EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201201244

Highly Efficient Construction of Trifluoromethylated Heterocycles; [3+2] Annulation of N,N′-Cyclic or C,N-Cyclic Azomethine Imines with Trifluoromethyl-Containing Electron-Deficient Olefins

De Wang,[a] Hong-Ping Deng,[b] Yin Wei,[b] Qin Xu,*[a] and Min Shi*[a,b]

Keywords: Synthetic methods / Nitrogen heterocycles / Fluorine / Diastereoselectivity / Annulation

A highly regio- and stereoselective synthesis of pyrazolidine analogues by the use of N,N′-cyclic or C,N-cyclic azomethine imines with two different trifluoromethyl-containing olefins has been developed. The method affords highly functionalized trifluoromethyl-containing pyrazolidine analogues in excellent yields with high diastereoselectivities under mild conditions.

Pyrazolidine is an important structural motif that exists in a broad range of biologically and pharmaceutically relevant compounds.[1] For example, bicyclic pyrazolidinones (**LY**) have potential use as antibiotics[2a,2b,2c] and their isoquinoline derivatives show antimicrobial activities (Figure 1).[2d] Synthetic methods to access these molecules include [3+2] cycloaddition reactions of azomethine imines, diazoalkanes, and nitrile imines with activated alkenes.[3] Among those, azomethine imines, as a class of 1,3-dipoles, have been widely used in [3+2] annulations with alkenes or alkynes,[4] and some effective asymmetric variants by using different chiral catalysts have been also reported.[5]

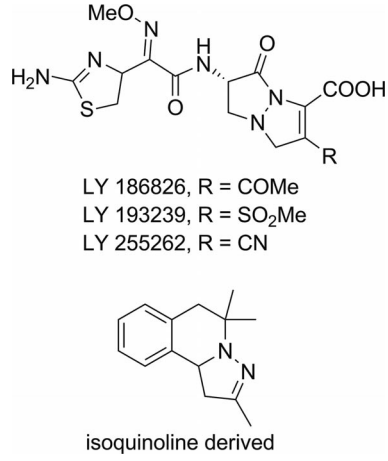


Figure 1. Examples of biologically active pyrazolidine and pyrazoline derivatives.

Recently, significant research efforts have focused on the strategic introduction of trifluoromethyl groups into drug-like molecules in medicinal and agricultural chemistry due to the unique physical properties of this group.[6] There are two general methods to achieve trifluoromethyl-containing compounds: one is direct introduction of the trifluoromethyl group through nucleophilic, electrophilic, or radical reactants; the second uses a building-block strategy involving the assembly of readily accessible trifluoromethyl-containing organic compounds as starting materials.[7–9] Both approaches have their own particular advantages; whereas the latter approach is well-suited for the valorization of readily available trifluoromethyl-containing building blocks, 2,2,2-trifluoroethylidene malonates are good substrates to construct stereogenic tertiary carbon centers bearing a trifluoromethyl group. In this research field, Lu and coworkers applied 2,2,2-trifluoroethylidene malonates to asymmetric Michael addition and Friedel–Crafts alkylation to give the desired products in good yields.[10] Fang and coworkers have synthesized aryl-substituted α-trifluoromethyl-α,β-unsaturated carboxylic acids (AFUCA), which are one of the most valuable building blocks for the synthesis of CF_3-containing molecules.[11]

The annulation of azomethine imines with trifluoromethyl-containing olefins is fascinating because it not only provides a method with which to construct five-membered heterocycles, but also leads to the generation of products containing the trifluoromethyl group. Great efforts have focused on [3+2] cycloaddition of azomethine imines with different olefins,[4,5] however, the reactivities of azomethine

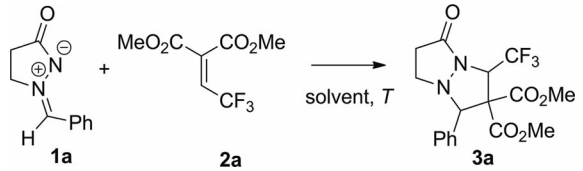
[a] Key Laboratory for Advanced Materials and Institute of Fine Chemicals, School of Chemistry & Molecular Engineering, East China University of Science and Technology,
130 Mei Long Road, Shanghai 200237, China
[b] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences,
345 Lingling Road, Shanghai 200032, China
E-mail: Mshi@mail.sioc.ac.cn
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201201244.

imines with trifluoromethyl-containing olefins has rarely been reported. Only Shibata's group reported one example of [3+2] annulation using N,N′-cyclic azomethine imines with α-trifluoromethyl acrylate (MAF-TBE),[12a] giving the products in 79–97% yields along with between 59:41 and 75:25 diastereoselectivities.[12b]

In this paper, we wish to report a highly regio- and stereoselective synthesis of trifluoromethyl-containing pyrazolidine analogues by the use of N,N′-cyclic or C,N-cyclic azomethine imines with two different trifluoromethyl-containing olefins under mild conditions.[13]

Initial examination was carried out using N,N′-cyclic azomethine imine **1a** (0.2 mmol) and trifluoroethylidene malonate **2a** (0.24 mmol) as the substrates in tetrahydrofuran (THF) at room temperature for 24 h (Table 1, entry 1). We found that the desired cycloadduct **3a** was obtained in 55% yield and more than 99:1 diastereoselectivity. Subsequently, we attempted to optimize the reaction conditions by screening several solvents; the results are summarized in Table 1 (entries 2–6). As can be seen, in acetonitrile (CH_3CN), the desired product **3a** could be obtained in 65% yield with 99:1 diastereoselectivity, and in toluene or ethyl acetate (EtOAc), **3a** was formed in 60 and 80% yields, respectively, with excellent diastereoselectivities (Table 1, entries 3 and 4). Using 1,2-dichloroethane (DCE) or dichloromethane (CH_2Cl_2) as solvent, the yield of **3a** increased to 92 and more than 99%, respectively, also with excellent diastereoselectivities (Table 1, entries 5 and 6). Thus, CH_2Cl_2 was found to be the most suitable solvent for this reaction. Lowering the reaction temperature to 0 °C or –20 °C in CH_2Cl_2 led to a significant decrease in the yield of **3a** to 30% or barely no product, respectively, even upon prolonging the reaction time to 48 h (Table 1, entries 7 and 8). Upon reducing the reaction time to 2 h, the reaction also proceeded smoothly to give **3a** in more than 99% yield (Table 1, entry 9). The relative configuration of **3a** was assigned on the basis of X-ray diffraction studies. The ORTEP drawing is shown in Figure 2 and the CIF data are summarized in the Supporting Information.

Table 1. Optimization of the reaction conditions for [3+2] annulation.



Entry[a]	Solvent	T (°C)	t [h]	dr[b]	Yield [%][c]
1	THF	r.t.	24	>99:1	55
2	CH_3CN	r.t.	24	>99:1	65
3	toluene	r.t.	24	>99:1	60
4	EtOAc	r.t.	24	>99:1	80
5	DCE	r.t.	24	>99:1	92
6	CH_2Cl_2	r.t.	24	>99:1	>99
7	CH_2Cl_2	0	48	>99:1	30
8	CH_2Cl_2	–20	48	–	trace
9	CH_2Cl_2	r.t.	2	>99:1	>99

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), solvent (1.0 mL). [b] Determined by ^1H and ^{19}F NMR spectroscopic analysis. [c] Isolated yield.

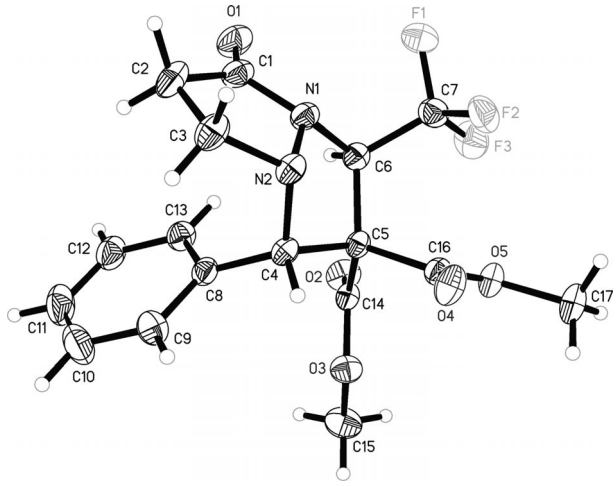
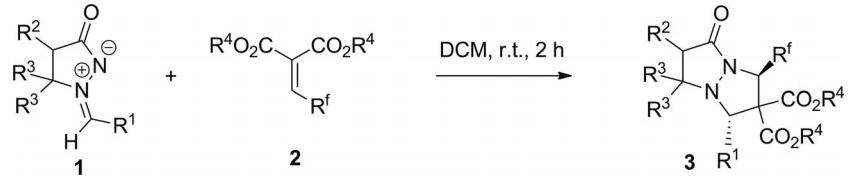


Figure 2. ORTEP drawing of product **3a**.

With the identification of the optimal reaction conditions, the generality of this catalyst-free [3+2] cycloaddition was examined by using a variety of azomethine imines **1** and trifluoroethylidene malonates **2**; the results are summarized in Table 2. All reactions proceeded smoothly to give the corresponding products **3** in good yields and moderate to excellent diastereoselectivities under the optimal conditions (Table 2). Excellent yields and diastereoselectivities were obtained when utilizing diethyl 2-(2,2,2-trifluoroethylidene)malonate (**2b**) or dimethyl 2-(2,2,3,3,3-pentafluoropropylidene)malonate (**2c**) instead of 2-(2,2,2-trifluoroethylidene)malonate (**2a**; Table 2, entries 2 and 3). Regardless of whether R^1 was an electron-rich or -deficient aromatic ring, the reactions proceeded smoothly to give the corresponding bicyclic pyrazolidinone products **3d**–**g** in good yields and good *dr* values (Table 2, entries 4–7). Only in the case of *p*-BrC_6H_4 azomethine imine **1b**, was the corresponding adduct **3d** obtained in a slightly lower yield (87%), but still with more than 99:1 *dr*; in this case the reaction time was lengthened to 24 h because **1b** is not very soluble in CH_2Cl_2 (Table 2, entry 4). Multisubstituted azomethine imine **1f** was also investigated in this reaction, affording the corresponding product **3h** in more than 99:1 *dr* and 89% yield (Table 2, entry 8). When R^1 was a heteroaromatic group (R^1 = 2-furan) or a sterically more bulky 2-naphthalene moiety, the reactions also proceeded efficiently to afford the corresponding products **3i**–**j** in 77 and 82% yields with high *dr* values, respectively (Table 2, entries 9 and 10). Changing the aromatic group to an aliphatic group provided the corresponding product **3k** in 94% yield with >99:1 *dr* (Table 2, entry 11). When R^2 was a methyl group, the desired bicyclic product **3l** was obtained in 88% yield with 2:1 *dr* (Table 2, entry 12). When R^3 was a methyl group, almost no reaction occurred (Table 2, entry 13).

Table 2. Substrate scope of [3+2] annulation of azomethine imine **1** with trifluoroethylidene malonate **2**.



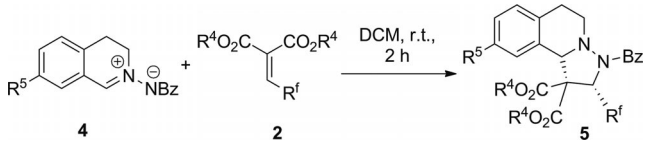
1 + **2** → **3**

Entry[a]	**1**	R^1	R^2	R^3	**2**	R^4	R^3	*dr*[b]	Product	Yield [%][c]
1	**1a**	Ph	H	H	**2a**	Me	CF_3	>99:1	**3a**	>99
2	**1a**	Ph	H	H	**2b**	Et	CF_3	>99:1	**3b**	96
3	**1a**	Ph	H	H	**2c**	Et	CF_2CF_3	>99:1	**3c**	90
4[d]	**1b**	4-BrC_6H_4	H	H	**2a**	Me	CF_3	>99:1	**3d**	87
5	**1c**	4-FC_6H_4	H	H	**2a**	Me	CF_3	>99:1	**3e**	98
6	**1d**	4-$CH_3C_6H_4$	H	H	**2a**	Me	CF_3	>99:1	**3f**	>99
7	**1e**	4-$CH_3OC_6H_4$	H	H	**2a**	Me	CF_3	>99:1	**3g**	92
8	**1f**	3,4,5-$(CH_3O)_3C_6H_4$	H	H	**2a**	Me	CF_3	>99:1	**3h**	89
9[d]	**1g**	2-furyl	H	H	**2a**	Me	CF_3	>99:1	**3i**	77
10	**1h**	2-naphthyl	H	H	**2a**	Me	CF_3	>99:1	**3j**	82
11	**1i**	*n*-Octyl	H	H	**2a**	Me	CF_3	>99:1	**3k**	94
12	**1j**	Ph	CH_3	H	**2a**	Me	CF_3	2:1	**3l**	88
13	**1k**	Ph	H	CH_3	**2a**	Me	CF_3	–	–	trace

[a] Reaction conditions: **1** (0.2 mmol), **2** (0.3 mmol), CH_2Cl_2 (2.0 mL), r.t., 2 h. [b] Determined by ^{19}F NMR spectroscopic analysis. [c] Isolated yield. [d] The reaction was carried out for 24 h and monitored by TLC.

Encouraged by the [3+2] annulation of N,N′-cyclic azomethine imine with trifluoroethylidene malonate, we next attempted to use C,N-cyclic azomethine imine **4** instead of N,N′-cyclic azomethine imine **1** to examine the reaction outcome. We found that the reactions also proceeded smoothly to give the annulation products in high yields and high diastereoselectivities; the results are summarized in Table 3. The reaction was tolerant of either electron-deficient or -rich aromatic rings on the azomethine imines **4a**–**c** (R^5 = H, Br, or Me) with various trifluoroethylidene malonates **2a**–**c**, providing a series of the corresponding products **5a**–**g** in 81–99% yields with excellent diastereoselectivities (Table 3, entries 1–7). The relative configuration of **5a** was assigned on the basis of X-ray diffraction studies. The ORTEP drawing of **5a** is shown in Figure 3 and the CIF data are summarized in the Supporting Information.

Table 3. Substrate scope of [3+2] annulation of azomethine imine **4** with trifluoroethylidene malonate **2**.



4 + **2** → **5**

Entry[a]	**4**	R^5	**2**	R^4	R^f	*dr*[b]	Product	Yield [%][c]
1	**4a**	H	**2a**	Me	CF_3	>99:1	**5a**	91
2	**4a**	H	**2b**	Et	CF_3	>99:1	**5b**	82
3	**4a**	H	**2c**	Me	CF_2CF_3	>99:1	**5c**	96
4[d]	**4b**	Br	**2a**	Me	CF_3	>99:1	**5d**	94
5[d]	**4b**	Br	**2b**	Et	CF_3	>99:1	**5e**	81
6[d]	**4b**	Br	**2c**	Me	CF_2CF_3	>99:1	**5f**	>99
7	**4c**	CH_3	**2a**	Me	CF_3	>99:1	**5g**	>99

[a] Reaction conditions: **4** (0.2 mmol), **2** (0.24 mmol), CH_2Cl_2 (2.0 mL), r.t., 2 h. [b] Determined by ^{19}F NMR spectroscopic analysis. [c] Isolated yield. [d] The reaction was carried out in 4–8 h and monitored by TLC.

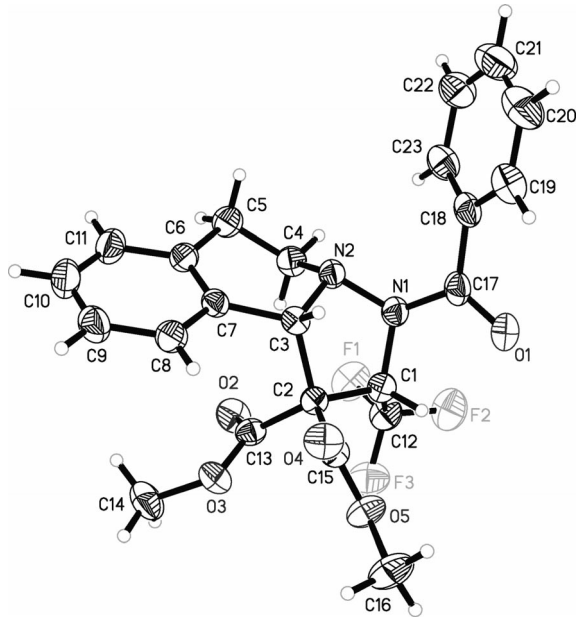
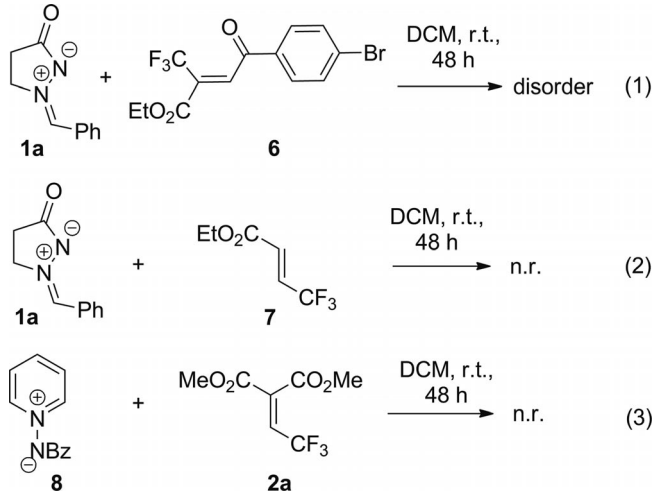


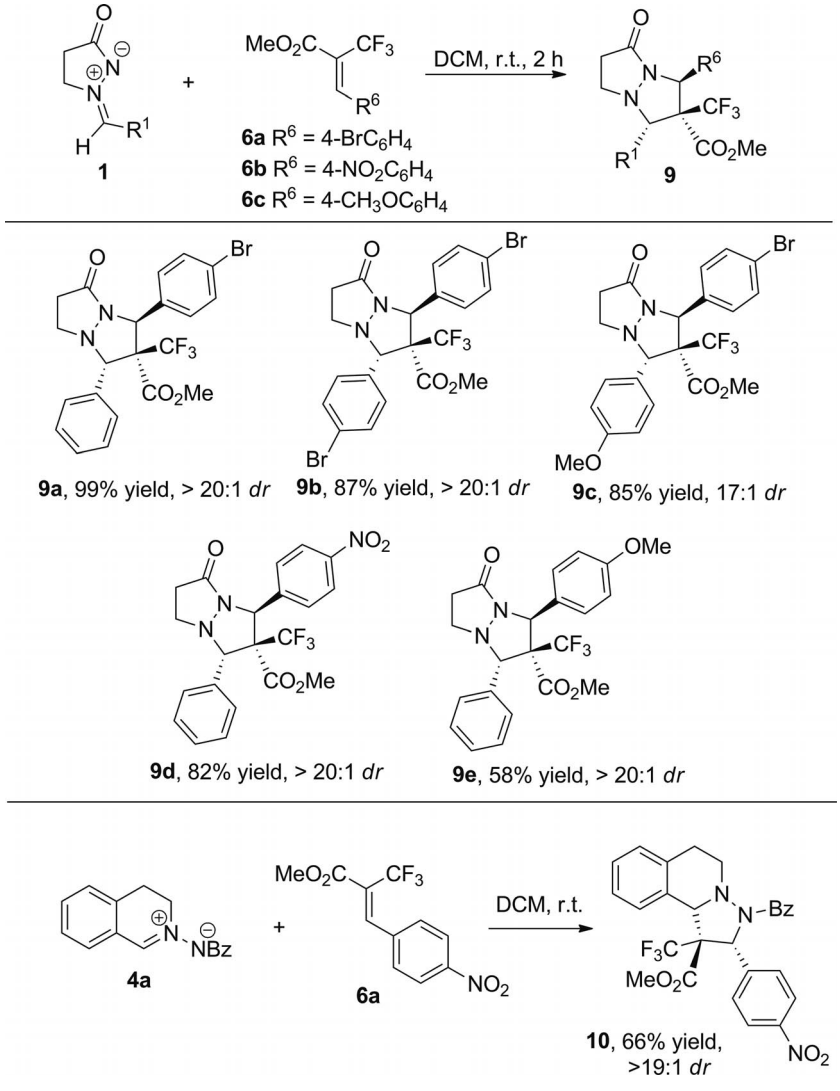
Figure 3. ORTEP drawing of product **5a**.

To extend this synthetic methodology to other trifluoromethyl-containing olefins or other 1,3-dipoles, we next attempted the reactions of **1a** with **6** or **7** under the standard conditions. However, none of the desired cycloadducts were formed [Scheme 1, Equations (1) and (2)]. Using compound **8** instead of **1a** to react with **2a**, no reaction occurred, probably because **8** is a relatively unreactive 1,3-dipole; see Scheme 1, Equation (3).



Scheme 1. Attempted reactions using other 1,3-dipoles and CF_3-containing olefins.

Because aryl-substituted α-trifluoromethyl α,β-unsaturated carboxylic acids (AFUCA)[11] are one of the most valuable building blocks for the synthesis of CF_3-containing molecules, we also prepared AFUCA esters **6a**–**c** and applied them to this [3+2] annulation reaction; the results are summarized in Scheme 2. Regardless of whether R^1 or R^6 were electron-rich or electron-deficient aromatic rings, the reactions proceeded smoothly to give the [3+2] annulation products in 58–99% yields along with 17:1–20:1 *dr* values (Scheme 2). Switching to azomethine imine **4a**, the desired annulation product **10** could also be obtained in 66% yield along with high diastereoselectivity. The relative configurations of **9c** and **10** were assigned on the basis of X-ray diffraction analysis. The ORTEP drawing of **9c** and **10** are shown in Figure 4 and the CIF data are summarized in the Supporting Information. Increasing the scale of the reaction (0.5 mmol) afforded **3a** in 98% yield and >99:1 *dr* under the standard conditions (Scheme 3).



Scheme 2. Substrate scope of [3+2] annulation of azomethine imine **1** or **4** with **6**.

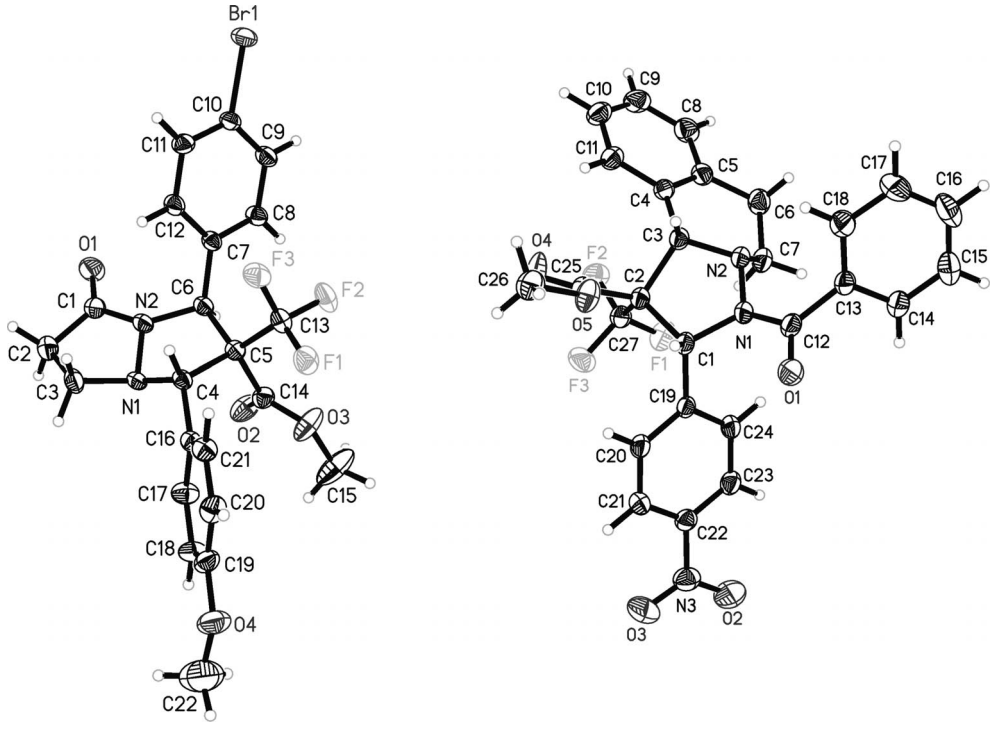
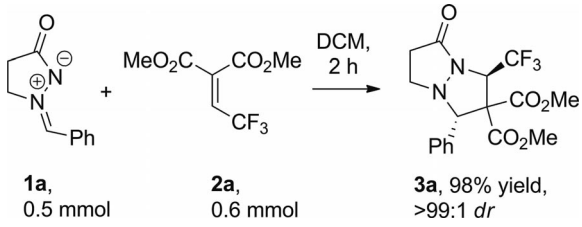


Figure 4. ORTEP drawing of products **9c** and **10**.



Scheme 3. The [3+2] annulation of **1a** and **2a** performed on a larger scale.

An asymmetric variant of these cyclizations has also been investigated by using a variety of chiral catalysts, but the cyclization products were obtained with low *ee* values (see the Supporting Information for details).

In conclusion, we have developed a novel [3+2] annulation of N,N′-cyclic or C,N-cyclic azomethine imines with CF_3-containing olefins, affording the corresponding trifluoromethyl-containing pyrazolidine analogues in excellent yields (up to >99%) with high diastereoselectivities (up to 99:1) under mild conditions. Current efforts focusing on developing an asymmetric version of this reaction and applying this methodology to synthesize biologically active products are in progress.

Experimental Section

General Procedure: Under an argon atmosphere, CF_3-containing olefin (0.25 mmol) was added to a solution of azomethine imine **1** or **4** (0.20 mmol) in CH_2Cl_2 (2.0 mL) and the resulting reaction mixture was stirred at room temperature for 2–48 h. The solvent was removed under reduced pressure and residue was purified by chromatography on silica gel (petroleum ether/EtOAc, 6:1→4:1) to provide the desired product.

Dimethyl 5-Oxo-1-phenyl-3-(trifluoromethyl)tetrahydropyrazolo[1,2-*a*]pyrazole-2,2(1*H*)-dicarboxylate (3a): Yield 78 mg (>99%); colorless solid; m.p. 172–173 °C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.37–7.34 (m, 3 H), 7.18–7.15 (m, 2 H), 5.51 (q, J = 7.2 Hz, 1 H), 4.86 (s, 1 H), 3.81 (s, 3 H), 3.40–3.32 (m, 4 H), 3.17–3.11 (m, 1 H), 2.37 (ddd, J_1 = 2.4, J_2 = 10.0, J_3 = 17.2 Hz, 1 H), 1.96 (dt, J_1 = 10.0, J_2 = 17.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.6, 166.5, 166.0, 132.4, 129.3, 129.0, 128.9, 122.9 (q, J = 280.4 Hz), 72.0, 69.4, 59.2 (q, J = 33.8 Hz), 53.6, 53.1, 44.3, 32.6 ppm. ^{19}F NMR (376 MHz, $CFCl_3$): δ = –69.6 (d, J = 7.5 Hz) ppm. IR (neat): $\tilde{\nu}$ = 2952, 2362, 1740, 1716, 1401, 1270, 1178, 1142, 933, 704 cm^{-1}. MS (ESI): *m*/*z* (%) = 387.1 (100) [M + H$^+$]. HRMS: Calcd. for $C_{17}H_{18}F_3N_2O_5^+$ [M + H$^+$] 387.1168; found 387.1162.

CCDC-866876 (for **3a**), -875407 (for **5a**), -876533 (for **9c**), and -895560 (for **10**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): Spectroscopic data of the compounds shown in Tables 1, 2, and 3, and Schemes 1 and 3, detailed descriptions of experimental procedures and the crystal structure data of **3a**, **5a**, **9c**, and **10**.

Acknowledgments

We thank the Shanghai Municipal Committee of Science and Technology (grant number 11JC1402600), the National Basic Research Program of China, (973)-2009CB825300, the Fundamental Research Funds for the Central Universities, and the National Natural Science Foundation of China (NSFC) for financial support

(grant numbers 21072206, 20472096, 20872162, 20672127, 21121062, and 20732008).

[1] a) V. V. Khau, M. J. Martinelli, *Tetrahedron Lett.* **1996**, *37*, 4323; b) J. H. Ahn, H.-M. Kim, S. H. Jung, S. K. Kang, K. R. Kim, S. D. Rhee, S.-D. Yang, H. G. Cheon, S. S. Kim, *Bioorg. Med. Chem. Lett.* **2004**, *14*, 4461; c) R. J. Ternansky, R. A. Holmes, *Drugs Future* **1990**, *15*, 149; d) L. N. Jungheim, S. K. Sigmund, *J. Org. Chem.* **1987**, *52*, 4007.

[2] a) L. Pezdirc, V. Jovanovski, D. Bevk, R. Jakše, S. Pirc, A. Meden, B. Stanovnik, J. Svete, *Tetrahedron* **2005**, *61*, 3977; b) L. Pezdirc, D. Bevk, U. Grošelj, A. Meden, B. Stanovnik, J. Svete, *J. Comb. Chem.* **2007**, *9*, 717; c) S. Hanessian, G. McNaughton-Smith, H.-G. Lombart, W. D. Lubell, *Tetrahedron* **1997**, *53*, 12789; and references cited therein d) X.-H. Liu, P. Cui, B.-A. Song, P. S. Bhadury, H.-L. Zhu, S.-F. Wang, *Bioorg. Med. Chem.* **2008**, *16*, 4075.

[3] For a general review on such cycloaddition reactions, see: P. A. Wade, In *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming), Pergamon Press, Oxford, **1991**, vol. 4, p. 1111.

[4] For a review, see: a) J. G. Schantl, *Sci. Synth.* **2004**, *27*, 731. For selected examples, see: b) D. K. Maiti, N. Chatterjee, P. Pandit, S. K. Hota, *Chem. Commun.* **2010**, *46*, 2022; c) M. Keller, A. S. S. Sido, P. Pale, J. Sommer, *Chem. Eur. J.* **2009**, *15*, 2810; d) L. Pezdirc, J. Cerkovnik, S. Pirc, B. Stanovnik, J. Svete, *Tetrahedron* **2007**, *63*, 991; e) N. D. Shapiro, Y. Shi, F. D. Toste, *J. Am. Chem. Soc.* **2009**, *131*, 11654.

[5] For a review, see: a) L. M. Stanley, M. P. Sibi, *Chem. Rev.* **2008**, *108*, 2887. For selected examples of *N*,*N*′-azomethine imine, see: b) M. P. Sibi, D. Rane, L. M. Stanley, T. Soeta, *Org. Lett.* **2008**, *10*, 2971; c) W. Chen, W. Du, Y.-Z. Duan, Y. Wu, S.-Y. Yang, Y.-C. Chen, *Angew. Chem.* **2007**, *119*, 7811; *Angew. Chem. Int. Ed.* **2007**, *46*, 7667; d) W. Chen, X.-H. Yuan, R. Li, W. Du, Y. Wu, L.-S. Ding, Y.-C. Chen, *Adv. Synth. Catal.* **2006**, *348*, 1818; e) H. Suga, A. Funyu, A. Kakehi, *Org. Lett.* **2007**, *9*, 97; f) R. Shintani, G. C. Fu, *J. Am. Chem. Soc.* **2003**, *125*, 10778; g) A. Suárez, C. W. Downey, G. C. Fu, *J. Am. Chem. Soc.* **2005**, *127*, 11244; h) R. Shintani, T. Hayashi, *J. Am. Chem. Soc.* **2006**, *128*, 6330; i) R. Shintani, M. Murakami, T. Hayashi, *J. Am. Chem. Soc.* **2007**, *129*, 12356; j) A. Chan, K. A. Scheidt, *J. Am. Chem. Soc.* **2007**, *129*, 5334. For recent examples of the cycloadditions of *C*,*N*-azomethine imines, see: k) C. Pereault, S. R. Goudreau, L. E. Zimmer, A. B. Charette, *Org. Lett.* **2008**, *10*, 689; l) T. Hashimoto, Y. Maeda, M. Omote, H. Nakatsu, K. Maruoka, *J. Am. Chem. Soc.* **2010**, *132*, 4076; m) T. Hashimoto, M. Omote, K. Maruoka, *Angew. Chem.* **2011**, *123*, 3551; *Angew. Chem. Int. Ed.* **2011**, *50*, 3489; n) T. Hashimoto, M. Omote, K. Maruoka, *Angew. Chem.* **2011**, *123*, 9114; *Angew. Chem. Int. Ed.* **2011**, *50*, 8952.

[6] For recent reviews in the developments of organofluorine chemistry in chemical, physical, and pharmacological properties, see: a) R. D. Chambers, *Fluorine in Organic Chemistry*, John Wiley & Sons, New York, **1973**; b) R. E. Banks, B. E. Smart, J. C. Tatlow, *Organofluorine Chemistry: Principles and Commercial Applications*; Plenum Press, New York, **1994**; c) R. Filler, Y. Kobayashi, L. M. Yagupolskii, *Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications*; Elsevier, New York, **1993**; d) D. Cahard, X. H. Xu, S. Couve-Bonnaire, X. Pannecoucke, *Chem. Soc. Rev.* **2010**, *39*, 558; e) S. Fustero, J. F. Sanz-Cervera, J. L. Aceña, M. Sánchez-Roselló, *Synlett* **2009**, 525; f) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320; g) K. Müller, C. Faeh, F. Diederich, *Science* **2007**, *317*, 1881; h) M. Schlosser, *Angew. Chem.* **2006**, *118*, 5558; *Angew. Chem. Int. Ed.* **2006**, *45*, 5432; i) M. Török, M. Abid, S. C. Mhadgut, B. Török, *Biochemistry* **2006**, *45*, 5377.

[7] For reviews of strategies for trifluoromethylation, see: a) Y. Zheng, J.-A. Ma, *Adv. Synth. Catal.* **2010**, *352*, 2745; b) J.-A. Ma, D. Cahard, *Chem. Rev.* **2008**, *108*, PR1; c) N. Shibata, S. Mizuta, H. Kawai, *Tetrahedron: Asymmetry* **2008**, *19*, 2633; d) J.-A. Ma, D. Cahard, *J. Fluorine Chem.* **2007**, *128*, 975; e) J.-A. Ma, D. Cahard, *Chem. Rev.* **2004**, *104*, 6119; f) O. A. Tomashenko, V. V. Grushin, *Chem. Rev.* **2011**, *111*, 4475.

[8] For a review on the construction of trifluoromethyl-containing stereogenicity from prochiral trifluoromethylated substrates, see: J. Nie, H.-C. Guo, D. Cahard, J.-A. Ma, *Chem. Rev.* **2011**, *111*, 455.

[9] For selected references of trifluoromethylation, see: a) H. Kawai, A. Kusuda, S. Nakamura, M. Shiro, N. Shibata, *Angew. Chem.* **2009**, *121*, 6442; *Angew. Chem. Int. Ed.* **2009**, *48*, 6324; b) T. Furukawa, T. Nishimine, E. Tokunaga, K. Hasegawa, M. Shiro, N. Shibata, *Org. Lett.* **2011**, *13*, 3972; c) H. Kawai, T. Furukawa, Y. Nomura, E. Tokunaga, N. Shibata, *Org. Lett.* **2011**, *13*, 3596; d) H. Kawai, K. Tachi, E. Tokunaga, M. Shiro, N. Shibata, *Org. Lett.* **2010**, *12*, 5104; e) E. J. Cho, S. L. Buchwald, *Org. Lett.* **2011**, *13*, 6552; f) T. D. Senecal, A. T. Pausons, S. L. Buchwald, *J. Org. Chem.* **2011**, *76*, 1174; g) V. V. Grushin, W. J. Marshall, *J. Am. Chem. Soc.* **2006**, *128*, 12644; h) N. D. Ball, J. W. Kampf, M. S. Sanford, *J. Am. Chem. Soc.* **2010**, *132*, 2878; i) Y. Ye, N. D. Ball, J. W. Kampf, M. S. Sanford, *J. Am. Chem. Soc.* **2010**, *132*, 14682; j) N. D. Ball, J. B. Gary, Y. Ye, M. S. Sanford, *J. Am. Chem. Soc.* **2011**, *133*, 7577; k) X. Wang, L. Truesdale, J.-Q. Yu, *J. Am. Chem. Soc.* **2010**, *132*, 3648; l) L. Chu, F.-L. Qin, *J. Am. Chem. Soc.* **2010**, *132*, 7262; m) L. Chu, F.-L. Qin, *J. Am. Chem. Soc.* **2012**, *134*, 1298; n) A. T. Parsons, T. D. Senecal, S. L. Buchwald, *Angew. Chem.* **2012**, *124*, 3001; *Angew. Chem. Int. Ed.* **2012**, *51*, 2947; o) A. T. Parsons, S. L. Buchwald, *Angew. Chem.* **2011**, *123*, 9286; *Angew. Chem. Int. Ed.* **2011**, *50*, 9120; p) Y. Ye, M. S. Sanford, *J. Am. Chem. Soc.* **2012**, *134*, 9034; q) R. Zhu, S. L. Buchwald, *J. Am. Chem. Soc.* **2012**, *134*, 12462; r) Y. Ji, T. Brueckl, R. D. Baxter, Y. Fujiwara, I. B. Seiple, S. Su, D. G. Blackmond, P. S. Baran, *Proc. Natl. Acad. Sci. USA* **2011**, *108*, 14411; s) E. J. Cho, T. D. Senecal, T. Kinzel, Y. Zhang, D. A. Watson, S. L. Buchwald, *Science* **2010**, *328*, 1679; t) T. Furuya, A. S. Kamlet, T. Ritter, *Nature* **2011**, *473*, 470; u) D. A. Nagib, D. W. C. MacMillan, *Nature* **2011**, *480*, 224; v) V. Matousek, A. Togni, V. Bizet, D. Cahard, *Org. Lett.* **2011**, *13*, 5762.

[10] a) L.-L. Wen, Q.-L. Shen, L. Lu, *Org. Lett.* **2010**, *12*, 4655; b) L.-L. Wen, Q.-L. Shen, X.-L. Wan, L. Lu, *J. Org. Chem.* **2011**, *76*, 2282.

[11] Y. Liu, H. Lai, B. Rong, T. Zhou, J. Hong, C. Yuan, S. Zhao, X. Zhao, B. Jiang, Q. Fang, *Adv. Synth. Catal.* **2011**, *353*, 3161.

[12] a) S. Ogawa, H. Yasui, E. Tokunaga, S. Nakamura, N. Shibata, *Chem. Lett.* **2009**, *38*, 1006; b) S. Ogawa, T. Nishimine, E. Tokunaga, N. Shibata, *Synthesis* **2010**, 3274.

[13] The recent papers in cycloaddition reaction from our group, see: a) G.-L. Zhao, J.-W. Huang, M. Shi, *Org. Lett.* **2003**, *5*, 4737; b) J.-W. Shi, M.-X. Zhao, Z.-Y. Lei, M. Shi, *J. Org. Chem.* **2008**, *73*, 305; c) Y.-L. Shi, M. Shi, *Org. Lett.* **2005**, *7*, 3057; d) H.-P. Deng, Y. Wei, M. Shi, *Org. Lett.* **2011**, *13*, 3348; e) D. Wang, Y. Wei, M. Shi, *Chem. Commun.* **2012**, *48*, 2764; f) Q.-Y. Zhao, Z. Lian, Y. Wei, M. Shi, *Chem. Commun.* **2012**, *48*, 1724; g) H.-P. Deng, Y. Wei, M. Shi, *Adv. Synth. Catal.* **2012**, *354*, 783.

Received: September 18, 2012
Published Online: November 9, 2012

