Molecular Compounds between Heterocyclic Compounds Containing Nitrogen[*]

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(Received August 30, 1956)

Although extensive researches[1-3] have been made on molecular compounds, little information[4] is found in the literature concerning those formed from heterocyclic compounds. In the present note the writers show that molecular compounds of a similar type are formed by heterocyclic compounds containing nitrogen atoms; further, interacting forces between the partner molecules are not essentially different from those acting in other molecular compounds.

Experimental

The following compounds (I—IX, group A) and their hydrogenated compounds (group B) were prepared for the examination.

Group A; benzo-[f]-quinoline (I), 5,6-dihydrobenzo-[f]-quinoline (II), benzo-[h]-quinoline (III), acridine (IV), 1,2,3,4-tetrahydroacridine (V), 7,8,9,10-tetrahydrophenanthridine (VI), 2,3-trimethylenequinoline (VII), quinoline (VIII), and 1,2,3,4-tetrahydrocarbazole (IX).

Preparation of Compounds.—The following compounds were prepared by the procedure described in the literature as cited. Solid compounds were recrystallized to constant melting point from the solvents indicated and, on the other hand, oily compounds were regenerated from their solid derivatives of constant melting point and redistilled before use: (I)[5], m. p. 93-93.5°C (benzine); 1,2,3,4,7,8,9,10 - octahydrobenzo - [f] - quinoline[6], m. p. 65-66°C (petroleum-ether), 1,2,3,4,5,6,4a, 4b-octahydrobenzo-[f]-quinoline[6], m. p. 90-91°C (petroleum-ether), (III)[7], m. p. 51-52.5°C (petroleum-ether); 1,2,3,4-tetrahydrobenzo-[h]-quinoline[7] m. p. 46-47°C (petroleum-ether); (IV), m. p. 109-110° (benzene); (V)[8], m. p. 54-55°C (benzene); *cis*-1,2,3,4,9,10,4a,4b - octahydroacridine[9], m. p. 71-73°C (petroleum-ether); *trans*-1,2,3,4,9,10,4a, 4b-octahydroacridine[10], m. p. 81-83°C (petroleum-ether); (VI)[11], m. p. 63-64°C (benzine); 5,6,7, 8,9,10,6a,10a - octahydrophenanthridine[12], m. p. 70-72°C (aqueous alcohol); (VII)[13], m. p. 60-61°C (benzine); *cis*-1,2,3,4-tetrahydro-2,3-trimethylenequinoline[14], oil, benzoyl derivative[14], m. p. 159-160°C (acetone), *trans* - 1,2,3,4-tetrahydro - 2,3-trimethylenequinoline[14], m. p. 68-68.5°C (petroleum-ether), (VIII), m. p. about −15°C, picrate, m. p. 228-230°C (ethanol); 1,2,3,4-tetrahydroquinoline[15], m. p. about 20°C, benzoyl derivative, m. p. 73-74°C (alcohol); (IX)[16], m. p. 117-118°C (methanol); *cis*-1,2,3,4,10,11-hexahydrocarbazole[17], m.p. 98-99°C (ethanol); *trans*-1,2,3,4,10,11-hexahydrocarbazole[17], m. p. 124-126°C (ethanol).

1,2,3,4-Tetrahydrobenzo-[f]-quinoline.—A mixture of 20 g. of benzo-[f]-quinoline and 20 g. of granulated tin was refluxed in 150 cc. of conc. hydrochloric acid for three hours until the tin was entirely consumed. The reaction mixture was made strongly alkaline with 6 N sodium hydroxide solution after cooling, and it was distilled with steam. The distillate was extracted with ether and recrystallized from ligroin after removal of ether, yielding 10 g. of pale yellow crystals[18], m. p. 93-93.5°C.

Anal. Found: C, 86.12, H, 6.00. Calcd. for $C_{13}H_{11}N$: C, 86.16, H, 6.12%.

This base was dissolved in 50 cc. of ether and treated with a small excess of equivalent benzoyl chloride and N sodium hydroxide solution. After the odor of benzoyl chloride had entirely disappeared, the ethereal layer was separated from

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[*] Partly presented at the Annual Meeting of the Chemical Society of Japan, April 3, 1956. The 8 th Part on "The Condensed Polynuclear Perhydro-Compounds Containing Nitrogen." The 7 th Part, T. Masamune and G. Homma, *J. Chem. Soc. Japan* (*Pure Chem. Sect.*), **77**, 1766 (1956).

[1] C. W. Wheland, "Advanced Organic Chemistry" John Wiley and Son's, 2nd ed., New York 1949 p. 54.

[2] Ch. Shinomiya, This Bulletin, **15**, 92, 137, 259, 281, 309 (1940).

[3] S. Seki and K. Suzuki, ibid., **26**, 63, 209, 372 (1953).

[4] It was found by Masamune and Kubota in this laboratory that a molecular compound is formed between tetrahydro-and octahydrophenanthridine. Ref., *J. Chem. Soc. Japan.* (*Pure Chem. Sect.*), **77**, 1467 (1956).

[5] H. C. A. Knueppel, *Ber*, **29**, 708 (1896).

[6] E. Bamberger, ibid., **24**, 2648 (1891).

[7] E. Bamberger and L. Stettenheimer, ibid., **24**, 2473 (1891).

[8] W. Borsche, ibid., **41**, 2203 (1908).

[9] W. H. Perkin and S. G. P. Plant, *J. Chem. Soc.*, **1928**, 2583.

[10] W. H. Perkin and W. G. Sedgwick. ibid., **1926**, 438.

[11] B. L. Hollingsworth and L. Petrow, ibid., **1948**, 1537.

[12] See Ref. (4).

[13] W. Borsche, *Ann.*, **377**, 120 (1910).

[14] W. H. Perkin and S. G. P. Plant, *J. Chem. Soc.*, **1928**, 638.

[15] H. Rupe, M. Seiberth and W. Kussmaul, *Helv. Chim. Acta*, **3**, 75 (1920).

[16] C. V. Rogers and B. B. Corson, *J. Am. Chem. Soc.*, **69**, 2910 (1947).

[17] J. Gurney, W. H. Perkin and S. G. P. Plant, *J. Chem. Soc.*, **1927**, 2676.

[18] This substance was shown to correspond to dihydro-derivative of benzo-[f]-quinoline from analytical value, and was proved to be a molecular compound between (I) and its pure tetrahydro-derivative in the present paper. Bamberger's "1,2,3,4-tetrahydrobenzo-[f]-quinoline" would probably be the same substance as this. See Ref. (5).

the aqueous solution and was washed with 2 N hydrochloric acid to remove unreacted benzo-[f]-quinoline. A benzoylated compound obtained from the ethereal solution by removal of the solvent, had m. p. 153-4°C on recrystallization from alcohol. It was refluxed with 12 g. of potassium hydroxide in 300 cc. aqueous alcoholic solution for four hours. The product was again extracted with ether, after distillation of alcohol under reduced pressure and addition of water. The ethereal solution was treated with 2 N hydrochloric acid. After separation from the ethereal layer, the acidic solution gave 7 g. of oily tetrahydrobenzo-[f]-quinoline, b. p. 200-202°C (14mm.), on alkalification, separation from aqueous solution and distillation under diminished pressure. The hydrochloride was prepared by passing hydrogen chloride into the ethereal solution of the base.

Anal. Found: C, 70.95; H, 6.39. Calcd. for $C_{13}H_{13}NHCl$: C, 71.03; H, 6.42%.

Its picrate had m. p. 167-168°C, when the base was added into saturated alcoholic solution of picric acid and was recrystallized from the same solvent.

5, 6-Dihydrobenzo-[f]-quinoline [II].—Benzo-[f]-quinoline (10 g.) was hydrogenated with 1 g. of Raney-nickel[19] at 100°C in an autoclave, starting at 70 atmospheric pressures and the reaction was stopped when one and a half mole of hydrogen were absorbed. The products were extracted with 200 cc. of ether. When the ethereal solution was concentrated up to 50 cc. and cooled, about 4 g. of pale yellow crystals were separated. The crystals thus isolated by filtration gave m. p. 88-90°C, on recrystallization from aqueous alcohol. On the other hand, when the solvent of the filtrate was entirely removed, the residue consisting of some oil and a small amount of solid was again filtered. The filtrate thus separated was proved to be tetrahydrobenzo-[f]-quinoline as above mentioned, by derivation of the benzoyl compound and by the mixed melting point determination. The yield of the base was 6 g.

The crystals of m. p. 88-90°C were dissolved in 100 cc. of ether and subjected to benzoylation with 3.3 g. of benzoylchloride and alkaline solution. After seven hours, the ethereal solution (a) was separated from the aqueous solution and treated with 100 cc. of 2 N-hydrochloric acid. As the acidic solution was made alkaline and extracted with ether, the ethereal solution gave 1.7 g. of an oily dihydrobenzo-[f]-quinoline. Its picrate and hydrochloride had m. p. 205-206°C and m. p. 255-257°C respectively.

Anal. Found: C, 71.72; H, 5.73. Calcd. for

System of (I) and 1, 2, 3, 4-tetrahydrobenzo-[f]-quinoline (Fig. 1).

Mol % of (I)	100	90	80	70	60	50	40	30	20	10
Melting points	92	66	80	88	92	93	92	87	80	63
Thawing points	90	64	64	79	87	91.5	88	78	—	—

System of (II) and 1, 2, 3, 4-tetrahydrobenzo-[f]-quinoline.

Mol % of (II)	70	60	50	40	30	20
Melting points	73	87	90	89	83	70
Thawing points	—	80	88	84	75	—

System of (V) and *cis*-1, 2, 3, 4, 9, 10, 4a, 9a-octahydroacridine (Fig. 2).

Mol % of (V)	100	90	85	80	70	60	50	40	30	20	10	0
Melting points	55	47	42	45	52	56	58	51	54	63	69	73
Thawing points	54	39	38	38	38	51	57	48	48	49	58	71

System of (VI) and 5, 6, 7, 8, 9, 10, 6a, 10a-octahydrophenanthridine.

Mol % of (VI)	100	90	85	80	70	60	50	40	33	30	20	10	0
Melting points	64	60	54	60	63	69	73	75	76	75	73	66	72
Thawing points	63	52	52	52	52	53	66	73	75	74	66	64	70

System of (V) and *trans*-1, 2, 3, 4, 9, 10, 4a, 9a-octahydroacridine.

Mol % of (V)	100	90	80	70	60	50	40	30	20	10	0
Melting points	55	51	47	43	51.5	57	63	68	75	80	83
Thawing points	54	43	42	42	43	43	44	45	51	64	81

System of (IV) and *cis*-1, 2, 3, 4, 9, 10, 4a, 9a-octahydroacridine.

Mol % of (IV)	100	90	80	70	60	50	40	30	20	10	0
Melting points	110	105	102	98	95	90	80	55	65	71	73
Thawing points	109	99	94	89	83	73	—	—	—	53	71

System of (I) and 1, 2, 3, 4, 7, 8, 9, 10-octahydrobenzo-[f]-quinoline.

Mol % of (I)	100	90	80	70	60	50	40	30	20	10	0
Melting points	93	91	85	78	69	55	42	40	50	61	66
Thawing points	92	80	66	47	36	34	33	33	35	43	65

System of (IX) and *cis*-1, 2, 3, 4, 10, 11-hexahydrocarbazole.

Mol % of (IX)	100	90	80	70	60	50	40	30	20	10	0
Melting points	118	114	106	99	92	84	72	83	88	94	99
Thawing points	116	85	74	71	70	70	70	71	73	78	98

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[19] R. Mozingo, "Org. Syntheses" Vol. 21 (1941), p. 15.

$C_{13}H_{11}NHCl$: C, 71.72; H, 5.55%.

On the other hand, the benzoylated compound of tetrahydrobenzo-[f]-quinoline was isolated from the ethereal solution (a).

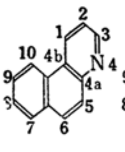
Melting Point-Composition Diagram. — A sample each of group (A) and group (B) was weighed (about 5 mg.) and dissolved in ether respectively. These ethereal solutions were mixed in a proper ratio, heated for a short time to remove the solvent and then poured into a capillary with a diameter 3-4 mm. The mixture was furthermore dried in a desiccator after complete removal of ether. The phase diagram was obtained by recording both the thawing and melting points of these mixtures, using the common procedures of melting point determination and sometimes using the method of Shinomiya[2].

Thawing and melting points of four combinations resulted in formation of a peak in the diagram (see below and Figs. 1 and 2). For the sake of comparison the same points of several representative cases not forming a molecular compound are also recorded in the following.

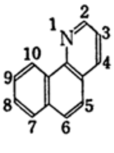
Ultraviolet Absorption Measurements. — The measurements were made by the use of a Beckmann quartz spectrophotometer, Model DU. Alcohol or iso-octane (dried over phosphorous pentoxide) was used as solvent. The spectrum was examined at 0.5 mμ intervals near maximum and at 3 mμ intervals at the region from 215 to 360 mμ.

Results and Discussion

The results of thermal analysis for mixtures of one of group (A) and one of group (B) were summarized in Table I and the diagrams of two representative pairs forming molecular compounds were shown in Figs. 1 and 2. Four combinations yielded a peak in the melting point diagram, viz., (I: 1,2,3,4-tetrahydrobenzo-[f]-quinoline), (II: 1,2,3,4-tetrahydrobenzo-[f]-quinoline), (V: *cis*-1,2,3,4,9,10,4a,9a-octahydroacridine) and (VI: 5,6,7,8,9,10,6a,10a-octahydrophenanthridine); but there was no peak in the others. It is to be noted that these molecular compounds are



(I)



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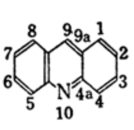
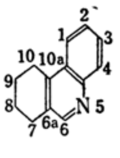
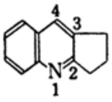


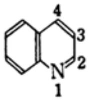
(IV)



(VI)



(VII)



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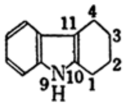

(IX)

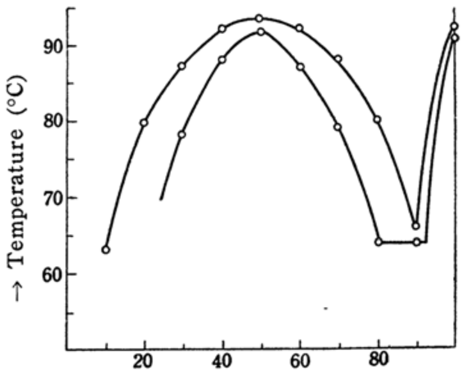

Fig. 1. Molecular compound between benzo-[f]-quinoline and 1,2,3,4-tetrahydrobenzo-[f]-quinoline.

TABLE I

ON THE FORMATION OF CRYSTALLINE MOLECULAR COMPOUNDS

Group A	Group B	Molecular compound	
		Molar ratio	Melting point (°C)
(I)	1,2,3,4-Tetrahydrobenzo-[f]-quinoline	1 : 1	93—93.5
(I)	1,2,3,4,7,8,9,10-Octahydrobenzo-[f]-quinoline	None	
(I)	1,2,3,4,5,6,4a,4b-Octahydrobenzo-[f]-quinoline	None	
(II)	1,2,3,4-Tetrahydrobenzo-[f]-quinoline	1 : 1	88—90
(III)	1,2,3,4-Tetrahydrobenzo-[h]-quinoline	None	
(IV)	*cis*-1,2,3,4,9,10,4a,9a-Octahydroacridine	None	
(V)	〃	1 : 1	56—58
(V)	*trans*-1,2,3,4,9,10,4a,9a-Octahydroacridine	None	
(VI)	5,6,7,8,9,10,6a,10a-Octahydrophenanthridine	1 : 2	75—76
(VII)	*cis*-1,2,3,4-Tetrahydro-2,3-trimethylenequinoline	None	
(VIII)	1,2,3,4-Tetrahydroquinoline	None	
(IX)	*cis*-1,2,3,4,10,11-Hexahydrocarbazole	None	
(IX)	*trans*-1,2,3,4,10,11-Hexahydrocarbazole	None	

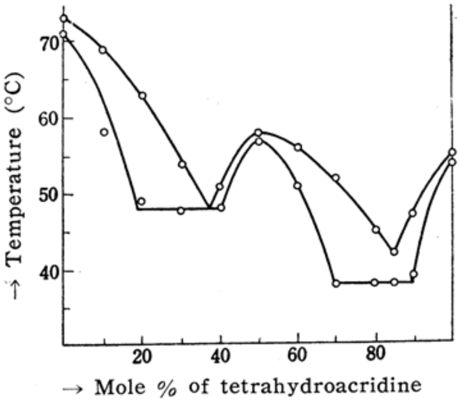

Fig. 2. Molecular compound between 1, 2, 3, 4-tetrahydroacridine and *cis*-1, 2, 3, 4, 9, 10, 4a, 9a-octahydroacridine.

formed between the compounds containing nitrogen of anilino-type and those of pyridino-type, but their mixture does not always result in the formation of a molecular compound.

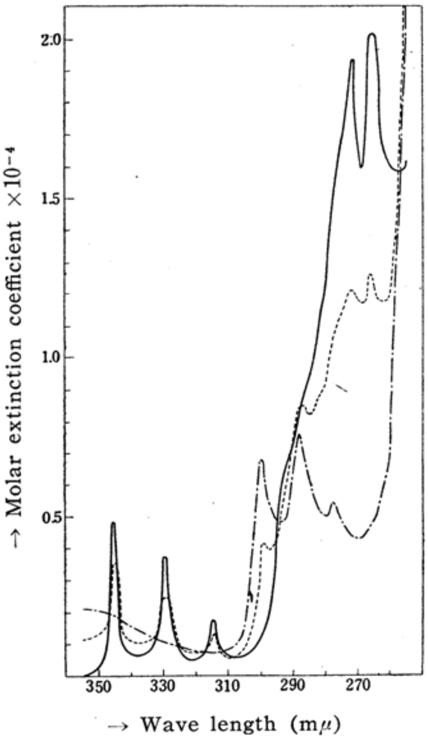

Fig. 3. Ultraviolet absorption spectrum of molecular compound between benzo-[f]-quinoline and its 1, 2, 3, 4-tetrahydro-derivative.

Solvent: isoöctane; conc.: $M \times 10^{-4}$

—— Benzo-[f]-quinoline

–·–· 1, 2, 3, 4-Tetrahydrobenzo-[f]-quinoline

------ Molecular compound

The ultraviolet absorption spectra of one of the molecular compounds examined are shown in Fig. 3 together with those of component molecules concerned. They refer to the measurements of the same concentration. Examination of Fig. 3 shows that the intensity of a molecular compound is half of the sum of intensity of partner molecules, indicating that the molecular compound concerned is in a state of complete dissociation. In the other three molecular compounds, a similar phenomenon is found.

There are several papers available which deal with the nature of intermolecular forces in molecular compounds[20–23]. However, no satisfactory explanation has been given even for the most familiar type of molecular compound, viz., quinhydrone formed from quinone and hydroquinone. According to Suzuki and Seki[22], the hydrogen bond is important in the same quinhydrone: they ascribed 4.6 to 1.6 kcal. of the total heat of formation (5.386 kcal.) to this cause. As the molecules of the substance in group A which form molecular compounds have one N atom and those of B have an N—H bond, a hydrogen bond of the N—H···N type may possibly be formed between the interacting molecules in the present case. But this is not the most important cause of the formation of such a molecular compound. For instance, it is to be noted that no molecular compound is formed between benzo-[f]-quinoline and 1, 2, 3, 4, 7, 8, 9, 10-octahydrobenzo-[f]-quinoline (see Table 1).

Contrary to Suzuki and Seki, Tsubomura[23] holds a view that the effect of charge transfer is most important in quinhydrone. However, no definite support was obtained for that theory of charge transfer from the present authors' measurement of ultraviolet absorption spectra. Therefore, further measurement under different conditions is desirable.* It may, however, suffice to point out here that all the molecules concerned have π-electrons and that the formation of molecular compounds seems to be affected by such a factor as the number of unsaturated rings.

Lastly it is of interest to note that the *cis*-isomer of hydrogenated acridine is

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20) K. Higasi and K. Hirota, "Riron Yuki-Kagaku," Asakura-Shoten, Tokyo (1951), p. 40.

21) H. Murakami, This Bulletin, **26**, 441 (1953).

22) S. Seki and K. Suzuki, ibid., **26**, 372 (1953).

23) H. Tsubomura, ibid., **26**, 304 (1953).

* The writers propose to study this problem in the future.

capable of participating in molecular compound formation, while the *trans*-isomer has no such capacity. Therefore, the spatial configuration seems to be one of the factors, suggesting the importance of van der Waal's force in the molecular compound formation.

The present research was conducted under the supervision of President H. Suginome of the University and the authors are especially indebted to Professor K. Higasi for his kind guidance and criticism.

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