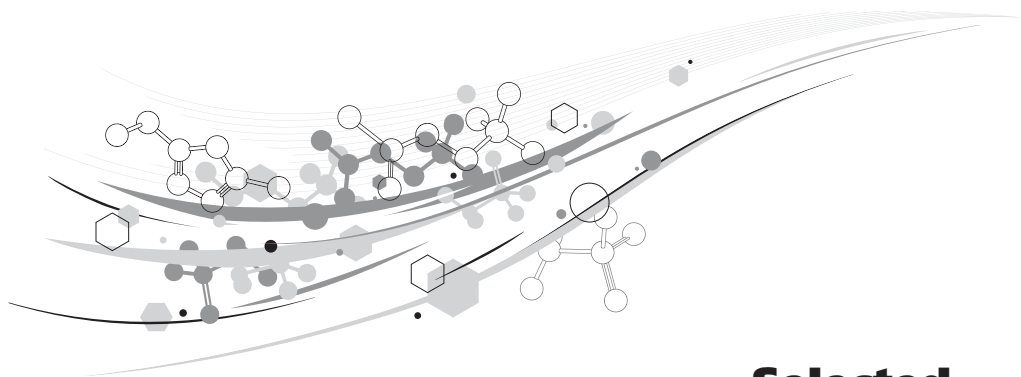




# ISO(THIO)CYANATES and their Analogues





## **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.

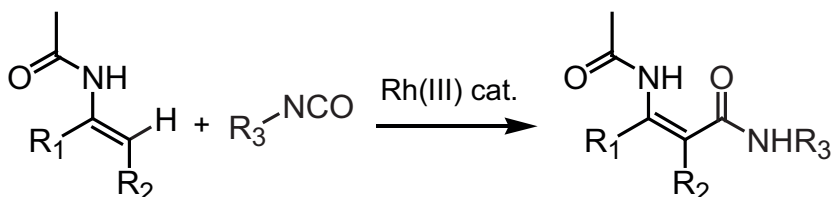
With over 100,000 building blocks synthesized and now available from our stock we are a recognized leader in the market. Our catalogue features versatile building block classes and adds 1,000 products each month. Although they all are available for purchase through [www.enaminestore.com](http://www.enaminestore.com) 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.

Isocyanates, isothiocyanates, and trifluoroethyl carbamates are important intermediates in organic synthesis and drug discovery. These reagents have successfully been used in the preparation of numerous pharmaceuticals and agrochemicals. Present mini-catalog comprises ca. 160 most demanded structures available from our stock. Full list of the title structures available from Enamine can be found in our downloadable catalog or browsed in the on-line Enamine store.

# Isocyanates, Isothiocyanates, and Trifluoroethyl Carbamates

## 1. Isocyanates

The chemistry of isocyanates involves two major types of reactions that are nucleophilic addition and cycloaddition. Thus, reactions of isocyanates with amines readily yield substituted urea derivatives.<sup>1</sup> Similarly, alcohols and phenols easily react with isocyanates to give carbamates, while reactions of isocyanates with carbon nucleophiles provide a useful synthetic access to substituted amides and related derivatives. The high yields and the lack of byproducts in the above reactions have led to their widespread use in the synthesis of biologically active substances and polymers. Isocyanates are also reported to undergo different cycloadditions, such as [2+2], [3+2] dipolar, and [4+2] reactions, with suitable substrates resulting in useful products (e.g. -lactams).<sup>2</sup> While classical aspects of the chemistry of isocyanates are described in a number of books and review articles<sup>3</sup> this class of compounds has recently been shown to be increasingly useful in a metal-mediated amidation of anilide and enamide C-H bonds<sup>4</sup> (Example 1).



Example 1

<sup>1</sup> (a) Gallou, I. *Org. Prep. Proced Int.* **2007**, 39, 355-383.

(b) Majer, P. et al. *J. Org. Chem.* **1994**, 59, 1937-1938.

(c) Bogolubsky, A. V et al. *Tetrahedron* **2011**, 67, 3619-3623.

<sup>2</sup> (a) Ulrich, H. *Acc. Chem. Res.* **1969**, 2, 186-192.

(b) Arbuзов, B. A. et al. *Synthesis*, **1982**, 433.

(c) Chmielewski, M. et al. *J. Org. Chem.*, **1986**, 51, 2397.

(d) Reddy, C. K. et al. *Indian J. Chem.* **1987**, 26B, 882.

<sup>3</sup> (a) Ozaki, S. *Chem. Rev.* **1972**, 72, 457-496.

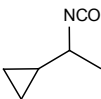
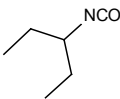
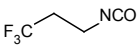
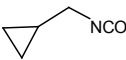
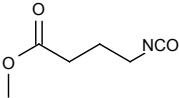
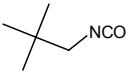
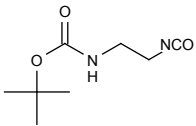
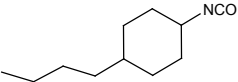
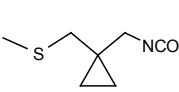
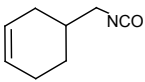

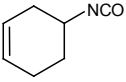
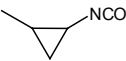
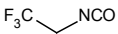
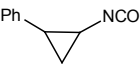
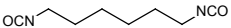
(b) Braunstein, P. et al. *Chem. Rev.*, **1989**, 89, 1927-1945.

(c) Ulrich, H. *Chemistry and Technology of Isocyanates*, Wiley, New York. (1996).

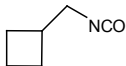
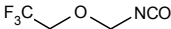

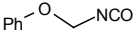
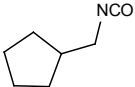
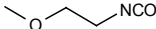
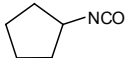
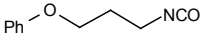
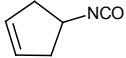
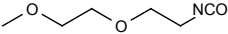
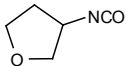
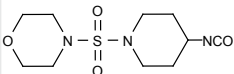
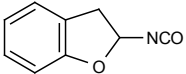
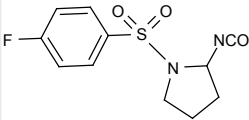
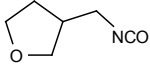
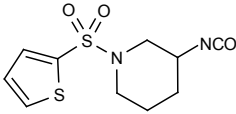
(d) Six, C. et al. *Organic Isocyanates in Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, vol. 20, pp 63-82 (2012).

<sup>4</sup> Hesp, K. D. et al. *J. Am. Chem. Soc.* **2011**, 133, 11430.

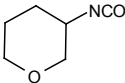
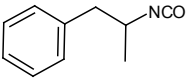
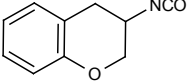
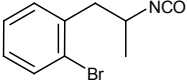
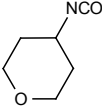
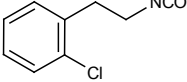
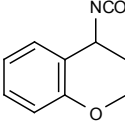
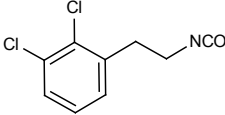
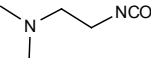
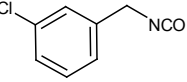
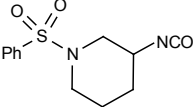
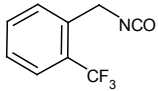
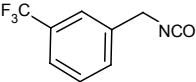
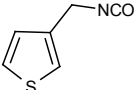
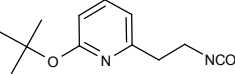
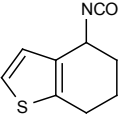
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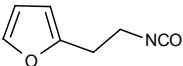
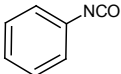
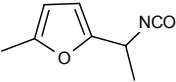
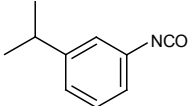
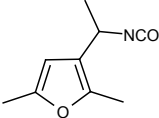
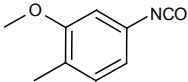
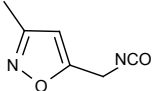
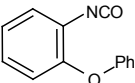
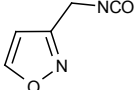
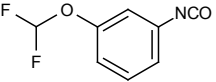
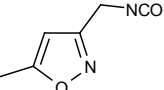
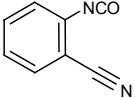
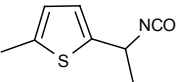
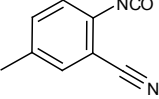
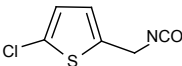
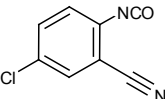
## Alkyl and Aryl Isocyanates

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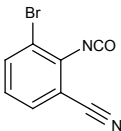
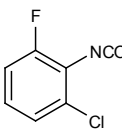
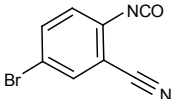
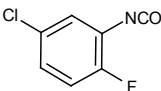
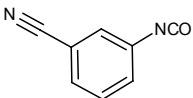
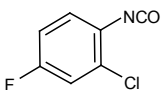
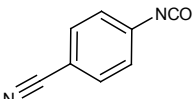
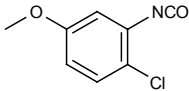
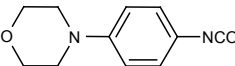
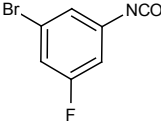
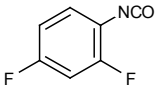
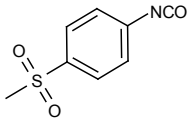
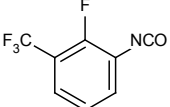
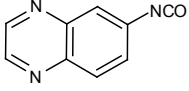
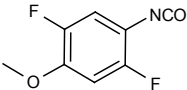
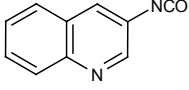
## Alkyl and Aryl Isocyanates

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## Alkyl and Aryl Isocyanates

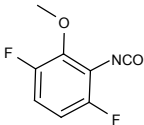
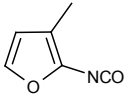

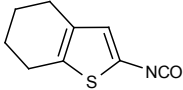
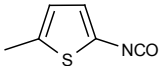
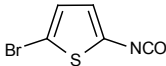
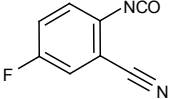
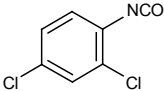
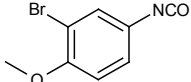
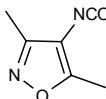
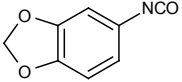
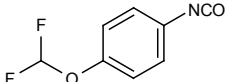
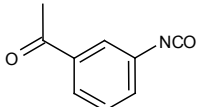
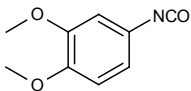
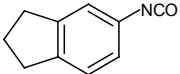
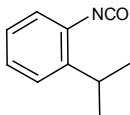
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<p><a href="#">EN300-111250</a></p>		<p><a href="#">EN300-54641</a></p>	
<p><a href="#">EN300-90397</a></p>		<p><a href="#">EN300-04017</a></p>	

## Alkyl and Aryl Isocyanates

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<p><a href="#">EN300-36951</a></p>		<p><a href="#">EN300-41905</a></p>	
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<p><a href="#">EN300-85430</a></p>		<p><a href="#">EN300-56533</a></p>	
<p><a href="#">EN300-20921</a></p>		<p><a href="#">EN300-98428</a></p>	
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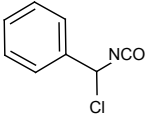
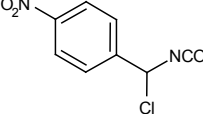
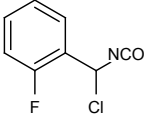
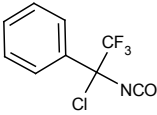
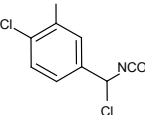
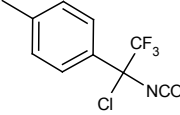
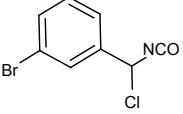
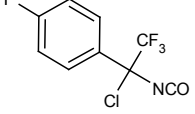
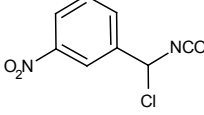
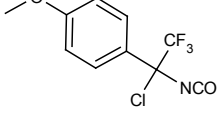
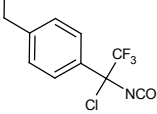
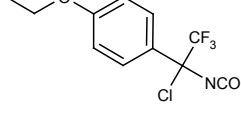


## Alkyl and Aryl Isocyanates

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<p><a href="#">EN300-70427</a></p>		<p><a href="#">EN300-110528</a></p>	
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<p><a href="#">EN300-48625</a></p>		<p><a href="#">EN300-111037</a></p>	

## $\alpha$ -Chloroalkyl Isocyanates

$\alpha$ -Chloroalkyl Isocyanates listed in this subsection are CNC-bis electrophiles that have been successfully used in many heterocyclization reactions resulting in functionalized derivatives of 1,3-benzoxazin-4-one,<sup>5</sup> dihydropyridine,<sup>6</sup> purine,<sup>7</sup> etc.

<a href="#">EN300-118425</a>		<a href="#">EN300-118430</a>	
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<a href="#">EN300-118428</a>		<a href="#">EN300-118423</a>	
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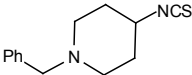
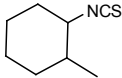
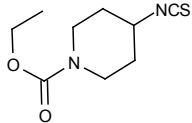
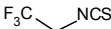
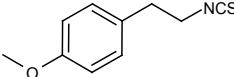
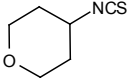
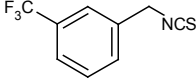
<sup>5</sup> Vovk M. V. et al. *J. Fluor. Chem.* **2002**, *116*, 97-101.

<sup>6</sup> Vovk M. V. et al. *Synlett* **2006**, *3*, 375-378.

<sup>7</sup> Yaroshenko V. O. et al. *Synthesis* **2007**, *21*, 3309-3318.

## 2. Isothiocyanates

Isothiocyanates react with nucleophiles in a similar manner as isocyanates do. Although rates of reactions involving isothiocyanates are usually lower compared to those with isocyanates, the isothiocyanates tend to be less sensitive to moisture and are easier to handle.<sup>8</sup> Isothiocyanates are very important building blocks in the synthesis of heterocycles. The large number of heterocyclization reactions with isothiocyanates giving access to a multitude of four-, five-, six-, and seven-membered ring heterocyclic systems have been discovered.<sup>9</sup>

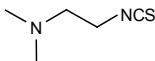
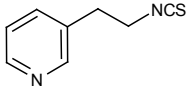
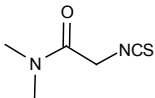
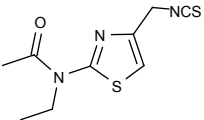
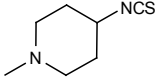
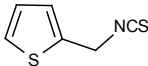
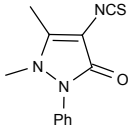
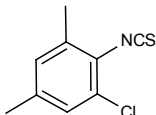
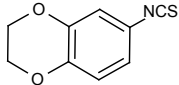
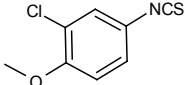
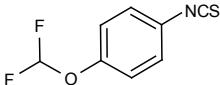
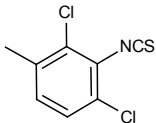
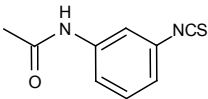
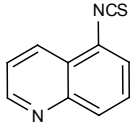
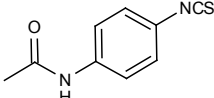
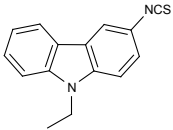
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<sup>8</sup> Romanowski, F. et al. *Organic Thiocyanates and Isothiocyanates in Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, vol. 36, pp 609-618 (2012).

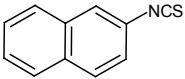
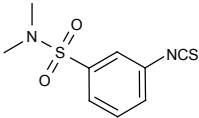
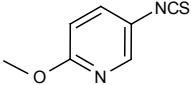
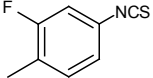
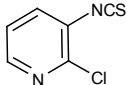
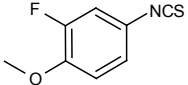
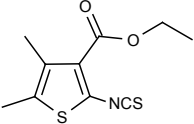
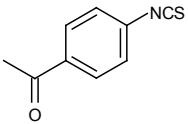
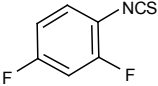
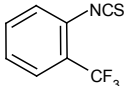
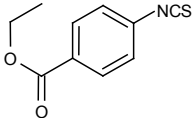
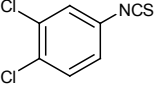
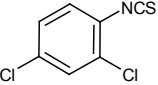
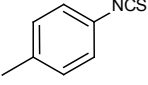
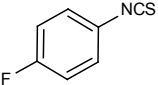
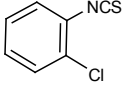
<sup>9</sup> (a) Mukerjee, A. K. et al. *Chem. Rev.* **1991**, 91, 1.

(b) M. Avalos et al. *Heterocycles* **1992**, 33, 973-1010

## Isothiocyanates

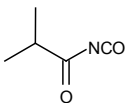
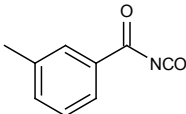
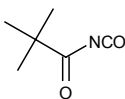
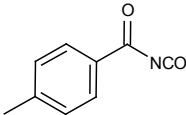
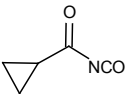
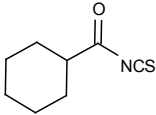
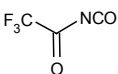
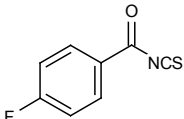
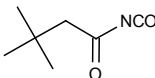
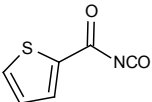
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## Isothiocyanates

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### 3. Acyl Isocyanates and Thioacyl Isocyanates

Acyl isocyanates and thioacyl isocyanates are chemically more reactive than their alkyl- or aryl congeners. Notably, the presence of the additional carbonyl group in acyl and thioacyl isocyanates not only increases the reactivity of their NCO and NCS groups, respectively, but is also responsible for their ability to undergo *e.g.*, 1,4-cycloaddition reactions.<sup>10</sup> On account of this property acyl and thioacyl isocyanates became irreplaceable building blocks in the synthesis of many important heterocyclic systems, such as substituted triazolinones,<sup>11</sup> furans,<sup>12</sup> and bicyclic 2-pyridones.<sup>13</sup>

EN300-114979		EN300-82407	
EN300-60380		EN300-82406	
EN300-116578		EN300-21044	
EN300-01256		EN300-21908	
EN300-26321		EN300-39924	

<sup>10</sup> For reviews, see: Nuridzhanyan, K. A. *Russ. Chem. Rev.* **1970**, *39*, 130.

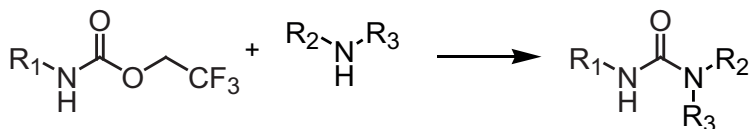
<sup>11</sup> Tsuge, O.; Kanemasa, S. *J. Org. Chem.* **1973**, *38*, 2972.

<sup>12</sup> Hari, Y.; Iguchi, T.; Aoyama, T. *Synthesis* **2004**, 1359.

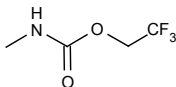
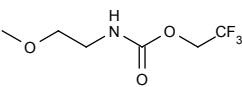
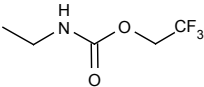
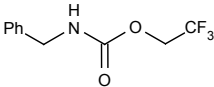
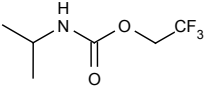
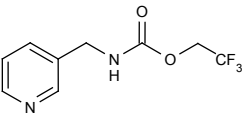
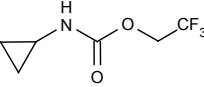
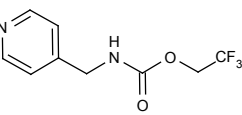
<sup>13</sup> Hari, Y.; Iguchi, T.; Aoyama, T. *Synthesis* **2005**, 2147.

## 4. Trifluoroethyl Carbamates

Trifluoroethyl carbamates included in this section possess moderate electrophilicity. They have effectively been used in combinatorial syntheses of unsymmetrically substituted urea (Example 2) and guanidine derivatives<sup>14</sup> which are useful as both synthetic intermediates and lead-like compounds for high throughput screening of biological activity. A simple workup procedure, the high yields obtained, and the purity of the isolated products make the method for the pre-preparation of substituted ureas and guanidines from amines and trifluoroethyl carbamates highly advantageous as compared to other available procedures.<sup>15</sup>



Example 2

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<a href="#">EN300-44207</a>		<a href="#">EN300-23881</a>	
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<sup>14</sup> (a) Bogolubsky, A. V et al. *Tetrahedron* **2011**, *67*, 3619-3623.

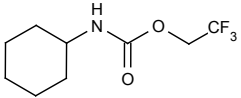
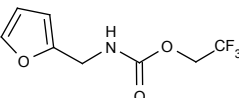
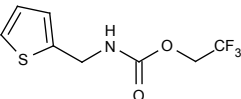
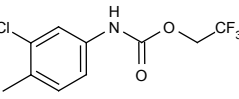
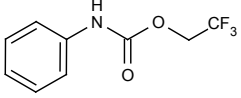
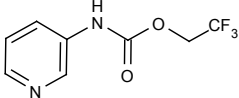
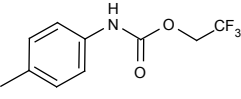
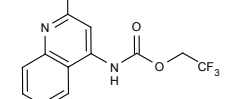
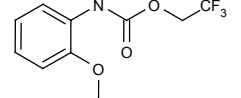
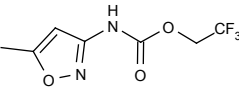
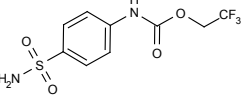
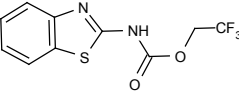
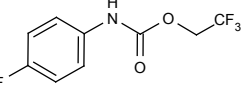
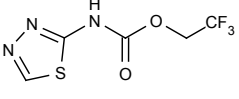
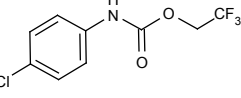
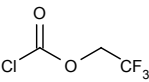
(b) Bogolubsky, A. V et al. unpublished results.

<sup>15</sup> (a) Gallou, I. *Org. Prep. Proced Int.* **2007**, *39*, 355-383.

(b) Delebecq, E. et al. *Chem. Rev. Article ASAP* DOI: 10.1021/cr300195n.

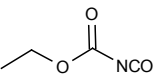
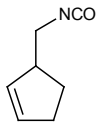
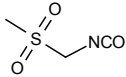
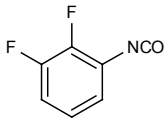
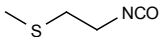
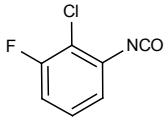
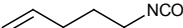
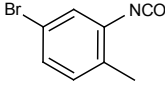
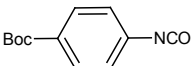
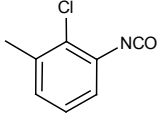
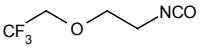
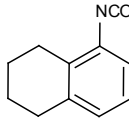
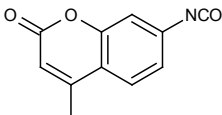
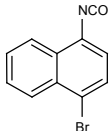
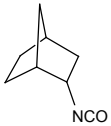
(c) Matsumura, Y. et al. *J. Org. Chem.* **2000**, *65*, 1549-1551.

## Trifluoroethyl Carbamates

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## New Arrivals

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