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BOOK REVIEWS

Heterocyclic Antitumor Antibiotics. Topics in Heterocyclic Chemistry, 02. Edited by Moses Lee (Hope College, Holland, MI). Series Edited by R. R. Gupta. Springer: Berlin, Heidelberg, New York. 2006. xiv + 252 pp. $149.00. ISBN 3-540-30982-9.

Heterocyclic antitumor antibiotics represent a broad class of natural products that are of widespread interest from the point of view of both their chemotherapeutic potential and, often, their chemical novelty. Thus, a well-written, up-to-date account of progress in the study of such compounds is expected to be well received. This monograph, however, is somewhat disappointing, although it is by no means poorly written or lacking in intrinsic scientific merit. The disappointment arises largely from the fact that its six chapters represent a rather eclectic collection of topics, several of which are only very loosely connected to compounds that should be classified as heterocyclic antitumor antibiotics in the normally accepted definition.

Chapter 1 covers the synthesis of analogues of the combretastatins, which are naturally occurring compounds that possess colchicine-like activity against tubulin assembly, thus leading to antimytotic activity and promise as anticancer agents. The combretastatins, however, are substituted stilbenes, and therefore the connection to the theme of heterocyclic antitumor antibiotics is somewhat of a stretch. (A connection to heterocyclic systems does exist in that the synthetic analogues described in this review are themselves heterocycles.) Although the synthetic chemistry presented is relatively routine, as is often the case in descriptions of studies of a medicinal chemistry nature, the compilation of structure−activity relationships (SAR) in these analogues is likely to be of value to those interested in antimytotic compounds of this class.

The next chapter on the structures of and synthetic approaches to a number of pyrrole-containing natural products with anticancer potential fits well within the theme implied by the title of this monograph. The synthetic approaches to these antibiotics are varied and include methodologies that have some novelty in their application to pyrrole chemistry. The review is of potential interest not only for its overview of the SAR for this class of anticancer compounds but also for its compilation of newer synthetic methods for this class of heterocycles.

Chapter 3 deals with synthetic approaches to carbolines, which are both bona fide natural heterocycles and anticancer agents. The methodology described, which focuses largely on β-carbolines, is rich in classical methodology as well as newer strategies and is recommended to indole chemists in general. The isomeric α-, γ-, and δ-carbolines, which are much more rare, are touched on briefly.

The following chapter seems particularly out of place in the context of the theme of the monograph because most of the natural products described here are not heterocycles. It does, however, deal with a relatively topical area of antitumor antibiotics. The kinamycin antitumor antibiotics, which are the principal focus of this chapter, were considered for some 30 years to be *N*-cyanobenzo[*b*]carbazoles but have been recognized for the past 13 years to be polyketide-derived carbocycles that incorporate a novel diazo group. Unlike the preceding chapters of this monograph, which emphasize synthetic methodology and SAR studies, this chapter focuses on hypothetical molecular modes of action of the kinamycins and related diazo natural products. Given the confusion concerning the structures of the kinamycins in the past, it is somewhat disappointing that a number of errors appear in the structures provided in this chapter. The existing speculation concerning possible mechanisms of action for DNA cleavage by the kinamycins is relatively well documented here but without much critical analysis. The addition of a new speculation at the end of this chapter regarding a possible photochemically induced mechanism of DNA cleavage is not helpful to the field, since there is absolutely no experimental evidence to indicate that photoactivation plays any role in the bioactivity or in the in vitro DNA-cleaving activity of these compounds.

Chapter 5 covers synthetic heterocyclic antibacterial agents of the quinolone and oxazolidinone categories, as well as certain heterocyclic hydroxamic acid derivatives. Although the compounds discussed are certainly of interest to medicinal chemists concerned with synthetic antibacterials, the compounds described are so diverse with respect to structure and mode-of-action that it is surprising to find them included in the same chapter.

The final chapter deals with natural, synthetic, and semisynthetic inhibitors of β-lactamases. This is a field that has been reviewed frequently but remains topical as a consequence of the serious threat to the effectiveness of antibacterial chemotherapy that has arisen with the emergence of bacterial strains possessing broad-spectrum resistance to β-lactam antibiotics. There are compilations here of the SAR for various classes of β-lactamase inhibitors that have not been presented in other reviews, so workers in this field may benefit from perusing this chapter, just as this reviewer has.

In summary, this monograph certainly has sufficient scientific value to merit inclusion in most academic libraries and in industrial laboratories concerned with antibacterial and anticancer agent discovery. Individual researchers, on the other hand, might first wish to weigh the extent to which this far-ranging collection of reviews deals sufficiently with topics of specific interest to their research groups before acquiring a personal copy.

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