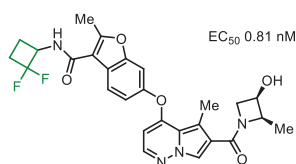


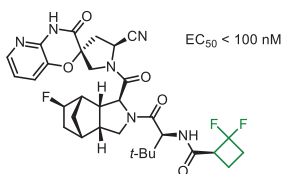
Fluoroalkyl Motif for Enhanced Solubility

Introduction

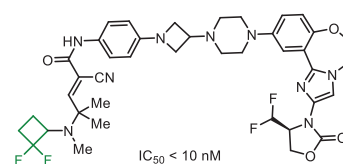
2,2-Difluorocyclobutyl is a recent and successful addition to the toolkit of fluoroalkyl groups. First introduced in 2019 by scientists at *Enamine*,¹ it serves as an analogue to the more widely used 3,3-difluorocyclobutyl motif. The latter has been incorporated into one FDA-approved drug (Ivosidenib, *Servier*)² and three other drugs that reached clinical trials. Unlike the 3,3-difluoro-variant, the 2,2-difluorocyclobutyl group is less symmetric, which typically enhances the solubility of compounds by over an order of magnitude.^{1,3} Discover our latest collection of 2,2-difluorocyclobutyl compounds, designed to deliver improved pharmacological properties.



inhibitor of vascular endothelial growth factor receptor 2
WO 2026/019977
Merck

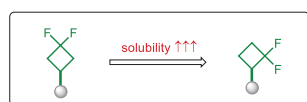


inhibitor of viral protease
WO 2025/221657
Aligos/Katholieke Universiteit

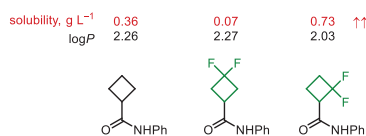


inhibitor of phosphoinositide 3-kinase alpha
WO 2025/237374
Wigen Biomedicine Technology

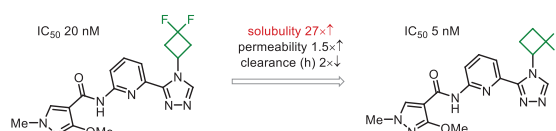
Concept



in drugs:
1 FDA-approved
3 in clinical trials



J. Org. Chem. **2019**, *84*, 8487
Enamine



inhibitor of apoptosis signal-regulating kinase 1, *ACS Med. Chem. Lett.* **2021**, *64*, 15402
Biogen

We offer: over 25 2,2-difluorocyclobutyl compounds from stock on 5-10 gram scale.

EN300-6496796	EN300-22112274	EN300-45480255	EN300-189763	EN300-51862012	EN300-6733481
EN300-27745789	EN300-218230	EN300-26978634	EN300-7374285	EN300-39868865	EN300-300540
EN300-7440128	EN300-127142	EN300-7440126	EN300-27735369	EN300-7546750	EN300-6513490
EN300-45220589	EN300-28694168	EN300-52781450	EN300-54912727	EN300-54912738	EN300-53429182
EN300-22112285	EN300-52681926	EN300-54679641	EN300-52600422	EN300-52413742	EN300-54771631

References

1. A. Chernykh et al. *J. Org. Chem.* **2019**, *84*, 8487.
2. J. Popovici-Muller et al. *ACS Med. Chem. Lett.* **2018**, *9*, 300.

3. J. Jones et al. *J. Med. Chem.* **2021**, *64*, 15402.



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