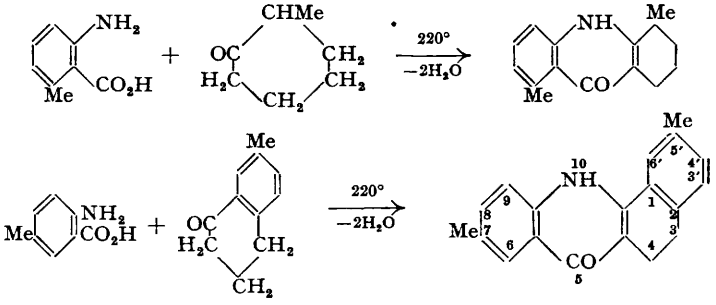
47. *Hydroacridones: Synthesis and Dehydrogenation. Part II.*

By R. A. Reed.

Dimethyltetrahydro-, methyldihydrobenz-, and dimethydihydrobenz-acridones have been prepared by condensation of the five methylanthranilic acids with 2- and 3-methyl*cyclo*hexanone, 1-tetralone, and 7-methyl-1-tetralone at 220°. Dehydrogenation has been effected by heating in air with copper powder at 360—400°. Orientation of the dimethylacridones has been established by absolute methods and by examination of their ultra-violet fluorescence colours.

Dimethyltetrahydroacridones, methyl- and dimethyl-dihydrobenzacridones have been prepared and dehydrogenated by methods similar to those used for methyltetrahydroacridones (J., 1944, 425).



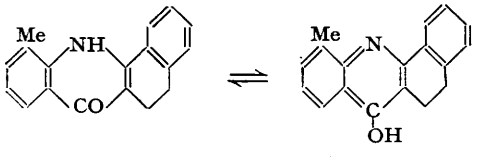
Only dimethyl-1 : 2 : 3 : 4-tetrahydroacridones containing both methyl groups in the same benzene ring have hitherto been described (Hughes and Lions, *Proc. Roy. Soc. N.S. Wales*, 1937, **71**, 458; Sen and Basu, *J. Indian Chem. Soc.*, 1930, **7**, 435; Huggill and Plant, J., 1939, 784), being prepared by condensation of the appropriate xylidine with ethyl *cyclo*hexenone-2-carboxylate, followed by cyclisation of the resultant anil at 260—280°. No dihydro-1 : 2-benzacridone derivatives have hitherto been described, although Bukhsh and Desai (*Proc. Indian Acad. Sci.*, 1939, **10**, *A*, 262) condensed anthranilic acid with *trans*-2-ketodecahydronaphthalene to obtain an octahydrobenzacridone of undetermined orientation.

The dimethyltetrahydroacridones obtained by using 3-methyl*cyclo*hexanone may contain this methyl group in either the 2- or the 4-position. Only one product has been isolated and this contains the methyl group in the 2-position. The orientation has been established in some cases by dehydrogenation and comparison of the resulting dimethylacridone with one of known orientation prepared by similar means. Thus 2 : 9-dimethylacridone may also be prepared by condensation of 4-methylanthranilic acid with 2-methyl*cyclo*hexanone and dehydrogenation of the product.

Examination under ultra-violet light of alcoholic solutions of the dimethylacridones produced on dehydrogenation, when made acid and alkaline by the addition of a few drops of 5N-hydrochloric acid and sodium hydroxide respectively, shows that a methyl group in position 4 or 6, *i.e.*, adjacent to the carbonyl group, results in both the acid and the alkaline solution fluorescing green. A methyl group in position 10 gives rise to a green colour in acid and a blue in alkaline solution. Methyl groups in any other positions give the normal acridone colours, *viz.*, blue in acid, green in alkali. On this evidence, the products arising from 3-methyl*cyclo*hexanone have the unfixed methyl group in position 2 and not 4. Obviously, however, when 6-methylanthranilic acid is condensed with the ketone, such evidence cannot determine the orientation of the dehydrogenated product. It is noteworthy that 4 : 10-dimethylacridone gives fluorescence colours similar to those of 10- and not 4-methylacridone, showing that the methyl group in position 10 has greater control over the fluorescence colours exhibited. By contrast, all the 1 : 2-benzacridone derivatives described show precisely the same colours, *viz.*, green in acid, blue in alkali. In this case, therefore, a methyl group in position 6 has no effect upon the colour given. The 1 : 2-benzacridones, when dissolved in alcohol, show only a faint blue-violet daylight fluorescence as opposed to the relatively strong fluorescence of the methyl- and dimethyl-acridones.

The dimethyltetrahydroacridones now reported are all soluble in dilute hydrochloric acid and give insoluble dichromates. Their solutions in cold concentrated sulphuric acid are yellow, showing no daylight fluorescence, unlike the hydroacridones containing three benzene rings, which yield yellow solutions exhibiting a blue or bluish-green fluorescence.

Only those methyl- or dimethyl-dihydrobenzacridones having a methyl group in position 9 are soluble in dilute acid, showing that the adjacent electron-repelling methyl group sends the equilibrium further towards the hydroxyacridine structure postulated by Tiedtke (*Ber.*, 1909, **42**, 621) for 1 : 2 : 3 : 4-tetrahydroacridone itself.



The introduction of a methyl group in position 9 generally has a marked lowering effect upon the melting point of both the hydroacridone and its dehydrogenation products.

All the hydroacridones described are soluble in alcoholic alkali except 10-phenyl-1 : 2 : 3 : 4-tetrahydroacridone; 2 : 10-dimethyl-1 : 2 : 3 : 4-tetrahydroacridone is, however, easily soluble in alcohol alone, as is 10-methyltetrahydroacridone (see Part I, *loc. cit.*). All the hydroacridones are insoluble in aqueous alkali, as are also the acridones obtained from them.

Experimental.

All m. p.'s recorded (liquid paraffin bath) are corrected and all nitrogen analyses (micro-Dumas) are by Dr. G. Weiler of Oxford.

1 : 9-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—3-Methylanthranilic acid (Part I, *loc. cit.*) (10 g.) and 2-methyl*cyclo*hexanone (93%; 12·5 ml.) were heated at 220° for 1½ hours. The liquid residue (solid when cold) was dissolved in boiling alcohol (25 ml.) and allowed to cool. The crystals were collected, washed with alcohol and with ether (yield, 5·7 g.; 40%), and recrystallised from alcohol (norit), giving almost colourless needles, m. p. 193—194°. The picrate, prepared in xylene solution and recrystallised from acetic acid, had m. p. 191—192° (decomp.). Titration of this with N/10-sodium hydroxide, and ethyl bis-2 : 4-dinitrophenylacetate as indicator, showed *M* for the base 225 (Calc. for $C_{15}H_{17}ON$: *M*, 227).

1 : 8-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—A mixture of 4-methylanthranilic acid (4 g.) and 2-methyl*cyclo*hexanone (93%; 5 ml.) was heated at 220° for 1½ hours. The cold solid residue was boiled with alcohol (10 ml.), cooled, filtered off, and washed with alcohol and ether (yield, 1·15 g.; 19%). The product crystallised from pyridine in cream-coloured prisms, m. p. 325°. The picrate separated overnight from alcohol in yellow needles, m. p. 204—206° (decomp.), titration indicating *M* for the base 228.

1 : 7-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—5-Methylanthranilic acid (7 g.) and 2-methyl*cyclo*hexanone (93%; 8 ml.), heated and worked up as above, gave 3·5 g. (34%) of crude product. This on recrystallisation from pyridine gave cream plates, m. p. 339°. Titration of the picrate, yellow prisms from acetic acid, m. p. 165—167° (decomp.), indicated *M* for the base 227.

1 : 6-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—From 2 g. of 6-methylanthranilic acid and 3 ml. of 2-methyl*cyclo*hexanone (93%), heated at 210° for 2½ hours, the crude product, isolated as before, amounted to 0·7 g. (23%). Recrystallisation from pyridine gave cream crystals, m. p. 311° (Found : N, 6·2. $C_{15}H_{17}ON$ requires N, 6·2%).

2 : 9-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—A yield of 3·2 g. (53%) of crude product was obtained from 4 g. of 3-methylanthranilic acid and 5 ml. of 3-methyl*cyclo*hexanone (98%) after 2½ hours' heating at 210°. Recrystallisation from pyridine gave cream-coloured crystals, m. p. 326°. Titration of the picrate, m. p. 218° (decomp.) (from acetic acid), indicated for the base *M* 227.

2 : 8-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—This was obtained (yield, 1·8 g.; 30%) from 4 g. of 4-methylanthranilic acid and 5 ml. of 3-methyl*cyclo*hexanone (98%) after 1 hour at 220°. Recrystallisation from much pyridine gave cream needles, m. p. above 385°. The hydrochloride crystallised when a hot solution in 2N-hydrochloric acid cooled. Titration of the picrate, m. p. 222° (from alcohol), gave *M* for the base 228.

2 : 7-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—This was produced by heating a mixture of 6 g. of 5-methylanthranilic acid and 8 ml. of 3-methyl*cyclo*hexanone (98%) at 220° for 30 mins. (yield, 4·2 g.; 40%). Recrystallisation from much pyridine gave colourless or faintly pink leaflets, m. p. 378°. This compound rapidly dissolved in 5N-hydrochloric acid, the hydrochloride soon separating. The picrate, m. p. 222° (decomp.) (from acetic acid), showed on titration *M* for the base 223.

2 : 6-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—Heated at 220° for 1½ hours, a mixture of 2 g. of 6-methylanthranilic acid and 3 ml. of 3-methyl*cyclo*hexanone (98%) gave this *compound* (0·8 g.; 27%). Colourless prisms, m. p. 365°, were obtained by recrystallisation from pyridine (Found : N, 6·2. $C_{15}H_{17}ON$ requires N, 6·2%). The picrate separated from acetic acid in yellow crystals, m. p. 168° (decomp.), containing acetic acid of crystallisation.

2 : 10-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—This was obtained (4·5 g.; 32%) from 10 g. of *N*-methylanthranilic acid (Part I, *loc. cit.*) and 12·5 ml. of 3-methyl*cyclo*hexanone (98%) at 220° for 2 hours, with crystallisation of the residue from 40 ml. of benzene. Recrystallisation from pyridine gave colourless crystals, m. p. 192—193°, becoming brownish on exposure and readily soluble in cold alcohol. The picrate, m. p. 173—174° (from acetic acid), gave, on titration, *M* for the base 229.

An attempt to prepare 1 : 10-dimethyl-1 : 2 : 3 : 4-tetrahydroacridone from *N*-methylanthranilic acid and 2-methyl-*cyclo*hexanone (93%) gave no solid product.

10-*Phenyl*-1 : 2 : 3 : 4-*tetrahydroacridone*.—Two hours' heating at 210° of a mixture of 10 g. of *N*-phenylanthranilic acid (*Org. Synth.*, **19**, 6) and 8 g. of *cyclo*hexanone (97·5%) and treatment of the residue with 100 ml. of benzene gave 3·5 g. (28%) of product. Recrystallisation from alcohol (norit) gave pale yellow prisms, m. p. 298°, insoluble in cold alcoholic alkali but soluble in fairly concentrated sulphuric acid, dilution precipitating the base. The solution in cold concentrated sulphuric acid showed a fluorescence (bluish-green). Titration of the picrate, m. p. 142° (from acetic acid), indicated *M* for the base 277 (Calc. for $C_{19}H_{17}ON$: *M*, 275).

Dehydrogenations.—These were accomplished by heating in a metal-bath with 2 parts of copper powder at 360—400° as described in Part I. The total sublimate was extracted with boiling 2N-hydrochloric acid, and the insoluble solid recrystallised from a suitable solvent.

1 : 9-Dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) gave 0·1 g. of 1 : 9-*dimethylacridone*, yellow leaflets, m. p. 230°, after recrystallisation from alcohol (Found : N, 6·4. $C_{15}H_{13}ON$ requires N, 6·3%), 1 : 8-dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·45 g.) gave 0·1 g. of 1 : 8-*dimethylacridone*, pale yellow needles, m. p. 301°, after two crystallisations from pyridine (Found : N, 6·55%), 1 : 7-dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·4 g.) gave 0·2 g. of 1 : 7-*dimethylacridone*, pale yellow needles, m. p. 343° after crystallisation from pyridine (Found : N, 6·8%), and 1 : 6-dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) yielded 0·2 g. of 1 : 6-*dimethylacridone*, pale yellow needles, m. p. 282° after recrystallisation from 50% pyridine (Found : N, 6·3%).

2 : 9-Dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) yielded 0·15 g. of product, pale yellow crystals, m. p. 314°, from pyridine (Found : N, 6·3%). A mixed m. p. with 1 : 8-dimethylacridone gave m. p. 301°, *i.e.*, no depression, and the ultra-violet fluorescence colours were identical. On this evidence 1 : 8-dimethylacridone would appear to be dimorphic.

2 : 8-Dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) gave 0·15 g. of product, yellow needles, m. p. 363°, from aqueous pyridine (Found : N, 6·45%). Since the ultra-violet fluorescence colours were blue in acid, green in alkali, the product was 2 : 8-*dimethylacridone*.

2 : 7-Dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) produced 0·1 g. of yellow needles, m. p. 328° (from alcohol) (Found : N, 6·55%). The fluorescence colours, blue in acid, green in alkali, show the product to be 2 : 7-*dimethylacridone*.

2 : 6-Dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·3 g.) yielded 0·1 g. of a product, pale yellow needles, m. p. 352°, from

pyridine (Found: N, 6·1%). In this case the fluorescence colours, green in acid, green in alkali, cannot confirm the orientation, but the high m. p. is evidence for 2 : 6-*dimethylacridone*.

2 : 10-Dimethyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) gave 0·05 g. of 2 : 10-dimethylacridone, m. p. 181°, after two crystallisations from aqueous alcohol and one from benzene. A specimen prepared by methylation of 2-methylacridone (Gleu and Nitzsche, *J. pr. Chem.*, 1939, **153**, 219) had the same m. p., and a mixture of the two showed no depression. The fluorescence colours were green in acid, blue in alkali.

10-Phenyl-1 : 2 : 3 : 4-tetrahydroacridone (0·5 g.) gave 0·2 g. of 10-phenylacridone, buff-coloured prisms, m. p. 275° (decomp.), from toluene (Goldberg and Nimerovsky, *Ber.*, 1907, **40**, 2450, record m. p. 276°). The colours given under ultra-violet light were bluish-green in acid, blue in alkali.

To establish the validity of the fluorescence technique in these orientation problems, the monomethylacridones (see Part I), 3 : 10- and 4 : 10-dimethylacridone (Gleu and Nitzsche, *loc. cit.*) were examined in alcoholic solution under ultra-violet light.

	Acid.	Alkali.		Acid.	Alkali.
Acridone	Blue	Green	4-Methylacridone	Green	Green
1-Methylacridone	,,	,,	10-Methylacridone	,,	Blue
2-Methylacridone	,,	,,	3 : 10-Dimethylacridone	,,	,,
3-Methylacridone	,,	,,	4 : 10-Dimethylacridone	,,	,,

That these rules do not apparently apply where the substituent groups in the acridone nucleus are other than methyl is shown by the fact that 2-chloro-7-methoxyacridone (May and Baker Ltd.) showed green fluorescence in acid and also in alkali.

3 : 4-*Dihydro*-1 : 2-*benzacridone*.—A mixture of 7 g. of anthranilic acid and 11 g. of 1-tetralone (Schroeter, D.R.P. 346,948; *p*-nitrophenylhydrazone, m. p. 231—232°) was heated to 200° during 1½ hours and maintained at 220° for a further hour. The residue was refluxed for 1½ hours with 50 ml. of benzene, cooled, and filtered. The solid was washed with pyridine to remove colour and then with ether, giving a yield of 5·4 g. (43%). Recrystallisation from acetic acid gave cream needles, m. p. 301°. Titration of the picrate, m. p. 175°, prepared in acetic acid solution and dried at 100°, gave *M* for the base 247 (Calc. for $C_{17}H_{13}ON$: *M*, 247).

9-*Methyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—3-Methylanthranilic acid (4 g.) and 1-tetralone (5 g.) were heated at 220° for 2½ hours, and the product extracted with 20 ml. of alcohol. The residue (2·5 g.; 36%), recrystallised from alcohol, gave cream leaflets, m. p. 216°. The picrate, m. p. 191—192°, prepared in alcohol and dried at 100°, showed on titration *M* for the base 264 (Calc. for $C_{18}H_{15}ON$: *M*, 261).

8-*Methyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—A mixture of 4 g. of 4-methylanthranilic acid and 6 g. of 1-tetralone, heated at 220° for 1½ hours, gave 1·8 g. (26%) of product, after extraction with alcohol. Recrystallisation of the brownish prisms from much pyridine gave cream prisms, m. p. 320° (Found: N, 5·8. $C_{18}H_{15}ON$ requires N, 5·4%).

7-*Methyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—5-Methylanthranilic acid (2 g.) and 1-tetralone (2·2 g.; 1·15 mols.), heated at 220—240° for ½ hour and extracted with benzene, gave a yield of 1·6 g. (46%). Recrystallisation from pyridine gave cream needles, m. p. 319°. Titration of the picrate, m. p. 199° (decomp.) (from acetic acid, and dried at 100°), indicated *M* for the base 262 (Calc., 261).

6-*Methyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—A mixture of 2 g. of 6-methylanthranilic acid and 2·5 g. of 1-tetralone was heated at 220° for 1½ hours. The cold liquid residue was heated with 10 ml. of benzene and allowed to cool; 0·75 g. (22%) of product then separated. Recrystallisation from pyridine–alcohol gave colourless needles, m. p. 257—258° (Found: N, 5·5. $C_{18}H_{15}ON$ requires N, 5·4%).

5′-*Methyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—One hour's heating at 220° of a mixture of 7 g. of anthranilic acid and 11 g. of 7-methyl-1-tetralone (Barnett and Sanders, J., 1933, 434; see also Fieser and Martin, *Org. Synth.*, **15**, 92; Martin, *ibid.*, **17**, 97; *p*-nitrophenylhydrazone, m. p. 192—193°) gave 5·8 g. (43·5%) of product after extraction with 50 ml. of benzene. Recrystallisation from pyridine produced cream needles, m. p. 300°. Titration of the picrate, m. p. 207° (from acetic acid), showed *M* for the base 255 (Calc., 261).

5′ : 9-*Dimethyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—3-Methylanthranilic acid (4 g.) and 7-methyl-1-tetralone (5 g.) were heated together at 220° for 2½ hours, and the residue extracted with 20 ml. of alcohol and washed with a little pyridine, alcohol, and finally ether. Recrystallisation of the product (2·7 g.; 37%) from dilute acetic acid yielded colourless needles, m. p. 240°. Titration of the picrate, m. p. 206—207° (from alcohol), showed *M* for the base 279 (Calc., 275). The picrate, prepared in acetic acid solution, had m. p. 187—188° and contained solvent of crystallisation.

5′ : 8-*Dimethyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—A yield of 4·0 g. (55%) was obtained as a brown crystalline solid from a mixture of 4 g. of 4-methylanthranilic acid and 7 g. of 7-methyl-1-tetralone by heating at 220° for 1½ hours and extracting the product with 100 ml. of alcohol. Recrystallisation from pyridine (norit) gave cream needles, m. p. 299° (Found: N, 5·4. $C_{19}H_{17}ON$ requires N, 5·1%). The picrate, m. p. 229° (decomp.) (from acetic acid), is not equimolecular.

5′ : 7-*Dimethyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—A mixture of 4 g. of 5-methylanthranilic acid and 5 g. of 7-methyl-1-tetralone, heated and worked up as for the 5′ : 9-compound, gave 4·7 g. (65%) of product, which crystallised from pyridine in cream needles, m. p. 304°. Titration of the picrate, m. p. 216° (decomp.) (from acetic acid), indicated *M* for the base 277 (Calc., 275).

5′ : 6-*Dimethyl*-3 : 4-*dihydro*-1 : 2-*benzacridone*.—6-Methylanthranilic acid (2 g.) and 7-methyl-1-tetralone (2·5 g.), heated at 220° for 1½ hours and extracted with 10 ml. of benzene, gave 1·0 g. (28%) of product as grey prisms. Recrystallisation from pyridine yielded colourless crystals, m. p. 303—304° (Found: N, 5·3. $C_{19}H_{17}ON$ requires N, 5·1%).

Dehydrogenations.—3 : 4-Dihydro-1 : 2-benzacridone (0·5 g.) gave 0·1 g. of 1 : 2-benzacridone, pale yellow needles, m. p. above 380°, from pyridine (Ullmann and Rasetti, *Annalen*, 1907, **355**, 351, give m. p. above 360°).

9-Methyl-3 : 4-dihydro-1 : 2-benzacridone (0·5 g.) yielded 0·05 g. of 9-*methyl*-1 : 2-*benzacridone*, pale yellow needles, m. p. 265°, from aqueous pyridine (Found: N, 5·4. $C_{18}H_{13}ON$ requires N, 5·4%), 8-methyl-3 : 4-dihydro-1 : 2-benzacridone (0·5 g.) produced 0·1 g. of 8-*methyl*-1 : 2-*benzacridone*, m. p. 364°, pale yellow needles from pyridine (Found: N, 5·75%), 7-methyl-3 : 4-dihydro-1 : 2-benzacridone (0·35 g.) gave 0·15 g. of 7-*methyl*-1 : 2-*benzacridone*, m. p. 378—379°, pale yellow needles from pyridine (Found: N, 5·65%), 6-methyl-3 : 4-dihydro-1 : 2-benzacridone (0·4 g.) yielded 0·2 g. of 6-*methyl*-1 : 2-*benzacridone*, m. p. 286°, pale yellow needles from 50% pyridine (Found: N, 5·3%), and 5′-methyl-3 : 4-dihydro-1 : 2-benzacridone (0·5 g.) gave rise to 0·15 g. of 5′-*methyl*-1 : 2-*benzacridone*, m. p. 341°, pale yellow needles from aqueous pyridine (Found: N, 6·0%).

5′ : 9-Dimethyl-3 : 4-dihydro-1 : 2-benzacridone (0·5 g.) produced 0·04 g. of 5′ : 9-*dimethyl*-1 : 2-*benzacridone*, m. p. 238°, yellow crystals from aqueous alcohol (Found: N, 5·4. $C_{19}H_{15}ON$ requires N, 5·1%), 5′ : 8-dimethyl-3 : 4-dihydro-1 : 2-benzacridone (0·4 g.) gave 0·1 g. of 5′ : 8-*dimethyl*-1 : 2-*benzacridone*, m. p. 320°, pale yellow needles from aqueous pyridine (Found: N, 4·95%), 5′ : 7-dimethyl-3 : 4-dihydro-1 : 2-benzacridone (0·5 g.) produced 0·2 g. of 5′ : 7-*dimethyl*-

1 : 2-*benzacridone*, m. p. 334°, pale yellow needles from aqueous pyridine (Found : N, 4·75%), and 5′ : 6-dimethyl-3 : 4-dihydro-1 : 2-benzacridone (0·4 g.) yielded 0·05 g. of 5′ : 6-*dimethyl*-1 : 2-*benzacridone*, m. p. 276°, pale yellow needles from 50% pyridine (norit) (Found : N, 5·0%).

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