ORGANIC LETTERS

2012
Vol. 14, No. 20
5330–5333

Regioselective Synthesis of Pyrazole Triflones Based on Triflyl Alkyne Cycloadditions

Hiroyuki Kawai, Zhe Yuan, Etsuko Tokunaga, and Norio Shibata*

Department of Frontier Materials, Graduate School of Engineering, Nagoya Institute of Technology, Gokiso, Showa-ku, Nagoya 466-8555, Japan

nozshiba@nitech.ac.jp

Received September 12, 2012

ABSTRACT

The regioselective synthesis of pyrazole triflones has been achieved by 1,3-dipolar cycloaddition of triflyl alkynes and hydrazonoyl chloride in the presence of Hünig's base. Pyrazolo[5,1-*a*]isoquinoline triflones were also regioselectively synthesized for the first time via tandem 1,3-dipolar cycloaddition/oxidative aromatization between triflyl alkynes and C,N-cyclic azomethine imines.

The trifluoromethanesulfonyl (triflyl, SO_2CF_3, Tf) group is the strongest electron-withdrawing group with high lipophilicity. The introduction of this functionality into organic compounds is an effective strategy to alter the fundamental character of parent molecules without majorly changing the molecular complexicity. In this context, attention has been paid to aryl trifluoromethyl sulfones **1** (aryl triflones, $ArSO_2CF_3$) in the development of bioactive compounds,[1] chiral catalysts,[2] and functional materials.[3]

A number of methodologies have been developed for the synthesis of aryl triflones including oxidation of aryl trifluoromethyl sulfides,[4] trifluoromethylation of aryl sulfonyl fluorides or aryl sulfonates,[5] thia-Fries rearrangement of aryl trifluoromethanesulfonates,[6] and direct trifluoromethanesulfonylation of aromatic compounds.[7] Recently, Taguchi et al. reported a regioselective synthesis of polysubstituted aryl triflones through a self-promoting

(1) (a) Park, C.-M.; Bruncko, M.; Adickes, J.; Bauch, J.; Ding, H.; Kunzer, A.; Marsh, K. C.; Nimmer, P.; Shoemaker, A. R.; Song, X.; Tahir, S. K.; Tse, C.; Wang, X.; Wendt, M. D.; Yang, X.; Zhang, H.; Fesik, S. W.; Rosenberg, S. H.; Elmore, S. W. *J. Med. Chem.* **2008**, *51*, 6902–6915. (b) Brown, B. S.; Keddy, R.; Zheng, G. Z.; Schmidt, R. G.; Koenig, J. R.; McDonald, H. A.; Bianchi, B. R.; Honore, P.; Jarvis, M. F.; Surowy, C. S.; Polakowski, J. S.; Marsh, K. C.; Faltynek, C. R.; Lee, C.-H. *Bioorg. Med. Chem.* **2008**, *16*, 8516–8525. (c) Wang, G.; Zhang, H.; Zhou, J.; Ha, C.; Pei, D.; Ding, K. *Synthesis* **2008**, 2398–2404.

(2) (a) Masui, M.; Ando, A.; Shioiri, T. *Tetrahedron Lett.* **1988**, *29*, 2835–2838. (b) Mouhtady, O.; Gaspard-Iloughmane, H.; Laporterie, A.; Roux, C. L. *Tetrahedron Lett.* **2006**, *47*, 4125–4128. (c) Kargbo, R.; Takahashi, Y.; Bhor, S.; Cook, G. R.; Lloyd-Jones, G. C.; Shepperson, I. R. *J. Am. Chem. Soc.* **2007**, *129*, 3846–3847. (d) Barta, K.; Franciò, G.; Leitner, W.; Lloyd-Jones, G. C.; Shepperson, I. R. *Adv. Synth. Catal.* **2008**, *350*, 2013–2023.

(3) (a) Wolff, J. J.; Gredel, F.; Oeser, T.; Irngartinger, H.; Pritzkow, H. *Chem.—Eur. J.* **1999**, *5*, 29–38. (b) Matsui, M.; Suzuki, M.; Hayashi, M.; Funabiki, K.; Ishigure, Y.; Doke, Y.; Shiozaki, H. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 607–612. (c) Porrès, L.; Mongin, O.; Katan, C.; Charlot, M.; Pons, T.; Mertz, J.; Blanchard-Desce, M. *Org. Lett.* **2004**, *6*, 47–50. (d) Droumaguet, C. L.; Mongin, O.; Werts, M. H. V.; Blanchard-Desce, M. *Chem. Commun.* **2005**, 2802–2804. (e) Mongin, O.; Porrès, L.; Charlot, M.; Katan, C.; Blanchard-Desce, M. *Chem.—Eur. J.* **2007**, *13*, 1481–1498.

(4) (a) Beaumont, A. J.; Clark, J. H. *J. Fluorine Chem.* **1991**, *52*, 295–300. (b) Chen, Q.-Y.; Duan, J.-X. *J. Chem. Soc., Chem. Commun.* **1993**, 918–919. (c) Su, W. *Tetrahedron Lett.* **1994**, *35*, 4955–4958. (d) González-Núñez, M. E.; Mello, R.; Royo, J.; Ríos, J. V.; Asensio, G. *J. Am. Chem. Soc.* **2002**, *124*, 9154–9163. (e) Liang, X.; Cheng, J.; Trudell, M. L. *J. Org. Chem.* **2003**, *68*, 5388–5391.

(5) (a) Kolomeitsev, A. A.; Movchun, V. N.; Kondratenko, N. V.; Yagupolski, Y. L. *Synthesis* **1990**, 1151–1152. (b) Movchun, V. N.; Kolomeitsev, A. A.; Yagupolski, Y. L. *J. Fluorine Chem.* **1995**, *70*, 255–257. (c) Singh, R. P.; Cao, G.; Kirchmeier, R. L.; Shreeve, J. M. *J. Org. Chem.* **1999**, *64*, 2873–2876.

(6) (a) Charmant, J. P.; Dyke, A. M.; Lloyd-Jones, G. C. *Chem. Commun.* **2003**, 380–381. (b) Zhao, Z.; Messinger, J.; Schön, U.; Wartchow, R.; Butenschön, H. *Chem. Commun.* **2006**, 3007–3009. (c) Crevatin, L. K.; Bonesi, S. M.; Erra-Balselle, R. *Helv. Chim. Acta* **2006**, *89*, 1147–1157. (d) Dyke, A. M.; Gill, D. M.; Harvey, J. N.; Hester, A. J.; Lloyd-Jones, G. C.; Muñoz, M. P.; Shepperson, I. R. *Angew. Chem., Int. Ed.* **2008**, *47*, 5067–5070. (e) Yoshioka, E.; Kohtani, S.; Miyabe, H. *Org. Lett.* **2010**, *12*, 1956–1959.

(7) (a) Hendrickson, J. B.; Bair, K. W. *J. Org. Chem.* **1977**, *42*, 3875–3878. (b) Creary, X. *J. Org. Chem.* **1980**, *45*, 2727–2729. (c) Magnier, E.; Blazejewski, J.-C.; Tordeux, M.; Wakselman, C. *Angew. Chem., Int. Ed.* **2006**, *45*, 1279–1282. (d) Macé, Y.; Raymondeau, B.; Pradet, C.; Blazejewski, J.-C.; Magnier, E. *Eur. J. Org. Chem.* **2009**, 1390–1397.

10.1021/ol3025154
Published on Web 10/04/2012

three-component reaction.[8] On the other hand, the synthesis of heteroaryl triflones has been considerably less studied. Our research group has recently developed the synthesis of indole triflones by direct trifluoromethanesulfonylation of indoles with the Tf_2O/TTBP (2,4,6-tri*tert*-butylpyridine) system.[9] Furthermore, novel heteroaryl triflones including oxindole, pyrazolone, pyridine, and quinoline derivatives have been regioselectively synthesized by LDA-mediated thia-Fries rearrangement.[10] We also reported the first practical synthesis of isoxazole triflones (4-triflyl isoxazoles) by an operationally simple procedure consisting of the reaction of α-triflyl ketones and imidoyl chloride.[11] As part of our ongoing research programs directed at the development of efficient methodologies for the preparation of fluorinated heterocycles,[12] we required pyrazole triflones **2** (4-trifluoromethanesulfonyl pyrazoles, 4-triflyl pyrazoles) as a key core unit for novel agrochemicals, in particular, 3,5-diarylpyrazole triflones (R^1 and R^2 = aromatic group, Figure 1).[13]

Figure 1. Aryl triflones **1**, pyrazole triflones **2**, and pyrazolo[5,1-*a*]isoquinoline triflones **5**.

Pyrazoles are a major class of five-membered nitrogen heterocycles and are important core components in natural products and valuable molecules in the pharmaceutical industry.[14] Numerous synthetic approaches for the construction of the pyrazole framework have been reported, for example, a condensation of 1,3-dicarbonyl compounds with hydrazines,[15] 1,3-dipolar cycloaddition of diazoalkanes or nitrilimines with alkenes or alkynes,[16] or the reaction between hydrazones and activated alkenes such as nitro olefins.[17] However, there are no synthetic methods for 3,5-diaryl pyrazole triflones, despite their clear potential usefulness and wide applicability for pharmaceuticals and agrochemicals. We disclose herein the first practical and regioselective synthesis of pyrazole 4-triflones **2** by a 1,3-dipolar cycloaddition between readily available materials, triflyl alkynes **3** and hydrazonoyl chloride **4**, in high yields with a broad scope. Pyrazolo[5,1-*a*]isoquinoline triflones **5** were also efficiently synthesized for the first time via regioselective, tandem 1,3-dipolar cycloaddition/oxidative aromatization of **3** and C,N-cyclic azomethine imines **6**.

We initiated our investigation with the cyclization of α-triflyl ketone **7** and hydrazonoyl chloride **4a**[18] in the presence of NEt_3, according to the modified procedure based on the synthesis of isoxazole triflones.[11] Unfortunately, 15% of desired pyrazole triflone **2a** was obtained (Scheme 1, top). We next attempted the cyclization using triflyl alkyne **3a**[19] instead of **7**. Gratifyingly, the desired cycloadduct **2a** was obtained in 43% regioselectively (Scheme 1, bottom). This preliminary result encouraged us to further investigate the optimization

(8) Yanai, H.; Fujita, M.; Taguchi, T. *Chem. Commun.* **2011**, *47*, 7245–7247.

(9) Xu, X.-H.; Liu, G.-K.; Azuma, A.; Tokunaga, E.; Shibata, N. *Org. Lett.* **2011**, *13*, 4854–4857.

(10) Xu, X.-H.; Wang, X.; Liu, G.-K.; Tokunaga, E.; Shibata, N. *Org. Lett.* **2012**, *14*, 2544–2547.

(11) Kawai, H.; Sugita, Y.; Tokunaga, E.; Shibata, N. *Eur. J. Org. Chem.* **2012**, 1295–1298.

(12) (a) Shibata, N.; Fujimoto, H.; Mizuta, S.; Ogawa, S.; Ishiuchi, Y.; Nakamura, S.; Toru, T. *Synlett* **2006**, 3484–3488. (b) Ogawa, S.; Iida, N.; Tokunaga, E.; Shiro, M.; Shibata, N. *Chem.—Eur. J.* **2010**, *16*, 7090–7095. (c) Ogawa, S.; Nishimine, T.; Tokunaga, E.; Shibata, N. *Synthesis* **2010**, 3274–3281. (d) Huang, Y.; Tokunaga, E.; Suzuki, S.; Shiro, M.; Shibata, N. *Org. Lett.* **2010**, *12*, 1136–1138. (e) Matoba, K.; Kawai, H.; Furukawa, T.; Kusuda, A.; Tokunaga, E.; Nakamura, S.; Shiro, M.; Shibata, N. *Angew. Chem., Int. Ed.* **2010**, *49*, 5762–5766. (f) Kawai, H.; Tachi, K.; Tokunaga, E.; Shiro, M.; Shibata, N. *Angew. Chem., Int. Ed.* **2011**, *50*, 7803–7806. (g) Kawai, H.; Sugita, Y.; Tokunaga, E.; Sato, H.; Shiro, M.; Shibata, N. *Chem. Commun.* **2012**, *48*, 3632–3634. (h) Kawai, H.; Kitayama, T.; Tokunaga, E.; Matsumoto, T.; Sato, H.; Shiro, M.; Shibata, N. *Chem. Commun.* **2012**, *48*, 4067–4069. (i) Kawai, H.; Okusu, S.; Tokunaga, E.; Sato, H.; Shiro, M.; Shibata, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 4959–4962.

(13) 3,5-Disubstituted (3,5 = carbon) pyrazole triflones are rare (25 compounds are registered in the SciFinder database), and none of the examples of 3,5-diarylpyrazole triflones **2** is reported. (a) Jensen-Korte, U.; Gehring, R.; Schallner, O.; Stetter, J.; Becker, B.; Homeyer, B. 1988, DE3711928A1. (b) Jensen-Korte, U.; Schallner, O.; Stetter, J.; Wroblowsky, H. J.; Marhold, A.; Becker, B.; Behrenz, W.; Homeyer, B.; Stendel, W.; Andrews, P. 1989, EP302327A1. (c) Huang, J.; Lowder, P. D.; Ray, N. C.; Hawkins, D. W. 1997, EP780378A1. (d) Huang, J.; Lowder, P. D.; Ray, N. C.; Hawkins, D. W. 1998, US5817688A. (e) Schnatterer, S.; Chou, D. T.-W.; Knauf, W.; Jans, D.; Seeger, K. 2005, WO2005090314A1. (f) Lee, H. Ik; Le Hir de Fallois, L. P.; Timmons, P. R.; Cawthorne, W. G.; De Leon, A. P. 2008, WO 2008005489A2. (g) Shibata, C.; Chiba, Y.; Akase, T.; Tomura, N. 2010, JP2010083763A. (h) Liu, C.; Wang, L.; Li, Z.; Sun, X.; Lan, J.; Ren, L.; Wu, Q.; Chi, H. 2012, WO2012059048A1.

(14) (a) Elguero, J. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 5. (b) Elguero, J.; Goya, P.; Jagerovic, N.; Silva, A. M. S. *Targets Heterocycl. Syst.* **2002**, *6*, 52–98. (c) Kumar, G. G.; Vikas, K.; Vinod, K. *Res. J. Chem. Environ.* **2011**, *15*, 90–103.

(15) (a) Norris, T.; Colon-Cruz, R.; Ripin, D. H. B. *Org. Biomol. Chem.* **2005**, *3*, 1844–1849. (b) Curini, M.; Rosati, O.; Campagna, V.; Montanari, F.; Cravotto, G.; Boccalinic, M. *Synlett* **2005**, 2927–2930. (c) Heller, S. T.; Natarajan, S. R. *Org. Lett.* **2006**, *8*, 2675–2678. (d) Gosselin, F.; O'Shea, P. D.; Webster, R. A.; Reamer, R. A.; Tillyer, R. D.; Grabowski, E. J. J. *Synlett* **2006**, 3267–3270. (e) Polshettiwar, V.; Varma, R. S. *Tetrahedron Lett.* **2008**, *49*, 397–400. (f) Sachse, A.; Penkova, L.; Noel, G.; Dechert, S.; Varzatskii, O. A.; Fritsky, I. O.; Meyer, F. *Synthesis* **2008**, 800–806. (g) Shen, L.; Cao, S.; Liu, N.; Wu, J.; Zhu, L.; Qian, X. *Synlett* **2008**, 1341–1344. (h) Fustero, S.; Roman, R.; Sanz-Cervera, J. F.; Simon-Fuentes, A.; Cunat, A. C.; Villanova, S.; Murguia, M. *J. Org. Chem.* **2008**, *73*, 3523–3529. (i) Fustero, S.; Roman, R.; Sanz-Cervera, J. F.; Simon-Fuentes, A.; Bueno, J.; Villanova, S. *J. Org. Chem.* **2008**, *73*, 8545–8552.

(16) (a) Foti, F.; Grassi, G.; Risitano, F. *Tetrahedron Lett.* **1999**, *40*, 2605–2606. (b) Aggarwal, V. K.; de Vicente, J.; Bonnert, R. V. *J. Org. Chem.* **2003**, *68*, 5381–5383. (c) Hari, Y.; Tsuchida, S.; Sone, R.; Aoyama, T. *Synthesis* **2007**, 3371–3375. (d) Gao, D.; Zhai, H.; Parvez, M.; Back, T. G. *J. Org. Chem.* **2008**, *73*, 8057–8068. (e) Babinski, D. J.; Aguilar, H. R.; Still, R.; Frantz, D. E. *J. Org. Chem.* **2011**, *76*, 5915–5923. (f) Jackowski, O.; Lecourt, T.; Micouin, L. *Org. Lett.* **2011**, *13*, 5664–5667.

(17) (a) Deng, X.; Mani, N. S. *Org. Lett.* **2006**, *8*, 3505–3508. (b) Deng, X.; Mani, N. S. *Org. Lett.* **2008**, *10*, 1307–1310. (c) Deng, X.; Mani, N. S. *J. Org. Chem.* **2008**, *73*, 2412–2415. (d) Ma, C.; Li, Y.; Wen, P.; Yan, R.; Ren, Z.; Huang, G. *Synlett* **2011**, 1321–1323.

(18) Paulvannan, K.; Chen, T.; Hale, R. *Tetrahedron* **2000**, *56*, 8071–8076.

(19) (a) Hanack, M.; Wilhelm, B.; Subramanian, L. R. *Synthesis* **1988**, 592–595. (b) Xiang, J. S.; Mahadevan, A.; Fuchs, P. L. *J. Am. Chem. Soc.* **1996**, *118*, 4284–4290.

of the reaction conditions using **3a** (Table 1). The reaction was next attempted using iPr$_2$NEt, yielding **2a** in a slightly better yield of 46% (entry 2). The choice of solvent was found to be important in the conversion (entries 3—9), and the yield was increased to 92% in MeCN (entry 9). The structure of **2a** was clearly determined after derivatization to a known 1,3,5-triphenyl-1*H*-pyrazole by reductive desulfonylation using $LiAlH_4$ (see Scheme S1 in Supporting Information, SI).[20]

Scheme 1. Synthesis of **2a** Using α-Triflyl Ketone **7** or Triflyl Alkyne **3a**

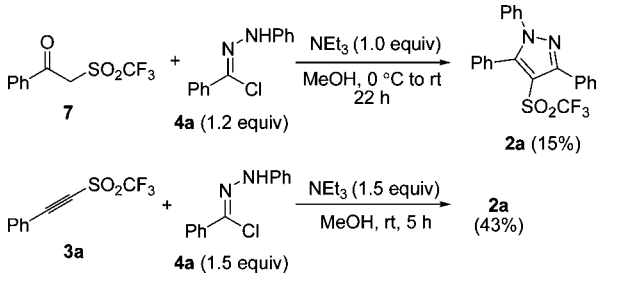
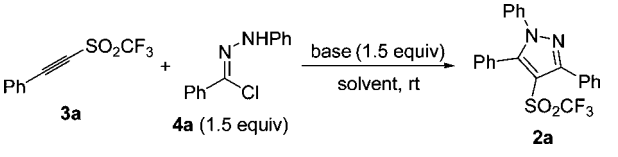


Table 1. Optimization of Bases and Solvents for 1,3-Dipolar Cycloaddition of **3a** and **4a**[a]

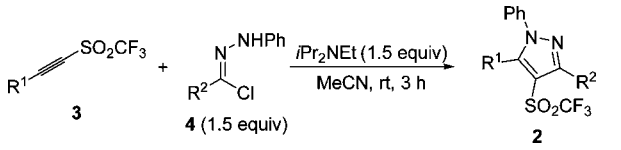


entry	base	solvent	time (h)	yield (%)[b]
1	NEt_3	MeOH	5	43
2	iPr$_2$NEt	MeOH	4	46
3	iPr$_2$NEt	CH_2Cl_2	8	63
4	iPr$_2$NEt	$CHCl_3$	24	78
5	iPr$_2$NEt	toluene	24	25
6	iPr$_2$NEt	THF	10	15
7	iPr$_2$NEt	DMF	2	49
8	iPr$_2$NEt	MeCN	3	92

[a] The reaction of **3a** with **4a** (1.5 equiv) was carried out in the presence of base (1.5 equiv) at rt. [b] Isolated yield.

With suitable conditions in hand, the scope of the 1,3-dipolar cycloaddition was explored with a variety of substrates selected in order to establish the generality of the process using this strategy, all affording good to excellent yields (Table 2). A series of triflyl alkynes **3b**—**e** with a variety of substituents at their aromatic rings (R^1), such as methyl, pentyl, and fluoro, were nicely converted to corresponding pyrazole triflones **2b**—**e** in high yields (80%—85%) (entries 2—5). We next examined the substrate scope differing in the nature of the aryl substituents of hydrazonoyl chlorides **4** under the same reaction conditions. A series of hydrazonoyl chlorides **4b**—**e** were nicely converted to pyrazole triflone **2f**—**i** in 80%—90% yields, these being almost independent of the functional groups on the aromatic ring of **4** such as methyl, chloro, and bromo as well as a sterically demanding naphthyl substrate (entries 6—9). Interestingly, when the reaction was attempted with imidoyl chloride **8a** under the same reaction conditions, isoxazole triflone **9a** was isolated in 82% yield (Scheme 2).

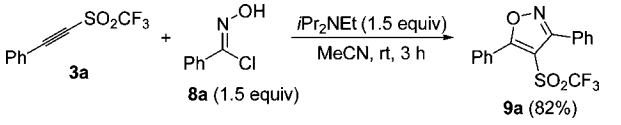
Table 2. Synthesis of Pyrazole Triflones **2**[a]



entry	**3**	R^1	**4**	R^2	**2**	yield (%)[b]
1	**3a**	Ph	**4a**	Ph	**2a**	92
2	**3b**	2-MeC_6H_4	**4a**	Ph	**2b**	85
3	**3c**	4-MeC_6H_4	**4a**	Ph	**2c**	80
4	**3d**	4-*n*-$C_5H_{11}C_6H_4$	**4a**	Ph	**2d**	85
5	**3e**	3-FC_6H_4	**4a**	Ph	**2e**	83
6	**3a**	Ph	**4b**	4-MeC_6H_4	**2f**	90
7	**3a**	Ph	**4c**	4-ClC_6H_4	**2g**	81
8	**3a**	Ph	**4d**	4-BrC_6H_4	**2h**	82
9	**3a**	Ph	**4e**	2-naphthyl	**2i**	80

[a] The reaction of **3** with **4** (1.5 equiv) was carried out in the presence of iPr$_2$NEt (1.5 equiv) in MeCN at rt. [b] Isolated yield.

Scheme 2. Synthesis of Isoxazole Triflone **9a**



We next examined the 1,3-dipolar cycloaddition of **3** with C,N-cyclic azomethine imines **6**[21] for the synthesis of the biologically attractive pyrazolo[5,1-*a*]isoquinoline framework.[22] Treatment of **3a** with **6a** in CH_2Cl_2 at ambient temperature regioselectively furnished unstable cycloadduct **10a**, which was isolated as pyrazolo[5,1-*a*]-isoquinoline triflone **5a** in 92% yield after aromatization

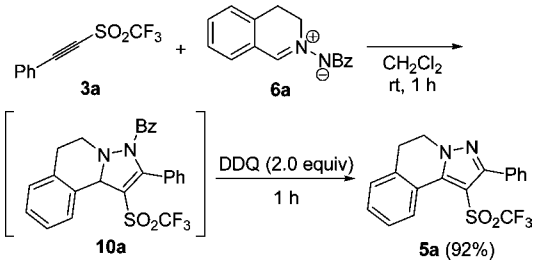
(20) Zora, M.; Kivrak, A. *J. Org. Chem.* **2011**, *76*, 9379–9390.

(21) (a) Hashimoto, T.; Maeda, Y.; Omote, M.; Nakatsu, H.; Maruoka, K. *J. Am. Chem. Soc.* **2010**, *132*, 4076–4077. (b) Hashimoto, T.; Omote, M.; Maruoka, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 3489–3492. (c) Hashimoto, T.; Omote, M.; Maruoka, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 8952–8955. (d) Soeta, T.; Tamura, K.; Ukaji, Y. *Org. Lett.* **2012**, *14*, 1226–1229.

(22) (a) Cruz, R.; Arias, M. S.; Arias, M. E.; Soliveri, J. *J. Antibiot.* **1996**, *49*, 700–702. (b) Cruz, R.; Arias, M. E.; Soliveri, J. *Appl. Microbiol. Biotechnol.* **2000**, *53*, 480–483. (c) Paronikyan, E. G.; Sirakanyan, S. N.; Noravyan, A. S.; Paronikyan, R. G.; Dzhagatspanyan, I. A. *Pharm. Chem. J.* **2001**, *35*, 8–10.

using DDQ (Scheme 3). The structure of **5a** was determined after derivatization to a known pyrazolo[5,1-*a*]-isoquinoline by reductive desulfonylation using Mg/MeOH (see Scheme S2 in SI).[23]

Scheme 3. Synthesis of Pyrazolo[5,1-*a*]isoquinoline Triflones **5a** via 1,3-Dipolar Cycloaddition/Oxidative Aromatization of **3a** with **6a**

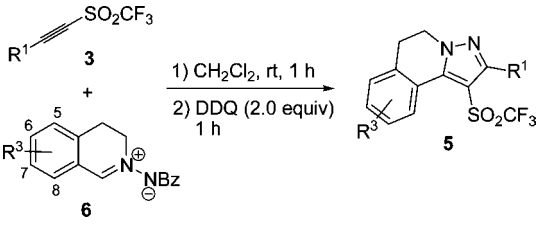


The scope of this tandem regioselective 1,3-dipolar cycloaddition/oxidative aromatization was investigated with a range of triflyl alkynes **3** and azomethine imines **6** (Table 3). High to excellent yields were obtained for all cases up to 98%, with these being almost independent of the functional groups and the positions of the aromatic ring of **3** (entries 2−5). Nonaromatic triflyl alkyne **3f** was also a suitable substrate for this transformation to afford **5f** in 74% yield (entry 6). Cyclic azomethine imines having a methyl or bromo group were also utilized in this transformation in excellent yields (87%−98%) (entries 7−9).

In summary, we disclose the first practical synthesis of pyrazole triflones **2** by regioselective 1,3-cycloaddition of triflyl alkynes **3** and hydrazonoyl chloride **4** in the presence of Hünig's base. Biologically attractive pyrazolo[5,1-*a*]-isoquinoline triflones **5** were also efficiently synthesized for the first time via regioselective tandem 1,3-dipolar cycloaddition/oxidative aromatization between triflyl alkynes **3** and C,N-cyclic azomethine imines **6**. The direct introduction of a triflyl group into pyrazoles through C−H activation with trifluoromethane sulfonylation is the next challenge in this field, and the subject is under active investigation.

(23) Ortega, H.; Ahmed, S.; Alper, H. *Synthesis* **2007**, 3683–3691.

Table 3. Synthesis of Pyrazolo[5,1-*a*]isoquinoline Triflones **5**[a]



entry	**3**	R^1	**6**	R^3	**5**	yield (%)[b]
1	**3a**	Ph	**6a**	H	**5a**	92
2	**3b**	2-MeC_6H_4	**6a**	H	**5b**	80
3	**3c**	4-MeC_6H_4	**6a**	H	**5c**	88
4	**3d**	4-*n*-$C_5H_{11}C_6H_4$	**6a**	H	**5d**	98
5	**3e**	3-FC_6H_4	**6a**	H	**5e**	90
6	**3f**	cyclopropyl	**6a**	H	**5f**	74
7	**3a**	Ph	**6b**	5-Me	**5g**	87
8	**3a**	Ph	**6c**	7-Me	**5h**	98
9	**3a**	Ph	**6d**	7-Br	**5i**	94

[a] The reaction of **3** with **6** (1.0 equiv) was carried out in CH_2Cl_2 at rt. [b] Isolated yield.

Acknowledgment. This study was financially supported in part by Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology (Project name: Advanced Molecular Transformation by Organocatalysts) (Project name: Platform for Drug Discovery, Informatics and Structural Life Science). We are grateful to Central Glass Co., Ltd. for the gift of triflic anhydride. We also thank the Asahi Glass Foundation.

Supporting Information Available. Experimental procedures, spectra data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.