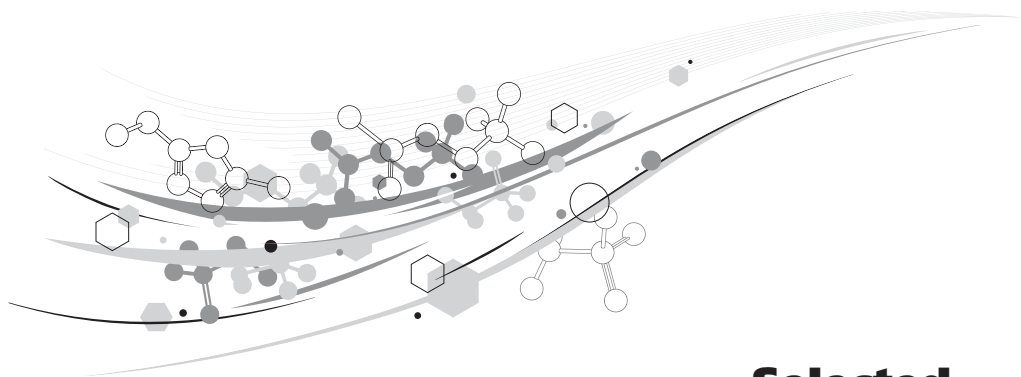


FLUORINATED ALIPHATIC AMINES





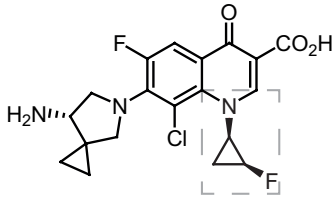
Selected Building Block Series

With development of on-line chemical directories acquiring necessary reagents and building blocks for day-to-day research activity has become a technical routine. Many thousands of building blocks are now available in the market and sub-structure search can efficiently provide a selection of reagents to buy. However, this approach might be limited.

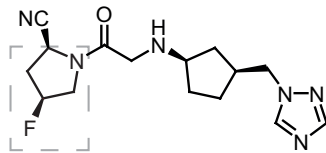
With over 100,000 building blocks synthesized and now available from our stock we are a recognized leader in the market. Our catalogue features versatile building block classes and adds 1,000 products each month. Although they all are available for purchase through www.enaminestore.com and many public or corporate chemical databases we wanted to gather together the most interesting and recently prepared building blocks to provide a series of useful guides to a novel and innovative chemistry.

Fluorinated aliphatic amines

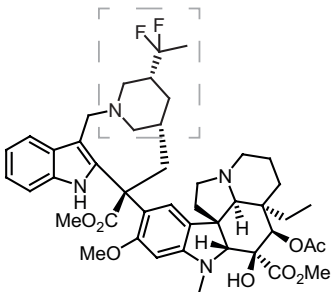
Motifs of fluorinated aliphatic amines are common in drug discovery.



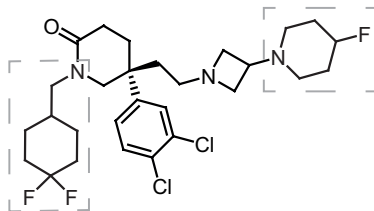
Citafloxacin
Daiichi Sankyo Co., 2008



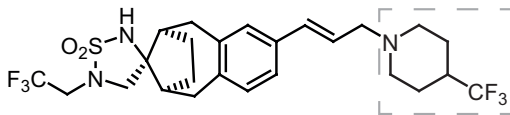
Melogliptin
Glenmark Pharm., 2006



Vinflunine
Laboratoires Pierre Fabre, 1998

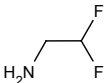
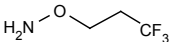
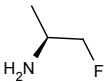
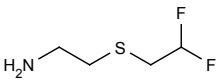
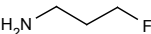
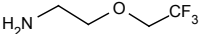
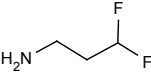
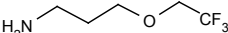
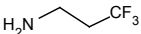
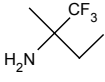
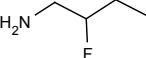
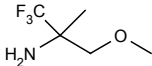

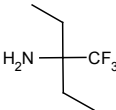

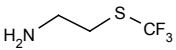


Antiurinary agent
Pfizer Inc., 2002



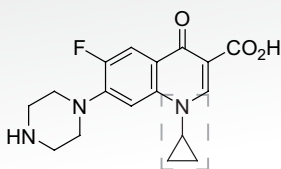
Nootropic agent
Marck Research Laboratories, 2005

Linear amines

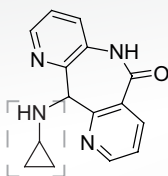
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<p>EN300-102325</p> <p>HCl</p>		<p>EN300-74923</p>	
<p>EN300-84693</p>		<p>EN300-35000</p> <p>HCl</p>	
<p>EN300-69309</p> <p>HCl</p>		<p>EN300-32020</p>	
<p>EN300-41781</p> <p>HCl</p>		<p>EN300-93182</p> <p>HCl</p>	
<p>EN300-100456</p> <p>HCl</p>		<p>EN300-94944</p> <p>HCl</p>	
<p>EN300-101814</p> <p>HCl</p>		<p>EN300-93912</p> <p>HCl</p>	
<p>EN300-90872</p>		<p>EN300-40766</p>	

***trans*-2-(Trifluoromethyl)-cyclopropanamine**

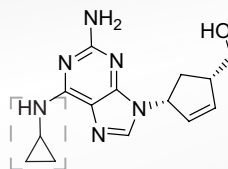
Fragment of cyclopropanamine is common in approved drugs:



Ciprofloxacin

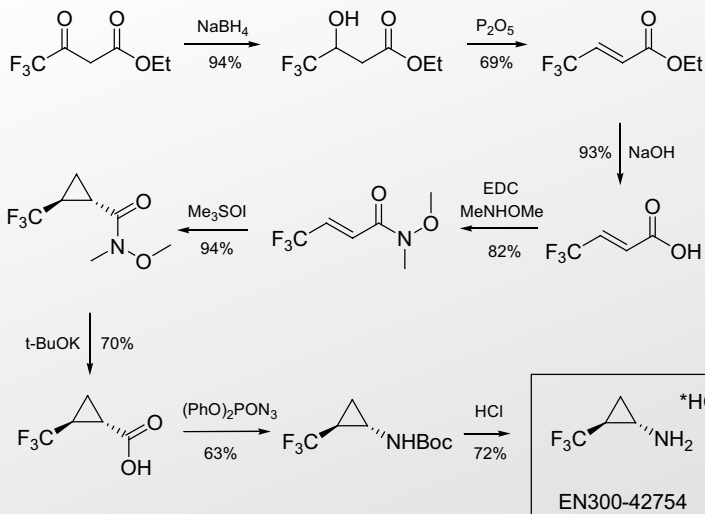


Nevirapine



Abocavir

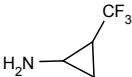
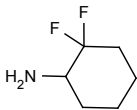

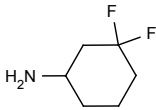
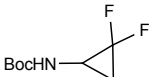
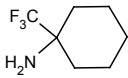
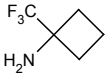
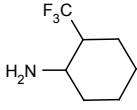
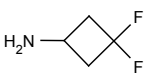
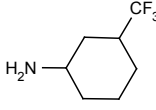
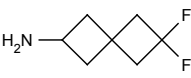
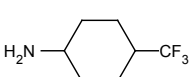
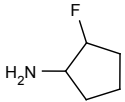
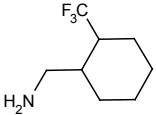
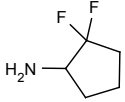
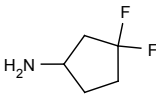
Recently we developed a practical synthesis of the novel building block:
trans-2-(trifluoromethyl)-cyclopropanamine.^{1,2}



1. A. V. Bezdudny et al. *Synthesis* **2011**, 1, 119.

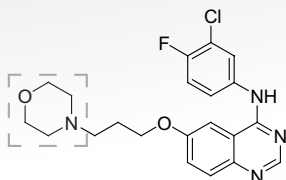
2. V. S. Yarmolchuk et al. *Synthesis* **2012**, 44, 1152.

Exocyclic amines

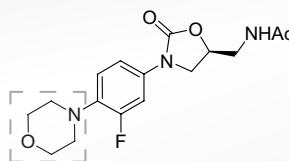
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<p>EN300-79761</p>		<p>EN300-112279</p> <p>HCl</p>	
<p>EN300-74868</p>		<p>EN300-75524</p> <p>HCl</p>	
<p>EN300-94391</p> <p>HCl</p>		<p>EN300-27688</p>	
<p>EN300-78062</p> <p>HCl</p>		<p>EN300-26926</p>	
<p>EN300-90484</p>		<p>EN300-27291</p>	
<p>EN300-115151</p> <p>HCl</p>		<p>EN300-96312</p>	
<p>EN300-99908</p> <p>HCl</p>		<p>EN300-109808</p> <p>HCl</p>	

Trifluoromethylated morpholines

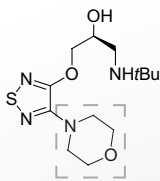
Motif of morpholine is highly common in drug discovery. Many FDA-approved drugs contain morpholine moiety.



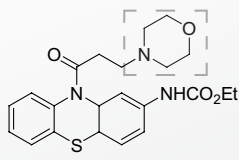
Gefitinib



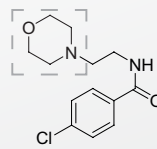
Linezolid



Timolol

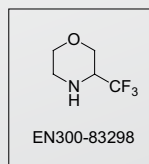
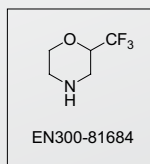
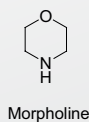


Moricizine



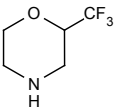
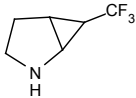
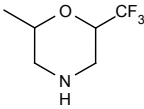
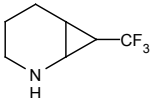
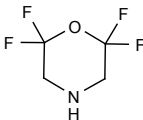
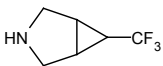
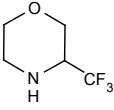
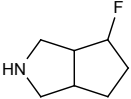
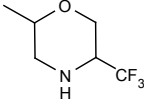
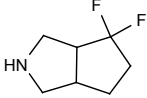
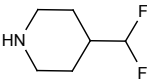
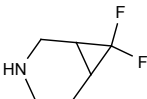
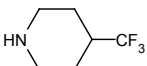
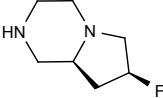
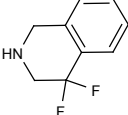
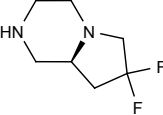
Moclobenide

Recently we developed a practical approach to trifluoromethylated morpholines. The trifluoromethyl substituent multidimensionally tuned the metabolic stability, basicity and lipophilicity of the parent structure.¹




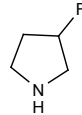
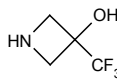
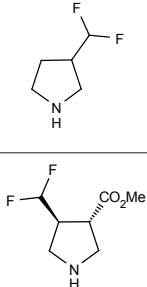

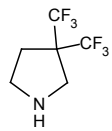
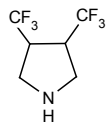


1. A. V. Shcherbatiuk et al. *Tetrahedron* 69 2013, 3796-3804.

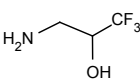
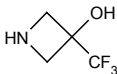
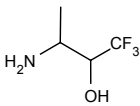
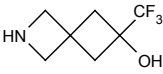
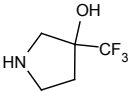
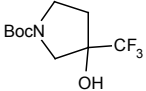
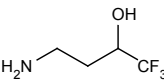
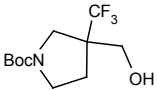
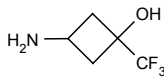
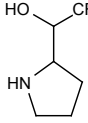
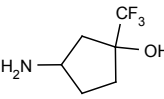
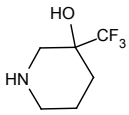
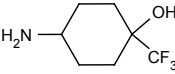
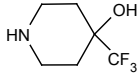
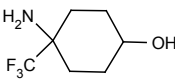
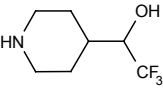
Morpholines, Piperidines and Bicyclic amines

<p>EN300-81684</p> <p>HCl</p>		<p>EN300-97937</p> <p>HCl</p>	
<p>EN300-90726</p>		<p>EN300-79100</p> <p>HCl</p>	
<p>EN300-52620</p>		<p>EN300-73968</p> <p>HCl</p>	
<p>EN300-83298</p> <p>HCl</p>		<p>EN300-113369</p> <p>HCl</p>	
<p>EN300-90738</p>		<p>EN300-109987</p> <p>HCl</p>	
<p>EN300-110108</p> <p>HCl</p>		<p>EN300-100245</p> <p>HCl</p>	
<p>EN300-93067</p>		<p>EN300-73116</p> <p>2HCl</p>	
<p>EN300-113083</p> <p>HCl</p>		<p>EN300-73117</p> <p>2HCl</p>	

Azetidines and Pyrrolidines

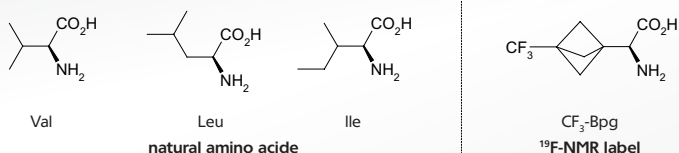
EN300-89727		EN300-100104	
HCl	EN300-110434	HCl	EN300-89584
EN300-94689		EN300-89757	
HCl	EN300-108152	HCl	EN300-102456
EN300-107382		EN300-109585	
HCl	EN300-116702	HCl	EN300-73354
EN300-90481		EN300-79916	
HCl	EN300-105150	EN300-95926	
HCl		HCl	

Amino alcohols

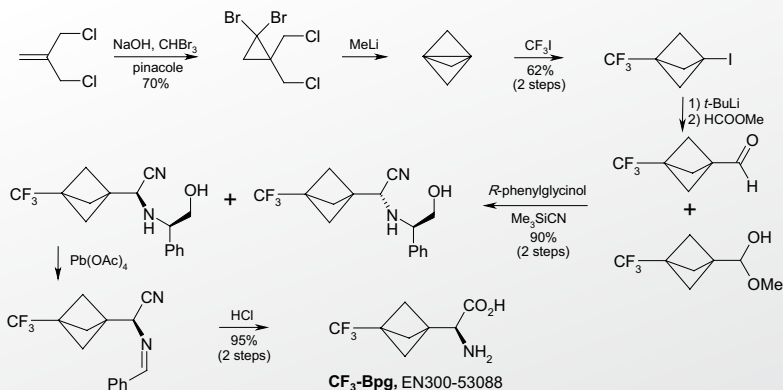
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<p>EN300-29780</p> <p>HCl</p>		<p>EN300-105150</p> <p>HCl</p>	
<p>EN300-84068</p> <p>HCl</p>		<p>EN300-89625</p>	
<p>EN300-74756</p> <p>HCl</p>		<p>EN300-102059</p>	
<p>EN300-111534</p> <p>HCl</p>		<p>EN300-71887</p> <p>HCl</p>	
<p>EN300-82765</p> <p>HCl</p>		<p>EN300-80830</p>	
<p>EN300-112237</p> <p>HCl</p>		<p>EN300-58599</p>	
<p>EN300-82572</p>		<p>EN300-110084</p> <p>HCl</p>	

¹⁹F NMR label for peptide studies

Fluorinated amino acid 3-(trifluoromethyl)bicyclo[1.1.1]hept-2-ylglycine, (CF_3 -Bpg), was designed,¹ synthesized^{1,2} and validated¹ as a ¹⁹F NMR label for structure analysis of membrane active peptides. The amino acid is perfectly suited to replace the residues of Val, Ile and Leu in peptides.



Synthesis:



Amino acid CF_3 -Bpg was already used to study the structure of several membrane-active peptides:³ gramicidin S, PGLa, SAP, (KIGAKI)₃, Magainin 2, Temporin A and to evaluate the coil-coiled interactions within a polypeptide sequence.⁴

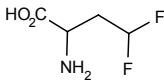
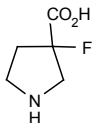
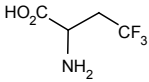
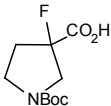
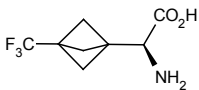
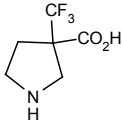
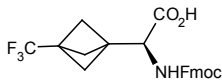
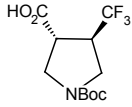
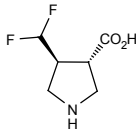
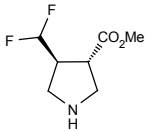
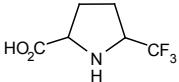
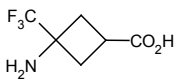
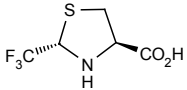
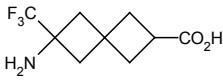
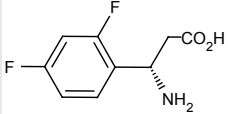
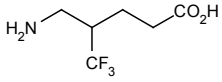
¹ P. K. Mikhailiuk et al. *Angew. Chem. Int. Ed.* **2006**, *45*, 5659.

² P. K. Mikhailiuk et al. *Fluorine Chem.* **2010**, *131*, 217.

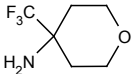
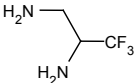
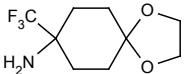
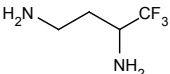
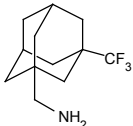
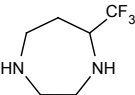
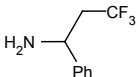
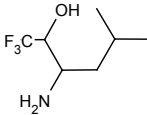
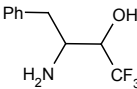
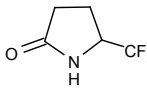
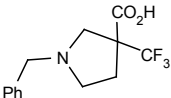
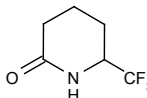
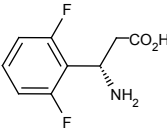
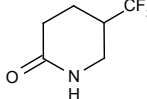
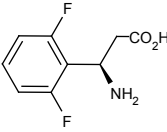
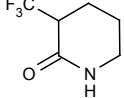
³ V. S. Kubyskhin et al. in *Fluorine in Pharmaceutical and Medicinal Chemistry: From Biophysical Aspects to Clinical Applications*. (Eds.: V. Gouverneur, K. Muller), Imperial College Press, London, **2012**, 91.

⁴ M. Salwiczek et al. *Amino Acids* **2010**, *39*, 1589.

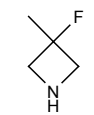
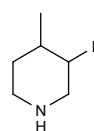
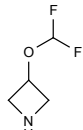
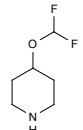
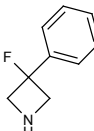
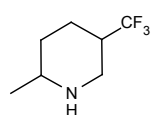
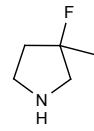
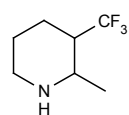
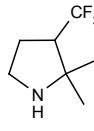
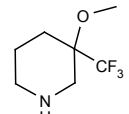
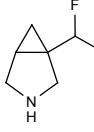
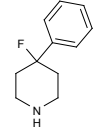
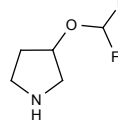
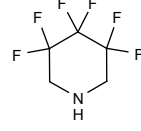
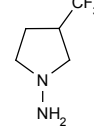
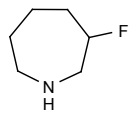
Amino acids

<p>EN300-65367</p>		<p>EN300-96908</p> <p>HCl</p>	
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<p>EN300-53088</p>		<p>EN300-61407</p> <p>HCl</p>	
<p>EN300-89327</p>		<p>EN300-76959</p>	
<p>EN300-110322</p> <p>HCl</p>		<p>EN300-109585</p> <p>HCl</p>	
<p>EN300-75802</p> <p>HCl</p>		<p>EN300-74301</p> <p>HCl</p>	
<p>EN300-34890</p>		<p>EN300-74493</p> <p>HCl</p>	
<p>EN300-85544</p> <p>HCl</p>		<p>EN300-07164</p> <p>HCl</p>	


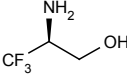
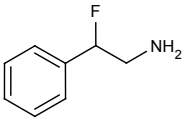
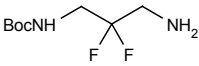
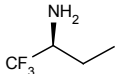
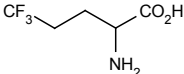
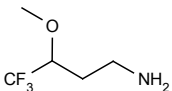
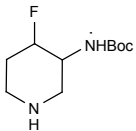

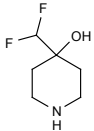
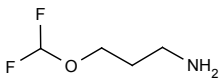
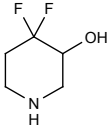
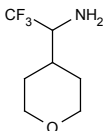
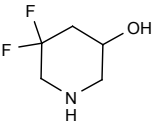
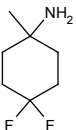
Diverse derivatives

<p>EN300-93520</p> <p>HCl</p>		<p>EN300-109961</p> <p>2HCl</p>	
<p>EN300-97552</p>		<p>EN300-74445</p> <p>2HCl</p>	
<p>EN300-116549</p> <p>HCl</p>		<p>EN300-78514</p> <p>2HCl</p>	
<p>EN300-50504</p>		<p>EN300-30697</p>	
<p>EN300-40849</p>		<p>EN300-90523</p>	
<p>EN300-58944</p>		<p>EN300-78403</p>	
<p>EN300-67015</p>		<p>EN300-29977</p>	
<p>EN300-84859</p> <p>HCl</p>		<p>EN300-35893</p>	

New Arrivals

<p>EN300-124674</p> <p>HCl</p>		<p>EN300-127532</p> <p>HCl</p>	
<p>EN300-156761</p> <p>HCl</p>		<p>EN300-156956</p> <p>HCl</p>	
<p>EN300-137256</p> <p>HCl</p>		<p>EN300-129123</p>	
<p>EN300-123357</p> <p>HCl</p>		<p>EN300-142149</p> <p>HCl</p>	
<p>EN300-157667</p>		<p>EN300-157661</p> <p>HCl</p>	
<p>EN300-160286</p> <p>HCl</p>		<p>EN300-137379</p> <p>HCl</p>	
<p>EN300-155382</p> <p>HCl</p>		<p>EN300-126976</p> <p>HCl</p>	
<p>EN300-126061</p> <p>HCl</p>		<p>EN300-127298</p> <p>HCl</p>	

New Arrivals

<p>EN300-141346</p> <p>HCl</p>		<p>EN300-142130</p> <p>HCl</p>	
<p>EN300-142012</p> <p>HCl</p>		<p>EN300-153048</p>	
<p>EN300-171143</p>		<p>EN300-128644</p> <p>HCl</p>	
<p>EN300-171045</p>		<p>EN300-159776</p>	
<p>EN300-157446</p> <p>HCl</p>		<p>EN300-155850</p> <p>HCl</p>	
<p>EN300-172096</p>		<p>EN300-171923</p>	
<p>EN300-130197</p>		<p>EN300-173310</p>	
<p>EN300-132383</p> <p>HCl</p>		<p>EN300-131174</p> <p>HCl</p>	