Poster Presentation

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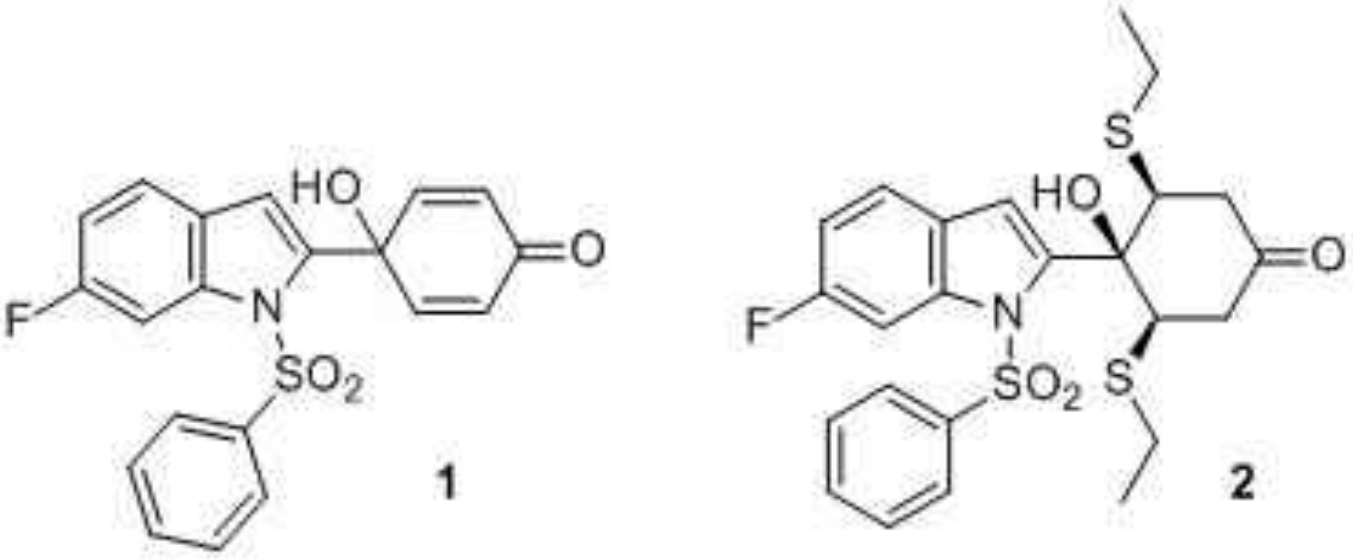
Influence of steric crowding on hydrogen bonding in anti-cancer quinols

C. Schwalbe[1], G. Wells[2], M. Stevens[3]

[1]Aston University, School of Life & Health Sciences, Birmingham, U.K., [2]University of London, UCL School of Pharmacy, London, U.K., [3]University of Nottingham, Centre for Biomolecular Sciences, Nottingham, U.K.

The quinol 4-(1-benzenesulfonyl-1*H*-6-fluoroindol-2-yl)-4-hydroxycyclohexa-2,5-dienone (1) is strongly active against cancer cells [1]. Two "Michael acceptor" electrophilic β-carbons on the quinol ring are believed necessary for optimal antitumor activity, and disruption of thioredoxin signaling is a possible mechanism of action. As a model for the possible product, the adduct (2) with two molecules of ethanethiol was prepared. These molecules have just one classical hydrogen bond (HB) donor group, the quinol OH, but a surfeit of acceptors, namely one C=O and two SO_2 oxygen atoms (designated O15, O17 and O18) as well as O14, the OH itself. In (1) paired molecules form a $R_2^2(14)$ ring by O14-H…O17 HB with H…O distance 2.15 Å and O-H…O angle 156°. In (2) the two EtS groups on the same side of the quinol ring as O14 interfere with this motif. Instead, a C(7) chain is formed by less optimal O14-H…O17 HB (2.34 Å and 134°). In apparent compensation, an intramolecular C-H…O HB to O17 is shorter and straighter in (2). In both structures all O atoms accept C-H…O HB. The unit cell dimensions are dissimilar, but a motif persists: one phenyl CH and one indole CH group bite onto the same O atom, O15 in (1) but O18 in (2).

[1] *J. M. Berry, T. D. Bradshaw, I. Fichtner et al. (2005) J. Med. Chem., 48, 639–644.*



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