

chromatography, and the melting and mixture melting points of the synthetic product (IV) with an authentic sample of dehydrocycloheximide (7) revealed that the two products were, in fact, identical.

Our research on the synthesis of IV was initiated on the model enamine (VI) prepared from piperidine and 2-methylcyclohexanone (V) since it has been suggested that enamines which are substituted in the 2-position might not undergo reaction (5). However, we have found that enamines of this type are reactive; thus, condensation of the model enamine (VI) with glutarimide- $\beta$ -acetyl chloride (III) resulted in the formation of a 25% yield of ( $\pm$ )-nordehydrocycloheximide (VII), thereby establishing that acylation at the 6-position is feasible. The reason that the yield of VII and of IV was not over 50% is most probably caused by the fact that the distilled enamine is actually a mixture of double bond isomers in which the double bond is either at C<sub>1</sub>-C<sub>6</sub> or C<sub>1</sub>-C<sub>2</sub>. Since only that isomer in which the double bond is at C<sub>1</sub>-C<sub>6</sub> (II or VI) can give IV or VII, the reduction in yield can readily be understood. Evidence that the enamine is a mixture of double bond isomers is available from its infrared spectrum. Thus, in the C=C region, II exhibits two peaks, one at 1680 cm.<sup>-1</sup> and one at 1645 cm.<sup>-1</sup> The enamine VI also exhibits peaks at 1670 cm.<sup>-1</sup> and 1640 cm.<sup>-1</sup> However, the enamine prepared from cyclohexanone and piperidine exhibits only one peak in the C=C region at 1645 cm.<sup>-1</sup> This result would be predicted for this enamine since it cannot exist in an isomeric form as can II or VI.

One final point which requires comment is the stereochemical assignment of the methyl groups

of dehydrocycloheximide (IV). It has been established that in cycloheximide the methyl groups are *trans* (1, 4), but no proof of the stereochemistry of dehydrocycloheximide has been reported. However, the present synthesis of dehydrocycloheximide (IV) establishes that the methyl groups are *trans* since IV was synthesized from (+)-*trans*-2,4-dimethylcyclohexanone (I). It might be argued that the  $\alpha$ -methyl group of I could be isomerized during the preparation of the enamine, but this hypothesis was shown to be rather unimportant when it was found that the acid catalyzed hydrolysis of the enamine (II) regenerated a 75% yield of (+)-*trans*-2,4-dimethylcyclohexanone (I). This result therefore offers strong support to the assignment of the *trans* methyl groups in dehydrocycloheximide (IV).

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## Book Notices

*Year Book of Drug Therapy*. 1962-1963 Series.

Edited by HARRY BECKMAN. Year Book Medical Publishers, Inc., 35 E. Wacker Drive, Chicago 1, Ill., 1962. 648 pp. 13 × 20 cm. Price \$8.50.

A new section has been added to this revised volume entitled "Precautions," replacing the section entitled "Critical Evaluation of the Year's New Drugs." As with prior editions, the major presentation is through abstracts covering reports of new therapeutic or prophylactic uses and applications of drugs during the "series year." The abstracts are well written in the concise and meaty form which has become characteristic of this series. In the newly added section, sketches of accumulated experience regarding the toxic actualities and poten-

tialities of drugs in current use will be of invaluable assistance to pharmaceutical and medical personnel.

*Protein Metabolism*. Edited by F. GROSS. Springer Verlag, Berlin-Wilmersdorf, Heidelberg Platz 3/, West Berlin, Germany, 1962. xi + 521 pp. 14 × 20.5 cm.

The proceedings of an international symposium are reported—the fourth in a series of such symposia sponsored by Ciba, Ltd., Basle. Major topics covered by the participants include: Action of hormones at the cellular level; Factors influencing protein metabolism in the organism; Evaluation and mode of action of anabolic steroids; Protein metabolism in human pathological states; and