244. *Studies in the* cyclo*Hexane Series. Part II.** *The Formation of Isomeric Arylaminocyanomethyl*cyclo*hexanes in the Condensation of the Cyanohydrins of the Methyl*cyclo*hexanones with Arylamines.*

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Qudrat-i-Khuda's claim (*J. Indian Chem. Soc.*, 1931, **8**, 277) to have isolated the four strainless forms of 1-carboxy-4-methyl*cyclo*hexane-1-acetic acid required by the Sasche–Mohr hypothesis led us to study the condensation of the cyanohydrins of the methyl*cyclo*hexanones with arylamines (cf. Walther and Hubner, *J. pr. Chem.*, 1916, **93**, 124). The reaction between the cyanohydrin of 4-methyl*cyclo*hexanone and aniline was studied by Betts and Plant from quite another point of view (J., 1928, 2073), but fractional crystallisation of the product led to the isolation of a more easily fusible isomeride in addition to the 1-anilino-1-cyano-4-methyl*cyclo*hexane described by these authors. The condensation of this cyanohydrin with *p*-bromoaniline, *o*-, *m*-, and *p*-toluidine, and α- and β-naphthylamine led, with the exception of the case of *o*-toluidine, to the formation of pairs of isomeric *arylaminocyanomethyl*cyclo*hexanes* (I), which were characterised by the corresponding *amides* (II), and also in certain cases by the *acids* (III) obtained from the latter by hydrolysis.

$$\mathrm{CHMe}{<}\begin{matrix}\mathrm{CH_2\cdot CH_2}\\\mathrm{CH_2\cdot CH_2}\end{matrix}{>}\mathrm{C}{<}\begin{matrix}\mathrm{CN}\\\mathrm{NHR}\end{matrix} \quad (\mathrm{I.}) \qquad {>}\mathrm{C}{<}\begin{matrix}\mathrm{CO\cdot NH_2}\\\mathrm{NHR}\end{matrix} \quad (\mathrm{II.}) \qquad {>}\mathrm{C}{<}\begin{matrix}\mathrm{CO_2H}\\\mathrm{NHR}\end{matrix} \quad (\mathrm{III.})$$

3-Methyl*cyclo*hexanone behaved similarly towards aniline and gave rise to two isomeric varieties of 1-*anilino*-1-*cyano*-3-*methyl*cyclo*hexane*, and in the condensation with *p*-bromoaniline, traces of a second isomeride also appeared to be present. With *o*- and *p*-toluidine and with the naphthylamines, however, only one individual was detected.

2-Methyl*cyclo*hexanone gave rise to pairs of isomerides with aniline and with β-naphthylamine, and in the condensation of the cyanohydrin with *p*-bromoaniline traces of a second isomeride appeared to be present. In the reactions with the toluidines and α-naphthylamine, however, only one product was isolated.

The arylaminocyanomethyl*cyclo*hexanes derived from all three methyl*cyclo*hexanones are therefore isolable in certain cases in two, but never more than two, modifications and there is no indication of isomerism connected with multiplanar forms.

Experimental.

1-*Anilino*-1-*cyano*-4-*methyl*cyclo*hexane*.—When a solution of potassium cyanide (35 g.) in water (100 c.c.) was added to a mixture of 4-methyl*cyclo*hexanone (56 g.) and aniline (46 g.) in

* The paper of Desai, Hunter, Ghulam Khan, and Saharia (this vol., p. 416) is to be regarded as Part I.

glacial acetic acid (250 c.c.), heat was evolved. The product, which separated over-night, was collected; dilution of the filtrate with water gave a further quantity. On recrystallisation from benzene, the A form of the anilinocyano-derivative separated in thick plates, m. p. 107° (Found : C, 78·2; H, 8·6. Calc. for $C_{14}H_{18}N_2$: C, 78·5; H, 8·4%). The mother-liquor, on being kept, deposited a further quantity; the filtrate from this, on being evaporated to dryness, yielded a residue, m. p. 65—75°, which was extracted with hexane. The sparingly soluble residue consisted of the A form, but the hexane extract deposited two types of crystal consisting of the A form, m. p. 107°, and thin plates of the *B form*, which were separated with the help of a lens and recrystallised from hexane. This isomeride had m. p. 92—93°, depressed to 80° by the A form (Found : C, 78·3; H, 8·1%).

The amide of the A form was prepared by dissolving the nitrile in cold concentrated sulphuric acid and keeping the mixture over-night. On dilution with water and treatment with ammonia, a precipitate formed, which separated from alcohol in needles, m. p. 166° (Found : C, 72·3; H, 8·7. Calc. for $C_{14}H_{20}ON_2$: C, 72·4; H, 8·6%). Betts and Plant (*loc. cit.*) recorded the m. p. as 161°. The *B form*, prepared in a similar manner from the B form of the nitrile, separated from alcohol in needles, m. p. 174° (Found : C, 72·1; H, 8·8%), depressed to 150—155° by the amide of the A form.

The A form of 1-anilino-4-methyl*cyclo*hexane-1-carboxylic acid was obtained by heating the A form of the amide with alcoholic hydrochloric acid for 20 hours, the residue obtained by removal of alcohol being treated with dilute aqueous sodium carbonate, and the acid recovered from the filtered solution by acidification with acetic acid. It separated from alcohol in needles, m. p. 186° [equiv., 235. Calc. for $C_{14}H_{19}O_2N$ (monobasic) : equiv., 233]. Betts and Plant record m. p. 179°.

The details of the preparation of the compounds described below are similar, but the experiments were carried out on a smaller scale; *e.g.*, the amount of ketone used for condensation in the 4-methyl series was 5·6 g., 11·2 g., and 5·6 g. in the cases of *p*-bromoaniline, *p*-toluidine, and β-naphthylamine respectively. (The theoretical percentages are given in parentheses.)

Compound.	Form.	M. p.	Analysis.	Remarks.
1-p-*Bromoanilino*-1-*cyano*-4-*methyl*cyclo*hexane*	A	126°	C, 57·5 (57·3); H, 5·7 (5·8)	Needles from hexane
	B	88—89	C, 57·4; H, 5·75	Nodules from hexane
1-p-*Bromoanilino*-4-*methyl*-cyclo*hexane*-1-*carboxyamide*	A	178	Br, 26·0 (25·7)	Needles from alcohol
	B	158	Br, 25·9	Needles from alcohol
1-p-*Bromoanilino*-4-*methyl*-cyclo*hexane*-1-*carboxylic acid*	A	184	Br, 25·9 (25·7)	
1-p-*Toluidino*-1-*cyano*-4-*methyl*cyclo*hexane*	A	104	C, 78·9 (78·9); H, 9·0 (8·8)	Needles from benzene
	B	79	C, 78·9; H, 7·9	Six-sided plates from hexane
1-p-*Toluidino*-4-*methyl*cyclo-*hexane*-1-*carboxyamide*	A	155	C, 73·0 (73·2); H, 9·2 (9·0)	Needles from alcohol
	B	145	C, 72·9; H, 9·1	Needles
1-m-*Toluidino*-1-*cyano*-4-*methyl*cyclo*hexane*	A	115	C, 78·9; H, 9·0	Needles from benzene
	B	82—83	C, 79·0; H, 8·7	Hexagonal plates from benzene
1-m-*Toluidino*-4-*methyl*cyclo-*hexane*-1-*carboxyamide*	A	137—138	C, 73·0; H, 9·1	Obtained by keeping the nitrile in conc. H_2SO_4 for 1 month
	B	117—118	C, 72·9; H, 9·0	
1-o-*Toluidino*-1-*cyano*-4-*methyl*cyclo*hexane*		100	C, 78·8; H, 8·9	Needles from benzene
1-o-*Toluidino*-4-*methyl*cyclo-*hexane*-1-*carboxyamide*		143	C, 73·0; H, 9·1	Plates from alcohol
1-α-*Naphthylamino*-1-*cyano*-4-*methyl*cyclo*hexane*	A	151—152	C, 81·8 (81·8); H, 7·6 (7·6)	Plates from benzene
	B	165	C, 81·6; H, 7·7	Soft needles from benzene
1-α-*Naphthylamino*-4-*methyl*-cyclo*hexane*-1-*carboxyamide*	A	138	C, 76·3 (76·6); H, 8·1 (7·8)	Plates from benzene–petrol
	B	204	C, 76·5; H, 7·9	
1-β-*Naphthylamino*-1-*cyano*-4-*methyl*cyclo*hexane*	A	152	C, 81·7; H, 7·8	Plates from benzene
	B	132	C, 81·5; H, 7·4	Needles from benzene
1-β-*Naphthylamino*-4-*methyl*-cyclo*hexane*-1-*carboxyamide*	A	270	C, 76·4; H, 8·0	Plates from benzene
	B	205	C, 76·5; H, 7·9	Minute plates from benzene
1-*Anilino*-1-*cyano*-3-*methyl*-cyclo*hexane*	A	75	C, 78·2 (78·5); H, 8·7 (8·4)	Needles from hexane
	B	95	C, 78·4; H, 8·4	Plates

Compound.	Form.	M. p.	Analysis.	Remarks.
1-*Anilino*-3-*methyl*cyclo*hexane*-1-*carboxyamide*	A	97	C, 72·2 (72·4); H, 8·8 (8·6)	Needles from alcohol
	B	92	C, 72·1; H, 8·7	Needles from benzene
1-p-*Bromoanilino*-1-*cyano*-3-*methyl*cyclo*hexane*		88—89	Br, 27·7 (27·3)	Needles from hexane
1-p-*Bromoanilino*-3-*methyl*-cyclo*hexane*-1-*carboxyamide*		137	Br, 25·9 (25·7)	Needles from alcohol
1-p-*Toluidino*-1-*cyano*-3-*methyl*cyclo*hexane*		78	C, 78·8 (78·9); H, 8·9 (8·8)	Rhomboids from alcohol
1-p-*Toluidino*-3-*methyl*cyclo*hexane*-1-*carboxyamide*		165	C, 73·0 (73·2); H, 9·2 (9·0)	Needles from alcohol
1-o-*Toluidino*-1-*cyano*-3-*methyl*cyclo*hexane*		86	C, 78·9; H, 9·0	Recovered unchanged after being kept in conc. H_2SO_4 for 4 months
1-α-*Naphthylamino*-1-*cyano*-3-*methyl*cyclo*hexane*		137	C, 81·6 (81·8); H, 7·8 (7·6)	Plates from benzene
1-α-*Naphthylamino*-3-*methyl*-cyclo*hexane*-1-*carboxyamide*		169	C, 76·5 (76·6); H, 8·0 (7·8)	Small prisms from benzene
1-β-*Naphthylamino*-1-*cyano*-3-*methyl*cyclo*hexane*		136	C, 81·4; H, 7·9	Rhombic plates from benzene
1-β-*Naphthylamino*-3-*methyl* cyclo*hexane*-1-*carboxyamide*		186	C, 76·7; H, 7·9	Needles from alcohol
1-*Anilino*-1-*cyano*-2-*methyl*-cyclo*hexane*	A	126	C, 78·3 (78·5); H, 8·6 (8·4)	Small plates from hexane containing a few drops of benzene
	B	88	C, 78·2; H, 8·3	Aggregates of soft needles
1-*Anilino*-2-*methyl*cyclo*hexane*-1-*carboxyamide*	A	128	C, 72·2 (72·4); H, 8·9 (8·6)	Obtained by keeping the nitrile in conc. H_2SO_4 for 6 weeks
	B	147	C, 72·3; H, 8·8	Plates from alcohol
1-*Anilino*-2-*methyl*cyclo*hexane*-1-*carboxylic acid*	A	187	C, 71·9 (72·1); H, 8·4 (8·1); equiv., 234 (233)	
1-p-*Bromoanilino*-1-*cyano*-2-*methyl*cyclo*hexane*		99	Br, 27·6 (27·3)	Short needles from hexane
1-p-*Bromoanilino*-2-*methyl*cyclo*hexane*-1-*carboxyamide*		154	Br, 26·0 (25·7)	Needles from alcohol
1-p-*Toluidino*-1-*cyano*-2-*methyl*cyclo*hexane*		140	C, 78·6 (78·9); H, 9·0 (8·8)	Plates from benzene
1-p-*Toluidino*-2-*methyl*cyclo*hexane*-1-*carboxyamide*		185	C, 73·0 (73·2); H, 9·1 (9·0)	Rectangular plates from benzene
1-m-*Toluidino*-1-*cyano*-2-*methyl*cyclo*hexane*		101	C, 78·7; H, 8·9	Needles from benzene
1-m-*Toluidino*-2-*methyl*cyclo*hexane*-1-*carboxyamide*		112	C, 73·1; H, 9·2	Obtained by keeping the nitrile in conc. H_2SO_4 for 4 months
1-o-*Toluidino*-1-*cyano*-2-*methyl*cyclo*hexane*		121	C, 78·8; H, 9·1	Needles from benzene. Recovered unchanged after keeping in conc. H_2SO_4 for 4 months
1-α-*Naphthylamino*-1-*cyano*-2-*methyl*cyclo*hexane*		118	C, 81·5 (81·8); H, 7·9 (7·6)	
1-β-*Naphthylamino*-1-*cyano*-2-*methyl*cyclo*hexane*	A	110—111	C, 81·4; H, 7·8	Nodules from benzene
	B	105	C, 81·5; H, 7·7	Plates from hexane
1-β-*Naphthylamino*-2-*methyl*-cyclo*hexane*-1-*carboxyamide*	A	178	C, 76·4 (76·6); H, 8·1 (7·8)	

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