Bioorganic & Medicinal Chemistry 22 (2014) 3537–3543

Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry

journal homepage: www . elsevier . com/locate/bmc

Oxidation of cyanobenzocycloheptatrienes: Synthesis, photooxygenation reaction and carbonic anhydrase isoenzymes inhibition properties of some new benzotropone derivatives

Murat Güney [a, b, ⇑], Ahmet Coskun [c, ⇑], Fevzi Topal [b, d], Arif Dastan [b], Ilhami Gülçin [b, e, ⇑], Claudiu T. Supuran [f, ⇑]

[a] Ağrı İbrahim Çeçen University, Faculty of Science and Art, Department of Chemistry, 04100 Agri, Turkey
[b] Atatürk University, Faculty of Science, Department of Chemistry, 25240 Erzurum, Turkey
[c] Konya Necmettin Erbakan University, Ahmet Kelesoglu Education Faculty, Department of Chemistry, 42099 Konya, Turkey
[d] Gumushane University, Vocational School of Health Services, Department of Medical Services and Techniques, 29100 Gumushane, Turkey
[e] King Saud University, Department Zoology, College of Science, Saudi Arabia
[f] Università degli Studi di Firenze, Laboratorio di Chimica Bioinorganica, Rm. 188, Via della Lastruccia 3, I-50019 Sesto Fiorentino (Firenze), Italy

article info

Article history:
Received 4 February 2014
Revised 2 April 2014
Accepted 6 April 2014
Available online 2 May 2014

Keywords:
Benzocycloheptatriene
Benzotropone
Oxidation
Rearrangement
Nitrile-substituted drugs
Carbonic anhydrase inhibition

abstract

The oxidation of some cyanocycloheptatrienes with CrO_3 and pyridine was investigated and a few new nitrile functionalised benzotropone derivatives were obtained. Photooxygenation reaction of these products was also studied. The structures of the formed products were determined on the basis of NMR spectroscopy and the formation mechanism of unusual products was discussed. Human carbonic anhydrase isoenzymes I, and II (hCA I and hCA II) inhibition properties of nitrile functionalized new benzotropone derivatives were also studied. Both CA isozymes were inhibited in the low micromolar range by these nitrile functionalized benzotropone analogues. The newly synthesized benzotropone derivatives showed inhibition constants in the sub-micromolar range (2.51–4.06 μM). The best hCA I inhibition was observed in 5H-benzocycloheptene-7-carbonitrile (K_i: 2.88 ± 0.86 μM). On the other hand, 5-oxo-5H-benzocycloheptatriene-7-carbonitrile showed the powerful inhibitory effect against hCA II (K_i: 2.51 ± 0.34 μM).