Oral presentation

Absolute structure determination of compounds even with only carbon as the heaviest element

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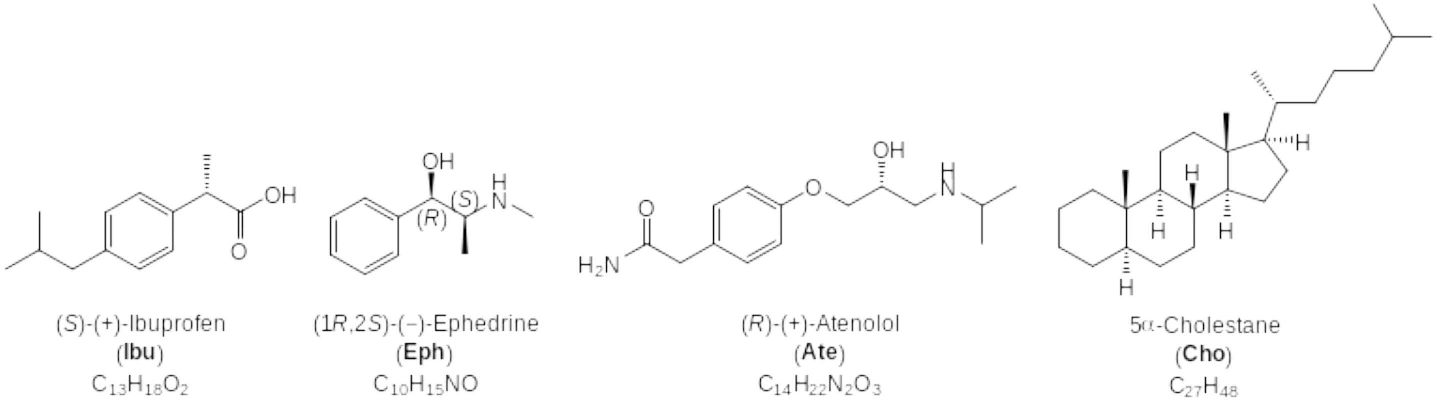
X-ray crystallography is a very powerful method for the determination of the absolute structure of compounds that contain elements heavier than oxygen [1, 2]. For all other compounds, absolute structure determination becomes more challenging and sometimes authors revert to chemical derivatisation [3], though this also can fail, e. g. in the case of tertiary alcohols [4]. Additionally, the Crystal Sponge method [5, 6], co-crystallization with heavy element containing co-solvates [7] and MircoED [8, 9] have been employed to determine the absolute structure. The Hooft parameter y [10] and the Parsons parameter Q [11] are less dependent upon the presence of a heavy element than the original Flack parameter x [12]. The calculation of the probability differentiating between a racemic, a correct or a false enantiomer by the Bayesian statistics, introduced in 2008, permits an even higher sensitivity [10]. However, we have noted that the usage of the probability calculation for the determination of the absolute structure is still limited.

In 2006, *Turner* reported that the absolute structures of (*S*)-(+)-ibuprofen (**Ibu**), (1*R*,2*S*)-(−)-ephedrine (**Eph**) and (*R*)-(+)-atenolol (**Ate**) could not be determined [13]. In this presentation, we will present our findings for these compounds as well as the more challenging case of cholestane (**Cho**) [11], which only consists of carbon and hydrogen, using a modern home source diffractometer without rotating anode. In addition, we have tested the hypothesis of Dittrich *et al.* who stated that a non-spherical atom model refinement improves the absolute structure parameters compared to the independent atom model (IAM) also for light-atom structures [14].



(*S*)-(+)-Ibuprofen (**Ibu**) $C_{13}H_{18}O_2$

(1*R*,2*S*)-(−)-Ephedrine (**Eph**) $C_{10}H_{15}NO$

(*R*)-(+)-Atenolol (**Ate**) $C_{14}H_{22}N_2O_3$

5α-Cholestane (**Cho**) $C_{27}H_{48}$

Figure 1. Studied compounds.

[1] Parsons, S. (2017). *Tetrahedron: Asymmetry* **28**, 1304.
[2] Linden, A. (2017). *Tetrahedron: Asymmetry* **28**, 1314.
[3] Burns, A. S., Dooley, C., III, Carlson, P. R., Ziller, J. W. & Rychnovsky, S. D. (2019). *Org. Lett.* **21**, 10125.
[4] Holstein, P. M., Holstein, J. J., Escudero-Adán, E. C., Baudoin, O. & Echavarren, A. M. (2017). *Tetrahedron: Asymmetry* **28**, 1321.
[5] Yoshioka, S., Inokuma, Y., Hoshino, M., Sato, T. & Fujita, M. (2015). *Chem. Sci.* **6**, 3765.
[6] Sairenji, S., Kikuchi, T., Abozeid, M. A., Takizawa, S., Sasai, H., Ando, Y., Ohmatsu, K., Ooi, T. & Fujita, M. (2017). *Chem. Sci.* **8**, 5132.
[7] Wang, J. R., Fan, X. W., Ding, Q. C. & Mei, X. F. (2016). *J. Mol. Struct.* **1119**, 269.
[8] Wang, B., Bruhn, J. F., Weldeab, A., Wilson, T. S., McGilvray, P. T., Mashore, M., Song, Q., Scapin, G. & Lin, Y. (2022). *Chem. Commun.* **58**, 4711.
[9] Klar, P. B., Krysiak, Y., Xu, H., Steciuk, G., Cho, J., Zou, X. & Palatinus, L. (2023). *Nat. Chem.* **15**, 848.
[10] Hooft, R. W. W., Straver, L. H. & Spek, A. L. (2008). *J. Appl. Cryst.* **41**, 96.
[11] Parsons, S., Flack, H. D. & Wagner, T. (2013). *Acta Cryst.* **B69**, 249.
[12] Flack, H. D. & Bernardinelli, G. (2000). *J. Appl. Cryst.* **33**, 1143.
[13] Turner, H. L. (2006). PhD thesis, University of Southampton.
[14] Dittrich, B., Strumpel, M., Schafer, M., Spackman, M. A. & Koritsanszky, T. (2006). *Acta Cryst.* **A62**, 217.

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