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Direct Synthesis of α-Fluoro-α-Triazol-1-yl Ketones from Sulfoxonium Ylides: A One-Pot Approach

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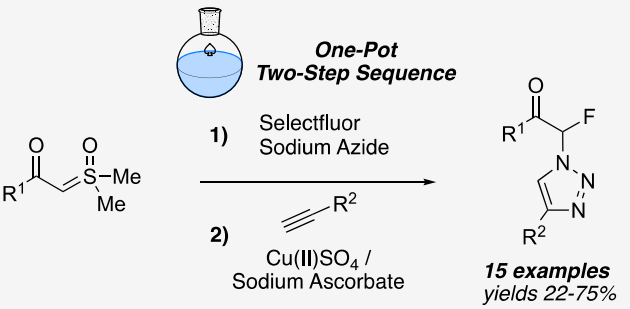
ABSTRACT: The work reported herein showcases a new route to access α-fluoro-α-triazol-1-yl ketones from sulfoxonium ylides via α-azido-α-fluoro ketone intermediates. In a one-pot, two-step sequence, the ketosulfoxonium reactant initially undergoes insertion of F^+ and N_3^-, followed by a subsequent CuAAC reaction with arylacetylenes to install a 1,4-triazolo moiety. The approach allows for modification to both the sulfoxonium ylide and arylacetylene reactants. Fifteen examples have been reported, with yields ranging between 22% and 75%.



Geminal difunctionalized ketones are among some of the most ubiquitous molecules in organic synthesis, highly desirable due to their applications in various biological studies in both academia and industry alike (Figure 1).[1] Important

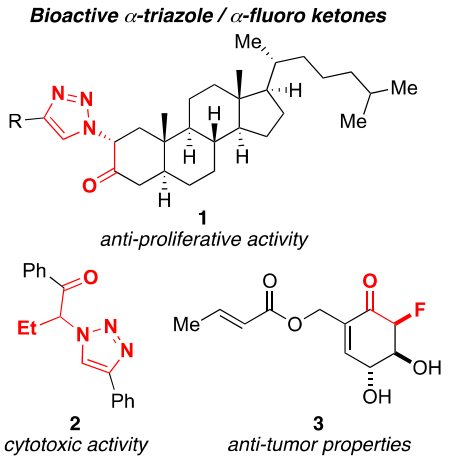


Figure 1. Selected examples of biologically active α-triazole/α-fluoro ketones.

examples have included the installation of 1,4-substituted triazoles α to the ketone functionality, such as steroid-derived substituted ketone **1**, which has shown antiproliferative activity against human cancer cell lines, along with butyrophenone **2** that exerts cytotoxic activity against A549, HT-29, and HeLa cancer cell lines. Important studies into cancer therapeutics are not limited to α-triazolo ketone; for example, α-fluorinated ketones such as cyclohexenone **3** exhibited antitumor properties against lung cancer.

As highlighted with these selected examples, synthetic chemists worldwide have exerted efforts to develop new routes to access α-functionalized ketones.[2] Two distinct subsections of this particular area of chemistry are that of α-azido ketones,[3] and their subsequent applications and transformations,[4] along with α-fluoroketones.[5] In our group, we have recently focused efforts toward accessing α-functionalized carbonyl-containing compounds from assorted sulfoxonium ylides (α-aryl, α-carbonyl).[6] More specifically, accessing S−H,[6a,b] N−H,[6c,f] halo−halo/halo-alkyl,[6d] and aryl[6e,h] derived insertion/arylation products. In search of developing new reactions and finding new modes of reactivities of ketosulfoxonium ylides, we herein present a one-pot, two-step sequence approach that employs ketosulfoxonium ylides as reactants to access α-fluoro-α-triazol-1-yl ketones. Inspired by recent works by Kirsch's[7] and Patonay's[8] groups in the field of α-azido ketone synthesis, and in tandem with the findings we reported on insertion reactions that sulfoxonium ylides can access α,α-dihalogenated ketones[6d] (as well as Wang's recent report on thiosulfonate insertions into sulfoxonium ylides[6g]), we present our latest findings that involve consecutive electrophilic fluorination/azide insertion into sulfoxonium ylides, followed by a Cu-catalyzed azide alkyne cycloaddition (CuAAC) process in a one-pot fashion. Arguably, the most attractive feature of this approach is that the installation of two medicinally relevant moieties, such as a fluorine atom, notable for fine-tuning pharmaceutical proper-

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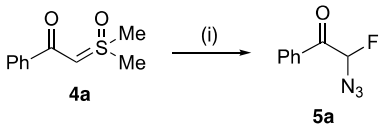
ties such as lipophilicity,[9] and triazoles, known bioisosteres that have mimicked various functional groups[10] and used in peptide ligations,[11] can be installed in a single pot reaction. Furthermore, the process benefits from the utilization of inexpensive and commercially available materials to access the sulfoxonium ylides employed, along with an inexpensive azide source (sodium azide) and a low-cost electrophilic fluorinating reagent (Selectfluor).[12] Classic Cu-catalyzed Click-Chemistry conditions were applied to affect the triazole formation ($CuSO_4$ and sodium ascorbate).[13] The overall approach allows for modification to both the sulfoxonium ylide and acetylene reactants to generate a library of compounds bearing divergent functionalities. To the best of our knowledge, only two single examples exist in the literature in which similar α,α,α-trifunctionalized ketones were synthesized by Shibatomi and Chung in 2011 and 2020, respectively.[14] Their reports highlight how a trifunctionalized ketone bearing a chloro substituent can undergo S_N2 reactions with sodium azide, followed by a Cu-catalyzed Click-Chemistry reaction to install a triazole moiety. With the desired target molecules identified, we set about investigating the optimization of the reaction conditions, employing sulfoxonium ylide **4a** as a reactant in the initial insertion step (Table 1). Our optimized conditions for

Table 1. Optimization of Reaction Conditions for the Transformation of Ylide 4a into α-Fluoro-α-azido Ketone 5a



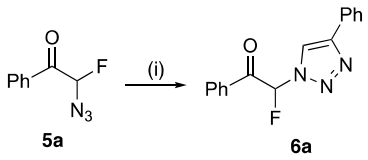
entry	deviation from optimized conditions	5a (%)[a]
1	none	61
2	1 equiv of NaN_3, 1 equiv of Selectfluor	45
3	1 equiv of NaN_3, 1.5 equiv of Selectfluor	52
4	1.5 equiv of NaN_3, 1 equiv of Selectfluor	37
5	2 equiv of NaN_3, 1 equiv of Selectfluor	30
6	2 equiv of NaN_3, 2 equiv of Selectfluor	55
7	THF as a solvent	40
8	MTBE as a solvent	25
9	EtOAc as a solvent	32
10	reaction conducted at 0 °C	40
11	reaction conducted at 50 °C	52
12	reaction left for 24 h	decomp
13	4-acetamidobenzenesulfonyl azide (1.5 equiv) as an azide source	NR
14	1.5 equiv of NaN_3, 1.5 equiv of 1-fluoro-2,4,6-trimethylpyridinium tetrafluoroborate	52
15	1.5 equiv of NaN_3, 1.5 equiv of *N*-fluorobenzenesulfonimide (NFSI)	33

[a]Isolated yield after chromatography. Optimized conditions: (i) **4a** (0.1 mmol), Selectfluor (1.5 equiv), sodium azide (1.5 equiv), acetonitrile (0.5 mL), rt, 1 h. NR = no reaction.

the first step found that using 1.5 equiv of Selectfluor and 1.5 equiv of sodium azide in acetonitrile as a reaction solvent proved effective to generate the α,α-azido,fluoro ketone **5a** (entry 1, 61% yield).[15]

Deviating away from these conditions with respect to modifying the molar ratios of azide and Selectfluor resulted in a loss of reaction yield in all cases trialed (entries 2−6). Investigating the role of solvent in the process was next evaluated; THF, MTBE, and ethyl acetate were all experimented (entries 7−9) but offered no improvement over acetonitrile. Conducting the reaction at lowered or elevated temperatures did not enhance the yield of **5a** (entries 10 and 11), while leaving the reaction for an extended time resulted in decomposition of the product **5a** (entry 12). To conclude studies on this first step, we questioned whether alternative azide or F^+ sources could offer further advances; the use of 4-acetamidobenzenesulfonyl azide gave no reaction (entry 13), while either 1-fluoro-2,4,6-trimethylpyridinium tetrafluoroborate (entry 14, 52% yield) or NFSI (entry 15, 33%) offered only lowered yields of **5a**. The second step of this approach was to conduct the CuAAC reaction on azide **5a** (Table 2). In this second step, we employed conditions from

Table 2. Optimized Reaction Conditions for the Transformation of Ketone 5a into α-Fluoro-α-triazolo Ketone 6a



entry	deviation from optimized conditions	6a (%)[a]
1	none	54
2	$CuSO_4·5H_2O$ (2 mol %), sodium ascorbate (5 mol %), *t*-BuOH/H_2O (1:1), 24 h	19
3	$CuSO_4·5H_2O$ (3 mol %), sodium ascorbate (12 mol %), DABCO (6 mol %), acetic acid (6 mol %), H_2O, rt, 15 min	NR
4	CuI (30 mol %)/sodium ascorbate (30 mol %)/MeCN/H_2O (2:1), rt, 16 h	26
5	CuI (10 mol %)/Et_3N (40 mol %), DMSO, rt, 24 h	32

[a]Isolated yield after chromatography. Optimized conditions: (i) alkyne (1.1 equiv), $CuSO_4·5H_2O$ (30 mol %), sodium ascorbate (30 mol %), *t*-BuOH/H_2O (10:1, 0.5 mL), rt, 16 h. NR = no reaction.

selected literature examples utilized on other azide−alkyne reactant systems, initially looking at using Cu(II)SO_4 as Cu source (entries 1−3). When 30 mol % of $CuSO_4·5H_2O$ and 30 mol % of sodium ascorbate in *tert*-butanol-water (10:1) for 16 h was employed, triazole product **6a** was isolated in 54% yield. Employing similar catalytic systems but using lower loadings of a Cu catalyst (entry 2)[13] afforded a lower yield of **6a**, while the addition of catalytic amounts of additives including DABCO and acetic acid (entry 3)[16] gave no reaction product **6a**. To investigate the effect of replacing the $CuSO_4$ as a Cu catalyst, we trialed literature conditions that employ CuI next (entries 4 and 5). Using 30 mol % of CuI in the presence of sodium ascorbate with the acetonitrile/water cosolvent system, product **6a** was obtained but in only 26% yield (entry 4).[17] Furthermore, changing the reaction solvent to DMSO and substituting sodium ascorbate for triethylamine (40 mol %) gave **6a** in 32% yield (entry 5).[18]

With the optimized conditions realized for the two individual steps, we decided to trial a one-pot approach. The main reasoning for this was linked to the volatility and apparent instability of compound **5a**,[15] but would also benefit from removing an unnecessary extra purification step of **5a**. As such, after the first step of the process had been completed, careful evaporation of the remaining acetonitrile solvent using a rotary evaporator would make **5a** immediately available to participate in the CuAAC reaction without purification. To our

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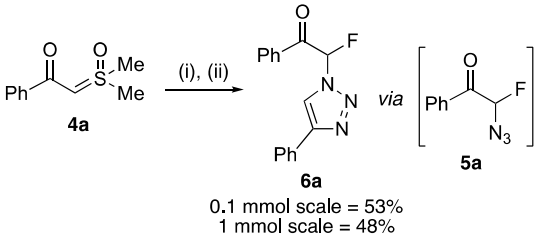
delight, this process proved to be very effective. After rotary evaporation, *tert*-butanol/water (10:1), 1.1 equiv of alkyne, 30 mol % of $CuSO_4{\cdot}5H_2O$, and 30 mol % of sodium ascorbate were added, and the mixture left to stir for 16 h afforded the final reaction product **6a** in a respectable 53% yield over the two-step, one-pot approach (Scheme 1). Additionally, on a 1 mmol scale, the one-pot approach could be replicated only with a slight drop in reaction yield for **6a** (48% yield).

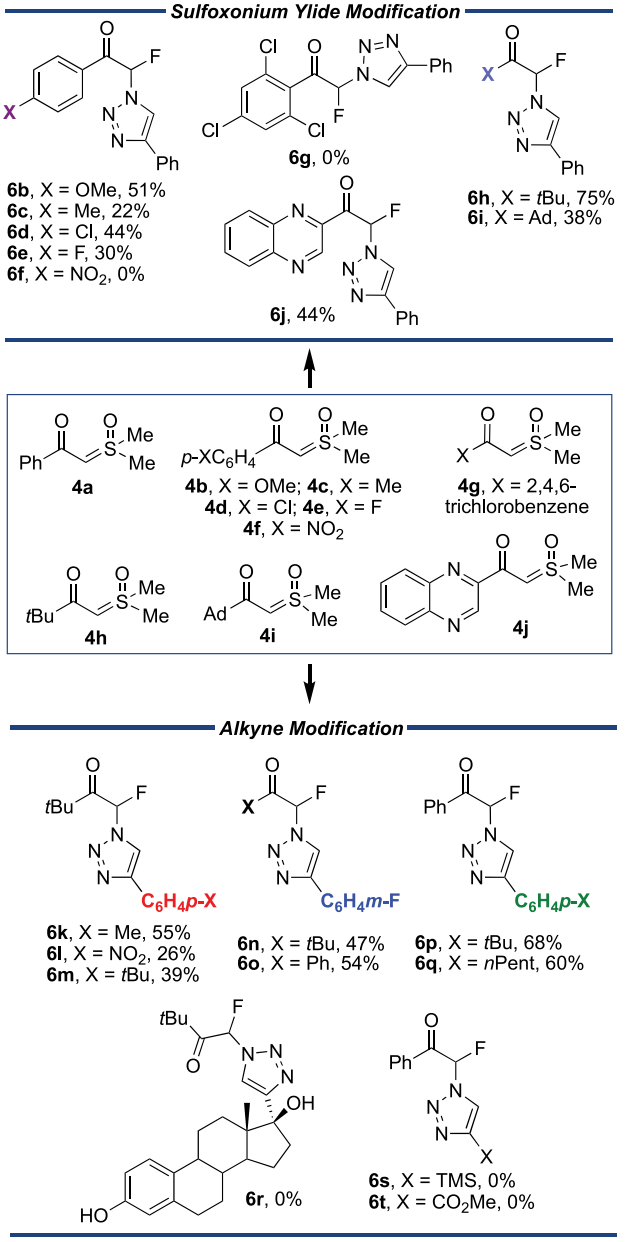
Scheme 1. Optimized Reaction Conditions for the Transformation of Ylide 4a into Ketone 6a[a]



[a]Reagents and conditions: (i) Selectfluor (1.5 equiv), sodium azide (1.5 equiv), acetonitrile, rt, 1 h (3 h on a 1 mmol scale). (ii) Alkyne (1.1 equiv), $CuSO_4{\cdot}5H_2O$ (30 mol %), sodium ascorbate (30 mol %), *t*-BuOH/H_2O (10:1), rt, 16 h.

Confirmation of the structure of product **6a** (and ketones **5a**, **6b**−**6q**) was determined using ^1H, $^{13}C\{^1H\}$, and ^{19}F NMR analysis. Distinctive ^2J coupling constants between hydrogen and fluorine atoms attached to the α-carbon to a ketone are about 48 Hz in similar fluorinated ketones,[19] and we were pleased to observe similar coupling constants in ketones **5a**, **6a**−**6q**, indeed confirming the presence of a single fluorine atom α to the carbonyl group appearing as a doublet signal. In addition, ^{19}F NMR analysis confirms this H−F coupling, with doublet signals observed and a J coupling constant of around 48 Hz for ketones **5a**, **6a**−**6q**. $^{13}C\{^1H\}$ NMR spectra corroborated the assigned structures, revealing an equally strong C−F coupling, with doublets observed at the ketone carbon atom (^2J coupling constant approximately 25 Hz), and at the α-carbon atom itself (larger ^1J coupling constant around 220 Hz).[19] With the optimized reaction conditions in hand, we next sought to investigate the scope and limitations of the approach (Scheme 2). First, we investigated the effects of introducing a range of substituents around the aryl ring of ketosulfoxonium ylides, resulting in the generation of a library of α-fluoro-α-triazol-1-yl ketones **6b**−**f** (Scheme 2, upper section). Initially, electron-rich substituents appended to the aryl ring of the ylides such as methoxy and methyl were well tolerated, affording triazole ketone products **6b** in 51% yield and **6c** in 22% yield, respectively. In addition, the incorporation of electronegative halogen atoms delivered the desired products **6d** and **6e** in moderate yields (44% and 30% each). Unfortunately, a *para*-nitro substituent (**6f**) proved unfruitful, and access to trichloroaryl insertion product **6g** also failed. Pleasingly, however, the incorporation of a quinoxaline moiety allowed access to heteroaryl-derived ketone **6j** in 44% yield. Alkyl variants such as *tert*-butyl-derived sulfoxonium ylide **4h** was next used under the optimized reaction conditions with phenylacetylene, and α,α-fluoro,triazole ketone **6h** was accessed in 75% yield. From a drug discovery viewpoint, the metabolic instability of *tert*-butyl groups[20] led us to investigate other relevant alkyl-derived ylides; adamantyl-containing molecules have desirable pharmaceutical properties

Scheme 2. Scope and Limitations of the One-Pot Approach to Access α-Fluoro-α-triazol-1-yl Ketones 6



such as enhanced lipophilicity and as such provide an interesting target to access.[21] Gratifyingly, we were able to observe the reactivity of the adamantyl ylide **4i** under the optimized conditions, affording α,α-substituted ketone **6i** in a moderate yield of 38%.

With modifications to the sulfoxonium reactants fulfilled, modification of the alkyne reactant was next investigated, more specifically, focusing on altering the substituents on the aromatic ring of the arylacetylene reactants (Scheme 2, lower section). The inclusion of diverse alkyl substituents at the *para*-position on the aryl ring of the acetylene reactants was studied first; methyl (**6k**, 55% yield), *tert*-butyl (**6m**, 39% yield and, **6p**, 68% yield), and *n*-pentyl (**6q**, 60% yield) all performed well under the optimized reaction conditions, modifying the *para*-substituent to a nitro group, however, led to a notable drop in the reaction yield (product **6l**, 26% yield). Following these reactions, we next tested 1-ethynyl-3-fluorobenzene under the

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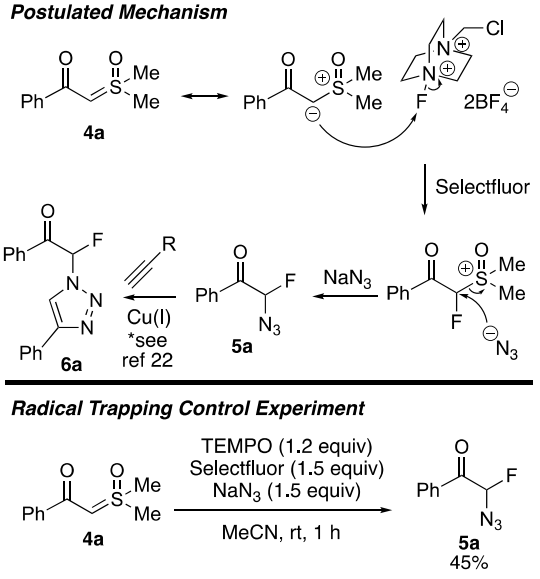
protocol,; pleasingly, two examples **6n** and **6o** were accessed in 47% and 54% yields, respectively. Incorporation of a larger steroid-derived alkyne such as ethinylestradiol to access structure **6r** (closely related to compound **1**, Figure 1), or attempts to incorporate more elementary alkyne reagents such as TMS-acetylene or methyl propiolate to access structures such as **6s−t**, proved unsuccessful.

To finalize these studies, the mechanism for this transformation is postulated in Scheme 3. Supported by our prior findings,[6d] the initial step would involve the nucleophilic nature of the α-carbon on ylide **4a** reacting with electrophilic fluorine (Selectfluor), followed by nucleophilic attack of the azide anion from sodium azide yielding α,α-azido,fluoro ketone intermediate **5a**. A radical-based pathway in this initial step was discounted since the reaction of **4a** under the standard conditions but in the presence of 1.2 equiv of TEMPO did not halt the reaction, with azido ketone intermediate **5a** confirmed by both TLC analysis and infrared spectroscopy against an authentic sample of **5a**. The subsequent introduction of the alkynyl reagent, in the presence of Cu(I) catalyst (generated from the reduction of Cu(II) to Cu(I) by sodium ascorbate), follows literature examples known for classic CuAAC (Cu-azide alkyne cycloaddition)-derived transformations,[13,22] allowing access to α-fluoro-α-triazol-1-yl ketones such as **6a**.

In summary, we have reported a one-pot, two sequence reaction that allows the conversion of assorted ketosulfoxonium ylides into α-fluoro-α-triazol-1-yl ketones, allowing the incorporation of two medicinally relevant moieties in a straightforward, cost-effective manner. Furthermore, the reaction tolerates modifications to both the ketosulfoxonium reactant (aryl- and alkyl-derived) and the arylacetylene reagents utilized in the process. We envisage in the future that the potential of these products and the methodology to access them may be utilized in drug discovery programs to access important and desirable pharmaceuticals in time to come.

Scheme 3. Postulated Mechanism and Radical Trapping Control Experiment



EXPERIMENTAL SECTION

General Comments. All commercially available reagents were used as purchased, and sulfoxonium ylide starting materials were prepared according to known literature procedures, with analytical data identical to those previously reported. TLC analyses were performed using silica gel plates, with detection by UV absorption (254 nm) for visualization. Flash column chromatography was performed using silica gel 200−400 mesh. All NMR analyses were recorded using $CDCl_3$ as a solvent and TMS as an internal standard (^{1}H NMR were recorded at 400, 500, or 600 MHz and $^{13}C\{^1H\}$ NMR at 100, 125, or 150 MHz using 400 (Agilent Technologies, 400/54 Premium Shielded), 500 (Agilent Technologies, 500/54 Premium Shielded), and 600 MHz (Bruker Ultrashield 600) instruments). Chemical shifts are reported in ppm downfield from TMS with a reference to the internal solvent. Infrared spectra were obtained using FT-IR (Bruker, model ALPHA) at 4.0 cm^{-1} resolution and are reported in wavenumbers. The samples were dispersed neat on a ZnSe crystal (ATR mode). Melting points were determined using a digital melting point apparatus (Fisatom, model 430D). High-resolution mass spectra (HRMS) were recorded using electron spray ionization in positive mode (ESI) on a Waters model Xevo G2 or in a Thermo Fischer model Orbitrap LTQ Velos.

Caution: This article details the use of sodium azide and generation of azide compounds, and caution should be taken when handling such sensitive compounds due to their associated toxicity and potential for explosions, especially on scale-up. The use of a blast shield is recommended when conducting such reactions.

General Procedure A: Synthesis of Sulfoxonium Ylides. The synthesis of sulfoxonium ylides was identical to our previously reported method,[6e] and a modification of that was highlighted by our group in 2017.[6d] A 125 mL oven-dried round-bottom flask was attached to a reflux condenser, under an argon atmosphere, to which 3.0 g of potassium *tert*-butoxide (27.2 mmol, 4.0 equiv) and 27.0 mL of anhydrous THF were added. Then, 4.48 g of trimethylsulfoxonium iodide (20.4 mmol, 3.0 equiv) was added in one portion. The suspension was heated at reflux for 2 h. After this time, the mixture was cooled at 0 °C, followed by the slow addition of the appropriate benzoyl chloride (6.8 mmol, 1.0 equiv). The reaction mixture temperature was slowly increased to room temperature, and this mixture stirred for an additional 3 h. Then, the solvent was removed on a rotary evaporator. After that, 70 mL of water was added, and the product was extracted with a 3:1 CH_2Cl_2/*i*-PrOH mixture (8 × 20 mL). The organic phase was washed with water (3 × 10 mL) and dried over Na_2SO_4, and the solvent was removed on a rotary evaporator. The crude material was purified by solubilization in the minimal amount of hot EtOAc (10−15 mL), followed by the slow addition of 15 mL of hexanes. The solid was filtered and washed with two portions of a 2:1 mixture of hexanes/EtOAc (2 × 10 mL), furnishing the respective sulfoxonium ylide.

General Procedure B: Synthesis of α-Fluoro-α-Triazolo-Ketones (6) From Sulfoxonium Ylides (4). A 5 or 10 mL round-bottom flask (fitted with rubber septa and outlet for gas release) was charged with sulfoxonium ylide (0.1 mmol), sodium azide (0.15 mmol), Selectfluor (0.15 mmol), and acetonitrile (0.5 mL per 0.1 mmol ylide) at room temperature under an air atmosphere, and the mixture left to stir for 1 h (thin-layer chromatography (TLC) was used to confirm the formation of the azide, using hexane/ethyl acetate, 10:1, as mobile phase). Evaporation of the acetonitrile solvent was performed on a rotary evaporator, followed by the addition of *tert*-butanol/water (10:1, 0.5 mL in total), alkyne (0.11 mmol), followed by $CuSO_4{\cdot}5H_2O$, and sodium ascorbate (30 mol % each, one portion) to the same reaction vessel, and the mixture was left to stir for 16 h (reaction monitored by TLC following the consumption of azide and appearance of triazole using hexane/ethyl acetate, 5:1). Upon completion, the reaction mixture was added directly to a column loaded with silica gel pre-eluted with the mobile phase solvent system (hexane/ethyl acetate, 5:1). Chromatography afforded the desired triazole products as either oils or solids.

2-(Dimethyl(oxo)-λ^6-sulfaneylidene)-1-phenylethan-1-one 4a.[6d] This compound was prepared according to general procedure A

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from benzoyl chloride. White solid (760 mg, 57%; mp = 116−118 °C). R_f = 0.38 (EtOAc/MeOH, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81−7.78 (2H, m), 7.45−7.36 (3H, m), 4.98 (1H, s), 3.51 (6H, s).

2-(Dimethyl(oxo)-λ^6-sulfanylidene)-1-(4-methoxyphenyl)-ethan-1-one 4b.[6b] This compound was prepared according to general procedure A from 4-methoxybenzoyl chloride. Cream solid (520 mg, 33%; mp = 157−159 °C). R_f = 0.29 (EtOAc/MeOH, 10:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (2H, d, J = 8.8 Hz), 6.89 (2H, d, J = 8.8 Hz), 4.91 (1H, s), 3.83 (3H, s), 3.50 (6H, s).

2-(Dimethyl(oxo)-λ^6-sulfanylidene)-1-(p-tolyl)ethan-1-one 4c.[6d] This compound was prepared according to general procedure A with the following modifications: 4-methylbenzoyl chloride (5 mmol), t-BuOK (20 mmol, 4 equiv), and trimethylsulfoxonium iodide (15 mmol, 3 equiv). White solid (800 mg, 76%; mp = 141−143 °C). R_f = 0.37 (EtOAc/MeOH, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (2H, d, J = 7.8 Hz), 7.19 (2H, d, J = 7.9 Hz), 4.95 (1H, s), 3.50 (6H, s), 2.38 (3H, s).

1-(4-Chlorophenyl)-2-(dimethyl(oxo)-λ^6-sulfanylidene)-ethan-1-one 4d.[6d] This compound was prepared according to general procedure A from 4-chlorobenzoyl chloride. White solid (810 mg, 52%; mp = 150−152 °C). R_f = 0.35 (EtOAc/MeOH, 10:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74−7.71 (2H, m), 7.37−7.34 (2H, m), 4.94 (1H, s), 3.51 (6H, s).

2-(Dimethyl(oxo)-λ^6-sulfanylidene)-1-(4-fluorophenyl)-ethan-1-one 4e.[6d] This compound was prepared according to general procedure A from 4-fluorobenzoyl chloride. White solid (1042 mg, 72%; mp = 138−140 °C). R_f = 0.38 (EtOAc/MeOH, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82−7.76 (2H, m), 7.08−7.02 (2H, m), 4.92 (1H, s), 3.51 (6H, s).

2-(Dimethyl(oxo)-λ^6-sulfaneylidene)-1-(4-nitrophenyl)-ethan-1-one 4f.[6e] This compound was prepared according to general procedure A with the following modifications: 4-nitrobenzoyl chloride (5 mmol), t-BuOK (5 mmol, 4 equiv), and trimethylsulfoxonium iodide (15 mmol, 3 equiv). Yellow solid (815 mg, 67%; mp = 198−200 °C). R_f = 0.33 (9:1 $CHCl_3$/MeOH). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.21 (2H, d, J = 8.9 Hz), 7.96 (2H, d, J = 8.9 Hz), 5.75 (1H, s), 3.55 (6H, s).

2-(Dimethyl(oxo)-λ^6-sulfaneylidene)-1-(2,4,6-trichlorophenyl)ethan-1-one 4g. This compound was prepared according to general procedure A with the following modifications: 2,4,6-trichlorobenzoyl chloride (5 mmol), t-BuOK (5 mmol), and trimethylsulfoxonium iodide (15 mmol). White solid (748 mg, 50%; mp = 176−178 °C). R_f = 0.60 (EtOAc/MeOH, 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.28 (2H, s), 4.52 (1H, s), 3.53 (6H, s). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 178.8, 138.8, 134.3, 132.7, 128.1, 72.9, 42.2. IR: ν (neat, ATR)/cm^{-1} 3081, 3014, 2926, 1543, 1370, 1176, 1100, 1028, 890, 853, 799, 738. HRMS (ESI/Q-TOF) m/z: [M + H]$^+$ calcd for $C_{10}H_{10}Cl_3O_2S$, 298.9467; found, 298.9465.

1-(Dimethyl(oxo)-λ^6-sulfanylidene)-3,3-dimethylbutan-2-one 4h.[6d] This compound was prepared according to general procedure A from pivaloyl chloride. White solid (1020 mg, 85%; mp = 170−172 °C). R_f = 0.35 (EtOAc/MeOH, 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.43 (1H, s), 3.37 (6H, s), 1.11 (9H, s).

1-((1*R*,3*R*,5*R*,7*R*)-Adamantan-2-yl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)ethan-1-one 4i. This compound was prepared according to general procedure A from adamantane carbonyl chloride. White solid (860 mg, 50%; mp = 161−163 °C). R_f = 0.38 (EtOAc/MeOH, 10:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.39 (1H, s), 3.36 (6H, s), 1.99 (3H, bs), 1.77 (6H, d, J = 2.0 Hz), 1.67 (6H, m). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 197.5, 66.4, 42.5, 39.8, 36.9, 28.6. IR: ν (neat, ATR)/cm^{-1} 3482, 3402, 3000, 2904, 2849, 1524, 1384, 1193, 1173, 1030, 856. HRMS (ESI/Q-TOF) m/z: [M + H]$^+$ calcd for $C_{14}H_{23}O_2S$, 255.1413; found, 255.1418.

2-(Dimethyl(oxo)-λ^6-sulfaneylidene)-1-(quinoxalin-2-yl)-ethan-1-one 4j. This compound was prepared according to general procedure A with the following modifications: quinoxaline-2-carbonyl chloride (1.3 mmol), t-BuOK (5.2 mmol, 4 equiv), and trimethylsulfoxonium iodide (3.9 mmol, 3 equiv). Light brown solid (178 mg, 55%; mp = 129−131 °C). R_f = 0.75 (9:1 $CHCl_3$/MeOH). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.54 (1H, s), 8.12−8.08 (2H, m), 7.80−7.75 (2H, m), 5.97 (1H, s), 3.58 (6H, s). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 179.3, 148.7, 143.5, 143.3, 141.0, 130.9, 130.4, 130.0, 129.4, 70.7, 42.2. IR: ν (neat, ATR)/cm^{-1} 3010, 2921, 1579, 1559, 1541, 1416, 1386, 1296, 1259, 1174, 1138, 1069, 1026, 854, 767. HRMS (ESI/Q-TOF) m/z: [M + H]$^+$ calcd for $C_{12}H_{13}N_2O_2S$, 249.0698; found, 249.0702.

2-Azido-2-fluoro-1-phenylethan-1-one 5a. To a 5 mL round-bottom flask were added 2-(dimethyl(oxo)-λ^6-sulfaneylidene)-1-phenylethan-1-one **4a** (19.6 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), and acetonitrile (0.5 mL), and the reaction was left to stir at room temperature for 1 h. The reaction solvent was then carefully evaporated using a rotary evaporator, and the remaining residue was purified on silica gel using hexane/ethyl acetate as an eluent (10:1). The desired product 2-azido-2-fluoro-1-phenylethan-1-one **5a** was isolated as a colorless oil (11 mg, 61%). R_f = 0.55 (10:1, hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (2H, d, J = 7.7 Hz), 7.67 (1H, t, J = 7.7 Hz), 7.53 (2H, t, J = 7.7 Hz), 6.13 (1H, d, J = 52.0 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 188.3 (d, J = 26.0 Hz), 135.0, 132.6, 129.6, 129.2, 96.4 (d, J = 225.0 Hz). ^{19}F NMR (377 MHz, $CDCl_3$): δ −144.3 (1F, d, J = 52.0 Hz). IR: ν (neat, ATR)/cm^{-1} 2956, 2919, 2850, 2121, 1699, 1598, 1451, 1218, 972, 688.

2-Fluoro-1-phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethan-1-one 6a. Following general procedure B, from 2-(dimethyl(oxo)-λ^6-sulfaneylidene)-1-phenylethan-1-one **4a** (19.6 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then t-BuOH/H_2O (10:1, 0.5 mL), phenylacetylene (12 μL, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 2-fluoro-1-phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethan-1-one **6a** was isolated as an off-white solid (15 mg, 53%; mp = 144−146 °C). R_f = 0.32 (5:1, hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04−8.02 (3H, m), 7.85−7.83 (2H, m), 7.72 (1H, d, J = 48.0 Hz), 7.70−7.65 (1H, m), 7.55−7.51 (2H, m), 7.45−7.41 (2H, m), 7.38−7.34 (1H, m). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 186.7 (d, J = 25.0 Hz), 149.4, 135.6, 132.4, 129.6, 129.5, 129.3 (d, J = 1.5 Hz), 129.1, 129.0, 126.1, 119.0 (d, J = 1.5 Hz), 91.5 (d, J = 218.0 Hz).^{19}F NMR (377 MHz, $CDCl_3$): δ −147.1 (1F, d, J = 48.0 Hz). IR: ν (neat, ATR)/cm^{-1} 3143, 2962, 2919, 2850, 1706, 1596, 1451, 1428, 1382, 1239, 1179, 1091, 1073, 1031, 1019, 962, 882, 823, 804, 761, 689, 668, 612. HRMS (ESI/Q-TOF) m/z: [M + H]$^+$ calcd for $C_{16}H_{13}FN_3O$, 282.1037; found, 282.1040.

Modification of General Procedure B: 1 mmol Scale. 2-(Dimethyl(oxo)-λ^6-sulfaneylidene)-1-phenylethan-1-one **4a** (196 mg, 1 mmol), sodium azide (98 mg, 1.5 mmol), Selectfluor (530 mg, 1.5 mmol), and acetonitrile (5 mL) reacted for 3 h; then t-BuOH/H_2O (10:1, 5 mL), phenylacetylene (120 μL, 1.1 mmol), $CuSO_4{\cdot}5H_2O$ (75 mg, 30 mol %), and sodium ascorbate (60 mg, 30 mol %) were used. 2-Fluoro-1-phenyl-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethan-1-one **6a** was isolated as an off-white solid (135 mg, 48%).

2-Fluoro-1-(4-methoxyphenyl)-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethan-1-one 6b. Following general procedure B, from 2-(dimethyl(oxo)-λ^6-sulfaneylidene)-1-(4-methoxyphenyl)ethan-1-one **4b** (22.6 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then t-BuOH/H_2O (10:1, 0.5 mL), phenylacetylene (12 μL, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 2-fluoro-1-(4-methoxyphenyl)-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethan-1-one **6b** was isolated as a white solid (16 mg, 51%; mp = 121−123 °C). R_f = 0.25 (5:1, hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04−8.00 (3H, m), 7.83 (2H, d, J = 7.5 Hz), 7.68 (1H, d, J = 48.0 Hz), 7.43 (2H, t, J = 7.5 Hz), 7.36 (1H, t, J = 7.5 Hz), 6.97 (2H, d, J = 9.0 Hz), 3.88 (3H, s). ^{13}C{^{1}H} NMR: (151 MHz, $CDCl_3$): δ 185.0 (d, J = 25.4 Hz), 165.4, 149.3, 131.9 (d, J = 2.0 Hz), 129.7, 129.1, 128.9, 126.1, 125.3, 119.0 (d, J = 1.5 Hz), 114.8, 91.4 (d, J = 218.0 Hz), 55.9. ^{19}F NMR (377 MHz, $CDCl_3$): δ −147.0 (1F, d, J = 48.0 Hz). IR: ν (neat, ATR)/cm^{-1} 3139, 2933, 2843, 1696, 1599, 1573, 1514, 1485, 1459, 1427, 1365, 1317, 1269, 1248, 1209, 1174, 1139, 1093, 1075, 1022, 965, 917, 872, 842, 817,

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765, 729, 694, 671, 610. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{15}FN_3O_2$, 312.1143; found, 312.1147.

2-Fluoro-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-1-(*p*-tolyl)ethan-1-one 6c. Following general procedure B, from 2-(dimethyl(oxo)-λ^6-sulfanylidene)-1-(*p*-tolyl) ethan-1-one **4c** (21 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then *t*-BuOH/H_2O (10:1, 0.5 mL), phenylacetylene (12 μL, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 2-fluoro-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-1-(*p*-tolyl)ethan-1-one **6c** was isolated as a white solid (6.5 mg, 22%; mp = 116−118 °C). R_f = 0.17 (5:1, hexane/ethyl acetate). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.03 (1H, s), 7.92 (2H, d, J = 8.3 Hz), 7.84−7.83 (2H, m), 7.70 (1H, d, J = 48.0 Hz), 7.44−7.43 (2H, m), 7.37−7.34 (1H, m), 7.32 (2H, d, J = 8.4 Hz), 2.43 (3H, s). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 186.3 (d, J = 26.0 Hz), 149.3, 147.1, 130.2, 129.9, 129.6, 129.4 (d, J = 1.5 Hz), 129.1, 129.0, 126.1, 119.0 (d, J = 1.8 Hz), 91.4 (d, J = 218.0 Hz), 22.1. ^{19}F NMR (376 MHz, $CDCl_3$): δ −147.2 (1F, d, J = 47.2 Hz). IR: ν (neat, ATR)/cm^{-1} 3140, 2950, 2921, 2852, 1704, 1605, 1459, 1370, 1252, 1182, 1093, 1022, 967, 871, 799, 765, 691, 621. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{15}FN_3O$, 296.1194; found, 296.1200.

1-(4-Chlorophenyl)-2-fluoro-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethan-1-one 6d. Following general procedure B, from 1-(4-chlorophenyl)-2-(dimethyl(oxo)-λ^6-sulfanylidene)ethan-1-one **4d** (23 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then *t*-BuOH/H_2O (10:1, 0.5 mL), phenylacetylene (12 μL, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 1-(4-chlorophenyl)-2-fluoro-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethan-1-one **6d** was isolated as a colorless oil (14 mg, 44%). R_f = 0.38 (5:1, hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (1H, s), 8.00−7.97 (2H, m), 7.85−7.83 (2H, m), 7.64 (1H, d, J = 48.0 Hz), 7.52−7.49 (2H, m), 7.45−7.43 (2H, m), 7.39−7.36 (1H, m). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 185.8 (d, J = 27.0 Hz), 149.4, 142.4, 130.72, 130.71, 129.9, 129.10, 129.06, 126.1, 119.1 (d, J = 2.0 Hz), 117.3, 91.7 (d, J = 218.0 Hz). ^{19}F NMR (377 MHz, $CDCl_3$): δ −146.7 (1F, d, J = 48.0 Hz). IR: ν (neat, ATR)/cm^{-1} 3139, 2923, 2851, 1711, 1589, 1570, 1487, 1460, 1433, 1403, 1365, 1279, 1243, 1207, 1180, 1139, 1093, 1015, 968, 916, 873, 764, 669. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{12}ClFN_3O$, 316.0647; found, 316.0655.

2-Fluoro-1-(4-fluorophenyl)-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethan-1-one 6e. Following general procedure B, from 2-(dimethyl(oxo)-λ^6-sulfanylidene)-1-(4-fluorophenyl)ethan-1-one **4e** (21.4 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then *t*-BuOH/H_2O (10:1, 0.5 mL), phenylacetylene (12 μL, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 2-fluoro-1-(4-fluorophenyl)-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethan-1-one **6e** was isolated as a white solid (9 mg, 30%; mp = 121−123 °C). R_f = 0.29 (5:1, hexane/ethyl acetate). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.14−8.06 (2H, m), 8.04 (1H, s), 7.86−7.80 (2H, m), 7.72−7.59 (1H, m), 7.47−7.40 (2H, m), 7.40−7.34 (1H, m), 7.23−7.18 (2H, m). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 185.3 (d, J = 26.0 Hz), 167.1 (d, J = 259.8 Hz), 149.5, 132.4 (d, J = 9.9 Hz), 129.5, 129.12, 129.06, 128.9 (d, J = 3.2 Hz), 126.1, 119.0, 116.9 (d, J = 22.2 Hz), 91.68 (d, J = 218.3 Hz). ^{19}F NMR (377 MHz, $CDCl_3$): δ −146.5 (1F, d, J = 47.3 Hz), −99.8 (1F). IR: ν (neat, ATR)/cm^{-1} 2957, 2923, 2852, 1708, 1598, 1459, 1432, 1365, 1238, 1177, 1093, 1073, 1019, 967, 874, 846, 802, 762, 692, 669, 617. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{12}F_2N_3O$, 300.0943; found, 300.0952.

1-Fluoro-3,3-dimethyl-1-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-butan-2-one 6h. Following general procedure B, from 1-(dimethyl-(oxo)-λ^6-sulfanylidene)-3,3-dimethylbutan-2-one **4h** (17.6 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then *t*-BuOH/H_2O (10:1, 0.5 mL), phenylacetylene (12 μL, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 1-fluoro-3,3-dimethyl-1-(4-phenyl-1*H*-1,2,3-triazol-1-yl)butan-2-one **6h** was isolated as a crystalline colorless solid (19.5 mg, 75%; mp = 105−107 °C). R_f = 0.40 (5:1, hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (1H, s), 7.87−7.85 (2H, m), 7.47−7.43 (2H, m), 7.40−7.35 (1H, m), 7.23 (1H, d, J = 48.0 Hz), 1.27 (9H, app. bd, J = 0.5 Hz). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 203.0 (d, J = 23.0 Hz), 149.1, 129.7, 129.1, 129.0, 126.1, 118.9 (d, J = 1.5 Hz), 89.6 (d, J = 218.0 Hz), 44.2, 25.8. ^{19}F NMR (377 MHz, $CDCl_3$): δ −145.2 (1F, d, J = 48.0 Hz). IR: ν (neat, ATR)/cm^{-1} 3140, 2974, 2876, 1732, 1480, 1459, 1433, 1369, 1241, 1191, 1139, 1111, 1074, 1045, 1034, 1020, 982, 918, 874, 837, 797, 765, 712, 694, 634. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{17}FN_3O$, 262.1350; found, 262.1356.

1-((1*R*,3*R*,5*R*,7*R*)-Adamantan-2-yl)-2-fluoro-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethan-1-one 6i. Following general procedure B, from 1-((1*R*,3*R*,5*R*,7*R*)-adamantan-2-yl)-2-(dimethyl(oxo)-λ^6-sulfaneylidene)ethan-1-one **4i** (25.4 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then *t*-BuOH/H_2O (10:1, 0.5 mL), phenylacetylene (12 μL, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 1-((1*R*,3*R*,5*R*,7*R*)-adamantan-2-yl)-2-fluoro-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethan-1-one **6i** was isolated as a colorless oil (13 mg, 38%). R_f = 0.45 (5:1, hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (1H, s), 7.87−7.84 (2H, m), 7.47−7.43 (2H, m), 7.40−7.35 (1H, m), 7.25 (1H, d, J = 48.0 Hz), 2.08 (3H, bs), 1.87 (6H, d, J = 3.0 Hz), 1.79−1.68 (6H, m). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 201.1 (d, J = 22.0 Hz), 149.1, 129.7, 129.1, 128.9, 126.1, 118.9 (d, J = 1.5 Hz), 88.8 (d, J = 218.0 Hz), 46.5, 38.8, 37.3, 36.6, 36.2, 28.0, 27.5. ^{19}F NMR (377 MHz, $CDCl_3$): δ −146.6 (1F, d, J = 48.0 Hz). IR: ν (neat, ATR)/cm^{-1} 3139, 2907, 2853, 1726, 1612, 1559, 1485, 1455, 1433, 1367, 1265, 1242, 1197, 1184, 1161, 1104, 1075, 1033, 1021, 999, 970, 933, 881, 846, 792, 763, 712, 694, 670, 628. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{23}FN_3O$, 340.1820; found, 340.1820.

2-Fluoro-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-1-(quinoxalin-2-yl)ethan-1-one 6j. Following general procedure B, from 2-(dimethyl(oxo)-λ^6-sulfaneylidene)-1-(quinoxalin-2-yl)ethan-1-one **4j** (24.8 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then *t*-BuOH/H_2O (10:1, 0.5 mL), phenylacetylene (12 μL, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 2-fluoro-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-1-(quinoxalin-2-yl)ethan-1-one **6j** was isolated as a crystalline yellow solid (14.5 mg, 44%; mp = 132−134 °C). R_f = 0.2 (dichloromethane). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.61 (1H, s), 8.34 (1H, d, J = 50.0 Hz), 8.21 (1H, s), 8.20 (1H, dd, J = 8.5, 1.0 Hz), 8.12 (1H, dd, J = 8.5, 1.0 Hz), 7.97−7.93 (1H, m), 7.89−7.85 (1H, m), 7.85−7.83 (2H, m), 7.45−7.41 (2H, m), 7.38−7.34 (1H, m). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 186.9 (1C, d, J = 26.0 Hz), 149.1, 144.8, 143.6, 143.5, 140.8, 133.9, 131.8, 130.8, 129.8, 129.6, 129.1, 129.0, 126.1, 119.5 (1C, d, J = 2.0 Hz) 89.8 (1C, d, J = 216.0 Hz). ^{19}F NMR (377 MHz, $CDCl_3$): δ −152.2 (1F, d, J = 52 Hz). IR: ν (neat, ATR)/cm^{-1} 3138, 2955, 2925, 2851, 1731, 1568, 1486, 1460, 1435, 1367, 1300, 1141, 1075, 989, 945, 807, 763, 695. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{13}FN_5O$, 334.1104; found, 334.1103.

1-Fluoro-3,3-dimethyl-1-(4-(p-tolyl)-1*H*-1,2,3-triazol-1-yl)-butan-2-one 6k. Following general procedure B, from 1-(dimethyl-(oxo)-λ^6-sulfanylidene)-3,3-dimethylbutan-2-one **4h** (17.6 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then *t*-BuOH/H_2O (10:1, 0.5 mL), 4-ethynyltoluene (14 μL, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 1-fluoro-3,3-dimethyl-1-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)butan-2-one **6k** was isolated as a cream solid (15 mg, 55%; mp = 108−110 °C). R_f = 0.36 (5:1, hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (1H, s), 7.76−7.73 (2H, m), 7.27−7.25 (2H, m), 7.22 (1H, d, J = 48.0 Hz), 2.39 (3H, s), 1.26 (9H, d, J = 0.5 Hz). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 203.0 (d, J = 23.0 Hz), 149.2, 138.9, 129.8, 126.9, 126.0, 118.5 (d, J = 2.0 Hz), 89.6 (d, J = 218.0 Hz), 44.2, 25.8, 21.5. ^{19}F NMR (377 MHz, $CDCl_3$): δ −145.3 (1F, d, J = 48.0 Hz).

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IR: ν (neat, ATR)/cm^{-1} 3089, 2974, 1736, 1479, 1438, 1367, 1238, 1192, 1110, 1045, 1028, 976, 817. HRMS (ESI/Q-TOF) m/z: [M + H]$^+$ calcd for $C_{15}H_{19}FN_3O$, 276.1507; found, 276.1511.

1-Fluoro-3,3-dimethyl-1-(4-(4-nitrophenyl)-1*H*-1,2,3-triazol-1-yl)butan-2-one 6l. Following general procedure B, from 1-(dimethyl(oxo)-λ^6-sulfanylidene)-3,3-dimethylbutan-2-one **4h** (17.6 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then *t*-BuOH/H_2O (10:1, 0.5 mL), 1-ethynyl-4-nitrobenzene (16.2 mg, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 1-fluoro-3,3-dimethyl-1-(4-(4-nitrophenyl)-1*H*-1,2,3-triazol-1-yl)butan-2-one **6l** was isolated as an off-white gum (8 mg, 26%). R_f = 0.20 (5:1, hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (2H, d, J = 8.8 Hz), 8.26 (1H, s), 8.05 (2H, d, J = 8.8 Hz), 7.26 (1H, d, J = 47.0 Hz), 1.31 (9H, s). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 202.8 (d, J = 23.0 Hz), 147.9, 146.9, 135.9, 126.7, 124.6, 120.8, 89.8 (d, J = 218.0 Hz), 29.9, 25.7. ^{19}F NMR (377 MHz, $CDCl_3$): δ −144.8 (1F, d, J = 47.0 Hz). IR: ν (neat, ATR)/cm^{-1} 3140, 2964, 2918, 2850, 1732, 1608, 1519, 1456, 1449, 1342, 1109, 1072, 1031, 982, 854, 756. HRMS (ESI/Q-TOF) m/z: [M + H]$^+$ calcd for $C_{14}H_{16}FN_4O_3$, 307.1201; found, 307.1202.

1-(4-(4-(*tert*-Butyl)phenyl)-1*H*-1,2,3-triazol-1-yl)-1-fluoro-3,3-dimethylbutan-2-one 6m. Following general procedure B, from 1-(dimethyl(oxo)-λ^6-sulfanylidene)-3,3-dimethylbutan-2-one **4h** (17.6 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then *t*-BuOH/H_2O (10:1, 0.5 mL), 4-*tert*-butylphenylacetylene (20 μL, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 1-(4-(4-(*tert*-butyl)phenyl)-1*H*-1,2,3-triazol-1-yl)-1-fluoro-3,3-dimethylbutan-2-one **6m** was isolated as a colorless oil (12.5 mg, 39%). R_f = 0.33 (5:1, hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (1H, s), 7.79 (2H, d, J = 8.4 Hz), 7.47 (2H, d, J = 8.4 Hz), 7.22 (1H, d, J = 48.0 Hz), 1.35 (9H, s), 1.26 (9H, s). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 203.0 (d, J = 23.0 Hz), 152.2, 149.1, 126.8, 126.0, 125.9, 118.5 (d, J = 1.5 Hz), 89.6 (d, J = 218.0 Hz), 44.2, 34.9, 31.4, 25.8. ^{19}F NMR (377 MHz, $CDCl_3$): δ −145.4 (1F, d, J = 48.0 Hz). IR: ν (neat, ATR)/cm^{-1} 3145, 2963, 2870, 1731, 1497, 1478, 1443, 1366, 1263, 1241, 1190, 1110, 1069, 1027, 1014, 961, 840, 828, 797. HRMS (ESI/Q-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{25}FN_3O$, 318.1976; found, 318.1976.

1-Fluoro-1-(4-(3-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)-3,3-dimethylbutan-2-one 6n. Following general procedure B, from 1-(dimethyl(oxo)-λ^6-sulfanylidene)-3,3-dimethylbutan-2-one **4h** (17.6 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then *t*-BuOH/H_2O (10:1, 0.5 mL), 1-ethynyl-3-fluorobenzene (13 μL, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 1-fluoro-1-(4-(3-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)-3,3-dimethylbutan-2-one **6n** was isolated as a colorless oil (13 mg, 47%). R_f = 0.30 (5:1, hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (1H, s), 7.63−7.58 (2H, m), 7.44−7.39 (1H, m), 7.23 (1H, d, J = 48.0 Hz), 7.10−7.05 (1H, m), 1.28 (9H, s). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 202.9 (d, J = 23.0 Hz), 163.3 (d, J = 246.0 Hz), 148.0 (d, J = 3.0 Hz), 131.8 (d, J = 8.0 Hz), 130.7 (d, J = 8.0 Hz), 121.7 (d, J = 3.0 Hz), 119.4 (d, J = 2.0 Hz), 115.8 (d, J = 21.0 Hz), 113.1 (d, J = 23.0 Hz), 89.7 (d, J = 218.0 Hz), 44.2, 25.8.^{19}F NMR (377 MHz, $CDCl_3$): δ −145.1 (1F, d, J = 48.0 Hz), −112.3 to −112.2 (1F, m). IR: ν (neat, ATR)/cm^{-1} 3143, 2974, 1732, 1620, 1591, 1480, 1456, 1437, 1370, 1253, 1223, 1155, 1129, 1111, 1081, 1067, 1044, 1030, 979, 867, 786, 685. HRMS (ESI/Q-TOF) m/z: [M + H]$^+$ calcd for $C_{14}H_{16}F_2N_3O$, 280.1256; found, 280.1259.

2-Fluoro-2-(4-(3-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)-1-phenylethan-1-one 6o. Following general procedure B, from 2-(dimethyl(oxo)-λ^6-sulfaneylidene)-1-phenylethan-1-one **4a** (19.6 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then *t*-BuOH/H_2O (10:1, 0.5 mL), 1-ethynyl-3-fluorobenzene (13 μL, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 2-fluoro-2-(4-(3-fluorophenyl)-1*H*-1,2,3-triazol-1-yl)-1-phenylethan-1-one **6o** was isolated as a colorless oil (16 mg, 54%). R_f = 0.28 (5:1, hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (1H, s), 8.04 (2H, d, J = 7.5 Hz), 7.73 (1H, d, J = 48.0 Hz), 7.71−7.67 (1H, m), 7.61−7.52 (4H, m), 7.42−7.37 (1H, m), 7.08−7.03 (1H, m). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 186.6 (d, J = 26.0 Hz), 163.3 (d, J = 246.0 Hz), 148.3, 135.6, 132.4, 131.7 (d, J = 8.0 Hz), 130.7 (d, J = 8.0 Hz), 129.5, 129.4 (d, J = 2.0 Hz), 121.7 (d, J = 3.0 Hz), 119.6 (d, J = 2.0 Hz), 115.9 (d, J = 21.5 Hz), 113.1 (d, J = 23.0 Hz), 91.6 (d, J = 218.0 Hz). ^{19}F NMR (377 MHz, $CDCl_3$): δ −146.7 (1F, d, J = 48.0 Hz), −112.3 to −112.2 (1F, m). IR: ν (neat, ATR)/cm^{-1} 2963, 2918, 2849, 1711, 1618, 1594, 1450, 1238, 1221, 1102, 877, 865, 785, 690. HRMS (ESI/Q-TOF) m/z: [M + H]$^+$ calcd for $C_{16}H_{12}F_2N_3O$, 300.0943; found, 300.0947.

2-(4-(4-(*tert*-Butyl)phenyl)-1*H*-1,2,3-triazol-1-yl)-2-fluoro-1-phenylethan-1-one 6p. Following general procedure B, from 2-(dimethyl(oxo)-λ^6-sulfaneylidene)-1-phenylethan-1-one **4a** (19.6 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then *t*-BuOH/H_2O (10:1, 0.5 mL), 4-*tert*-butylphenylacetylene (20 μL, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 2-(4-(4-(*tert*-butyl)phenyl)-1*H*-1,2,3-triazol-1-yl)-2-fluoro-1-phenylethan-1-one **6p** was isolated as a yellow solid (23 mg, 68%; mp = 118−120 °C). R_f = 0.30 (5:1, hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03−8.01 (2H, m), 7.99 (1H, s), 7.76 (2H, d, J = 8.5 Hz), 7.71 (1H, d, J = 48.5 Hz), 7.68−7.65 (1H, m), 7.53−7.50 (2H, m), 7.45 (2H, d, J = 8.6 Hz), 1.34 (9H, s). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 186.8 (d, J = 26.0 Hz), 152.2, 149.4, 135.5, 132.4, 129.5, 129.3 (d, J = 1.6 Hz), 126.7, 126.0, 125.9, 118.7 (d, J = 1.9 Hz), 91.5 (d, J = 218.0 Hz), 34.9, 31.4. ^{19}F NMR (377 MHz, $CDCl_3$): δ −147.3 (1F, d, J = 48.0 Hz). IR: ν (neat, ATR)/cm^{-1} 3142, 2963, 2905, 2868, 1708, 1597, 1497, 1450, 1364, 1244, 1206, 1094, 1071, 1025, 1016, 841, 825, 687. HRMS (ESI/Q-TOF) m/z: [M + H]$^+$ calcd for $C_{20}H_{21}FN_3O$, 338.1663; found, 338.1666.

2-Fluoro-2-(4-(4-pentylphenyl)-1*H*-1,2,3-triazol-1-yl)-1-phenylethan-1-one 6q. Following general procedure B, from 2-(dimethyl(oxo)-λ^6-sulfaneylidene)-1-phenylethan-1-one **4a** (19.6 mg, 0.1 mmol), sodium azide (9.8 mg, 0.15 mmol), Selectfluor (53 mg, 0.15 mmol), acetonitrile (0.5 mL), then *t*-BuOH/H_2O (10:1, 0.5 mL), 1-ethynyl-4-pentylbenzene (21.5 μL, 0.11 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 30 mol %), and sodium ascorbate (6 mg, 30 mol %), the desired product 2-fluoro-2-(4-(4-pentylphenyl)-1*H*-1,2,3-triazol-1-yl)-1-phenylethan-1-one **6q** was isolated as a cream solid (21 mg, 60%; mp = 96−98 °C). R_f = 0.42 (5:1, hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03−8.01 (2H, m), 7.99 (1H, s), 7.74 (2H, d, J = 8.2 Hz), 7.70 (1H, d, J = 48.0 Hz), 7.68−7.65 (1H, m), 7.53−7.50 (2H, m), 7.24 (2H, d, J = 8.2 Hz), 2.62 (2H, t, J = 7.8 Hz), 1.62 (2H, *pent*, J = 7.6 Hz), 1.36−1.31 (4H, m), 0.89 (3H, t, J = 6.9 Hz). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 186.8 (d, J = 26.0 Hz), 149.5, 144.1, 135.5, 132.4, 129.5, 129.3 (d, J = 2.0 Hz), 129.1, 126.9, 126.0, 118.6 (d, J = 2.0 Hz), 91.5 (d, J = 218.0 Hz), 35.9, 31.6, 31.2, 22.7, 14.2. ^{19}F NMR (377 MHz, $CDCl_3$): δ −147.3 (1F, d, J = 48.0 Hz). IR: ν (neat, ATR)/cm^{-1} 2956, 2928, 2856, 1708, 1597, 1506, 1450, 1363, 1244, 1094, 1073, 1027, 1017, 825, 799, 688. HRMS (ESI/Q-TOF) m/z: [M + H]$^+$ calcd for $C_{21}H_{23}FN_3O$, 352.1820; found, 352.1820.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c01441.

Copies of ^{1}H, ^{13}C{^{1}H}, and ^{19}F NMR spectra (PDF)

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The manuscript was written through contributions of all authors.

Notes

The authors declare no competing financial interest.

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