 9). Finally, using 5 mo l% of $Cu(F_3acac)_2$ in boiling toluene resulted in a 100 % conversion of the diazo reagent 1 after 3 h and rearrangement product 2 was isolated in an 79 % yield (entry 10).

With the optimised reaction conditions in hand, the substrate scope of the Doyle-Kirmse reaction of selected propargyl and allyl sulfides with diazo compound 1 was examined. The results are available in Scheme 1. All reactions were carried out successfully, and the corresponding rearrangement products 2 and 3a-d were isolated in moderate to good yields (Scheme 1). In the [2,3]–sigmatropic rearrangement reaction with phenyl propargyl sulfide, allenyl sulfide (2) was the corresponding product obtained in a 63 % yield. Furthermore, reactions with allyl sulfides bearing phenyl or sec-butyl group resulted in even higher yields, 72 % and 79 %, as seen in rearrangement products 3a and 3d, respectively. In comparison, allyl sulfides with a methyl (3b) or ethyl group (3c) resulted with significantly lower yields (53 % and 37 %, respectively). Higher yields were observed in reactions with allyl sulfides that had a bulky substituent, such as phenyl and sec–butyl group connected to the sulfur atom, probably due to steric effects. Notably, in the reaction with allyl sec-butyl sulfide, a mixture of diastereoisomers 3d was isolated as product in a 1 : 1 ratio.

Theoretically, in the catalytic reaction, the sulfonium ylides from the [2,3]–sigmatropic rearrangement are formed through the reaction of allyl or propargyl sulfides and metal carbenes that are generated by a metal-catalysed reaction with diazo substrates.[23,24] To confirm the experimentally observed reactivity, density functional theory (DFT) calculations were performed for both Cu(I)- and Cu(II)-mediated pathways (Table 2, Figure 2) for the [2,3]–sigmatropic rearrangement of allyl methyl sulphide with the diazo compound 1. Frontier orbital analysis of the Cu(I)- and Cu(II)-mediated diazo complexes reveals very similar HOMO / LUMO distributions, with the LUMO delocalized over the $C–N_2$ unit and the HOMO centered on the catalyst (Figure S1). Although the initial mechanistic proposal involves the formation of a Cu(II) carbene species upon reaction of $Cu(F_3acac)_2$ with diazo compound 1, the computed energy profile indicates that this pathway is associated with a prohibitively high activation barrier. Formation of the Cu(II) carbene intermediate is preceded by a highly endergonic transition state ($TS1$, $\Delta G^{\ddagger}$ = 1.83 eV), rendering this route kinetically unfavourable under the reaction conditions. In contrast, the pathway involving a Cu(I)-F_3acac catalyst proceeds with significantly lower energetic demands. Generation of the corresponding copper carbene intermediate occurs through a low-barrier transition state ($TS1$, $\Delta G^{\ddagger}$ = 0.34 eV), followed by formation of a stabilised carbene-derived intermediate (Int2). To rationalize differences in activation barriers for N_2 extrusion, a reduced density gradient (RDG) analysis of $TS1$ was performed for both Cu(I) and Cu(II) pathways (Figure S2). Red regions between the carbon and the Cu(II) center and between the carbon atom and nitrogen indicate pronounced steric/repulsive interactions, which are not observed for Cu(I). Together with the significantly longer Cu–C distance, this suggests weaker metal–substrate stability in the Cu(II) complex, accounting for the much higher activation barrier. The subsequent reaction with allyl methyl sulfide leads to the formation of a metal-bound sulfonium ylide (Int3), which, upon dissociation of the copper catalyst, furnishes a free ylide intermediate (Int4). This ylide then undergoes a facile [2,3]-sigmatropic rearrangement via a low-energy transition state ($TS2$, $\Delta G^{\ddagger}$ = 0.22 eV), ultimately affording the corresponding Doyle-Kirmse rearrangement product 3b.

Notably, the computed activation barriers for the [2,3]–sigmatropic rearrangement step are comparable for both oxidation states of copper, indicating that this transformation is intrinsically facile once the free ylide is formed. The decisive factor governing the overall reactivity is therefore the initial carbene formation step, which strongly favours the Cu(I)-mediated pathway. It was formerly thought that both Cu(I) and Cu(II) could act as catalytically active species, however, kinetic data reported by Kochi et al.[25] show that Cu(I) is significantly more active than Cu(II), and that Cu(II) is readily reduced to Cu(I) by diazo compounds.[26] Taken together, these computational and experimental observations support the conclusion that Cu(II) primarily functions as a precatalyst, being reduced in situ to the catalytically competent Cu(I) species.

Table 2. Relative Gibbs free energies (ΔG) expressed in eV. Reaction 1 is modelled using CuF_3acac catalyst, and energetically unfavourable reaction 2 using $Cu(F_3acac)_2$.

	Int1	TS1 (Gact)	Int2	Int3	Int4	TS2 (Gact)	Pr
1	0.20	0.54 (0.34)	–0.45	–0.56	–0.07	0.15 (0.22)	–1.55
2	0.46	2.29 (1.83)	1.63	0.85	–0.11	0.09 (0.20)	–1.68

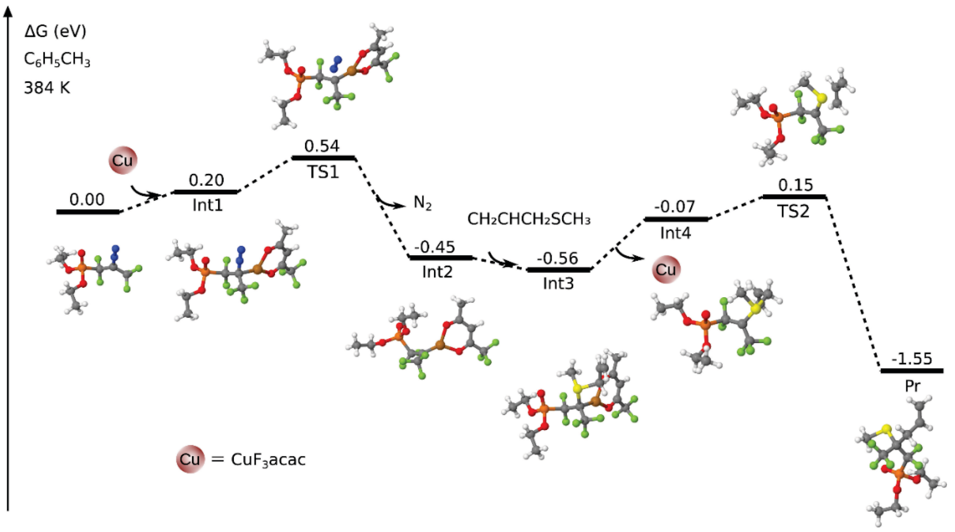


Figure 2. DFT calculated energy profile of the reaction mechanism for the [2,3]–sigmatropic rearrangement of allyl methyl sulphide with the diazo compound 1.

CONCLUSION

This work highlights the utility of fluorinated diazo compounds in Cu(II) catalysed [2,3]–sigmatropic rearrangement reactions, demonstrating efficient formation of fluorinated rearrangement products. Computational and kinetic studies confirm that Cu(I), generated in situ from Cu(II), serves as the active catalytic species, providing mechanistic insight into the Doyle-Kirmse reaction.

Acknowledgment. The authors gratefully acknowledge the financial support from the German Research Foundation (Grant RO 362/74–1). We express our gratitude to Mrs Anja Müller (Constructor University) and Prof. Nikolai Kuhnert (Constructor University) for recording HRMS spectra. Also, computational resources provided by the University of Zagreb (Croatia) Computing Center SRCE are gratefully acknowledged by the authors.

Supplementary Information. Supporting information to the paper is attached to the electronic version of the article at: https://doi.org/10.5562/cca4248.

REFERENCES

[1] J. Durka, J. Turkowska, D. Gryko, *ACS Sustainable Chem. Eng*. **2021**, *9*, 8895–8918. https://doi.org/10.1021/acssuschemeng.1c01976

[2] W. Kirmse, M. Kapps, *Chem. Ber*. **1968**, *101*, 994–1003. https://doi.org/10.1002/cber.19681010333

[3] M. P. Doyle, W. H. Tamblyn, V. Bagheri, *J. Org. Chem*. **1981**, *46*, 5094–5102. https://doi.org/10.1021/jo00338a008

[4] Z. Sheng, Z. Zhang, C. Chu, Y. Zhang, J. Wang, *Tetrahedron* **2017**, *73*, 4011–4022. https://doi.org/10.1016/j.tet.2016.11.045

[5] A. C. Jones, J. A. May, R. Sarpong, B. M. Stoltz, *Angew. Chem. Int. Ed*. **2014**, *53*, 2556–2591. https://doi.org/10.1002/anie.201302572

[6] M. Inoue, Y. Sumii, N. Shibata, *ACS Omega* **2020**, *5*, 10633–10640. https://doi.org/10.1021/acsomega.0c00830

[7] I. Ojima, 'Fluorine in medicinal chemistry and chemical biology', John Wiley & Sons, Chichester, UK, 2009. https://doi.org/10.1002/9781444312096

[8] D. O'Hagan, Y. Wang, M. Skibinski, A. M. Z. Slawin, *Pure and Applied Chemistry* **2012**, *84*, 1587–1595. https://doi.org/10.1351/PAC-CON-11-09-26,

[9] N. P. Ramirez, G. Pisella, J. Waser, J. *Org. Chem.* **2021**, **86**, 10928–10938. https://doi.org/10.1021/acs.joc.1c01423

[10] K. J. Hock, L. Mertens, R. Hommelsheim, R. Spitzner, R. M. Koenigs, *Chem. Commun*. *2017*, *53*, 6577–6580. https://doi.org/10.1039/C7CC02801F

[11] D. V. Vorobyeva, A. K. Mailyan, A. S. Peregudov, N. M. Karimova, T. P. Vasilyeva, I. S. Bushmarinov, C. Bruneau, P. H. Dixneuf, S. N. Osipov, *Tetrahedron* **2011**, *67*, 3524–3532. https://doi.org/10.1016/j.tet.2011.03.031,

[12] I. Hajdin, R. Pajkert, M. Keßler, J. Han, H. Mei, G.-V. Röschenthaler, Beilstein J. *Org. Chem*. **2023**, *19*, 541–549. https://doi.org/10.3762/bjoc.19.39

[13] I. Hajdin, R. Pajkert, H. Mei, J. Han, G.-V. Röschenthaler, *J. Fluor. Chem.* **2024**, *273*, 110218 https://doi.org/10.1016/j.jfluchem.2023.110218

[14] I. Hajdin, R. Pajkert, H. Mei, J. Han, A. Mravak, D. Duvinage, J. Beckmann, G.-V. Röschenthaler, *Org. Lett.* **2025**,*49*,13498–13503. https://doi.org/10.1021/acs.orglett.5c04281

[15] A. D. Becke, *Phys. Rev. A* **1988**, *38*, 3098. https://doi.org/10.1103/PhysRevA.38.3098

[16] C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785. https://doi.org/10.1103/PhysRevB.37.785

[17] A. D. Becke, *J. Chem. Phys*. **1993**, *98*, 5648–5652. https://doi.org/10.1063/1.464913

[18] H. F. Schaefer, ‘Methods of electronic structure theory’, Springer Science & Business Media, 2013.

[19] W. R. Wadt, P. J. Hay*, J. Chem. Phys*. *1985*, *82*, 284–298. https://doi.org/10.1063/1.448800

[20] P. J. Hay, W. R. Wadt, *J. Chem. Phys*. **1985**, *82*, 299–310. https://doi.org/10.1063/1.448975

[21] G. Scalmani, M. J. Frisch, *J. Chem. Phys*. **2010**, *132*, 114110. https://doi.org/10.1063/1.3359469

[22] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, et al., ‘Gaussian 16’, Gaussian Inc., Wallingford CT, 2016.

[23] Z. Zhang, Z. Sheng, W. Yu, G. Wu, R. Zhang, W.-D. Chu, Y. Zhang, J. Wang, *Nature Chem*. **2017**, *9*, 970–976. https://doi.org/10.1038/nchem.2789

[24] J. B. Sweeney, *Chem. Soc. Rev*. **2009**, *38*, 1027–1038. https://doi.org/10.1039/b604828p

[25] R. G. Salomon, J. K. Kochi, *J. Am. Chem. Soc*. **1973**, *95*, 3300–3310. https://doi.org/10.1021/ja00791a038,

[26] C. Özen, N. Ş. Tüzün, *Organometallics* **2008**, *27*, 4600–4610. https://doi.org/10.1021/om800094k