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FORMATION AND STEREOCHEMISTRY OF 2-ALLYL-2-ETHYL-1,2,3,5,6,11b-HEXAHYDRO-11H-INDOLO[3,2-g]INDOLIZINE PREVIOUSLY TAKEN FOR TO BE 3,4-DEHYDROQUEBRACHAMINE

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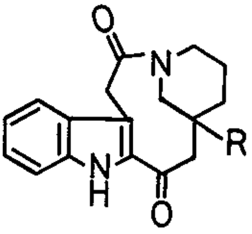
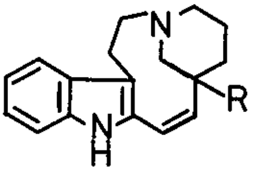
Formation and stereochemistry of 2-allyl-2-ethyl-1,2,3,5,6,11b-hexahydro-11H-indolo[3,2-g]indolizine(3:R=Et) previously taken for to be 3,4-dehydroquebrachamine (2:R=Et) is reported.

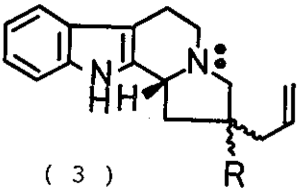
In 1969, Ziegler and co-workers[1] proposed a structure(2:R=Et; 3,4-dehydroquebrachamine) for the major product obtained from the tetracyclic ketolactam(1:R=Et) with lithium aluminum hydride in boiling dioxane. Later, Nagata and co-workers[2] called the proposed structure(2:R=Et) in question on the basis of their observation encountered in the synthesis of (*dl*)-velbanamine in which the tetracyclic ketolactam(1:R=H) afforded the allylic compound(3:R=H) instead of des-ethyl-3,4-dehydroquebrachamine (2:R=H) under the same condition described by Ziegler and co-workers[1]. Recently Ziegler and Bennett[3] claimed an amendment to the 3,4-dehydro structure(2:R=Et) giving a new structure represented as 3(R=Et), since the compound previously assigned as 2(R=Et) was not identical with the compound(2:R=Et) prepared through an unambiguous route. However the validity of the newly proposed structure(3:R=Et) and its stereochemistry is still uncertain because of lack of the unambiguous synthesis.



(1)



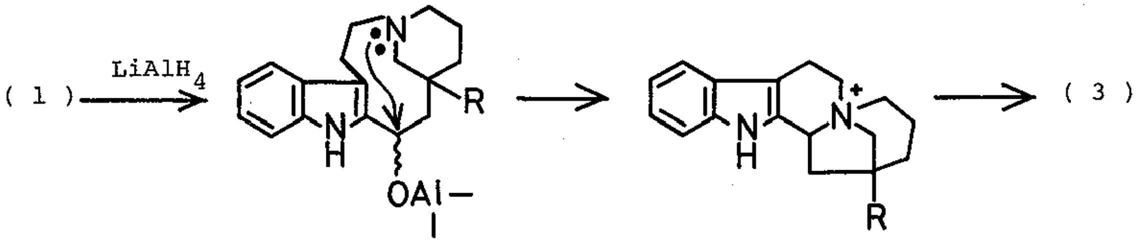
(2)



(3)

We wish to report a formation of 3(R=Et) and the determination of its stereochemistry which substantiated the newly proposed structure(3:R=Et). Based on the results known so far[1,2], it could be postulated that a pentacyclic quaternary base(5), formed through a tertiary amine(4), intervened in the course of the reaction to be collapsed into 3 through the Hofmann type elimination reaction. Pentacyclic quaternary base(5:R=Et) which could have two diastereomers would afford the allylic tertiary base(3:R=Et) with a stereochemistry correlated to the progenitors on treatment with lithium aluminum hydride. Each of stereochemically defined quaternary bases[5],5a and 5b, was treated with lithium aluminum hydride in boiling tetrahydrofuran respectively. To our surprise, the product[5] obtained from each of the isomer was identical and its physical and spectroscopic properties are completely in accord with those of the compound previously assigned as 2(R=Et). Its nmr spectrum, which was not reported by Ziegler and co-workers[1], exhibited typical allylic vinyl protons at δ 4.90-5.28(2H,m) and

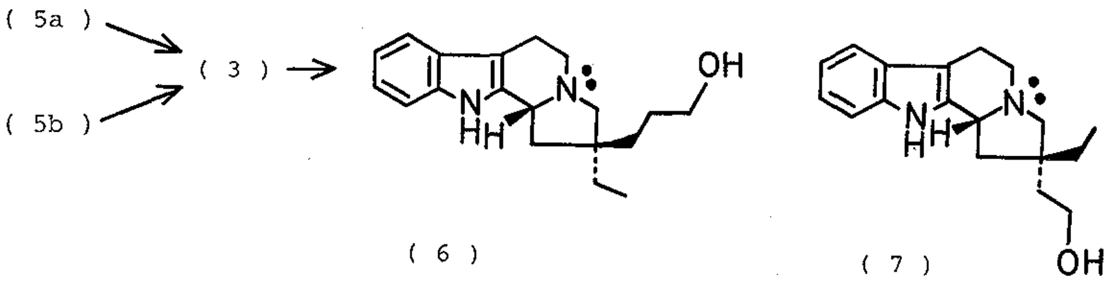
Ziegler's(R=Et) and Nagata's(R=H) reactions:



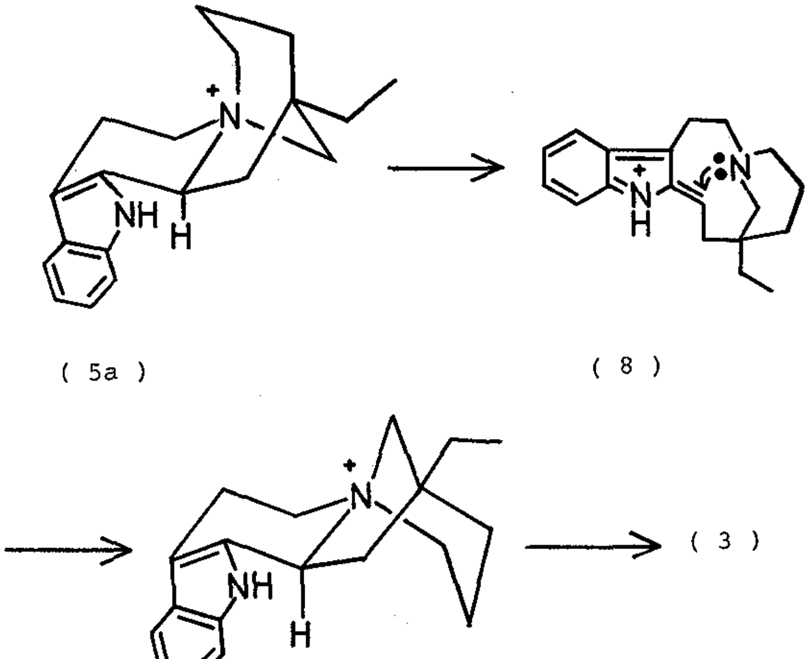
(4)　　　(5)

5.51-6.20(1H,m) which ruled out the previously proposed structure (2:R=Et)[6] and supported the newly proposed structure(3:R=Et). Although this experiment proved the intervention of the quaternary base(5:R=Et) in the reaction, stereochemistry of 3(R=Et) remained uncertain. Thus 3(R=Et) was transformed into the corressponding primary alcohol by treating with excess diborane, followed by alkaline hydrogen peroxide for the comparison with the authentic stereochemically defined alcohols; 6 and 7 which were prepared through the established route[7]. Identity of the former(6) with the alcohol derived from 3(R=Et) revealed the stereochemistry of its allylic precursor to be represented by 3(R=Et) with α-oriented ethyl and β-oriented allylic functions. The exclusive formation

Preparation of (3):



of one of the two possible isomers could be due to serious non-bonded(1,3-diaxial type) interactions in one(5a) of the quaternary bases. In the course of the reaction, an interconversion of 5a into more stable isomer(5b) through a C/D seco-intermediate (8) might take place at first to relieve stereochemical congestions and 5b could undergo the Hofmann type elimination reaction to afford only one isomer exclusively.



(5a)

(8)

(5b)

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2. M. Narisada, F. Watanabe, and W. Nagata, Tetrahedron Letters, 3681(1971).

3. F.E. Ziegler and G.B. Bennett, J. Amer. Chem. Soc., **95**, 7458(1973), see footnote(31).

4. S. Takano, S. Hatakeyama, and K. Ogasawara, J. Amer. Chem. Soc., **98**, 3022(1976).

5. Obtained in 23% and 40% yield with small amount of quebrachamine[4] from 5a and 5b, respectively; mp 108-109° (lit: mp 107-108°); nmr(δ) ($CDCl_3$) 0.72(3H,t,J=7.0Hz), 1.26(2H,q,J=7.0Hz), 1.50-2.33(4H,m), 2.46-3.50(6H,m), 4.18(1H,br.t,J=7.5Hz), 4.90-5.28(2H,m), 5.51-6.20(1H,m), 6.90-7.60(4H,m), 7.85(1H,br.s).

6. We would like to extend our appreciation to Professor F.E. Ziegler, Yale University, for providing copies of nmr spectra through Dr. M. Narisada, Shionogi Research Laboratory.

7. S. Takano, M. Hirama, T. Araki, and K. Ogasawara, J. Amer. Chem. Soc., in press.

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