R1415D

SYNTHESIS AND PROPERTIES OF BENZOTRIAZOLE DERIVATIVES

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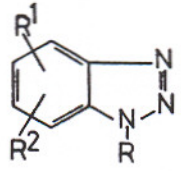
A considerable number of antiinflammatory agents have in common an anellated heterocyclic ring system as the characteristical structural moiety. It has been shown that benzotriazole may serve as such a ring system and that antiinflammatory activity depends largely on the kind of substitution. Thus, significant activity results from substitution in 1-position by the cinnamoyl[1] and 3.4.5-trimethoxybenzoyl[2] rests. Various substitution patterns have now been investigated based on the general formula as follows:



Representative for various ways of synthesis to arrive at such structures is the reaction of 5,6-dichlorobenzotriazole with carboxylic acid halides. Also, alkyl halides are amenable to this reaction. In the case of benzotriazoles carrying only one substituent in the carbocyclic ring, unequivocal syntheses

were sought. As an example, 1-(4-chlorobenzoyl)-5-methoxybenzotriazole may be synthesized by causing 4-methoxy-2-nitroaniline to react with 4-chlorobenzoylchloride first and only afterwards closing the triazole ring by reducing the nitro group and cyclizing the two amino groups by means of nitrous acid. So far, in this series of compounds, 1-cinnamoyl-5-nitrobenzotriazole has been found to exhibit the strongest anti-inflammatory activity.

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1) A. Kreutzberger and E. Dietz, Arzneim.-Forsch. 20, 1723 (1970).

2) A. Kreutzberger and H. van der Goot, J. Heterocycl. Chem. 12, 665 (1975).