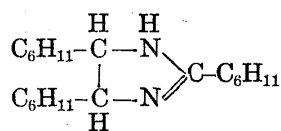


The Stereoisomerism of 2,4,5-Tricyclohexyl-imidazole

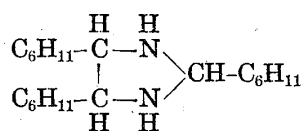
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In order to obtain stereoisomers of 2,4,5-tricyclohexyl-4,5-dihydroimidazole (A)⁽¹⁾ or stereoisomers of 2,4,5-tricyclohexyl-imidazolidine (B)⁽²⁾ which are the compounds of the substituted five-membered heterocyclic ring, containing two nitrogen atoms, the present authors studied the hydrogenation of amarine and isoamarine which are respectively *cis*- and *trans*-2,4,5-triphenyl-4,5-dihydroimidazole⁽³⁾.



(A)



(B)

The present authors obtained one compound, m.p. 162–3° (I), from isoamarine by the hydrogenation over Raney nickel in ethylalcohol and also over platinum black in glacial acetic acid, and two compounds, m.p. 174–5° (II) and m.p. 202–3° (III)⁽⁴⁾, from amarine by the hydrogenation over Raney nickel in ethylalcohol. In the latter case a small quantity of lophine (2,4,5-triphenyl-imidazole) was obtained.

It was reported by Waser and Gratsos⁽⁵⁾ that two compounds, m.p. 171–2° and m.p. 211–3°, were obtained from amarine and the latter was also obtained from lophine by the hydrogenation over platinum black in glacial acetic acid. They reported that the former was 2,4,5-tricyclohexyl-imidazolidine (B) and the latter was 2,4,5-tricyclohexyl-4,5-dihydroimidazole (A). However, they did not consider the configuration of these compounds at all. The compounds m.p. 174–5° and 202–3°, obtained by the present authors, are probably identical respectively with the two compounds obtained by Waser and Gratsos.

Considering the facts that the catalytic hydrogenation of imidazole ring (for example, in histidine, lysidine, trimethyl-imidazole and imidazole) over platinum black was hardly brought about⁽⁵⁾ and lophine was obtained in the present experiment in which amarine was treated with Raney nickel and hydrogen in ethylalcohol, it is doubtful whether the compounds, m.p. 174–5° (II) and m.p. 202–3° (III) (171–2° and 211–3° of Waser and

(1) Two stereoisomers theoretically exist.

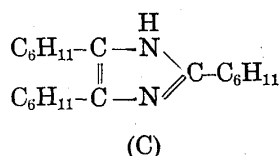
(2) Four stereoisomers are theoretically expected to exist.

(3) Snape: J. Chem. Soc., 77, 781 (1900).

(4) A part of this experiment was carried out by Miss Kōko Maeda.

(5) Waser and Gratsos: Helv. Chim. Acta, 11, 944 (1928).

and Gratsos) are respectively 2,4,5-tricyclohexyl-imidazolidine (B) and 2,4,5-tricyclohexyl-4,5-dihydroimidazole (A), as Waser and Gratsos reported⁽⁵⁾. From the chemical properties of the compound m.p. 202-3° (III) and the fact that it was also obtained from lophine⁽⁵⁾ by the hydrogenation,



(III) is considered probably to be 2,4,5-tricyclohexyl-imidazole (C) which can be explained to yield from amarine by the hydrogenation of phenyl groups and the dehydrogenation of *cis*-4,5-dihydroimidazole ring. The

fact that lophine was produced from amarine (*cis*) by the treatment with Raney nickel, while it was not produced from isoamarine (*trans*) by the similar treatment, also can be explained by the catalytic dehydrogenation which took place on *cis*-4,5-dihydroimidazole ring of amarine only.

From the consideration above-mentioned and the chemical property such as the stability for the treatment with hydrochloric acid, the present authors consider that the compounds m.p. 162-3° (I) and m.p. 174-5° (II) are probably *trans*- and *cis*-2,4,5-tricyclohexyl-4,5-dihydroimidazole (A) respectively, in which only the hydrogenation of phenyl groups is brought about and the configuration of 4,5-dihydroimidazole ring does not change.

Experimental

2,4,5-Tricyclohexyl-*trans*-4,5-dihydroimidazole (I)

A solution of 0.5 g of isoamarine⁽⁶⁾ m.p. 198-9°, which was prepared by the transformation of amarine, in 30 cc of absolute ethylalcohol was mixed with Raney nickel catalyst which was prepared from 1.5 or 3.0 g of nickel aluminum alloy powder. The mixture was shaken with hydrogen under ordinary pressure at 20° or 40° for about 100 hours.⁽⁷⁾ When about 300 cc of hydrogen was absorbed, the catalyst was filtered off and the solvent was distilled out. The white crystalline residue was fractionated by the recrystallization from acetone and 2,4,5-tricyclohexyl-*trans*-4,5-dihydroimidazole (I) was obtained. It was recrystallized from acetone as colorless prisms, m.p. 162-3°, soluble in ethylalcohol, acetone, benzene, ethylacetate, chloroform and petroleumether.

Anal. Calcd. for $\text{C}_{21}\text{H}_{38}\text{N}_2$: C 79.70, H 11.38, N 8.86; Found: C 79.24, H 11.38, N 9.26.

It was slightly soluble in boiling water, and the solution showed the weak alkaline reaction for litmus paper.

(6) Japp and Moir: J. Chem. Soc., 77, 781 (1900).

(7) The shaking was continued during the day-time. The number of the hours was the sum total of the shaking hours.

This compound (I) was also obtained by the hydrogenation of isoamarine (0.1 g) over platinum black⁽⁸⁾ prepared from chloroplatinic acid (0.5 g), in 20 cc of glacial acetic acid. Isoamarine was not hydrogenated over palladinised charcoal⁹ in ethylalcohol at 20°.

Styphnate of 2,4,5-tricyclohexyl-trans-4,5-dihydroimidazole (I)

An ethylalcoholic solution of 2,4,5-tricyclohexyl-4,5-dihydroimidazole (0.1 g) and an ethylalcoholic solution of styphnic acid⁽¹⁰⁾ (2,4,6-trinitro-resorcine) (0.08 g) were mixed. Water was added until slight turbidity appeared, and the mixture was heated to a clear solution. The styphnate separated on cooling as light yellow plates, m.p. 188–9° dec.

Anal. Calcd. for $C_{21}H_{36}N_2 \cdot C_6H_3N_3O_8$: N 12.47, Found: N 12.35.

Chloroplatinate of 2,4,5-tricyclohexyl-trans-4,5-dihydroimidazole (I)

A hot concentrated ethylalcoholic solution of the compound (I) (0.1 g) and a hot concentrated aqueous solution of chloroplatinic acid (0.2 g) were mixed. Chloroplatinate soon separated as light reddish orange plates, m.p. 240–3° dec.

Anal. Calcd. $(C_{21}H_{36}N_2)_2H_2PtCl_6$: Pt 18.71, N 5.37, Found: Pt 19.39, N 5.80.

2,4,5-Tricyclohexyl-cis-4,5-dihydroimidazole (II)

A solution of 0.5 g of amarine⁽¹¹⁾ in 30 cc of absolute ethylalcohol was mixed with Raney nickel catalyst which was prepared from 3.5 g of nickel alloy powder. The mixture was shaken with hydrogen at 20° for about 150 hours, until about 300 cc of hydrogen was absorbed. The catalyst was filtered off and the solvent was removed by distillation. The crystalline residue was fractionated by the recrystallization from acetone. Colorless prisms, m.p. 172–4° were obtained. Recrystallization from ethylalcohol yielded colorless needles, m.p. 174–5°, which were also recrystallized from acetone or benzene. This compound is probably identical with the compound m.p. 171–2° obtained by Waser and Gratsos⁽⁵⁾ who reported it to be 2,4,5-tricyclohexyl-imidazolidine.

Anal. Calcd. for $C_{21}H_{36}N_2$: C 79.70, H 11.38, N 8.86, Found: C 79.57, H 11.30, N 9.00.

This compound (II) is probably 2,4,5-tricyclohexyl-*cis*-4,5-dihydroimidazole (A).

Styphnate of the compound (II)

By the method similar to that of the preparation of styphnate of the

(8) Willstätter and Waldschmidt-Leitz: B., 54, 121 (1921).

(9) Ott and Schröter: B., 60, 633 (1927).

(10) When dinitrosoresorcine (Beilstein, H., VII 885) was warmed with 4N-HNO₃ in the water bath for several minutes, styphnic acid, pale yellow plates, m.p. 175–6°, separated.

(11) Bahrmann: J. prakt. Chem., (2) 27, 296 (1883). m.p. 99–100°.

compound (I), styphnate of (II) was obtained as light yellow needles, m.p. 175-6°.⁽¹²⁾

Anal. Calcd. for $C_{21}H_{36}N_2 \cdot C_6H_3N_3O_8$: N 12.47, Found: N 12.43.

Chloroplatinate of the compound (II)

By the method similar to that of the preparation of chloroplatinate of the compound (I), chloroplatinate of the compound (II) was obtained as light orange crystals, m.p. 216-7°. which is identical with the melting point of chloroplatinate of the compound m.p. 171-2° of Waser and Gratsos.⁽⁵⁾

Anal. Calcd. for $(C_{21}H_{36}N_2)_2H_2PtCl_6$: Pt 18.27, N 5.37, Found: Pt 19.01, N 5.91.

2,4,5-Tricyclohexyl-imidazole (III)

In the hydrogenation of amarine over Raney nickel in ethylalcohol, some experiments yielded only the compound m.p. 174-5° and some yielded the compound m.p. 202-3° and a small quantity of lophine⁽¹³⁾ and the others yielded the compound m.p. 174-5° and a small quantity of the compound m.p. 202-3° and lophine. The compound m.p. 202-3° (III) was separated by the fractional crystallization from acetone as colorless prisms which were also recrystallized from ethylalcohol or benzene.

Anal. Calcd. for $C_{21}H_{34}N_2$: C 80.20, H 10.90, N 8.89, Found: C 80.60, H 10.01, N 9.07.

It is slightly soluble in boiling water and the solution showed the very weak alkaline reaction for litmus paper.

Styphnate of the compound (III) could not be obtained in the crystalline form by the method similar to that of the preparation of the styphnate of the compounds (I) and (II).

The compound (III) was treated with hydrogen over Raney nickel at 20°. The hydrogenation did not take place.

Lophine was treated with hydrogen over Raney nickel at 20°. The hydrogenation hardly took place.

Summary

cis- and *trans*-2,4,5-Tricyclohexyl-4,5-dihydroimidazole were obtained respectively from amarine and isoamarine by the hydrogenation over Raney nickel and 2,4,5-tricyclohexyl-imidazole was obtained from amarine.

Part of the cost of this study was defrayed by a Grant of the Ministry of Education.

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(12) The styphnate of the compound m.p. 171-2° of Waser and Gratsos was reported to melt at 168.5-9.5° by them.

(13) Lophine was identified by the mixed melting point determination.