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The co-crystal structure of etoricoxib–phthalic acid (1/1), C_{18}H_{15}ClN_{2}O_{2}S·C_{8}H_{6}O_{4}

Table 1: Data collection and handling.

<table>
<thead>
<tr>
<th>Crystal:</th>
<th>Block</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size: 0.30 × 0.20 × 0.10 mm</td>
<td></td>
</tr>
<tr>
<td>Wavelength: Mo Kα radiation (0.71073 Å)</td>
<td></td>
</tr>
<tr>
<td>μ: 0.29 mm⁻¹</td>
<td></td>
</tr>
<tr>
<td>Diffractometer, scan mode: Nonius CAD4, ωθ</td>
<td></td>
</tr>
<tr>
<td>R_{int} measured, N(hkl)unique, R_{int}: 25.4°, &gt;99%</td>
<td></td>
</tr>
<tr>
<td>N(hkl)gt: 4813, 4484, 0.022</td>
<td></td>
</tr>
<tr>
<td>Criterion for Igt: 2σ(Igt), 3445</td>
<td></td>
</tr>
<tr>
<td>N(param)refined: 333</td>
<td></td>
</tr>
<tr>
<td>Programs: Olex2 [1], SHELX [2, 3]</td>
<td></td>
</tr>
</tbody>
</table>

Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

1 Source of material

In representative experiments, the etoricoxib (ETR) was presented by Nanjing Pujun Technology Co., Ltd. with no further purification. A mixture of ETR (35.9 mg, 0.1 mmol) and phthalic acid (16.6 mg, 0.1 mmol) was dissolved in a mixture of 5.0 mL methanol, and the resulting mixture was stirred and dissolved at 60 °C to obtain a clear solution. Then the solution was filtered and placed in a sample vial, covered with membrane and punctured. Crystals of the title compound were obtained by slow evaporation of the solution at room temperature within one week.

1.1 Experimental details

The crystal structure was determined using a CAD4 diffractometer. Using Olex2 [1], the structure was solved with the ShelXT [2] and refined with the ShelXL [3] refinement package. The H atoms were placed in idealized positions and treated as riding on their parent atoms, with the d(C–H) = 0.96 Å (methyl) and d(C–H) = 0.93 Å (aromatic) and d(O–H) = 0.85 Å. And Uiso(H) = 1.2 times Uiso(C) and Uiso(H) = 1.5 times Uiso(O).

2 Comment

Etoricoxib (ETR), a selective inhibitor of cyclooxygenase-2, is used to treat osteoarthritis, rheumatoid arthritis, and acute gouty arthritis. According to the biopharmaceutics classification system (BCS) [4], etoricoxib is classified as a BCS class II drug due to its poor aqueous solubility, which limits its clinical application [5, 6]. A cocrystal was reported to improve the physical and chemical stability, dissolution rate, and mechanical properties of drugs [7]. To date, four cocrystals including ETR–succinic acid, ETR–glutaric acid, ETR–adipic acid, ETR–suberic acid and ETR–caprolactam have been reported [8, 9].
In the crystal structure, the asymmetric unit contains
one ETR molecule and one pthalic acid molecule (see the
figure). It indicates that the hydrogen bond plays an
important role in maintaining the crystal structure. The N2
atom on the pyridine group of ETR is a hydrogen bond
acceptor, and the H atom on the carboxyl (O4–H4 of
the pthalic acid molecule is a hydrogen bond donor, forming
the intermolecular hydrogen bond O4–H4···N2 [length
1.697 Å, angle 173.1°]. The N2 atom of ETR shows more
basic than N1, perhaps because N1 is deactivated as an acceptor
by the m-chloro group. The C–C bond lengths of the aromatic
rings and bond angles of the phenyl rings were within
normal ranges. The C–Cl bond lengths of the benzene ring
was 1.730(3) Å. In general, all bond lengths and angles are in
the expected ranges in both molecules [10].

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manuscript and approved submission.

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References
1. Dolomanov O. V., Bourhis L. J., Gildea R. J., Howard J. A. K.,
Puschmann H. OLEX2: a complete structure solution, refinement and
2. Sheldrick G. M. Crystal structure refinement with SHELXL. Acta
4. FDA. Waiver of In vivo Bioavailability and Bioequivalence Studies for
Immediate–Release Solid Oral Dosage Forms Based on a Biopharmaceutics
Classification System; Food and Drug Administration: Silver Spring, MD, USA, 2002.
5. Yazdanian M., Briggs K., Jankovsky C., Hawi A. The ‘high solubility’
definition of the current FDA guidance on biopharmaceutical classification
system may be too strict for acidic drugs. Pharm. Res. 2004, 21, 293–299.
6. Yu L. X., Amidon G. L., Polli J. E., Zhao H., Mehta M. U., Conner D. P.,
Shah V. P., Lesko L. J., Chen M. L., Lee V. H., Hussain A. S.
Biopharmaceutics classification system: the scientific basis for

