823. *Application of the Bruckner Method to the Synthesis of Phenanthridine Derivatives.*

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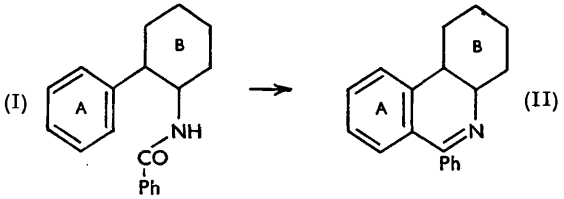
1-Aryl*cyclo*hexenes have been converted into 1-aryl-2-nitro*cyclo*hexenes and compounds regarded as 1-aryl-2-nitro-1-nitroso*cyclo*hexanes. *cis*-2-Aryl*cyclo*hexylamines are obtained by reduction of the 1-aryl-2-nitro*cyclo*hexenes, and their benzoates are cyclised to 1 : 2 : 3 : 4 : 4*a* : 10*a*-hexahydrophenanthridines. 6-Methoxy-9-phenylphenanthridine is formed readily by dehydrogenation of the corresponding hexahydro-compound. *N*-Benzoyl-2-phenyl*cyclo*pentylamine is prepared by the same route and cyclised to 3 : 4-dihydro-1-phenyl*cyclo*penta[*c*]*iso*quinoline.

Bruckner and his co-workers[1] synthesised 3-methyl*iso*quinolines by a method in which addition of dinitrogen trioxide to 1-arylpropenes is the first step. We report here our extension of this method to the synthesis of phenanthridine derivatives by the use of 1-aryl*cyclo*hexenes in place of 1-arylpropenes.

Addition of dinitrogen trioxide to 1-phenyl*cyclo*hexene yields, according to the conditions, predominantly either 1-nitro-2-phenyl*cyclo*hexene or a compound, m. p. 224° (decomp.), regarded as 2-nitro-1-nitroso-1-phenyl*cyclo*hexane.* The latter gave in cold alcoholic alkali a deep red solution from which the original nitrosite was recovered by acidification. It was unchanged by acetic anhydride–sulphuric acid under conditions which convert 1-arylpropene nitrosites into 1-aryl-2-nitropropyl acetates.[1] With acetic anhydride in pyridine, the acetate of the *aci*-form of the nitrosite was formed, which regenerated the original substance on hydrolysis with alcoholic alkali. Oxidation of the nitrosite with potassium permanganate gave benzoic acid. 1-*o*-, 1-*m*-, and 1-*p*-Tolyl-, and 1-*m*-methoxphenyl-*cyclo*hexene similarly gave 1-aryl-2-nitro*cyclo*hexenes or solid nitrosites. 1-Aryl*cyclo*hexanols were formed in all cases by concomitant hydration, and in some cases could not be eliminated from the 1-aryl-2-nitro*cyclo*hexenes.

The 1-aryl-2-nitro*cyclo*hexenes were reduced in good yields to *cis*-2-aryl*cyclo*hexylamines by lithium aluminium hydride. Heating the benzamide derived from 1-nitro-2-phenyl*cyclo*hexene with palladised charcoal in *p*-cymene gave 2-benzamidodiphenyl and *N*-benzoyl-*trans*-2-phenyl*cyclo*hexylamine.[2] The m. p. of the *N*-phenylthioureide of the amine was in agreement with that reported for the *N*-phenylthioureide of *cis*-2-phenyl*cyclo*hexylamine prepared by a different method.[3] The 2-aryl-*N*-benzoyl*cyclo*hexylamines (I) were cyclised to 1 : 2 : 3 : 4 : 4*a* : 10*a*-hexahydrophenanthridines (II) by phosphoric oxide–phosphorus oxychloride :[4] good yields were obtained from the benzoyl derivatives of 2-*m*-tolyl- and 2-*m*-methoxyphenyl-*cyclo*hexylamine; in the other cases, since ring B is alicyclic and there is no activation, the poor yields realised were to be expected. As a test case, the dehydrogenation of 1 : 2 : 3 : 4 : 4*a* : 10*a*-hexahydro-6-methoxy-9-phenylphenanthridine was found to proceed readily with palladised charcoal, yielding 6-methoxy-9-phenylphenanthridine.



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* Part of this work was published in *Chem. and Ind.*, 1954, 757.

[1] Bruckner, *Annalen*, 1935, **518**, 227; Bruckner and Kramli, *J. prakt. Chem.*, 1936, **145**, 291; Bruckner, Fodor, Kiss, and Kovacs, *J.*, 1948, 885; Bruckner and Fodor, *Ber.*, 1943, **76**, 466.

[2] Nightingale and Tweedie, *J. Amer. Chem. Soc.*, 1944, **66**, 1963.

[3] Arnold and Richardson, *ibid.*, 1954, **76**, 3649.

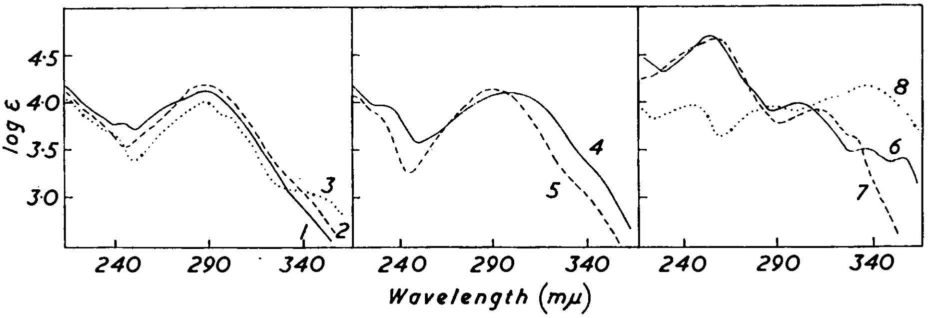
[4] Whaley and Hartung, *J. Org. Chem.*, 1949, **14**, 650.

Under conditions employed for the preparation of 1-aryl-2-nitro*cyclo*hexenes, 1-nitro-2-phenyl*cyclo*pentene and 1-nitro-2-phenyl*cyclo*heptene were obtained from 1-phenyl*cyclo*pentene and 1-phenyl*cyclo*heptene respectively. 2-Phenyl*cyclo*pentylamine was prepared by lithium aluminium hydride reduction of the nitro-compound, and its benzoyl derivative was cyclised to 3 : 4-dihydro-1-phenyl*cyclo*penta[*c*]*iso*quinoline. The ultraviolet absorption spectra of the cyclised bases and of 6-methoxy-9-phenylphenathridine are presented in the Figures.

EXPERIMENTAL

Addition of Dinitrogen Trioxide to 1-*Phenyl*cyclo*hexene*.—(*a*) A saturated aqueous solution (50 ml.) of sodium nitrite and ether (50 ml.) containing 1-phenyl*cyclo*hexene [5] (2 g.), cooled by ice-water, were treated with 4N-sulphuric acid at such a rate as to maintain continuous evolution of nitrous fumes. The ethereal layer developed an intense blue colour which faded to light yellow in 2 hr., indicating completion of reaction. The ethereal layer was *immediately* separated, washed with water, and dried (Na_2SO_4). The combined ether extracts from 20 such experiments were treated with sodium (10 g.) in methanol (150 ml.) with vigorous shaking. Water (150 ml.) was added to the solution with stirring and the deep red aqueous layer separated. The ethereal layer was repeatedly washed with dilute aqueous sodium hydroxide, till the aqueous layer was no longer coloured, dried (Na_2SO_4), and evaporated. Two distillations of the residual oil in a vacuum gave 1-phenyl*cyclo*hexanol (4 g.), b. p. 90—95°/3 mm., m. p. and mixed m. p. 62°, and 1-*nitro*-2-*phenyl*cyclo*hexene* (25 g.), b. p. 145—150°/3 mm. (Found : C, 72·3; H, 7·3; N, 7·4. $C_{12}H_{13}O_2N$ requires C, 70·9; H, 6·4; N, 6·9%). The alkaline extract was cooled and acidified with concentrated hydrochloric acid, to yield 2-*nitro*-1-*nitroso*-1-*phenyl*cyclo*hexane* (7 g.), yellow needles (from methanol), m. p. 224° (decomp.) (Found : C, 61·5; H, 6·2; N, 11·8. $C_{12}H_{14}O_3N_2$ requires C, 61·6; H, 6·0; N, 12·0%).

Absorption spectra of (1) 3 : 4-*dihydro*-4-*methyl*-1-*phenyl*iso*quinoline hydrochloride*, (2) 1 : 2 : 3 : 4 : 4a : 10a-*hexahydro*-9-*phenyl*-, (3) -7-*methyl*-9-*phenyl*-, *and* (4) -6(8)-*methyl*-9-*phenyl*-*phenanthridine hydrochloride*, (5) 3 : 4-*dihydro*-1-*phenyl*cyclo*penta*[c]iso*quinoline hydrochloride*, (6) 9-*phenyl*- *and* (7) 6-*methoxy*-9-*phenyl*-*phenanthridine*, (8) 1 : 2 : 3 : 4 : 4a : 10a-*hexahydro*-6-*methoxy*-9-*phenylphenanthridine hydrochloride* (*all in* EtOH).



(*b*) An ice-cooled mixture of saturated aqueous sodium nitrite (50 ml.) and ether (50 ml.) containing 1-phenyl*cyclo*hexene (2 g.) was treated with 4N-sulphuric acid gradually till the initial blue colour faded to yellow, then the whole was set aside with periodical addition of dilute sulphuric acid, for 6 hr. The combined ether layers from 20 such experiments were worked up as previously. Very little 1-nitro-2-phenyl*cyclo*hexene was obtained. The main product was 2-nitro-1-nitroso-1-phenyl*cyclo*hexane (40 g.), m. p. and mixed m. p. 224° (decomp.). The *acetyl derivative*, obtained with acetic anhydride in pyridine at 100°, crystallised from methanol in colourless needles, m. p. 102—103° (Found : C, 61·0; H, 5·4; N, 9·8. $C_{14}H_{16}O_4N_2$ requires C, 60·9; H, 5·8; N, 10·2%).

cis-2-*Phenyl*cyclo*hexylamine*.—To a stirred solution of lithium aluminium hydride (12 g.) in ether (200 ml.) was added gradually a solution of 1-nitro-2-phenyl*cyclo*hexene (20 g.) in ether (200 ml.). The mixture was left at 30° for 24 hr., then decomposed by water. The ether layer was decanted and extracted repeatedly with 2N-hydrochloric acid (ether layer A). The combined acid extracts were cooled strongly, made alkaline with concentrated aqueous ammonia,

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[5] Nametkin and Iwanoff, *Ber.*, 1923, **56**, 1805.

and extracted with ether. The extract on evaporation left 2-*phenyl*cyclo*hexylamine* (9 g.), b. p. 90°/0·3 mm. The *benzoyl derivative* (Schotten–Baumann method), crystallised from light petroleum, had m. p. 122—123° (Found : C, 81·9; H, 7·2; N, 4·7. $C_{19}H_{21}ON$ requires C, 81·7; H, 7·5; N, 5·0%). The *N*-phenylthioureide melted at 138° (Arnold and Richardson [3] reported m. p. 137—138°).

The ether layer A on evaporation gave a gummy *substance* (1·5 g.), which crystallised from alcohol as colourless needles, m. p. 153—155° (Found : C, 75·8; H, 8·1; N, 7·5. $C_{12}H_{15}ON$ requires C, 76·2; H, 7·9; N, 7·4%).

Dehydrogenation of N-*Benzoyl*-cis-2-*phenyl*cyclo*hexylamine*.—The benzamide (1 g.) was dehydrogenated with 15% palladised charcoal (0·4 g.) in *p*-cymene (50 ml.); 150 ml. of hydrogen were evolved (60% dehydrogenation). The solution was cooled and filtered. The residue was extracted with hot benzene and filtered. Evaporation of the filtrate left *N*-benzoyl-*trans*-2-phenyl*cyclo*hexylamine [2] (0·2 g.), which crystallised from benzene in feathery needles, m. p. and mixed m. p. 178° (Found : C, 82·1; H, 7·7; N, 5·2. Calc. for $C_{19}H_{21}ON$: C, 81·7; H, 7·5; N, 5·0%). The *p*-cymene filtrate was evaporated and the residue dissolved in benzene. Addition of light petroleum to turbidity gave more (0·1 g.) of the benzamide, m. p. 178°. The mother-liquor on evaporation gave a solid (0·4 g.), m. p. 80—85°, raised by chromatography to 83—85°, mixed m. p. with 2-benzamidodiphenyl,[6] 84—85°.

1 : 2 : 3 : 4 : 4a : 10a-*Hexahydro*-9-*phenylphenanthridine*.—A mixture of *N*-benzoyl-*cis*-2-phenyl*cyclo*hexylamine (3 g.) in xylene (75 ml.), phosphorus oxychloride (15 ml.), and phosphoric oxide (15 g.) was refluxed for 3 hr., cooled, and decomposed with ice. The aqueous layer was made alkaline and extracted with ether. The base in the ethereal layer was purified by one more passage through acid, to give 1 : 2 : 3 : 4 : 4*a* : 10*a*-hexahydro-9-phenylphenanthridine as an oil (0·3 g.). The *hydrochloride* crystallised from dry acetone as colourless plates, m. p. 240—241° (Found : C, 76·4; H, 6·4. $C_{19}H_{20}NCl$ requires C, 76·6; H, 6·7%).

Addition of Dinitrogen Trioxide to 1-m-*Methoxyphenyl*cyclo*hexene*.—The cyclo*hexene* was prepared by a Grignard reaction with *cyclo*hexanone and subsequent dehydration with 50% sulphuric acid; it had b. p. 120°/5 mm. (Found : C, 82·4; H, 8·1. $C_{13}H_{16}O$ requires C, 83·0; H, 8·5%). Treatment of the olefin (40 g.) with dinitrogen trioxide as in (*a*) above gave 1-m-*methoxyphenyl*-2-*nitro*cyclo*hexene* (28 g.), b. p. 130°/0·1 mm. (Found : C, 66·5; H, 6·6. $C_{13}H_{15}O_3N$ requires C, 66·9; H, 6·4%), and 1-m-*methoxyphenyl*-2-*nitro*-1-*nitroso*cyclo*hexane* (7 g.), yellow needles (from methanol), m. p. 161° (Found : C, 59·0; H, 6·0; N, 10·6. $C_{13}H_{16}O_4N_2$ requires C, 58·6; H, 5·5; N, 10·6%).

cis-2-m-*Methoxyphenyl*cyclo*hexylamine*.—Reduction of the foregoing nitro-olefin (25 g.) by lithium aluminium hydride gave the *cyclo*hexylamine (11 g.), b. p. 112—115°/3 mm., characterised as the *benzoyl derivative*, m. p. 165—168° (from ether) (Found : C, 78·2; H, 7·8; N, 4·9. $C_{20}H_{23}O_2N$ requires C, 77·7; H, 7·4; N, 4·5%). The neutral *substance* (0·8 g.) obtained in the reduction crystallised from alcohol, then having m. p. 154° (Found : C, 77·5; H, 8·0; N, 7·4. $C_{13}H_{15}ON$ requires C, 77·6; H, 7·5; N, 7·0%).

1 : 2 : 3 : 4 : 4a : 10a-*Hexahydro*-6-*methoxy*-9-*phenylphenanthridine*.—Cyclisation of the above benzoyl derivative (3·3 g.) in xylene (25 ml.) by phosphorus oxychloride (10 ml.) and phosphoric oxide (10 g.) gave the phenanthridine as an oil (1·95 g.). The *hydrochloride* crystallised from acetone–ether in colourless needles, m. p. 189° (decomp.) (Found : C, 73·1; H, 6·2. $C_{20}H_{22}ONCl$ requires C, 73·3; H, 6·7%).

6-*Methoxy*-9-*phenylphenanthridine*.—The above hexahydrophenanthridine (0·35 g.) was dehydrogenated in *p*-cymene (20 ml.) by 50% palladised charcoal (0·2 g.) during 8 hr. The solution was filtered and extracted with dilute hydrochloric acid. Basification of the extract and crystallisation of the precipitate from dilute alcohol gave the *phenanthridine*, m. p. 100—101° (Found : C, 83·9; H, 5·7. $C_{20}H_{15}ON$ requires C, 84·2; H, 5·3%).

Addition of Dinitrogen Trioxide to 1-o-*Tolyl*cyclo*hexene*.—Treatment of the olefin [7] (40 g.) with nitrous fumes according to procedure (*a*) above gave 1-*nitro*-2-o-*tolyl*cyclo*hexene* (30 g.), b. p. 128°/0·3 mm. (Found : C, 73·4; H, 7·1. $C_{13}H_{15}O_2N$ requires C, 71·9; H, 6·9%), and by procedure (*b*) 2-*nitro*-1-*nitroso*-1-o-*tolyl*cyclo*hexane* (35 g.), yellow needles (from methanol), m. p. 210° (decomp.) (Found : C, 63·1; H, 5·9. $C_{13}H_{16}O_3N_2$ requires C, 62·9; H, 6·5%). The *acetyl derivative*, prepared by acetic anhydride and sulphuric acid and crystallised from methanol, had m. p. 99° (Found : C, 62·7; H, 5·7; N, 10·2. $C_{15}H_{18}O_4N_2$ requires C, 62·1; H, 6·2; N, 9·7% .

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[6] Pictet and Hubert, *Ber.*, 1896, **29**, 1186.

[7] Sherwood, Short, and Stansfield, *J.*, 1932, 1832.

cis-2-o-*Tolyl*cyclo*hexylamine*.—Reduction of the preceding nitro-olefin (25 g.) as above gave the amine (13 g.), b. p. 95—100°/0·5 mm., whose *benzoyl derivative* had m. p. 127—129° (from ether) (Found : C, 82·3; H, 8·1; N, 5·2. $C_{20}H_{23}ON$ requires C, 81·9; H, 7·9; N, 4·8%). The neutral *substance* (0·8 g.) obtained crystallised from alcohol in colourless needles, m. p. 172—174° (Found : C, 77·4; H, 8·2; N, 7·1. $C_{13}H_{17}ON$ requires C, 76·9; H, 8·4; N, 6·9%).

1 : 2 : 3 : 4 : 4a : 10a-*Hexahydro-5-methyl-9-phenylphenanthridine*.—The above benzoyl derivative (3·1 g.), by the usual procedure, yielded the phenanthridine (0·45 g.) whose *picrate* crystallised from alcohol in greenish-yellow plates, m. p. 186—187° after sintering at 176° (Found : C, 62·4; H, 5·1. $C_{26}H_{24}O_7N_4$ requires C, 61·9; H, 4·8%).

Addition of Dinitrogen Trioxide to 1-m-*Tolyl*cyclo*hexene*.—Treatment of the *cyclo*hexene[7] (40 g.) with dinitrogen trioxide according to procedure (*a*) gave 1-*nitro*-2-m-*tolyl*cyclo*hexene* (28 g.), b. p. 138—140°/0·5 mm. (Found : C, 74·2; H, 7·4%), and 2-*nitro*-1-*nitroso*-1-m-*tolyl*-cyclo*hexane* (1 g.), colourless needles (from pyridine–light petroleum), m. p. 195—197° (Found : C, 63·2; H, 6·3; N, 11·4%).

The former afforded, as above, the amine (10 g. from 20 g.), b. p. 125°/3 mm. [*benzoyl derivative*, needles (from ether), m. p. 120—123° (Found : C, 82·3; H, 8·1; N, 5·1%)], and a neutral *substance*, m. p. 124—125° (from methanol) (Found : C, 77·3; H, 8·5; N, 6·9. $C_{13}H_{17}ON$ requires C, 76·9; H, 8·4; N, 6·9%), and finally 1 : 2 : 3 : 4 : 4a : 10a-*hexahydro*-6(*or* 8)-*methyl*-9-*phenylphenanthridine hydrochloride*, m. p. 226—227° (from acetone–ether) (Found : C, 76·9; H, 6·6%).

Addition of Dinitrogen Trioxide to 1-p-*Tolyl*cyclo*hexene*.—Treatment of the *cyclo*hexene[8] (40 g.) according to procedure (*a*) gave 1-*nitro*-2-p-*tolyl*cyclo*hexene* (20 g.), b. p. 139°/0·1 mm. (Found : C, 72·0; H, 6·8%), and 2-*nitro*-1-*nitroso*-1-p-*tolyl*cyclo*hexane* (4 g.), yellow needles (from methanol), m. p. 228° (decomp.) (Found : C, 62·8; H, 6·4; N, 11·2%).

The former gave, as above, *cis*-2-*p*-tolyl*cyclo*hexylamine, b. p. 97°/0·4 mm. [*benzoyl derivative*, needles (from ether), m. p. 136—137° (Found : C, 81·5; H, 7·6; N, 5·2%)], a neutral *substance*, needles (from alcohol), m. p. 173° (Found : C, 76·6; H, 8·6; N, 7·0%), and 1 : 2 : 3 : 4 : 4a : 10a-*hexahydro*-7-*methyl*-9-*phenylphenanthridine hydrochloride* (from alcohol–ether), m. p. 209° (Found : C, 76·8; H, 7·2%).

Addition of Dinitrogen Trioxide to 1-*Phenyl*cyclo*pentene*.—Treatment of the *cyclo*pentene[9] (19 g.) according to procedure (*a*) gave 1-*nitro*-2-*phenyl*cyclo*pentene* (9 g.), b. p. 105—108°/0·2 mm. (Found : C, 69·6; H, 5·7. $C_{11}H_{11}O_2N$ requires C, 69·8; H, 5·8%).

This afforded 2-phenyl*cyclo*pentylamine, b. p. 80—82°/0·7 mm. [*benzoyl derivative* (from ether), needles, m. p. 154° (Found : C, 82·0; H, 7·5; N, 5·3. $C_{18}H_{19}ON$ requires C, 81·5; H, 7·2; N, 5·3%)], and 3 : 4-*dihydro*-1-*phenyl*cyclo*penta*[c]iso*quinoline hydrochloride* (0·3 g. from 3 g.) (from alcohol–ether), m. p. 214° (Found : C, 71·7; H, 6·9. $C_{18}H_{18}NCl,H_2O$ requires C, 71·6; H, 6·6%).

Addition of Dinitrogen Trioxide to 1-*Phenyl*cyclo*heptene*.—Treatment of 1-phenyl*cyclo*heptene[10] (5 g.) according to procedure (*a*) gave 1-*nitro*-2-*phenyl*cyclo*heptene* (3 g.), b. p. 128°/2 mm. (Found : C, 72·0; H, 7·1. $C_{13}H_{15}O_2N$ requires C, 71·9; H, 6·9%).

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[8] Sabatier and Mailhe, *Compt. rend.*, 1904, **138**, 1323.
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