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Diverse Trifluoromethyl Heterocycles from a Single Precursor

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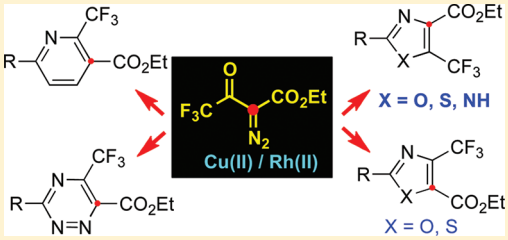
Supporting Information

ABSTRACT: Ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate is a highly versatile intermediate for the synthesis of a wide range of trifluoromethyl heterocycles. With the use of rhodium(II) or copper(II) catalyzed carbene X−H insertion reactions as key steps, a diverse set of trifluoromethyl-oxazoles, -thiazoles, -imidazoles, -1,2,4-triazines, and -pyridines are available from the diazoketoester, either directly in a single step or with just one additional step.



INTRODUCTION

Fluorine-containing compounds rarely occur in nature, but an increasing number of synthetic bioactive pharmaceuticals and agrochemicals contain fluorine.[1] At present, ca. 20% of marketed medicines and ca. 30% of agrochemicals contain at least one fluorine atom. In many such compounds, the fluorine is incorporated in the form of a trifluoromethyl group, and examples include well-known pharmaceuticals such as fluoxetine (Prozac), celecoxib (Celebrex), and mefloquin (Lariam) and a recently developed 5-trifluoromethyl oxazole,[2] a diacylglycerol acyltransferase-1 (DGAT-1) inhibitor (Figure 1).

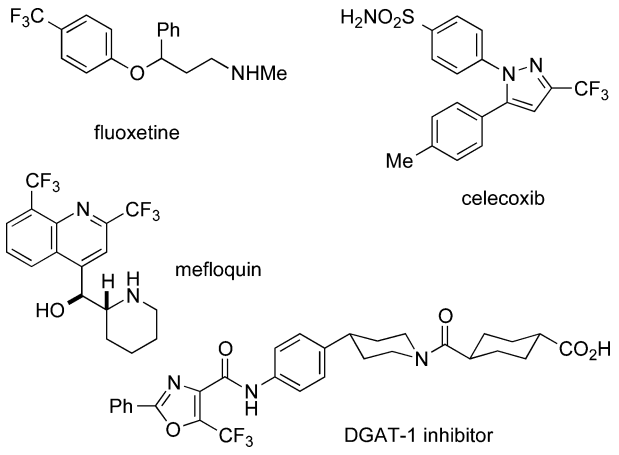
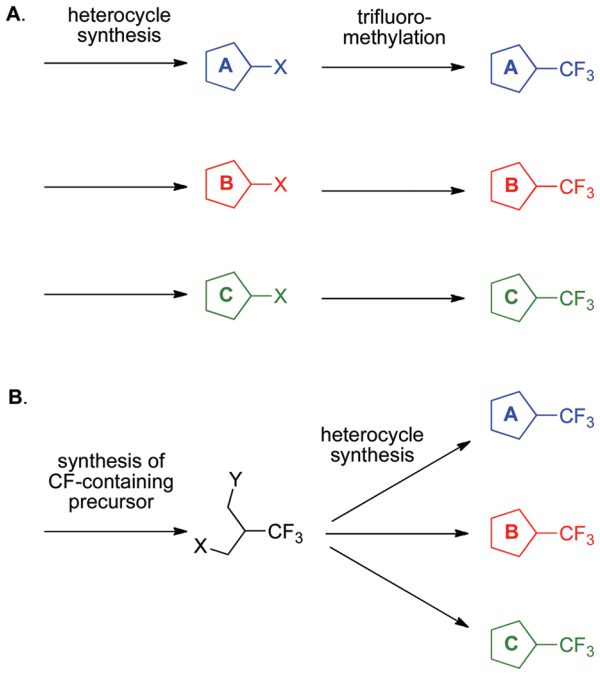


Figure 1. Some trifluoromethyl-containing pharmaceuticals.

As a consequence, a number of methods have been developed for the introduction of trifluoromethyl groups into molecules.[3,4]

Given the importance of trifluoromethyl groups in bioactive compounds and the fact that a large majority of modern medicines and agrochemicals contain one or more heterocyclic rings, it is not surprising that the synthesis of trifluoromethyl heterocycles is a topic of current interest to the chemical community. There are two main options for the construction of trifluoromethyl heterocycles. First is the trifluoromethylation of preformed heterocyclic rings (Scheme 1A) using, for example, one of the methods developed recently.[5−9] Alternatively, in a complementary approach, one could access a carefully chosen single CF_3-containing precursor that can be subsequently converted into a range of different heterocycles (Scheme 1B). In certain circumstances, we believe that the second approach might be more efficient and versatile, and we therefore have investigated the metal-catalyzed reactions of a trifluoroacetyl diazo compound, ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate (**1**),

Scheme 1. Possible Routes to a Diverse Set of Trifluoromethyl-Substituted Heterocyclic Rings



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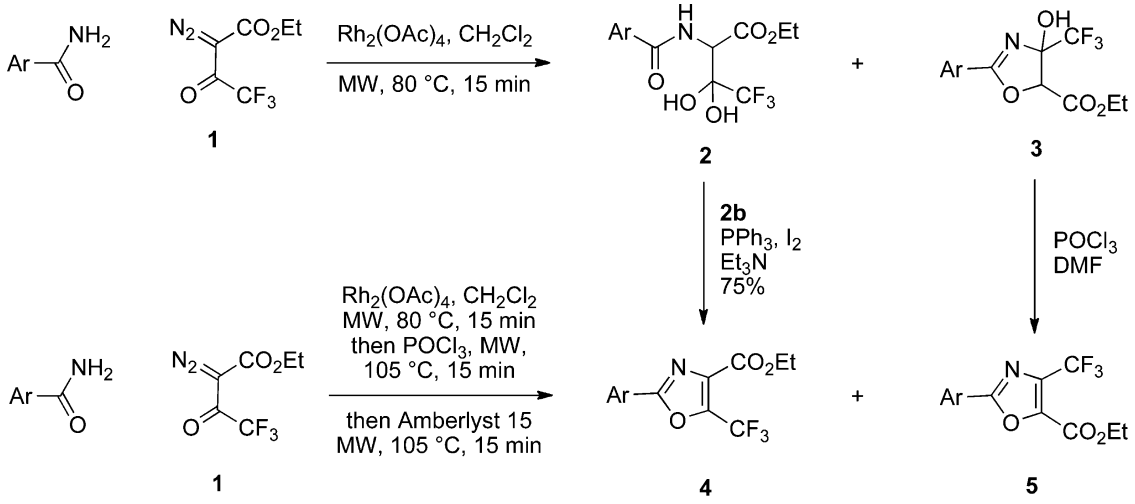
Scheme 2. Formation of 5- and 4-Trifluoromethyloxazoles



in heterocycle construction. We now report the use of this versatile reagent in the synthesis of a wide range of trifluoromethyloxazoles, -thiazoles, -imidazoles, -1,2,4-triazines, and -pyridines.

RESULTS AND DISCUSSION

In continuation of our work on metal carbene N−H insertion reactions in synthesis,[10−17] we were keen to explore the potential of similar reactions using trifluoroacetyl diazo compounds as starting materials. Although ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate (**1**) is a known diazo-β-ketoester, it has been sparingly used in synthesis and has only seen use in a limited number of heterocycle-forming reactions. Thus, as early as 1968, Dworschak and Weygard reported its photochemical reaction with acetonitrile to give ethyl 2-methyl-4-trifluoromethyloxazole-2-carboxylate in 60% yield,[18] while Hoffmann and Wenkert reported the first rhodium(II)-acetate-catalyzed reaction of the diazo compound.[19] Thus, reaction with ethyl vinyl ether gave a dihydrofuran, which upon reaction with amines gave 2-trifluoromethylpyrroles. Non-metal-catalyzed reactions with ynamines or with phosphoranes followed by Ph_3P gave pyrazoles and pyridazines, respectively,[20−22] before Wang and Zhu reinvestigated the reaction with nitriles but under rhodium(II) acetate catalysis.[23] Wang and Zhu also reinvestigated the reaction with vinyl ethers[24] as a route to dihydrofurans and furans. Trifluoromethylfurans are also obtained from reaction of the diazo compound **1** with alkynes.[25] Hence, the conversion of diazo β-ketoester **1** into trifluoromethyl heterocycles has been exemplified in a few cases, although none of this work has involved the N−H insertion chemistry that has proved so versatile in the synthesis of a series of nonfluorinated N-containing heterocycles.

Ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** is readily prepared either by diazo transfer to ethyl trifluoroacetoacetate[22] or by trifluoroacetylation of commercially available ethyl diazoacetate with trifluoroacetic anhydride.[23] We preferred the latter method and routinely prepared the compound in 5-g batches. Initially, we investigated oxazole formation by reaction of diazocarbonyl compound **1** with carboxamides under our previously reported rhodium(II)-acetate-catalyzed conditions,[16] expecting to isolate the N−H insertion products, β-ketoamides. In this event, these were isolated in modest yields but as their hydrates **2**,[26,27] presumably because of the enhanced electrophilicity of the trifluoromethyl ketone toward adventitious water during chromatography. The structure of the 4-bromophenyl derivative **2d** was confirmed by X-ray crystallography (see the Supporting Information). The remaining material was largely made up by the product of carbene O−H insertion and cyclization, the oxazolines **3** (Scheme 2), with the structures of the 2-bromo- and 4-methoxy-phenyl derivatives **3b** and **3c** being confirmed by X-ray crystallography (see the Supporting Information). Hence, the trifluoroacetyl diazoketoester **1** behaves somewhat differently to its nonfluorinated counterpart, presumably the enhanced oxophilicity of the rhodium carbene intermediate derived from **1** causing the competing O−H insertion process. We have only previously observed significant amounts of products derived from competing O−H insertion when using perfluorinated ligands on rhodium, where the ligands also influence the electrophilicity of the intermediate rhodium carbene.[16]

As expected, both compounds **2** and **3** could be dehydrated to the corresponding oxazoles. Thus, the hydrated ketoamide **2b** underwent cyclodehydration to the 5-trifluoromethyloxazole **4b** in 75% yield using the Wipf protocol (Scheme 2).[28] Likewise, the 4-hydroxyoxazolines **3** underwent dehydration to the corresponding 4-trifluoromethyloxazoles **5** upon treatment with phosphorus oxychloride (Scheme 2). The intermediates **2** and **3** need not be isolated; repeating the rhodium(II)-acetate-catalyzed reaction of **1** with carboxamides, but with subsequent addition of phosphorus oxychloride to the reaction mixture, leads directly to a separable mixture of the 5-trifluoromethyl and 4-trifluoromethyl oxazoles **4** and **5** in modest yields (Scheme 2), with the 4-isomer, the product of initial O−H insertion, predominating (Table 1). Although in general, the

Table 1. Formation of 5- and 4-Trifluoromethyloxazoles 4 and 5

	Ar	2 yield/%	3 yield/%	3 → 5 yield/%	1 → 4 yield/%	1 → 5 yield/%
a	Ph	43	35	73	13	30
b	2-BrC_6H_4	32	40	69	14	35
c	4-$MeOC_6H_4$	40	38	72	28	33
d	4-BrC_6H_4	38	33	67	23	31

oxazole-4- and -5-carboxylates **4** and **5** were distinguishable by ^{13}C NMR spectroscopy (the CF_3-bearing ring carbon occurring at δ 141.4−142.5 and δ 135.9−136.7, respectively),

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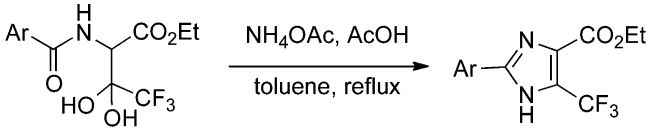
the structures of oxazoles **4b**, **5b**, and **5c** were confirmed by crystallography (see the Supporting Information). Oxazole **4a** was also obtained in 50% yield by rhodium(II)-acetate-catalyzed reaction of **1** with benzonitrile, in confirmation of earlier findings.[23]

With N−H insertion products **2** in hand, albeit in modest yield, we were able to prepare 5-trifluoromethyl imidazoles **6** simply by treatment with ammonium acetate in acetic acid/toluene (Scheme 3).[29]

Scheme 3. Formation of 5-Trifluoromethylimidazoles[a]

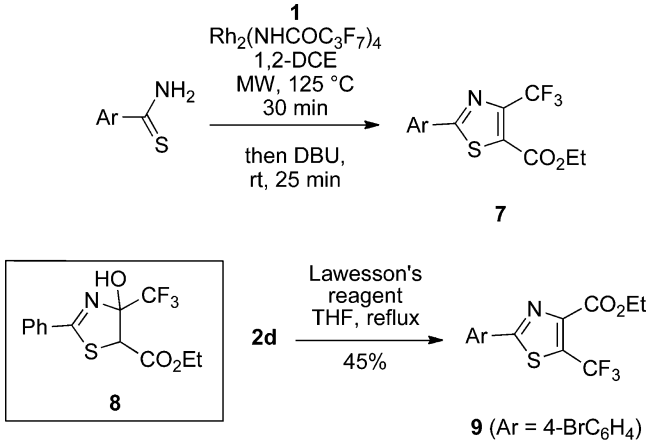


2 **6**

[a]**2a**, Ar = Ph; **2c**, Ar = 4-MeOC$_6$H$_4$; **2d**, Ar = 4-BrC$_6$H$_4$; **6a**, Ar = Ph (42%); **6b**, Ar = 4-MeOC$_6$H$_4$ (45%); **6c**, Ar = 4-BrC$_6$H$_4$ (40%).

Finally, within the 1,3-azole series, we investigated the preparation of trifluoromethylthiazoles by reaction of diazoketoester **1** with thiocarboxamides. Although the reaction of diazocarbonyl compounds with thioamides is less well-known than the corresponding reaction with amides, we have recently shown that with the right choice of rhodium catalyst, it proceeds readily.[16] Thus, rhodium(II)-heptafluorobutyramide-catalyzed reaction of diazocarbonyl compound **1** with a range of thiocarboxamides under microwave irradiation followed by addition of DBU to the reaction mixture gave the 4-trifluoromethyl thiazoles **7** in good yield (Scheme 4). As expected, the reaction

Scheme 4. Formation of Trifluoromethylthiazoles[a]



7

8

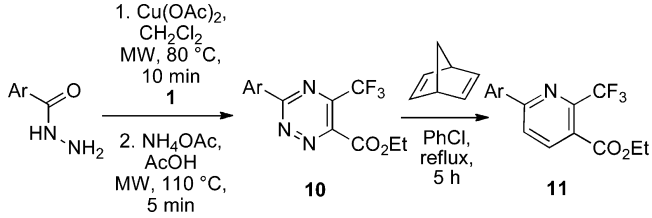
9 (Ar = 4-BrC$_6$H$_4$)

[a]**7a**, Ar = Ph (64%); **7b**, Ar = 4-BrC$_6$H$_4$ (63%); **7c**, Ar = 4-CF$_3$C$_6$H$_4$ (65%); **7d**, Ar = 2-quinolinyl (68%).

proceeds by C−S bond formation to the carbene intermediate (S−H insertion into the thiocarboxamide imino tautomer), although the thiazole **4c** was subjected to X-ray crystallographic analysis to confirm its structure (see the Supporting Information). If DBU is not added, the reaction stops at the 4-hydroxy-thiazoline stage. In the case of thiobenzamide, the intermediate thiazoline **8** was isolated in 54% yield, and its structure was confirmed by X-ray crystallography (see the Supporting Information). The regioisomeric 5-trilfluoromethylthiazoles are also available by treating the initial N−H insertion product, or in this case its hydrate, with Lawesson's reagent.[29] This was exemplified by the conversion of ketoamide hydrate **2d** into thiazole **9** in modest yield (Scheme 4).

In order to explore further the utility of diazoketoester **1** in the synthesis of trifluoromethyl heterocycles, we next investigated its reaction with aryl hydrazides (Scheme 5). Despite the wide range

Scheme 5. Synthesis of 2-Trifluoromethylnicotinates[a]



10 **11**

[a]**10a**, Ar = Ph (28%); **10b**, Ar = 3-MeOC$_6$H$_4$ (35%); **10c**, Ar = 4-BrC$_6$H$_4$ (31%); **11a**, Ar = Ph (89%); **11b**, Ar = 3-MeOC$_6$H$_4$ (86%); **11c**, Ar = 4-BrC$_6$H$_4$ (91%).

of N−H compounds that have been reported to undergo metal carbene N−H insertion reactions, the reaction of hydrazides has only recently been reported from our laboratory.[30] Microwave-assisted reaction of **1** with benzhydrazide in the presence of copper(II) acetate, followed by reaction with ammonium acetate in acetic acid as previously described,[30] gave after chromatography the 1,2,4-triazines **10** in modest yield (Scheme 5). The structure of the 5-trifluoromethyl-1,2,4-triazine **10a** was confirmed by X-ray crystallography (see the Supporting Information). 1,2,4-Triazines are known to act as electron-deficient dienes in aza Diels−Alder reactions,[31−33] and therefore we investigated their conversion into pyridines by Diels−Alder reaction with norbornadiene as an ethyne equivalent.[34−37] Thus, heating triazines **10** with an excess of norbornadiene in chlorobenzene gave 6-aryl-2-trifluoromethylnicotinates **11** in excellent yield (Scheme 5).

In conclusion, the present work not only further confirms the utility of carbene X−H insertion reactions as a key step in the synthesis of heterocycles, but also establishes ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate as a highly versatile intermediate for the synthesis of a wide range of trifluoromethyl heterocycles as summarized in Scheme 6. Oxazoles, thiazoles, imidazoles, 1,2,4-triazines, and pyridines are available directly from diazoketoester **1**, either directly in a single step or with just one additional step. In the case of oxazoles and thiazoles, the same diazoketoester precursor can give rise to 4- or 5-trifluoromethyl d erivatives depending on the reaction conditions, adding to the versatility.

EXPERIMENTAL SECTION

General Information. Commercially available reagents were used throughout without purification unless otherwise stated. Anhydrous solvents were used as supplied. Tetrahydrofuran was distilled from sodium benzophenone ketyl under nitrogen atmosphere. Dichloromethane was distilled from calcium hydride under a nitrogen atmosphere. Light petroleum refers to the fraction with bp 40−60 °C. Ether refers to diethyl ether. Reactions were routinely carried out under a nitrogen or argon atmosphere. Analytical thin layer chromatography was carried out on aluminum-backed plates coated with silica gel and visualized under UV light at 254 and/or 360 nm and/or potassium permanganate or ethanolic vanillin dip. Chromatography was carried out on silica gel. Fully characterized compounds were chromatographically homogeneous. Infrared spectra were recorded on an FT-IR spectrometer in the range 4000−600 cm^{-1} as solutions in chloroform. NMR spectra were recorded at 400 or

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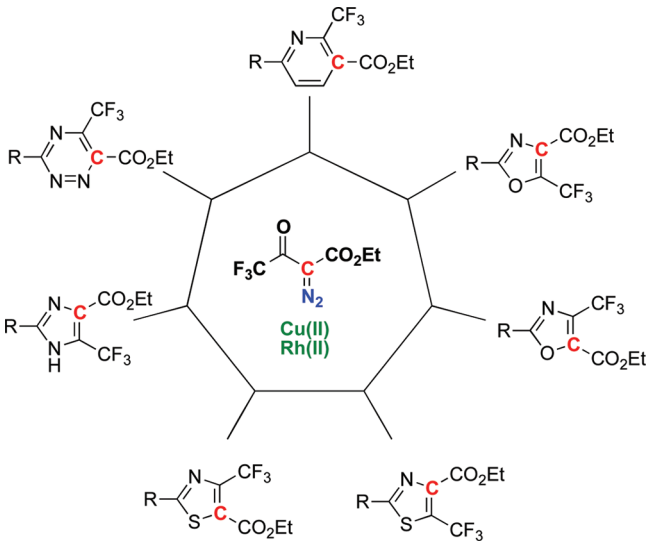
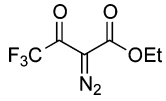
Scheme 6. Ethyl 2-Diazo-4,4,4-trifluoro-3-oxobutanoate[a]



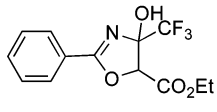
[a]A highly versatile precursor to a wide range of heterocyclic products via carbene insertion reactions (the carbon that originates from the carbene is indicated).

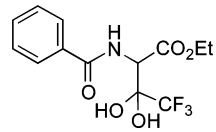
500 MHz (^{1}H frequency, 100 or 125 MHz ^{13}C frequency, 377 MHz ^{19}F frequency). Chemical shifts are quoted in ppm and *J*-values in Hz. Chemical shift values are referenced against residual proton in the deuterated solvents. In the ^{13}C NMR spectra, signals corresponding to CH, CH_2, or CH_3 are assigned from DEPT-90 and -135 spectra; all others are quaternary C. Mass spectra were recorded on a time-of-flight mass spectrometer using electrospray ionization (ESI). Microwave reactions were carried out in a CEM Discover TM S-class microwave reactor at 300 W with IR temperature sensor.



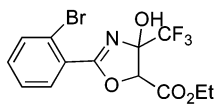
Ethyl 2-Diazo-4,4,4-trifluoro-3-oxobutanoate 1. To a solution of ethyl diazoacetate (3.1 mL, 30.0 mmol) in dichloromethane (33 mL) at 0 °C was added dropwise pyridine (2.7 mL, 33.0 mmol). The mixture was stirred for 15 min. A solution of trifluoroacetic anhydride (4.7 mL, 33.0 mmol) in dichloromethane (8.0 mL) was added dropwise and stirred for 30 min. The reaction mixture was poured into water (30 mL) and neutralized with $NaHCO_3$. The organic layer was isolated, and the solvent was removed under reduced pressure, yielding a dark yellow oil. The crude product was purified over a silica cartridge (100 g) using a gradient of 0−50% ethyl acetate in cyclohexane over a period of 40 min. The appropriate fractions were combined to give the title compound as a yellow oil (5.3 g, 84%): ν_{max} ($CHCl_3$)/cm^{-1} 2990, 2164, 1740, 1711, 1671, 1377, 1360, 1305, 1279, 1203, 1164, 1014; δ_H (400 MHz; $CDCl_3$) 4.37 (2 H, q, *J* 7.1 Hz), 1.36 (3 H, t, *J* 7.1 Hz); δ_C (100 MHz; $CDCl_3$) 172.1 (q, *J* 39 Hz, C), 158.3 (C), 115.7 (q, *J* 287 Hz, CF_3), 71.9 (C), 62.6 (CH_2), 13.9 (Me).

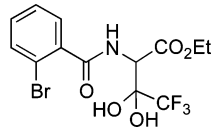
Oxazoles. *General Method A.* To a solution of ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (200 mg, 0.95 mmol) and the benzamide (1.26 mmol) in dichloromethane (5 mL) was added rhodium(II) acetate (8.4 mg, 2 mol %). The reaction vessel was sealed, and the solution was heated in a microwave reactor to 80 °C for 20 min. The reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The residue was purified over silica using a solvent system of 30% ethyl acetate in light petroleum to give (i) the ethyl 4-hydroxy-2-aryl-4-trifluoromethyl-4,5-dihydrooxazole-5-carboxylate **3** and (ii) the ethyl 2-benzamido-4,4,4-trifluoro-3,3-dihydroxybutanoate **2**.



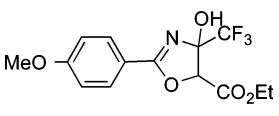


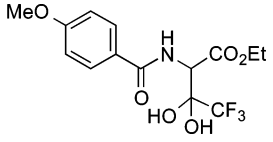
*Ethyl 4-Hydroxy-2-phenyl-4-trifluoromethyl-4,5-dihydrooxazole-5-carboxylate **3a** and Ethyl 2-Benzamido-4,4,4-trifluoro-3,3-dihydroxybutanoate **2a**.* According to General Method A, ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (200 mg, 0.95 mmol), benzamide (152 mg, 1.26 mmol), and rhodium(II) acetate (8.4 mg, 2 mol %) gave (i) ethyl 4-hydroxy-2-phenyl-4-trifluoromethyl-4,5-dihydrooxazole-5-carboxylate **3a** as a colorless solid (100 mg, 35%): mp 92−95 °C (lit.,[38] no data); (Found: M + Na^+, 326.0598. $C_{13}H_{12}F_3NO_4$ + Na^+ requires 326.0611); ν_{max} ($CHCl_3$)/cm^{-1} 3569, 2987, 1759, 1645, 1582, 1496, 1452, 1376, 1355, 1301, 1256, 1192, 1159; δ_H (400 MHz; $CDCl_3$) 8.45 (2 H, d, *J* 8.0 Hz), 7.62 (1 H, t, *J* 8.0 Hz), 7.48 (2 H, t, *J* 8.0 Hz), 6.57 (1H, s), 5.23 (1 H, s), 4.35 (2 H, m), 1.35 (3 H, t, *J* 7.2 Hz); δ_C (100 MHz; $CDCl_3$) 169.9 (C), 165.0 (C), 133.5 (CH), 129.5 (CH), 128.8 (C), 124.6 (CH), 122.8 (q, *J* 283.0 Hz, CF_3), 98.4 (q, *J* 35.0 Hz, C), 80.2 (CH), 62.2 (CH_2), 14.0 (Me); δ_F (377 MHz; $CDCl_3$) −82.05 (s, CF_3). (ii) Ethyl 2-benzamido-4,4,4-trifluoro-3,3-dihydroxybutanoate **2a** was also given as a colorless crystalline solid (115 mg, 38%): mp 69−71 °C; (Found: M + Na^+, 344.0700. $C_{13}H_{14}F_3NO_5$ + Na^+ requires 344.0716); ν_{max} ($CHCl_3$)/cm^{-1} 3569, 3437, 2987, 1738, 1676, 1640, 1580, 1517, 1446, 1375, 1301, 1259, 1191, 1144; δ_H (400 MHz; $(CD_3)_2SO$) 8.24 (1 H, d, *J* 8.8 Hz), 7.85 (2 H, d, *J* 8.4 Hz), 7.58−7.64 (2 H, m), 7.50−7.57 (3 H, m), 4.94 (1 H, d, *J* 8.8 Hz), 4.15 (2 H, q, *J* 7.2 Hz), 1.21 (3 H, t, *J* 7.2 Hz); δ_C (100 MHz; $CDCl_3$) 169.4 (C), 166.6 (C), 133.7 (C), 132.3 (CH), 129.0 (CH), 127.8 (CH), 123.5 (q, *J* 288.0 Hz, CF_3), 92.8 (q, *J* 31.0 Hz, C), 61.4 (CH_2), 56.4 (CH), 14.5 (Me); δ_F (377 MHz; $CDCl_3$) −81.6 (s, CF_3).





*Ethyl 2-(2-Bromophenyl)-4-hydroxy-4-trifluoromethyl-4,5-dihydrooxazole-5-carboxylate **3b** and Ethyl 2-(2-Bromobenzamido)-4,4,4-trifluoro-3,3-dihydroxybutanoate **2b**.* According to General Method A, ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (200 mg, 0.95 mmol), 2-bromobenzamide (252 mg, 1.26 mmol), and rhodium(II) acetate (8.4 mg, 2 mol %) gave (i) ethyl 4-hydroxy-2-(2-bromophenyl)-4-trifluoromethyl-4,5-dihydrooxazole-5-carboxylate **3b** as a colorless solid (144 mg, 40%): mp 139−141 °C; (Found: M + Na^+, 403.9716. $C_{13}H_{11}{}^{79}BrF_3NO_4$ + Na^+ requires 403.9721); ν_{max} ($CHCl_3$)/cm^{-1} 3688, 3566, 3008, 1758, 1652, 1601, 1567, 1439, 1395, 1376, 1351, 1303, 1246, 1191, 1161; δ_H (400 MHz; $(CD_3)_2SO$) 8.27 (1 H, s), 7.84 (2 H, m), 7.58 (2 H, m), 5.47 (1 H, s), 4.23 (2 H, m), 1.25 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 167.1 (C), 165.4 (C), 134.7 (C), 134.2 (CH), 132.1 (CH), 127.5 (CH), 126.9 (CH), 123.5 (q, *J* 283.7 Hz, CF_3), 121.5 (C), 98.8 (q, *J* 32.5 Hz, C), 80.2 (CH), 61.8 (CH_2), 14.5 (Me); δ_F (377 MHz; $CDCl_3$) −82.0 (s, CF_3). (ii) Ethyl 2-(2-bromobenzamido)-4,4,4-trifluoro-3,3-dihydroxybutanoate **2b** was also given as a colorless crystalline solid (120 mg, 32%): mp 111−114 °C; (Found: M + Na^+, 421.9822. $C_{13}H_{13}{}^{79}BrF_3NO_5$ + Na^+ requires 421.9827); δ_H (400 MHz; $(CD_3)_2SO$) 8.46 (1 H, d, *J* 9.2 Hz), 7.68 (1 H, d, *J* 8.0 Hz), 7.58−7.64 (2 H, m), 7.50−7.57 (3 H, m), 4.89 (1 H, d, *J* 9.2 Hz), 4.17 (2 H, q, *J* 7.2 Hz), 1.23 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 169.1 (C), 167.3 (C), 138.6 (C), 133.8 (CH), 131.8 (CH), 129.5 (CH), 128.4 (CH), 123.3 (q, *J* 292.3 Hz, CF_3), 119.3 (C), 92.6 (q, *J* 30.2 Hz, C), 61.4 (CH_2), 56.2 (CH), 14.4 (Me); δ_F (377 MHz; $CDCl_3$) −81.6 (s, CF_3).





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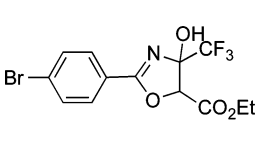
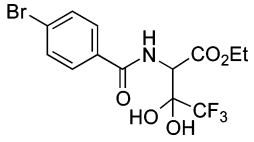
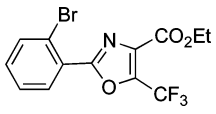
Ethyl 4-Hydroxy-2-(4-methoxyphenyl)-4-trifluoromethyl-4,5-dihydrooxazole-5-carboxylate ***3c*** *and Ethyl 2-(4-Methoxybenzamido)-4,4,4-trifluoro-3,3-dihydroxybutanoate* ***2c***. According to General Method A, ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (200 mg, 0.95 mmol), 4-methoxybenzamide (190 mg, 1.26 mmol), and rhodium(II) acetate (8.4 mg, 2 mol %) gave (i) ethyl 4-hydroxy-2-(4-methoxyphenyl)-4-trifluoromethyl-4,5-dihydrooxazole-5-carboxylate **3c** as a colorless solid (120 mg, 38%): mp 125−127 °C; (Found: M + Na^+, 356.0700. $C_{14}H_{14}F_3NO_5$ + Na^+ requires 356.0716); ν_{max} ($CHCl_3$)/cm^{-1} 3689, 3568, 3011, 1758, 1639, 1610, 1513, 1464, 1425, 1377, 1356, 1307, 1259, 1192, 1173, 1096; δ_H (400 MHz; $CDCl_3$) 8.02 (2 H, d, *J* 8.8 Hz), 6.97 (2 H, d, *J* 8.8 Hz), 5.20 (1 H, s), 4.36 (2 H, m), 4.19 (1 H, br), 3.90 (3 H, s), 1.36 (3 H, t, *J* 7.0 Hz); δ_C (126 MHz; $CDCl_3$) 169.6 (C), 165.3 (C), 163.7 (C), 131.5 (CH), 122.6 (q, *J* 284.8 Hz, CF_3), 117.1 (C), 114,0 (CH), 98.5 (q, *J* 32.7 Hz, C), 79.9 (CH), 62.2 (CH_2), 55.5 (Me), 14.0 (Me); δ_F (377 MHz; $CDCl_3$) −81.6 (s, CF_3). (ii) Ethyl 4,4,4-trifluoro-3,3-dihydroxy2-(4-methoxybenzamido)butanoate **2c** was also given as a colorless crystalline solid (133 mg, 40%): mp 71−74 °C; (Found: M + Na^+, 374.0815. $C_{14}H_{16}F_3NO_6$ + Na^+ requires 374.0822); ν_{max} ($CHCl_3$)/cm^{-1} 3690, 3571, 3007, 1738, 1668, 1606, 1577, 1496, 1442, 1375, 1343, 1311, 1259, 1182, 1096, 1030; δ_H (400 MHz; $(CD_3)_2SO$) 8.10 (1 H, d, *J* 9.0 Hz), 7.83 (2 H, d, *J* 8.7 Hz), 7.59 (1 H, s), 7.52 (1 H, s), 7.05 (2 H, d, *J* 8.7 Hz), 4.93 (1 H, d, *J* 9.0 Hz), 4.13 (2 H, q, *J* 7.1 Hz), 3.83 (3 H, s), 1.20 (3 H, t, *J* 7.1 Hz); δ_C (100 MHz; $CDCl_3$) 168.6 (C), 166.0 (C), 162.5 (C), 129.7 (CH), 125.8 (CH), 122.0 (q, *J* 287.8 Hz, CF_3), 114.2 (C), 93.0 (q, *J* 32.2 Hz, C), 61.4 (CH_2), 56.3 (Me), 55.9 (CH), 13.8 (Me); δ_F (377 MHz; $CDCl_3$) −81.6 (s, CF_3).



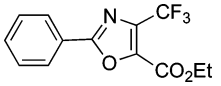


Ethyl 2-(4-bromophenyl)-4-hydroxy-4-trifluoromethyl-4,5-dihydrooxazole-5-carboxylate ***3d*** *and Ethyl 2-(4-Bromobenzamido)-4,4,4-trifluoro-3,3-dihydroxybutanoate* ***2d***. According to General Method A, ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (200 mg, 0.95 mmol), 4-bromobenzamide (252 mg, 1.26 mmol), and rhodium(II) acetate (8.4 mg, 2 mol %) gave (i) ethyl 4-hydroxy-2-(4-bromophenyl)-4-trifluoromethyl-4,5-dihydrooxazole-5-carboxylate **3d** as a colorless solid (119 mg, 33%): mp 103−105 °C; (Found: M + Na^+, 403.9716. $C_{13}H_{11}{}^{79}BrF_3NO_4$ + Na^+ requires 403.9721); ν_{max} ($CHCl_3$)/cm^{-1} 3690, 3011, 1759, 1646, 1584, 1569, 1489, 1403, 1377, 1354, 1300, 1256, 1182, 1160; δ_H (400 MHz; $(CD_3)_2SO$) 8.18 (1 H, s), 7.90 (2 H, d, *J* 8.7 Hz), 7.80 (2 H, d, *J* 8.7 Hz), 5.50 (1 H, s), 4.22 (2 H, q, *J* 7.1 Hz), 1.22 (3 H, t, *J* 7.1 Hz); δ_C (126 MHz; $CDCl_3$) 169.1 (C), 164.9 (C), 132.1 (CH), 131.0 (CH), 128.8 (C), 123.6 (C), 122.6 (q, *J* 284.8 Hz, CF_3), 98.5 (q, *J* 33.0 Hz, C), 80.2 (CH), 62.4 (CH_2), 14.0 (Me); δ_F (377 MHz; $CDCl_3$) −81.9 (s, CF_3). (ii) Ethyl 2-(4-bromobenzamido)-4,4,4-trifluoro-3,3-dihydroxybutanoate **2d** was also given as a colorless crystalline solid (162 mg, 43%): mp 111−114 °C; (Found: M + Na^+, 421.9822. $C_{13}H_{13}{}^{79}BrF_3NO_5$ + Na^+ requires 421.9827); ν_{max} ($CHCl_3$)/cm^{-1} 3690, 3568, 3011, 1740, 1716, 1645, 1593, 1568, 1516, 1480, 1398, 1341, 1314, 1258, 1145, 1070; δ_H (400 MHz; $(CD_3)_2SO$) 8.37 (1 H, d, *J* 9.0 Hz), 7.80 (2 H, d, *J* 8.7 Hz), 7.72 (2 H, d, *J* 8.7 Hz), 7.59 (1 H, s), 7.52 (1 H, s), 4.93 (1 H, d, *J* 9.0 Hz), 4.13 (2 H, q, *J* 7.1 Hz), 1.20 (3 H, t, *J* 7.1 Hz); δ_C (126 MHz; $CDCl_3$) 169.1 (C), 167.6 (C), 132.1 (CH), 131.3 (C), 128.9 (CH), 127.5 (C), 122.0 (q, *J* 287.8 Hz, CF_3), 93.8 (q, *J* 32.2 Hz, C), 63.5 (CH_2), 55.3 (CH), 13.8 (Me); δ_F (377 MHz; $CDCl_3$) −81.6 (s, CF_3).

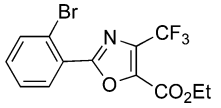


Conversion of ***2*** *and* ***3*** *into Oxazoles* ***4*** *and* ***5***. *Ethyl 2-(2-Bromophenyl)-5-trifluoromethyloxazole-4-carboxylate* ***4b***. To a dry flask were added triphenylphosphine (157 mg, 0.60 mmol), iodine (152 mg, 0.60 mmol), and anhydrous dichloromethane (15 mL). Once the solids had dissolved completely, triethylamine (173 μL, 1.24 mmol) and a solution of ethyl 2-(2-bromobenzamido)-4,4,4-trifluoro-3,3-dihydroxybutanoate **2b** (119.7 mg, 0.30 mmol) in dichloromethane (5 mL) were added. The mixture was allowed to stir under argon overnight at room temperature and then concentrated in vacuo. The product was purified by chromatography over silica using 20% ethyl acetate in light petroleum to give the title compound **4b** as colorless solid (25.7 mg, 75%): mp 52−55 °C; (Found: M + H^+, 363.9807. $C_{13}H_9{}^{79}BrF_3NO_3$ + H^+ requires 363.9791); ν_{max} ($CHCl_3$)/cm^{-1} 3684, 3409, 2986, 2854, 1740, 1605, 1571, 1459, 1398, 1379, 1361, 1317, 1246, 1153, 1028; δ_H (400 MHz, $CDCl_3$) 8.04 (1 H, d, *J* 8.0 Hz), 7.78 (1 H, d, *J* 8.0 Hz), 7.49 (1 H, t, *J* 8.0 Hz), 7.42 (1 H, t, *J* 8.0 Hz), 4.50 (2 H, q, *J* 7.2 Hz), 1.46 (3 H, t, *J* 7.2 Hz); δ_C (100 MHz; $CDCl_3$) 160.5 (C), 159.2 (C), 142.5 (q, *J* 44.0 Hz, C), 134.6 (CH), 133.2 (C), 133.1 (CH), 133.2 (CH), 127.5 (C), 126.3 (C), 121.7 (CH), 118.3 (q, *J* 269.0 Hz, CF_3), 62.3 (CH_2), 13.9 (Me); δ_F (377 MHz; $CDCl_3$) −61.01 (s, CF_3).

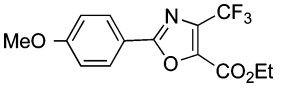
General Method B. Phosphoryl chloride (20 μL, 0.21 mmol) was added to a solution of the ethyl 4-hydroxy-2-aryl-4-trifluoromethyl-4,5-dihydrooxazole-5-carboxylate 3 (0.09 mmol) in DMF (300 μL) at 0 °C. The mixture was stirred at room temperature for 16 h, poured into ice-water (1 mL), and then extracted with EtOAc (3 × 2 mL). The organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified over silica using 10% ethyl acetate in light petroleum to give the ethyl 2-aryl-4-trifluoromethyloxazole-5-carboxylate 5.



Ethyl 2-Phenyl-4-trifluoromethyloxazole-5-carboxylate ***5a***. According to General Method B, ethyl 4-hydroxy-2-phenyl-4-trifluoromethyl-4,5-dihydrooxazole-5-carboxylate **3a** (28.5 mg, 0.09 mmol) gave ethyl 2-phenyl-4-trifluoromethyloxazole-5-carboxylate **5a** as a colorless solid (19.5 mg, 73%): mp 44−47 °C (lit.,[38] no data); (Found: M + H^+, 286.0687. $C_{13}H_{10}F_3NO_3$ + H^+ requires 286.0686); ν_{max} ($CHCl_3$)/cm^{-1} 2987, 2929, 1739, 1609, 1560, 1488, 1451, 1398, 1379, 1362, 1329, 1315, 1276, 1151, 1037; δ_H (400 MHz, $CDCl_3$) 8.17 (2 H, d, *J* 8.0 Hz), 7.50−7.60 (3 H, m), 4.48 (2 H, q, *J* 7.2 Hz), 1.44 (3 H, t, *J* 7.2 Hz); δ_C (100 MHz; $CDCl_3$) 162.7 (C), 156.1 (C), 139.9 (C), 136.7 (q, *J* 44.0 Hz, C), 132.4 (CH), 129.2 (CH), 127.7 (CH), 125.2 (C), 119.8 (q, *J* 268.0 Hz, CF_3), 62.7 (CH_2), 14.0 (Me); δ_F (377 MHz; $CDCl_3$) −61.84 (s, CF_3).



Ethyl 2-(2-Bromophenyl)-4-trifluoromethyloxazole-5-carboxylate ***5b***. According to General Method B, ethyl 2-(2-bromophenyl)-4-hydroxy-4-trifluoromethyl-4,5-dihydrooxazole-5-carboxylate **3b** (36.1 mg, 0.09 mnmol) gave ethyl 2-(2-bromophenyl)-4-trifluoromethyloxazole-5-carboxylate **5b** as colorless solid (23.7 mg, 69%): mp 62−63 °C; (Found: M + H^+, 363.9807. $C_{13}H_9{}^{79}BrF_3NO_3$ + H^+ requires 363.9791); ν_{max} ($CHCl_3$)/cm^{-1} 3689, 3606, 3053, 2988, 1737, 1602, 1549, 1523, 1472, 1455, 1398, 1382, 1322, 1296, 1255, 1175, 1157, 1012; δ_H (400 MHz, $CDCl_3$) 8.06 (1 H, d, *J* 8.0 Hz), 7.78 (1 H, d, *J* 8.0 Hz), 7.39−7.52 (2 H, m), 4.50 (2 H, q, *J* 7.2 Hz), 1.46 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 161.2 (C), 155.9 (C), 140.4 (C), 135.9 (q, *J* 41.0 Hz, C), 134.8 (CH), 133.2 (CH), 132.1 (CH), 127.6 (C), 126.4 (CH), 120.7 (C), 119.7 (q, *J* 268.0 Hz, CF_3), 62.5 (CH_2), 14.0 (Me); δ_F (377 MHz; $CDCl_3$) −61.71 (s, CF_3).



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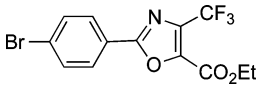
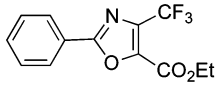
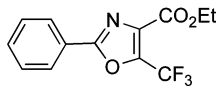
Ethyl 2-(4-Methoxyphenyl)-4-trifluoromethyloxazole-5-carboxylate ***5c***. According to General Method B, ethyl 4-hydroxy-2-(4-methoxyphenyl)-4-trifluoromethyl-4,5-dihydrooxazole-5-carboxylate **3c** (33 mg, 0.09 mmol) gave ethyl 2-(4-methoxyphenyl)-4-trifluoromethyloxazole-5-carboxylate **5c** as a colorless solid (22 mg, 72%): mp 104−106 °C; (Found: M + H^+, 316.0813. $C_{14}H_{13}F_3NO_4$ + H^+ requires 316.0791); ν_{max} ($CHCl_3$)/cm^{-1} 3011, 2932 2842, 1738, 1613, 1564, 1500, 1464, 1442, 1425, 1397, 1378, 1361, 1322, 1258, 1150, 1079, 1036, 840; δ_H (400 MHz, $CDCl_3$) 8.12 (2 H, d, *J* 9.2 Hz), 7.02 (2 H, d, *J* 9.2 Hz), 4.46 (2 H, q, *J* 7.2 Hz), 3.90 (3 H, s), 1.43 (3 H, t, *J* 7.2 Hz); δ_C (100 MHz; $CDCl_3$) 162.8 (C), 156.2 (C), 139.4 (C), 136.5 (q, *J* 43.0 Hz, C), 133.4 (C), 129.2 (CH), 119.7 (q, *J* 268.0 Hz, CF_3), 117.6 (C), 114.5 (CH) 62.3 (CH_2), 55.5 (Me), 14.0 (Me); δ_F (377 MHz; $CDCl_3$) −61.85 (s, CF_3).



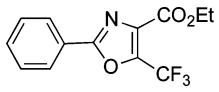
Ethyl 2-(4-Bromophenyl)-4-trifluoromethyloxazole-5-carboxylate ***5d***. According to General Method B, ethyl 2-(4-bromophenyl)-4-hydroxy-4-trifluoromethyl-4,5-dihydrooxazole-5-carboxylate **3d** (36.1 mg, 0.09 mmol) gave ethyl 2-(4-bromophenyl)-4-trifluoromethyloxazole-5-carboxylate **5d** as a colorless solid (23.0 mg, 67%): mp 58−61 °C; (Found: M + Na^+, 385.9611. $C_{13}H_9{}^{79}BrF_3NO_3$ + Na^+ requires 385.9616); ν_{max} ($CHCl_3$)/cm^{-1} 3687, 3012, 2415, 1737, 1603, 1544, 1479, 1407, 1382, 1323, 1306, 1288, 1176, 1158; δ_H (400 MHz; $CDCl_3$) 8.06−8.02 (2 H, m), 7.69−7.66 (2 H, m), 4.48 (2 H, q, *J* 7.2 Hz), 1.44 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 161.8 (C), 156.0 (C), 140.1 (q, *J* 2.8 Hz, C), 136.7 (q, *J* 41.1 Hz, C), 132.5 (CH), 128.9 (CH), 127.4 (C), 124.1 (C), 119.6 (q, *J* 269.8 Hz, CF_3), 62.6 (CH_2), 14.0 (Me); δ_F (377 MHz; $CDCl_3$) −61.85 (s, CF_3).

Direct Preparation of Oxazoles ***4*** *and* ***5***. *General Method C.* To a solution of the benzamide (0.32 mmol) and ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (73 mg, 0.35 mmol) in dichloromethane (1 mL) was added rhodium(II) acetate (3.1 mg, 2 mol %). The reaction vessel was sealed and heated in a microwave reactor to 80 °C for 15 min. The solution was cooled to room temperature, and phosphorus oxychloride (98 mg, 60 μL, 0.64 mmol) was added. The reaction mixture was resealed and heated in a microwave reactor to 105 °C for 20 min. The solution was again cooled to room temperature, and Amberlyst 15 (100 mg) was added. The reaction vessel was resealed and heated in a microwave reactor at 105 °C for 15 min. The solution was cooled to room temperature and filtered, and the filtrate was concentrated under reduced pressure. The residue was purified over silica using a solvent system of 10−20% ethyl acetate in light petroleum to give (i) the ethyl 2-aryl-4-trifluoromethyloxazole-5-carboxylate **5** and (ii) the ethyl 2-aryl-5-trifluoromethyloxazole-4-carboxylate **4**.

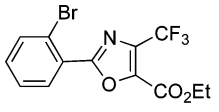


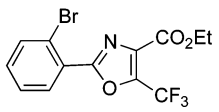


Ethyl 2-Phenyl-4-trifluoromethyloxazole-5-carboxylate ***5a*** *and Ethyl 2-Phenyl-5-trifluoromethyloxazole-4-carboxylate* ***4a***. According to General Method C, benzamide (38 mg, 0.32 mmol), ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (73 mg, 0.35 mmol), and rhodium(II) acetate (3.1 mg, 2 mol %) gave (i) ethyl 2-phenyl-4-trifluoromethyloxazole-5-carboxylate **5a** as a colorless solid (27 mg, 30%), data given above, and (ii) ethyl 2-phenyl-5-trifluoromethyloxazole-4-carboxylate **4a** as a colorless solid (16 mg, 13%): mp 59−61 °C; (lit.,[23] mp 57−58 °C); (Found: M + H^+, 286.0687. $C_{13}H_{10}F_3NO_3$ + H^+ requires 286.0686); ν_{max} ($CHCl_3$)/cm^{-1} 3011, 2929, 1735, 1608, 1549, 1486, 1450, 1399, 1382, 1363, 1329, 1315, 1299, 1177, 1157, 1013; δ_H (400 MHz, $CDCl_3$) 8.17 (2 H, d, *J* 8.0 Hz), 7.51−7.61 (3 H, m), 4.49 (2 H, q, *J* 7.2 Hz), 1.45 (3 H, t, *J* 7.2 Hz); δ_C (100 MHz; $CDCl_3$) 161.8 (C), 159.4 (C), 141.8 (q, *J* 41.1 Hz, C), 133.5 (CH), 132.2 (CH), 129.0 (CH), 127.4 (C), 125.9 (C), 118.3 (q, *J* 267.0 Hz, CF_3), 62.3 (CH_2), 13.9 (Me); δ_F (377 MHz; $CDCl_3$) −60.93 (s, CF_3).

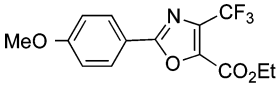


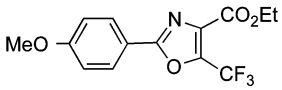
Ethyl 2-Phenyl-5-trifluoromethyloxazole-4-carboxylate ***4a*** *from Benzonitrile.* A solution of 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (420 mg, 2.0 mmol) in benzonitrile (1.5 mL) was added dropwise over a 6 h period to a stirred mixture of rhodium(II) acetate (44 mg, 5 mol %) and benzonitrile (1.5 mL) at 80 °C, and the stirring continued at this temperature for 2 h. The solvent was evaporated under vacuum and purified by chromatography using 10% ethyl acetate in petroleum ether to give ethyl 2-phenyl-5-trifluoromethyloxazole-4-carboxylate **4a** as a colorless solid (285 mg, 50%), data given in the previous experiment.



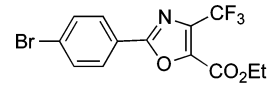


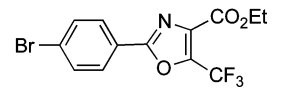
Ethyl 2-(2-Bromophenyl)-4-trifluoromethyloxazole-5-carboxylate ***5b*** *and Ethyl 2-(2-Bromophenyl)-5-trifluoromethyloxazole-4-carboxylate* ***4b***. According to General Method C, 2-bromobenzamide (64 mg, 0.32 mmol), ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (73 mg, 0.35 mmol), and rhodium(II) acetate (3.1 mg, 2 mol %) gave (i) ethyl 2-(2-bromophenyl)-4-trifluoromethyloxazole-5-carboxylate **5b** as colorless solid (40 mg, 35%), data given above, and (ii) ethyl 2-(2-bromophenyl)-5-trifluoromethyloxazole-4-carboxylate **4b** as a colorless solid (16 mg, 14%), data given above.





Ethyl 2-(4-Methoxyphenyl)-4-trifluoromethyloxazole-5-carboxylate ***5c*** *and Ethyl 2-(4-Methoxyphenyl)-5-trifluoromethyloxazole-4-carboxylate* ***4c***. According to General Method C, 4-methoxybenzamide (48 mg, 0.32 mmol), ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (73 mg, 0.35 mmol), and rhodium(II) acetate (3.1 mg, 2 mol %) gave (i) ethyl 2-(4-methoxyphenyl)-4-trifluoromethyloxazole-5-carboxylate **5c** as a colorless solid (33 mg, 33%), data given above, and (ii) ethyl 2-(4-methoxyphenyl)-5-trifluoromethyloxazole-4-carboxylate **4c** as a colorless solid (28 mg, 28%): mp 53−55 °C; (Found: M + H^+, 316.0813. $C_{14}H_{13}F_3NO_4$ + H^+ requires 316.0791); ν_{max} ($CHCl_3$)/cm^{-1} 2986, 2931 2842, 1734, 1612, 1558, 1495, 1465, 1442, 1426, 1397, 1381, 1362, 1326, 1309, 1036; δ_H (400 MHz, $CDCl_3$) 8.10 (2 H, d, *J* 8.8 Hz), 7.02 (2 H, d, *J* 8.8 Hz), 4.46 (2 H, q, *J* 7.2 Hz), 3.90 (3 H, s), 1.43 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 162.8 (C), 162.0 (C), 159.5 (C), 141.4 (q, *J* 41.1 Hz, C), 133.4 (CH), 129.4 (CH), 120.3 (q, *J* 269.9 Hz, CF_3), 117.6 (C), 114.7 (CH), 62.3 (CH_2), 55.5 (Me), 13.9 (Me); δ_F (377 MHz; $CDCl_3$) −60.84 (s, CF_3).





Ethyl 2-(4-Bromophenyl)-4-trifluoromethyloxazole-5-carboxylate ***5d*** *and Ethyl 2-(4-Bromophenyl)-5-trifluoromethyloxazole-4-carboxylate* ***4d***. According to General Method C, 4-bromobenzamide (63 mg, 0.32 mmol), ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (73 mg, 0.35 mmol), and rhodium(II) acetate (3.1 mg, 2 mol %) gave (i) ethyl 2-(4-bromophenyl)-4-trifluoromethyloxazole-5-carboxylate **5d** as a colorless solid (36 mg, 31%), data given above, and (ii) ethyl 2-(4-bromophenyl)-5-trifluoromethyloxazole-4-carboxylate **4d** as a colorless solid (26 mg, 23%): mp 47−49 °C; (Found: M + Na^+, 385.9611. $C_{13}H_9BrF_3NO_3$ + Na^+ requires 385.9616); ν_{max} ($CHCl_3$)/cm^{-1} 3691, 3606, 3011, 2928, 2855, 2360, 1740, 1603, 1571, 1459, 1398, 1379, 1361, 1317, 1239, 1153, 1047, 1027; δ_H (400 MHz, $CDCl_3$) 8.04 (2 H, d, *J* 8.0 Hz), 7.68 (2 H, d, *J* 8.0 Hz), 4.49 (2 H, q, *J* 7.2 Hz), 1.44 (3 H, t, *J* 7.2 Hz); δ_C (100 MHz; $CDCl_3$) 161.0 (C),

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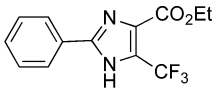
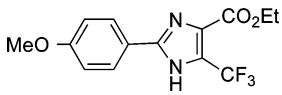
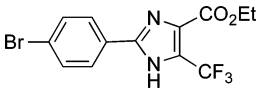
159.2 (C), 141.8 (q, *J* 41.1 Hz, C), 133.6 (C), 132.4 (CH), 128.7 (CH), 127.2 (C), 123.9 (C), 118.3 (q, *J* 269.9 Hz, CF_3), 62.3 (CH_2), 13.9 (Me); δ_F (377 MHz; $CDCl_3$) −60.91 (s, CF_3).



Imidazoles. *Ethyl 2-Phenyl-5-trifluoromethyl-1H-imidazole-4-carboxylate* ***6a.*** Ethyl 2-benzamido-4,4,4-trifluoro-3,3-dihydroxybutanoate **2a** (120 mg, 0.51 mmol), ammonium acetate (51 mg, 0.70 mmol), and glacial acetic acid (180 μL) were dissolved in toluene (4.5 mL), and the solution was heated under reflux for 3 h. The mixture was cooled, washed with brine (3 mL), dried ($MgSO_4$), and concentrated in vacuo, and the residue was purified over silica using a solvent system of 30% ethyl acetate in light petroleum to yield the title compound **6a** as a colorless solid (61 mg, 42%): mp 168−171 °C; (Found: M + Na^+, 307.0659. $C_{13}H_{11}F_3N_2O_2$ + Na^+ requires 307.0665); ν_{max} ($CHCl_3$)/cm^{-1} 3418, 3011, 1703, 1602, 1581, 1535, 1478, 1437, 1415, 1368, 1285, 1264, 1174, 1146, 1050; δ_H (400 MHz; $CDCl_3$) 14.06 (1 H, br), 8.14 (2 H, d, *J* 7.8 Hz), 7.50−7.52 (3 H, m), 4.34 (2 H, q, *J* 7.2 Hz), 1.33 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 158.4 (C), 148.3 (C), 134.1−135.2 (m, C), 130.5 (CH), 129.3 (CH), 128.7 (CH), 127.0 (C), 122.8 (C), 121.5 (q, *J* 272.8 Hz, CF_3), 61.8 (CH_2), 14.3 (Me); δ_F (377 MHz; $CDCl_3$) −59.45 (s, CF_3).

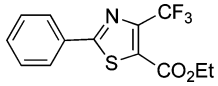


Ethyl 2-(4-Methoxyphenyl)-5-trifluoromethyl-1H-imidazole-4-carboxylate ***6b.*** Ethyl 2-(4-methoxybenzamido)-4,4,4-trifluoro-3,3-dihydroxybutanoate **2c** (63 mg, 0.19 mmol), ammonium acetate (22 mg, 0.29 mmol), and glacial acetic acid (86 μL) were dissolved in toluene (2.2 mL), and the solution was heated under reflux for 2 h. Work up as for compound **6a** gave the title compound **6b** as a colorless solid (27 mg, 45%): mp 175−177 °C; (Found: M + H^+, 315.0938. $C_{14}H_{14}F_3N_2O_3$ + H^+ requires 315.0951); ν_{max} ($CHCl_3$)/cm^{-1} 3419, 2989, 1704, 1602, 1581, 1535, 1478, 1437, 1415, 1368, 1285, 1264, 1174, 1146, 1050; δ_H (400 MHz; $CDCl_3$) 13.86 (1H, br), 8.09 (2 H, d, *J* 8.0 Hz), 7.07 (2 H, d, *J* 8.0 Hz), 4.36 (2 H, q, *J* 7.2 Hz), 3.82 (3 H, s), 1.33 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 161.1 (C), 158.4 (C), 148.4 (C), 134.0−135.0 (m, C), 129.3 (CH), 126.9 (C), 122.2 (C), 121.5 (q, *J* 272.8 Hz, CF_3), 114.7 (CH), 61.7 (CH_2), 55.8 (Me), 14.3 (Me); δ_F (377 MHz; $CDCl_3$) −59.41 (s, CF_3).

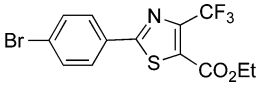


Ethyl 2-(4-Bromophenyl)-5-trifluoromethyl-1H-imidazole-4-carboxylate ***6c.*** Ethyl 2-(4-bromobenzamido)-4,4,4-trifluoro-3,3-dihydroxybutanoate **2d** (150 mg, 0.54 mmol), ammonium acetate (54 mg, 0.70 mmol), and glacial acetic acid (210 μL) were dissolved in toluene (5.3 mL), and the solution was heated under reflux for 2 h. Work up as for compound **6a** gave the title compound **6c** as a colorless solid (78 mg, 40%), mp 184−186 °C; (Found: M + H^+, 362.9950. $C_{13}H_{11}{}^{79}BrF_3N_2O_2$ + H^+ requires 362.9951); ν_{max} ($CHCl_3$)/cm^{-1} 3420, 3012, 1704, 1601, 1581, 1535, 1478, 1437, 1415, 1368, 1285, 1265, 1174, 1146, 1071, 1050; δ_H (400 MHz; $CDCl_3$) 14.18 (1H, br), 8.09 (2 H, d, *J* 8.0 Hz), 7.73 (2 H, d, *J* 8.0 Hz), 4.37 (2 H, q, *J* 7.2 Hz), 1.33 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 158.3 (C), 147.3 (C), 133.8−135.1 (m, C), 132.3 (CH), 128.9 (CH), 128.4 (C), 128.1 (C), 124.0 (C), 123.2 (C), 121.5 (q, *J* 272.8 Hz, CF_3), 61.8 (CH_2), 14.3 (Me); δ_F (377 MHz; $CDCl_3$) −59.49 (s, CF_3).

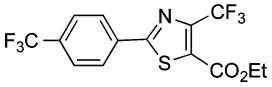
Thiazoles. *General Method D.* To the thiobenzamide (0.22 mmol) and ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (51 mg, 0.24 mmol) in 1,2-dichloroethane (1 mL) was added rhodium(II) heptafluorobutyramide (5.0 mg, 2 mol %). The reaction vessel was sealed and heated in a microwave reactor to 125 °C for 30 min. The reaction vessel was allowed to cool to room temperature, and DBU (100 mg, 0.66 mmol) was added. The reaction mixture was resealed and stirred at room temperature for 20 min. The solvent was removed under reduced pressure, and the residue was purified over silica using a solvent system of 15% diethyl ether in light petroleum to give the ethyl 2-aryl-4-trifluoromethylthiazole-5-carboxylate 7.



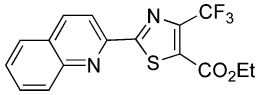
Ethyl 2-Phenyl-4-trifluoromethylthiazole-5-carboxylate ***7a.*** According to General Method D, thiobenzamide (30 mg, 0.22 mmol), ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (51 mg, 0.24 mmol), and rhodium(II) heptafluorobutyramide (5.0 mg, 2 mol %) gave the title compound **7a** as a colorless solid (43 mg, 64%): mp 109−111 °C (lit.,[39] no data); (Found: M + Na^+, 324.0274. $C_{13}H_{10}F_3NO_2S$ + Na^+ requires 324.0282); ν_{max} ($CHCl_3$)/cm^{-1} 3689, 3012, 1733, 1602, 1531, 1458, 1432, 1372, 1355, 1302, 1271, 1170; δ_H (400 MHz; $CDCl_3$) 8.02−7.99 (2 H, m), 7.56−7.47 (3 H, m), 4.43 (2 H, q, *J* 7.2 Hz), 1.42 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 170.6 (C), 159.1 (C), 146.8 (q, *J* 37.9 Hz, C), 131.9 (CH), 131.8 (C), 129.4 (C), 129.2 (CH), 126.9 (CH), 119.8 (q, *J* 272.8 Hz, CF_3), 62.6 (CH_2), 14.0 (Me); δ_F (377 MHz; $CDCl_3$) −60.97 (s, CF_3).



Ethyl 2-(4-Bromophenyl)-4-trifluoromethylthiazole-5-carboxylate ***7b.*** According to General Method D, 4-bromothiobenzamide (60 mg, 0.28 mmol), ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (70 mg, 0.34 mmol), and rhodium(II) heptafluorobutyramide (7.2 mg, 2 mol %) gave the title compound **7b** as a colorless solid (67 mg, 63%): mp 94−96 °C; (Found: M + Na^+, 401.9383. $C_{13}H_9{}^{79}BrF_3NO_2S$ + Na^+ requires 401.9387); ν_{max} ($CHCl_3$)/cm^{-1} 3011, 1735, 1591, 1533, 1443, 1396, 1371, 1299, 1271, 1240, 1169, 1091, 1073, 1013; δ_H (400 MHz; $CDCl_3$) 7.88−7.85 (2 H, m), 7.65−7.62 (2 H, m), 4.43 (2 H, q, *J* 7.2 Hz), 1.42 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 169.2 (C), 158.9 (C), 146.9 (q, *J* 38.0 Hz, C), 132.5 (CH), 130.7 (C), 129.8−129.8 (m, C), 128.3 (CH), 126.5 (C), 119.7 (q, *J* 272.8 Hz, CF_3), 62.7 (CH_2), 14.0 (Me); δ_F (377 MHz; $CDCl_3$) −60.98 (s, CF_3).

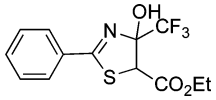


Ethyl 4-Trifluoromethyl-2-(4-(trifluoromethyl)phenyl)thiazole-5-carboxylate ***7c.*** According to General Method D, 4-trifluoromethythiobenzamide (60 mg, 0.29 mmol), ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (74 mg, 0.31 mmol), and rhodium(II) heptafluorobutyramide (6.5 mg, 2 mol %) gave the title compound **7c** as a colorless solid (70 mg, 65%): mp 80−82 °C (lit.,[40] no data); (Found: M + Na^+, 392.0149. $C_{14}H_9F_6NO_2S$ + Na^+ requires 392.0156); ν_{max} ($CHCl_3$)/cm^{-1} 3012, 1736, 1523, 1447, 1409, 1372, 1325, 1302, 1272, 1172, 1112, 1091, 1069, 1018; δ_H (400 MHz; $CDCl_3$) 8.12 (2 H, d, *J* 8.0 Hz), 7.76 (2 H, d, *J* 8.0 Hz), 4.45 (2 H, q, *J* 7.2 Hz), 1.43 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 168.4 (C), 158.8 (C), 147.1 (q, *J* 38.1 Hz, C), 134.8 (C), 133.3 (q, *J* 33.0 Hz, C), 130.7−130.7 (m, C), 127.2 (CH), 126.3 (q, *J* 3.6 Hz, CH), 123.5 (q, *J* 272.5 Hz, CF_3), 119.7 (q, *J* 272.9 Hz, CF_3), 62.9 (CH_2), 14.0 (Me); δ_F (376 MHz; $CDCl_3$) −60.99 (s, CF_3), −63.08 (s, CF_3).

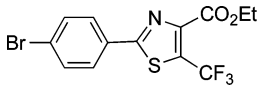


Ethyl 2-(Quinolin-2-yl)-4-trifluoromethylthiazole-5-carboxylate ***7d.*** According to General Method D, quinoline-2-thiocarboxamide (52.6 mg, 0.28 mmol), ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1**

(70 mg, 0.34 mmol), and rhodium(II) heptafluorobutyramide (7.2 mg, 2 mol %) gave the title compound **7d** as a colorless solid (67 mg, 68%): mp 143−147 °C; (Found: M + H^+, 353.0578. $C_{16}H_{12}F_3N_2O_2S$ + H^+ requires 353.0566); ν_{max} ($CHCl_3$)/cm^{-1} 2987, 1735, 1594, 1484, 1409, 1372, 1352, 1302, 1298, 1260, 1171, 1152, 1092, 1013; δ_H (400 MHz; $CDCl_3$) 8.39 (1 H, d, *J* 8.0 Hz), 8.33 (1 H, d, *J* 8.0 Hz), 8.16 (1 H, d, *J* 8.0 Hz), 7.90 (1 H, d, *J* 8.0 Hz), 7.81 (1 H, t, *J* 8.0 Hz), 7.65 (1 H, t, *J* 8.0 Hz), 4.45 (2 H, q, *J* 7.2 Hz); 1.43 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 171.7 (C), 159.2 (C), 149.6 (C), 147.7 (C), 146.7 (q, *J* 38.1 Hz, C), 137.4 (CH), 132.1 (CH), 130.5 (CH), 129.6 (C), 129.2 (C), 128.0 (CH), 127.8 (CH), 120.5 (q, *J* 272.5 Hz, CF_3), 117.5 (CH), 62.9 (CH_2), 14.0 (Me); δ_F (376 MHz; $CDCl_3$) −61.11 (s, CF_3).

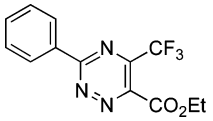


Ethyl 4-Hydroxy-2-phenyl-4-trifluoromethyl-4,5-dihydrothiazole-5-carboxylate ***8***. To thiobenzamide (30 mg, 0.22 mmol) and ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (51 mg, 0.24 mmol) in 1,2-dichloroethane (1 mL) was added rhodium(II) heptafluorobutyramide (5.1 mg, 2 mol %). The reaction vessel was sealed and heated in a microwave reactor to 125 °C for 30 min. The reaction vessel was allowed to cool to room temperature, and the solvent was removed under reduced pressure. The residue was purified over silica using a solvent system of 8% ethyl acetate in light petroleum. The title compound **8** was isolated as a colorless solid (38 mg, 54%): mp 109−111 °C; (Found: M + Na^+, 342.0377. $C_{13}H_{12}F_3NO_3S$ + Na^+ requires 342.0388); ν_{max} ($CHCl_3$)/cm^{-1} 3566, 3011, 2360, 1740, 1606, 1578, 1493, 1449, 1372, 1312, 1192, 1138; δ_H (400 MHz; $CDCl_3$) 7.91−7.88 (2 H, m), 7.60−7.55 (1 H, m), 7.48−7.44 (2 H, m), 4.84 (1 H, s), 4.72 (1 H, s), 4.38−4.26 (2 H, m), 1.34 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 174.8 (C), 167.8 (C), 133.1 (CH), 131.0 (C), 128.9 (CH), 128.8 (CH), 123.0 (q, *J* 286.3 Hz, CF_3), 106.4 (q, *J* 31.1 Hz, C), 63.0 (CH_2), 53.1 (CH), 13.9 (Me); δ_F (377 MHz; $CDCl_3$) −83.08 (s, CF_3).

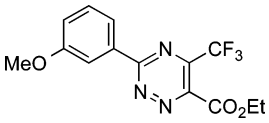


Ethyl 2-(4-Bromophenyl)-5-trifluoromethylthiazole-4-carboxylate ***9***. A solution of ethyl 2-(4-bromobenzamido)-4,4,4-trifluoro-3,3-dihydroxybutanoate **2d** (150 mg, 0.46 mmol) and Lawesson's reagent (282 mg, 0.70 mmol) in dry THF (2.5 mL) was heated to reflux for 4 h. The reaction mixture was then evaporated in vacuo, and the residue was purified over silica gel eluting with ethyl acetate−light petroleum (3:7) to yield the title compound **9** as a colorless solid (78 mg, 45%): mp 108−110 °C; (Found: M + Na^+, 401.9383. $C_{13}H_9{}^{79}BrF_3NO_2S$ + Na^+ requires 401.9387); ν_{max} ($CHCl_3$)/cm^{-1} 3007, 2941 1734, 1590, 1569, 1454, 1335, 1288, 1248, 1165, 1072, 1031; δ_H (400 MHz; $CDCl_3$) 7.88 (2 H, d, *J* 8.0 Hz), 7.65 (2 H, d, *J* 8.0 Hz), 4.50 (2 H, q, *J* 7.2 Hz), 1.45 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 167.5 (C), 160.0 (C), 146.6 (C), 132.5 (CH), 130.6 (q, *J* 3.6 Hz, CH), 130.5 (C), 128.4 (CH), 126.4 (C), 121.0 (q, *J* 272.8 Hz, CF_3), 62.5 (CH_2), 13.9 (Me); δ_F (377 MHz; $CDCl_3$) −52.47 (s, CF_3).

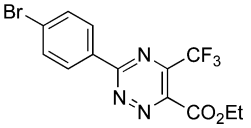
1,2,4-Triazines. *General Method E.* To ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (108 mg, 0.51 mmol) and the benzhydrazide (0.73 mmol) in dichloromethane (1 mL) was added anhydrous copper(II) acetate (2.8 mg, 3 mol %). The reaction vessel was sealed and heated in a microwave reactor to 80 °C for 10 min. The solvent was removed under reduced pressure, and acetic acid (0.5 mL) was added. To the acetic acid solution was added ammonium acetate (198 mg, 2.57 mmol), and the reaction mixture was heated in a microwave reactor to 110 °C for 5 min. The reaction mixture was allowed to cool to room temperature and was neutralized with saturated sodium hydrogen carbonate solution (5 mL). The organic material was extracted with ethyl acetate (3 × 10 mL), washed with brine (10 mL), and dried over $MgSO_4$. The mixture was filtered, and the filtrate was concentrated under reduced pressure. The residue was purified over silica using 10% ethyl acetate in light petroleum to give the ethyl 3-aryl-5-trifluoromethyl-1,2,4-triazine-6-carboxylate **10**.



Ethyl 3-Phenyl-5-trifluoromethyl-1,2,4-triazine-6-carboxylate ***10a***. According to General Method E, ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (108 mg, 0.51 mmol), benzhydrazide (100 mg, 0.73 mmol), and anhydrous copper(II) acetate (2.8 mg, 3 mol %) gave the title compound **10a** as a yellow solid (45 mg, 28%): mp 114−116 °C (lit.,[41] no data); (Found: M + Na^+, 320.0614. $C_{13}H_{10}F_3N_3O_2$ + Na^+ requires 320.0622); ν_{max} ($CHCl_3$)/cm^{-1} 3066, 1746, 1602, 1537, 1474, 1406, 1395, 1316, 1286, 1174, 1081; δ_H (400 MHz; $CDCl_3$) 8.67−8.64 (2 H, m), 7.69−7.59 (3 H, m), 4.60 (2 H, t, *J* 7.2 Hz), 1.49 (3 H, q, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 163.9 (C), 162.3 (C), 147.0 (C), 145.9 (q, *J* 38.8 Hz, C), 133.6 (CH), 132.5 (C), 129.3 (CH), 129.3 (CH), 119.8 (q, *J* 276.9, CF_3), 63.7 (CH_2), 13.9 (Me); δ_F (377 MHz; $CDCl_3$) −67.12 (s, CF_3).

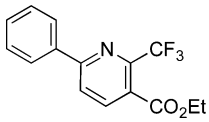


Ethyl 3-(3-Methoxyphenyl)-5-trifluoromethyl-1,2,4-triazine-6-carboxylate ***10b***. According to General Method E, ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (108 mg, 0.51 mmol), 3-methoxybenzhydrazide (121 mg, 0.75 mmol), and anhydrous copper(II) acetate (2.8 mg, 3 mol %) gave the title compound **10b** as a yellow solid (57 mg, 35%): mp 78−82 °C; (Found: M + Na^+, 350.0731. $C_{14}H_{12}F_3N_3O_3$ + Na^+ requires 350.0723); ν_{max} ($CHCl_3$)/cm^{-1} 3682, 3011, 1746, 1601, 1533, 1494, 1458, 1406, 1393, 1374, 1287, 1174, 1080; δ_H (400 MHz; $CDCl_3$) 8.25 (1 H, d, *J* 8.0 Hz), 8.18 (1 H, s), 7.52 (1 H, t, *J* 8.0 Hz), 7.22 (1 H, d, *J* 8.0 Hz), 4.60 (2 H, q, *J* 7.2 Hz), 3.96 (3 H, s), 1.50 (3 H, t, *J* 7.2 Hz); δ_C (100 MHz; $CDCl_3$) 163.7 (C), 162.2 (C), 160.3 (C), 147.1 (C), 146.1 (q, *J* 38.0 Hz, C), 133.8 (C), 130.3 (CH), 123.9 (CH), 121.8 (CH), 120.1 (CH), 119.6 (q, *J* 275.0, CF_3), 113.5 (CH), 63.7 (CH_2), 55.5 (Me), 13.9 (Me); δ_F (377 MHz; $CDCl_3$) −67.11 (s, CF_3).

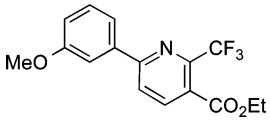


Ethyl 3-(4-Bromophenyl)-5-trifluoromethyl-1,2,4-triazine-6-carboxylate ***10c***. According to General Method E, ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate **1** (108 mg, 0.51 mmol), 4-bromobenzohydrazide (155 mg, 0.75 mmol), and anhydrous copper(II) acetate (2.8 mg, 3 mol %) gave the title compound **10c** as a yellow solid (59 mg, 31%): mp 88−93 °C; (Found: M + Na^+, 397.9710. $C_{13}H_9{}^{79}BrF_3N_3O_2$ + Na^+ requires 397.9722); ν_{max} ($CHCl_3$)/cm^{-1} 3691, 2988, 1746, 1592, 1534, 1446, 1412, 1391, 1303, 1288, 1175, 1076; δ_H (400 MHz; $CDCl_3$) 8.53 (2 H, d, *J* 8.0 Hz), 7.77 (2 H, d, *J* 8.0 Hz), 4.60 (2 H, q, *J* 7.2 Hz), 1.49 (3 H, t, *J* 7.2 Hz); δ_C (100 MHz; $CDCl_3$) 163.2 (C), 162.1 (C), 147.2 (C), 146.1 (q, *J* 39.0 Hz, C), 132.7 (CH), 131.4 (C), 130.6 (CH), 128.9 (C), 119.5 (q, *J* 275.0, CF_3), 63.7 (CH_2), 13.9 (Me); δ_F (377 MHz; $CDCl_3$) −67.09 (s, CF_3).

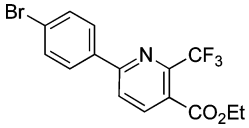
Pyridines. *General Method F.* The ethyl 3-aryl-5-trifluoromethyl-1,2,4-triazine-6-carboxylate **10** (0.044 mmol) was dissolved in chlorobenzene (0.5 mL), and norbornadiene (40.0 mg, 0.437 mmol, 44.5 μL) was added. The reaction vessel was sealed and heated to 131 °C for 5 h. The reaction mixture was allowed to cool to room temperature, and the solvent was removed under reduced pressure. The residue was purified over silica using a solvent system of 10% ethyl acetate in light petroleum to give the ethyl 6-aryl-2-trifluoromethylnicotinate **11**.



Ethyl 6-Phenyl-2-trifluoromethylnicotinate ***11a***. According to General Method F, ethyl 3-phenyl-5-trifluoromethyl-1,2,4-triazine-6-carboxylate **10a** (13.0 mg, 0.044 mmol) and norbornadiene (40.0 mg, 0.437 mmol, 44.5 μL) gave the title compound **11a** as a colorless solid (11.5 mg, 89%): mp 32−35 °C; (Found: M + Na^+, 318.0707. $C_{15}H_{12}F_3NO_2$ + Na^+ requires 318.0718); ν_{max} ($CHCl_3$)/cm^{-1} 2987, 1729, 1595, 1462, 1451, 1397, 1370, 1223, 1302, 1283, 1192, 1154, 1074, 1057, 1015; δ_H (400 MHz; $CDCl_3$) 8.19 (1 H, d, *J* 8.3 Hz), 8.13−8.10 (2 H, m), 7.98 (1 H, d, *J* 8.3 Hz), 7.55−7.48 (3 H, m), 4.45 (2 H, q, *J* 7.2 Hz), 1.43 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 165.6 (C), 158.4 (C), 145.6 (q, *J* 35.2 Hz, C), 139.4 (CH), 136.8 (C), 130.5 (CH), 129.0 (CH), 127.3 (CH), 125.8 (C), 121.8 (CH), 120.9 (q, *J* 275.4 Hz, CF_3), 62.5 (CH_2), 13.9 (Me); δ_F (377 MHz; $CDCl_3$) −64.38 (s, CF_3).



Ethyl 6-(3-Methoxyphenyl)-2-trifluoromethylnicotinate ***11b***. According to General Method F, ethyl 3-(3-methoxyphenyl)-5-trifluoromethyl-1,2,4-triazine-6-carboxylate **10b** (14.3 mg, 0.04 mmol) and norbornadiene (40.0 mg, 0.43 mmol, 44.5 μL) gave the title compound **11b** as a colorless solid (12.2 mg, 86%): mp 96−98 °C; (Found: M + Na^+, 348.0830. $C_{16}H_{14}F_3NO_3$ + Na^+ requires 348.0823); ν_{max} ($CHCl_3$)/cm^{-1} 3691, 3011, 2987, 1731, 1592, 1493, 1460, 1415, 1369, 1321, 1192, 1154, 1075, 1058, 1010; δ_H (400 MHz; $CDCl_3$) 8.20 (1 H, d, *J* 8.3 Hz), 7.98 (1 H, d, *J* 8.3 Hz), 7.72 (1 H, s), 7.68 (1 H, d, *J* 8.3 Hz), 7.45 (1 H, t, *J* 8.3 Hz), 7.07 (1 H, d, *J* 8.3 Hz), 4.45 (2 H, q, *J* 7.2 Hz), 3.93 (3 H, s), 1.43 (3 H, t, *J* 7.2 Hz); δ_C (126 MHz; $CDCl_3$) 165.6 (C), 160.2 (C), 158.4 (C), 145.6 (q, *J* 35.2 Hz, C), 139.4 (CH), 138.2 (C), 130.0 (CH), 125.9 (CH), 121.9 (CH)), 120.9 (q, *J* 275.4 Hz, CF_3), 119.6 (C), 116.2 (CH) 112.7 (CH), 62.5 (CH_2), 55.4 (Me) 13.9 (Me); δ_F (377 MHz; $CDCl_3$) −64.43 (s, CF_3).



Ethyl 6-(4-Bromophenyl)-2-trifluoromethylnicotinate ***11c***. According to General Method F, ethyl 3-(4-bromophenyl)-5-trifluoromethyl-1,2,4-triazine-6-carboxylate **10c** (16.4 mg, 0.044 mmol) and norbornadiene (40.0 mg, 0.437 mmol, 44.5 μL) gave the title compound **11c** as a colorless oil (14.8 mg, 91%): (Found: M + Na^+, 395.9829. $C_{15}H_{11}{}^{79}BrF_3NO_2$ + Na^+ requires 395.9823); ν_{max} ($CHCl_3$)/cm^{-1} 3008, 2941, 1731, 1594, 1495, 1466, 1393, 1369, 1292, 1192, 1153, 1074, 1057, 1015; δ_H (400 MHz; $CDCl_3$) 8.20 (1 H, d, *J* 8.3 Hz), 8.02 (1 H, d, *J* 8.3 Hz), 7.97-8.03 (3 H, m), 7.68 (1 H, d, *J* 8.3 Hz), 4.47 (2 H, q, *J* 7.2 Hz), 1.44 (3 H, t, *J* 7.2 Hz); δ_C (100 MHz; $CDCl_3$) 165.5 (C), 157.2 (C), 145.6 (q, *J* 35.2 Hz, C), 139.6 (C), 135.6 (C), 132.2 (CH), 128.8 (CH), 126.1 (CH), 125.3 (CH), 121.5 (C), 120.5 (q, *J* 275.4 Hz, CF_3), 62.5 (CH_2), 13.9 (Me); δ_F (377 MHz; $CDCl_3$) −64.37 (s, CF_3).

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^1H and ^{13}C NMR spectra for all compounds, X-ray figures (ORTEP), and X-ray CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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