*Medium Ring-size Effect in 2′, 3-Polymethylen-3-alkyl-2-phenylindolenines**

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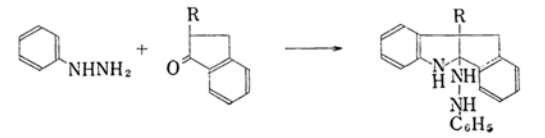
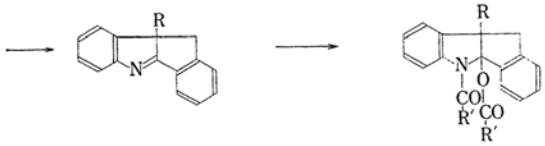
The pronounced reactivity of the C=N group of indolenine[1] to add various reagents was first observed when Leuchs and his co-workers[2] heated 2-benzyl-1-indanone (Ia) with excess phenylhydrazine at 130°C to yield a substance, $C_{28}H_{25}N_3$, m. p. 192°C, which, on treatment with hydrochloric acid, lost the phenylhydrazine and formed the hydrochloride (decomp. p. 206～208°C) of the expected indolenine IIIa ($C_{22}H_{17}N$, m. p. 123～124°C). It was soon

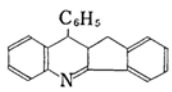


Ia R=$CH_2C_6H_5$ IIa R=$CH_2C_6H_5$
b R=CH_2CH_3 b R=CH_2CH_3

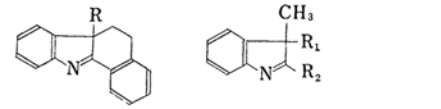


IIIa R=$CH_2C_6H_5$ IV
b R=CH_2CH_3

found that the indolenine IIIa was formed directly without a catalyst and that IIIa then immediately added phenylhydrazine to form the addition compound IIa. The C=N group adds not only amines, ammonia and phenylhydrazine, but also acid anhydrides (acetic, benzoic and phthalic anhydride) to give the indoline derivatives which have the general formula of IV.



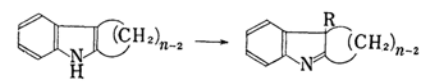
V



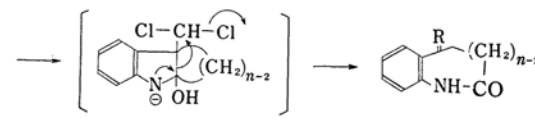
VIa R=$CH_2C_6H_5$ VIIa R_1=CH_3, R_2=C_6H_5
b R=CH_2CH_3 b R_1=$CH_2C_6H_5$, R_2=CH_3

A possibility that the active methylene of the benzyl group might be involved in the ring closure reaction giving the dihydroquinoline V, and that it is V instead of the indolenine IIIa which is responsible for the facile addition reactions, was ruled out by their subsequent findings. It was found that 2-ethyl-1-indanone (Ib) also gave a compound ($C_{17}H_{15}N$, m. p. 79～80°C) which, because of the lack of the active methylene of the benzyl group, should have the indolenine structure of IIIb, but which behaved like an aldehyde[3], e. g., by the addition of amines, ammonia and acid anhydrides as well as of sodium bisulfite.

Their further observation[4] that VIIa and the six-membered analogues of IIIa, b (VIa, b) were incapable of adding phenylhydrazine and sodium bisulfite led them to the conclusion that ring system III, with a five-membered ring fused to the indolenine nucleus, is essential to



VIIIa n=5 IXa n=5, R=$CHCl_2$
b n=6 b n=6, R=$CHCl_2$
c n=5, R=OOH
d n=6, R=OOH



Xa n=5, R=CHCl
b n=6, R=CHCl
c n=5, R=O
d n=6, R=O

* A preliminary communication has appeared in *Chem. & Ind.*, **1960**, 719.

1) For a general discussion of the reactions of indolenines, see P. L. Julian, E. W. Meyer and H. C. Pring, "The Chemistry of Indoles", in R. Elderfield, "Heterocyclic Compounds", Vol. 3, John Wiley and Sons, Inc., New York (1952), p. 108.

Unfortunately, the formula which appear on pp. 108—110 of their article are incorrect as a result of mistaking β-benzyl-α-hydrindone as 1-benzyl-2-indanone.

2) a) H. Leuchs, J. Wutke and E. Giesler, *Ber.*, **46**, 2200 (1913); b) H. Leuchs and K. Winzer, ibid., **58**, 1520 (1925); c) H. Leuchs, C. D. Philpot, P. Sauder, A. Heller and K. Köhler, *Ann*, **461**, 27 (1928).

3) Facile addition reactions to the C=N bond in the indolenines without a fused ring have been noticed. G. Plancher, *Ber.*, **31**, 1488 (1898); G. Plancher and D. Bettinelli, *Gazz. chim. ital.*, **29**, I, 106 (1899).

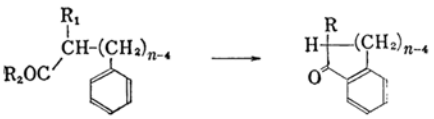
4) H. Leuchs, A. Heller and A. Hoffmann, *Ber.*, **62**, 871 (1932).

smooth addition reactions. The same sort of ring-size effect on the reactions of indolenines was encountered in our study[5] of "Plancher's base"[6] (Xa) and of the mechanism of its formation from pentindole (VIIIa) with alkali and chloroform.

Whereas tetrahydrocarbazole (VIIIb) affords stable 11-dichloromethyltetrahydrocarbazolenine (IXb), which can be converted into the lactam Xb only by prolonged reflux in the presence of alkali[7], the lactam Xa ("Plancher's base) is a sole product isolated from the reaction mixture of pentindole (VIIIa) with alkali and chloroform, presumably because of the enhanced reactivity of the C=N group in the intermediate IXa, which has a five-membered ring fused to the indolenine nucleus. It is not surprising, therefore, to find that the hydroperoxide, IXd, is stable enough to be isolated as such, but that the hydroperoxide IXc, from pentindole, is directly rearranged to the lactam Xc[8], suggesting a close relationship between the reactivity of indolenine and the size of the ring fused with it.

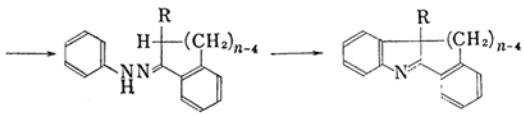
This paper will report on the preparation of 2′,3-polymethylen-3-alkyl-2-phenylindolenines (XIV) and on the observations of the changes of their properties as the ring members are varied from 5 to 6, 7 and 8, compared with those of 3,3-dimethyl-2-phenylindolenine (VIIa)[9] and 2,3-dimethyl-3-benzylindolenine (VIIb)[10].

The indolenines (XIV)[11,12] were prepared by Fischer-Brunner's method from 4-alkyl-1,2-benzocycl-1-en-3-one (XII); of these the seven-membered ketone (XIIa) (b. p. 153~160°C/28 mmHg; semicarbazone, m. p. 197~198°C) and



XIa $n=7$, $R_1=CH_3$
b $n=8$, $R_1=CH_3$

XIIa $n=7$, $R=CH_3$
b $n=8$, $R=CH_3$
c $n=6$, $R=CH_3$
d $n=5$, $R=CH_2CH_3$



XIII

XIVa $n=5$, $R=C_2H_5$
b $n=6$, $R=CH_3$
c $n=7$, $R=CH_3$
d $n=8$, $R=CH_3$

the eight-membered ketone (XIIb) (b. p. 109~111°C/1 mmHg; 2,4-dinitrophenylhydrazone, m. p. 170~171°C) were prepared from the corresponding acids (XIa, b) by polyphosphoric acid cyclization[13] (61%) and high dilution

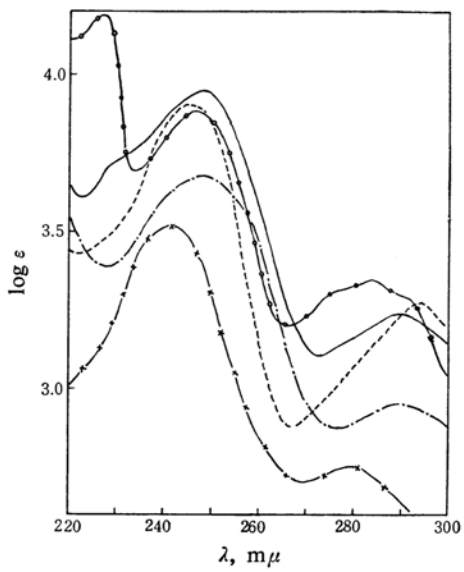
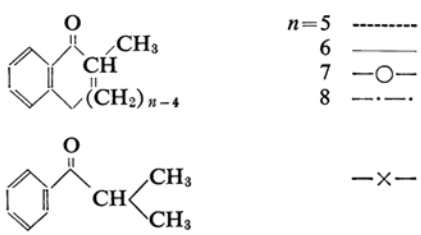


Fig. 1



5) M. Nakazaki, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zassi*), **76**, 1169 (1955).

6) G. Plancher, B. Cecchetti and E. Ghigi, *Gazz. chim. ital.*, **59**, 340 (1929).

7) M. F. Bartlett, D. F. Dickel and W. I. Taylor, *J. Am. Chem. Soc.*, **80**, 126 (1958).

8) B. Witkop, J. B. Patrick and M. Rosenblum, ibid., **73**, 2641 (1951).

9) H. M. Kissman, D. W. Farnsworth and B. Witkop, ibid., **74**, 3948 (1952); M. Nakazaki, K, Yamamoto and K. Yamagami, This Bulletin, **33**, 471 (1960). According to a recent publication (F. J. Evans and R. E. Lyle, *Chem. & Ind.*, **1960**, 597.), 3,3-dimethyl-2-phenylindolenine prepared by the polyphosphoric acid method is contaminated by isomeric 2,3-dimethyl-3-phenylindolenine.

The indolenine VIIa used here was regenerated from the purified picrate, m. p. 170~171°C, recrystallized from ethanol.

10) T. Hoshino, *Ann.*, **500**, 35 (1932); M. Nakazaki, S. Isoe and K. Tanno, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zassi*), **76**, 1263 (1955).

11) See footnote 2 c). Several attempts to prepare XIV, $n=5$, $R=CH_3$ failed.

12) M. Nakazaki, K. Yamamoto and K. Yamagami, (This Bulletin, **33**, 471 (1960)) reported 6a-methyl-5,6-dihydro-6a-benzo(a)carbazole (XIVb) as an oil, b. p. 160~164°C/2 mmHg; picrate, m. p. 169~170°C, but XIVb crystallized on prolonged standing in a refrigerator. The specimen used in the present work was recrystallized from diluted ethanol and melted at 98~98.5°C.

13) R. Gilman, Jr., and W. J. Horton, *J. Am. Chem. Soc.*, **73**, 1411 (1951).

TABLE I

Indolenine	M. p. or b. p., °C	M. p. of picrate, °C	UV spectra λ_{max}, mμ (log ε)		pK_a'	$-E_{1/2}$(S.C.E.) pH 2.20	pH 4.95	IR spectra μ
XIVa	150~155/1 mmHg	165~167	240(3.96)	304(3.67)	—	—	0.88	6.35
XVIIa	156~159/1 mmHg	154~155	227(4.11)	308(4.18)	2.2	0.88	1.17	
XIVb	98~98.5	167~168	235(4.16)	309(4.18)	2.6	0.92	1.13	6.44
XIVc	105~106	183~184	226(4.22)	290(4.16)	2.1	1.01	1.11	6.48
XIVd	145~147	119~120		266(3.97)	1.8	>1.1	1.28	6.48
VIIb	48~49	141~142		260(3.72)	—	>1.1	>1.3	6.37

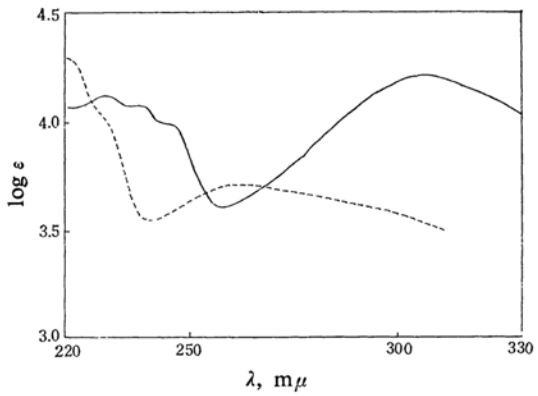
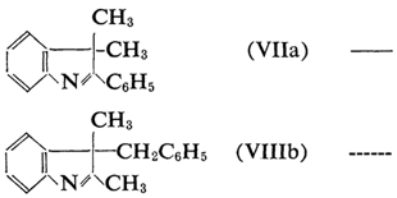


Fig. 2



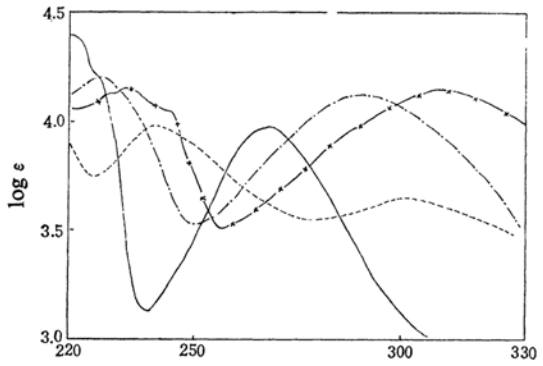
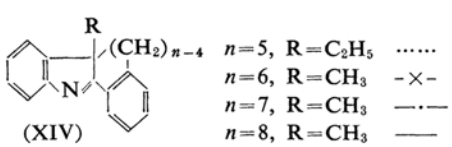


Fig. 3



Friedel-Crafts cyclization (62%) respectively[14].

The ultraviolet absorption spectra of the ketone XIIa, b, c, d[15] and isobutyrophenone are shown in Fig. 1.

In Table I the properties of these indolenines are summarised, together with those of VIIa and VIIb.

Ultraviolet Absorption Spectra[16] (See Table I, Figs. 2 and 3).—The six-membered indolenine XIVb exhibits almost the same ultraviolet spectrum as the indolenine VIIa, which has a phenyl group capable of conjugating with the indolenine system by free rotation. Moreover, the coincidence of the fine structures of their absorption pattern at a shorter wavelength is remarkable. However, a different situation arises in the seven- and eight-membered indolenines (XIVa, b), in which the polymethylene bridge pushs the ortho position of the phenyl group aside so as to force the benzene ring to pivot around out of the plane of the indolenine conjugate system, thus decreasing the effective conjugation between the indolenine system and the benzene ring. An inspection of the molecular model of the eight-membered indolenine (Fig. 4) reveals

Fig. 4

14) R. Huisgen, W. Rapp, I. Ugi and H. Walz, *Ann.*, **586**, 52 (1952). Their yield for the eight-membered ketone (XIIb, without a methyl group) was 70% by the high dilution Friedel-Crafts cyclization technique. For a general discussion of the synthetic methods of large ring compounds, see K. Ziegler's excellent article in Houben-Weyl, "Methoden der organischen Chemie", Ed. by E. Muller, Band IV, Teil 2, George-Thiem Verlag, Stuttgart (1955), p. 930.

15) The ultraviolet spectra of 1,2-benzocycl-1-en-3-one (XII) without methyl substitution have been thoroughly discussed. R. Huisgen, W. Rapp, I. Ugi, H. Walz and E. Mergenthaler, *Ann.*, **586**, 1 (1954).

16) Their infrared absorption spectra (C=N streching band) are summarized in Table I, but no conspicuous regular change in absorption maximum with the ring size can be found.

17) Free from Baeyer strain. The conformational relationships among the four methylene groups, 1—2 is semieclipsed, while 2—3 and 3—4 are skew.

that, to achieve the most favorable conformation[17], the benzene ring must be brought almost perpendicular to the indolenine ring, which explains the fact that eight-membered indolenine XIVd shows marked hypsochromic shifts of the absorption bands associated with its diminished extinction coefficients. Although its ultraviolet absorption maximum and ultraviolet absorption minimum become quite close to those of VIIb, which has no phenyl group at the C_2 position, the higher extinction coefficient of XIVd seems to show that complete steric inhibition of the mesomerism is not attainable, even in the eight-membered indolenine. The parallel observation of the medium ring-size effect on ultraviolet spectra in the indole series XV was reported by Huisgen and Ugi[18].

It is of interest also to note the extraordinarily low extinction coefficient of the absorption (in both the 240 mμ and 300 mμ regions) of the five-membered indolenines XIVa, whose positions of absorption bands are not shifted much from that of the six-membered indolenine XIVb. Although its detailed theoretical interpretation presents considerable difficulties[19,20], there is no doubt that the Baeyer strain imposed upon the five-membered ring (normal bond angle: 108°) with three sp^2 carbon atoms (normal bond angle: 120°) deforms the conjugated system of the indolenine to a great extent, thus causing the pattern of the absorption band to deviate considerably from that of the indolenines, which do not suffer Baeyer strain[21].

Dissociation Constant[22].—As can be seen from Table I, the p*K*a′ values of the indolenines XIV are also effected by the size of the ring fused to the indolenine nucleus.

Table I summarizes the values of p*K*a′ of the conjugated acids of the indolenines determined spectrophotometrically[23], while Fig. 5 reproduces typical spectra of the seven-membered indolenine at different pH values which show clearly marked isosbestic points. If the

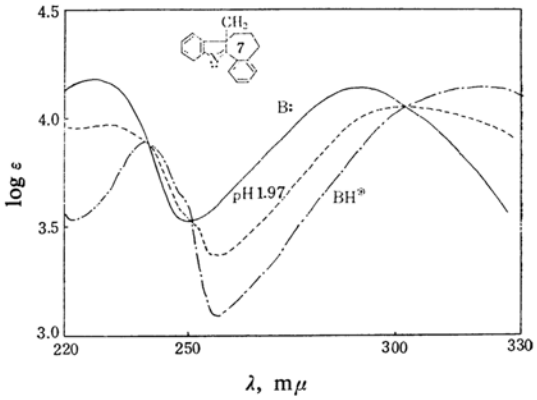
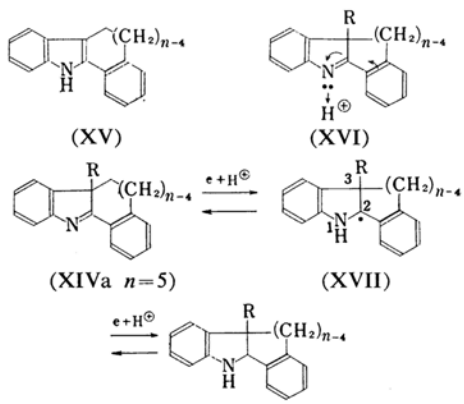


Fig. 5

phenyl group is allowed to be coplanar with the indolenine conjugation system, the +M effect of the phenyl group will be such as to increase the electron density at the nitrogen atom (XVI), i. e., to increase the basic strength of the indolenine. From the evidence previously adduced from the spectroscopic data (vide supra), there can be expected a considerable steric inhibition of the mesomerism and, hence, a decrease in the basic strength of the eight-membered indolenine XIVd; Table I shows this to be the case.

Polarographic Half-wave Potential.—If the polarographic electrode process[24] of indolenine



(XV) (XVI)

(XIVa $n=5$) (XVII)

(XVIII)

Fig. 6

18) R. Huisgen and I. Ugi, *Ann.*, **610**, 57 (1957).

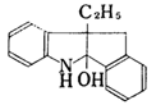
19) For the medium ring-size effect in 1,2-benzocycl-1-en-3-one and related compounds, see Huisgen's excellent review. R. Huisgen, *Angew. Chem.*, **69**, 341 (1957).

20) Ultraviolet absorption in relation to steric conformation about a single bond in a conjugated system is fully discussed in W. Klyne, "Progress in Stereochemistry", Vol. 1, Butterworths Pub. Ltd., London (1954), p. 136 and Vol. 2, (1958), p. 99. Numerous papers presented in G. W. Gray, "Steric Effects in Conjugated Systems", Butterworths Pub. Ltd., London (1958) are also worth consulting.

21) This Baeyer strain is reflected much more clearly in the polarographic study and will be discussed more thoroughly there.

22) H. C. Brown, D. H. McDaniel and O. Häfliger, "Dissociation Constants", in E. A. Braude and F. C. Nachod, "Determination of Organic Structures by Physical Methods", Academic Press, Inc., New York (1955), p. 567, and the literature cited in footnotes 19) and 20).

23) Attempts to measure the dissociation constant of XIVa were fruitless because its ultraviolet absorption spectra at various pH values did not show any clear isosbestic points, probably owing to the irreversible formation of (i) by the addition of water.



(i)

24) J. M. Kolthoff and J. K. Kingane, "Polarography", Vol. 1, Interscience Pub. Inc., New York (1952), p. 685; P. Pasternak, *Helv. Chim. Acta*, **31**, 753 (1948).

can be expressed as in Fig. 6, the stability of the intermediate free radical XVII may be expected to influence the half-wave potential.

When the π-orbital of the sp^2 center of XVII at C_2 can overlap effectively with the π-orbital of the phenyl group at C_2, the intermediate XVII will be stabilized and the half-wave potential will shift to positive. The high value of $-E_{1/2}$ of the eight-membered indolenine is clearly to be ascribed to the non-co-planarity of the iodolenine system and the phenyl group at the C_2 carbon atom.

The remarkable susceptibility of five-membered indolenine XIVa to polarographic reduction[25] is remarkable, conceivably because of the Baeyer strain being relieved in a five-membered ring with three sp^2 carbon atoms fused to a five-membered indolenine ring.

Experimental[26]

Diethyl Benzylethylmalonate.—To a stirred suspension of 4.6 g. of sodium powder (pulverized under boiling xylene and decanted from it) in 30 cc. of benzene was added slowly 23 cc. of absolute ethanol. After the sodium had been completely converted into sodium ethoxide, 35.4 g. of diethyl benzylmalonate was added over a 10 min. period. This mixture was refluxed while being stirred for 10 min.; then 46.5 g. of ethyl iodide was added over a period of 25 min. The temperature of the mixture was kept at 60~70°C for 5.5 hr. and then at 70~80°C for 7.5 hr. The solvent was then removed on a water bath, and water was added to dissolve the precipitated salt. The reaction mixture was extracted with ether. After the ether extract had been washed with water and dried over anhydrous sodium sulfate, the solvent was removed to yield an oil, b. p. 143~147°C/3 mmHg, 33.4 g. (85% yield) (literature[27]; b. p. 184°C/18 mmHg).

1-Benzyl-*n*-butyric Acid (XI) ($n=5$, $R_1=C_2H_5$, $R_2=OH$).—A mixture of 32.6 g. of diethyl benzylethylmalonate and 100 cc. of 45% aqueous potassium hydroxide was refluxed for 2 hr. (the mixture became homogenous after 20 min.) The aqueous solution was made acidic with dilute hydrochloric acid and extracted continuously with ether for 6 hr. Removal of the solvent gave a residue which was decarboxylated by heating at 180°C for 1 hr.; the residual oil was distilled to give 20.0 g. of a viscous oil (96% yield), b. p. 127~140°C/3 mmHg (literature[28]; b. p. 172~174°C/13 mmHg).

1-Benzyl-*n*-butyroyl Chloride (XI) ($n=5$, $R_1=C_2H_5$, $R_2=Cl$).—After a mixture of 19 g. of 1-benzyl-*n*-butyric acid and 17.8 g. of thionyl chloride had been heated on a water bath, the excess thionyl chloride was removed in a vacuum. Distillation of the residue afforded an oil, b. p. 124~131°C/15 mmHg, 20 g. (96% yield) (literature[27]; b. p. 128~131°C/15 mmHg). The anilide prepared from it was recrystallized from diluted ethanol, m. p. 86~87°C (literature[28]; m. p. 88~89°C).

2-Ethyl-1-indanone (XIId).—To a stirred mixture of 18.8 g. of powdered aluminum chloride and 50 cc. of carbon disulfide was added a solution of 1-benzyl-*n*-butyroyl chloride in 50 cc. of carbon disulfide over a period of 15 min. After being refluxed for 50 min., the reaction mixture was decomposed with ice and water. The usual working up gave an liquid with a pleasant smell, b. p. 130~136°C/13 mmHg, 14.8 g. (91% yield) (literature[29]; b. p. 143~144°C/22 mmHg). The semicarbazone was recrystallized from ethanol, m.p. 201.5~202.5°C (literature[29]; m.p. 202°C).

8b-Ethyl-2, 3-benzo-1, 2, 3, 4-tetrahydrocyclopent-(b)*pseudo*indole (XIVa)[30].—After a mixture of 2.0 g. of the indanone XIId, 1.4 g. of phenylhydrazine and 0.5 g. of sodium acetate was heated on a water bath for 2 hr., a solution of 12.5 g. of zinc chloride in 10 cc. of ethanol was added; this reaction mixture was kept at 150~155°C for 4 hr. Then 1 N hydrochloric acid was added to precipitate a complex salt which was collected and washed with 1 N hydrochloric acid and then with ether. Aqueous ammonia was added to the suspension of the complex salt on ether to liberate the indolenine XIVa, which was extracted with ether. After being washed with water and dried over anhydrous sodium sulfate, the solvent was evaporated to give a residual oil which distilled at 156°C/1 mmHg and which weighed 1.9 g. The crude indolenine was directly converted into the picrate and was recrystallized from ethanol to give yellow crystals, m. p. 164~165°C which were suspended on ether and decomposed with 0.5 N sodium hydroxide to regenerate the indolenine XIVa, b. p. 150~155°C/1 mmHg[31].

Found: C, 87.35; H, 6.61; N, 6.01. Calcd. for $C_{17}H_{15}N$: C, 87.51; H, 6.48; N, 6.00%.

The picrate was recrystallized from ethanol, m.p. 166~167°C.

Found: C, 59.49; H, 3.84; N, 12.33. Calcd. for $C_{23}H_{18}O_7N_4$: C, 59.74; H, 3.92; N, 12.12%.

Diethyl 3-Phenylpropylmalonate.—After 6 g. of sodium had been pulverized by vigorous stirring under 60 cc. of boiling toluene, the toluene was removed by decantation and was replaced by 50 cc. of benzene. Then 27 cc. of absolute ethanol was carefully added in order to convert the sodium powder into sodium ethoxide, and 63 cc. of freshly distilled diethyl malonate was added over a 45 min. period. To the refluxing reaction mixture was added a solution of 35 g. of 3-phenylpropyl bromide[32] in

25) On the medium ring-size effect of 1, 2-benzocyclo-1-en-3-one and related compounds on its half-wave potential, see the literature cited in footnote 15) and also H. Adkins, R. M. Elofson, A. G. Rossow and C. C. Robinson, *J. Am. Chem. Soc.*, **71**, 2622 (1949).

26) All ultraviolet spectra were measured in ethanol with an EP-2 Hitachi pen-recording spectrophotometer. The analyses were performed in the Microanalytical Laboratory of the Department of Chemistry, Osaka City University.

27) E. Mohr, *J. prakt. Chem.*, (2), **71**, 330 (1905).

28) B. Anschütz and W. Berns, *Ann.*, **261**, 307 (1891).

29) E. A. Speight, A. Stevenson and J. F. Thorpe, *J. Chem. Soc.*, **125**, 2191 (1924).

30) According to the nomenclature of A. M. Patterson and L. T. Capell, "The Ring Index", Reinhold Pub. Corp., New York (1940).

31) Leuchs and his coworkers (cf. footnote 2 c)) reported this indolenine as a crystal, m.p. 79~80°C, b.p. 202~204°C/14 mmHg, but our attempts to crystallize failed.

32) Prepared from 3-phenylpropanol according to the procedure of O. Kamm and C. S. Marvel, "Organic Syntheses", Coll. Vol. I, 25 (1948). B. p. 128~134°C/30 mmHg (86% yield).

50 cc. of benzene; the refluxing was then continued for 7 hr. on a water bath. After water was added, the reaction mixture was made acidic with dilute hydrochloric acid, and the benzene layer was separated. The aqueous solution was extracted with ether, and the ether extract was combined with benzene extract. After the mixture had been washed with water and dried over anhydrous sodium sulfate, the solvent was removed to give an oil which distilled at 143~149°C/1 mmHg and which weighed 44.7 g. (91.4% yield) (literature[33]; b. p. 189~194°C/13 mmHg).

Diethyl Methyl-3-phenylpropylmalonate.—To a sodium ethoxide solution prepared from 5.3 g. of sodium and 80 cc. of ethanol was added 44.4 g. of diethyl 3-phenylpropylmalonate. Into the stirred, refluxing solution, 39.2 g. of methyl iodide was add and then, after 2 hr. 10 g. of methyl iodide was added to make the solution neutral to wet litmus paper.

After the solvent had been removed, water was added and the mixture was extracted with ether. After the ether extract had been washed with water and dried over anhydrous magnesium sulfate, the ether was removed and the residual oil was distilled. The malonate distilled at 140~145°C/1 mmHg, and weighed 40.6 g. (87% yield) (literature[34]; b. p. 194°C/13 mmHg).

1-(3-Phenylpropyl)propionic Acid (XIa) (R_2=OH).—A mixture of 39.9 g. of diethyl methyl-3-phenylpropylmalonate, 90 g. of potassium hydroxide and 110 cc. of water was refluxed for 2~3 hr. The reaction mixture was then chilled in an ice bath and was made acidic with concentrated hydrochloric acid to precipitate crystals (methyl-3-phenylpropylmalonic acid), which were collected and washed with water. The malonic acid was decomposed by heating at 180°C and was distilled to give the acid XIa, b. p. 141~143°C/1 mmHg, 23.1 g. (88% yield) (literature[35]; b. p. 190°C/12 mmHg).

Found: C, 74.77; H, 8.89. Calcd. for $C_{12}H_{16}O$: C, 74.87; H, 8.39%.

The anilide was recrystallized from aqueous ethanol, m. p. 78.5~79.5°C.

Found: C, 80.85; H, 8.03; N, 5.45. Calcd. for $C_{18}H_{21}ON$: C, 80.86; H, 7.92; N, 5.24%.

4-Methyl-1,2-benzocyclohept-1-en-3-one (XIIa).—To stirred polyphosphoric acid prepared from 60.5 g. of phosphorus pentoxide and 38.7 g. of concentrated phosphoric acid was added 10 g. of the acid XIa; the reaction mixture was then heated at 100°C for 2 hr. The temperature of the mixture was raised to 160°C over a 1-hour period, and the reaction mixture was decomposed with water and extracted with ether. The ether extract was washed with 2 N sodium hydroxide and water, then dried over anhydrous sodium sulfate. Removal of the solvent gave a residual oil which distilled at 153~160°C/28 mmHg and which weighed 5.5 g. (61% yield). From alkaline washing, 1 g. of the acid XIa was recovered.

Found: C, 84.36; H, 8.14. Calcd. for $C_{12}H_{14}O$: C, 82.72; H, 8.10%.

The semicarbazone was recrystallized from aqueous ethanol, m. p. 197~198°C.

Found: C, 69.19; H, 7.51. Calcd. for $C_{13}H_{17}ON_3$: C, 67.50; H, 7.41%.

10a-Methyl-6,7-benzo-5,6,7,8,9,10-hexahydrocyclohept(b)*pseudo*indole (XIVc)[30]. — A mixture of 2 g. of the ketone XIIa and 1.3 g. of phenylhydrazine was heated on a water bath for 1.5 hr., the generated water was then removed by azeotropic distillation with benzene. After removal of the benzene, the residue was dissolved in 20 cc. of absolute ethanol and the solution was saturated with dry hydrogen chloride gas while being chilled in an ice-salt cooling bath. After being allowed to stand at room temperature for 5 hr., the solution was diluted with water and washed with ether to remove any neutral substance. The ether washing was extracted with dilute hydrochloric acid, and the acidic aqueous extracts were combined. The combined aqueous solution was then made basic with 2 N sodium hydroxide to precipitate the indolenine XIVc, which was extracted with ether. Removal of the solvent afforded a viscous oil which was purified via picrate. The picrate (2.1 g.) melted at 182~183°C after being recrystallized from ethanol and was decomposed with 0.5 N sodium hydroxide, then extracted with ether. The pale yellow ether extract was washed three times with 0.5 N sodium hydroxide until the ether layer became colorless; it was then washed with water and dried over anhydrous sodium sulfate. The solvent was removed to give a residue which was recrystallized from aqueous ethanol, m. p. 105~106°C.

Found: C, 87.56; H, 6.92; N, 5.91. Calcd. for $C_{18}H_{17}N$: C, 87.41; H, 6.93; N, 5.66%.

The picrate was recrystallized from ethanol to give yellow needles, m. p. 182~183°C.

Found: C, 60.61; H, 4.29; N, 11.58. Calcd. for $C_{24}H_{20}O_7N_4$: C, 60.50; H, 4.23; N, 11.76%.

4-Phenyl-*n*-butanol.—A mixture of 56 g. of ethyl 3-phenyl butyrate[36] and 7 g. of copper chromite catalyst was hydrogenated in a 500 cc. steel bomb at 98 atm. of hydrogen and at 256°C for 2 hr. After being separated from the catalyst, the alcohol was distilled to give a viscous oil, b. p. 145~151°C/26 mmHg, 33.5 g. (76.6% yield) (literature[37]; b. p. 137°C/14 mmHg).

4-Phenylbutyl Bromide.—This bromide was prepared from 4-phenyl-*n*-butanol following Kamm and Marvel's procedure[32], b. p. 142~148°C/24 mmHg (literature[38]; b. p. 132°C/12 mmHg).

Diethyl 4-Phenylbutylmalonate.—This was prepared from 4-phenylbutyl bromide following the procedure described in the preparation of diethyl 3-phenylpropylmalonate, b. p. 148~155°C/1 mmHg (91% yield) (literature[33]; b. p. 215~218°C/11 mmHg)

Diethyl Methyl-4-phenylbutylmalonate. — This was prepared from diethyl 4-phenylbutylmalonate by alkylation with methyl iodide following the procedure described in the preparation of diethyl

33) J. v. Braun and O. Kruber, *Ber.*, **45**, 386 (1912).
34) J. v. Braun and G. Kirschbaum, ibid., **45**, 1257 (1912).
35) J. v. Braun, H. Deutsch and A. Schmatloch, ibid., **45**, 1257 (1912).
36) B. p. 144~149°C/18 mmHg. Prepared from 3-phenylpropyl bromide by malonic ester synthesis.
37) H. Adkins, B. Wojcik and L. W. Covert, *J. Am. Chem. Soc.*, **55**, 1669 (1933).
38) P. W. Clutterbuck and J. B. Cohen, *J. Chem. Soc.*, **123**, 2510 (1923).

methyl-3-phenylpropylmalonate. The yield was 87.3%, and the malonate distilled at 155~160°C/1 mmHg.

Methyl-4-phenylbutylmalonic Acid.—Diethyl methyl-4-phenylbutylmalonate was hydrolyzed with 45% potassium hydroxide to give the malonic acid, which melted at 109~110°C after recrystallization from aqueous ethanol.

Found: C, 67.69; H, 7.50. Calcd. for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25%.

1-(4-Phenylbutyl)propionic Acid. (XIb) (R_2=OH).—Methyl-4-phenylbutylmalonic acid was decomposed by heating at 180°C, and the propionic acid XIb was distilled, b. p. 138~149°C/1 mmHg (75.6% yield).

Found: C, 75.86; H, 9.15. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80%.

The anilide was recrystallized from aqueous ethanol, m. p. 118~119°C.

Found: C, 80.89; H, 8.73; N, 5.09. Calcd. for $C_{19}H_{23}ON$: C, 81.10; H, 8.24; N, 4.98%.

1-(4-Phenylbutyl)propionyl Chloride (XIb) (R_2=Cl).—A mixture of 21.3 g. of the acid XIb and 17.8 g. of thionyl chloride was heated on a water bath for 1 hr., and the excess thionyl chloride was distilled off. The residual oil distilled at 161~167°C/15 mmHg, and weighed 23.2 g.

4-Methyl-1, 2-benzocyclooct-1-en-3-one (XIIb).—The simplified Ziegler's high dilution apparatus[39] consists of a 3-l. three-necked round-bottomed flask equipped with a Vibro-Mischer and an efficient Dimroth condenser. The acid chloride solution is introduced at the middle point of the arm which connects the flask and the condenser, so the solution is immediately diluted and is carried down into the reaction flask by the solvent running down from the condenser. In the flask was placed 900 cc. of carbon disulfide; a small amount of the solvent was distilled off through the condenser in order to dry the apparatus while the cooling water was temporarily cut off. Then 37 g. of powdered aluminum chloride was introduced, and the mixture was refluxed on a water bath while being vigorously stirred. To the mixture was added a solution of 23.2 g. of the acid chloride XIb (R_2=Cl) in 750 cc. of carbon disulfide over a period of 76.5 hr., during which time 11 g. of powdered aluminum chloride was added at the 24th, 34th, 49th, 64th and 74th hr. from the starting point of the reaction. After 1.2 l. of the solvent had been removed, the reaction complex was decomposed with ice, water and concentrated hydrochloric acid. After being saturated with sodium chloride, the mixture was extracted with ether. A dark colored solid which appeared between the aqueous layer and ether layer was collected and treated separately.

After the ether extract had been washed and dried over anhydrous sodium sulfate, the solvent was removed to give a residual oil which distilled at 105~110°C/1 mmHg and which weighed 6.0 g. The collected dark colored solid was continuously extracted with benzene for 6 hr., and the benzene extract was washed with water and dried over anhydrous sodium sulfate. After removal of the solvent, the extract gave 6.1 g. of an oil which distilled at 109~111°C/1 mmHg and which raised the total yield to 62.3%. On one more distillation, 9.8 g. of the crude ketone gave 8.6 g. of purified ketone, which boiled at 104~112°C/1 mmHg.

Found: C, 82.91; H, 8.74. Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57%.

The 2, 4-dinitrophenylhydrazone was recrystallized from ethanol, m. p. 170~171°C.

Found: C, 61.68; H, 5.27; N, 14.95. Calcd. for $C_{19}H_{20}O_4N_4$: C, 61.94; H, 5.47; N, 15.21%.

11a-Methyl-6,7-benzo-5, 6, 7, 8, 9, 10-hexahydrocyclooct(b)*pseudo*indole (XIVd)[30].—A mixture of 2.0 g. of the ketone XIIb and 1.2 g. of phenylhydrazine was heated on a water bath, and the generated water was removed by azeotropic distillation with benzene. After removal of the benzene, the residue was dissolved in 19 cc. of absolute ethanol, and the chilled solution was saturated with dry hydrogen chloride gas. After the solvent had been evaporated in a vacuum, the reaction mixture was diluted with water and washed with ether. The aqueous layer was made basic with a concentrated ammonia solution, and the basic fraction liberated was extracted with ether. Removal of the solvent afforded a solid which crystallized upon cooling and trituration. Recrystallization from aqueous ethanol yielded crystals, m. p. 145.5~146.5°C.

Found: C, 87.15; H, 7.40; N, 5.41. Calcd. for $C_{19}H_{19}N$: C, 87.31; H, 7.33; N, 5.36%.

The picrate was recrystallized from ethanol to give yellow crystals which deteriorated on heating at 100°C and were found to have 1 mol. of ethanol of crystallization.

Found: C, 60.19; H, 5.38; N, 10.46. Calcd. for $C_{25}H_{22}O_7N_4 \cdot C_2H_5OH$: C, 60.44; H, 5.26; N, 10.44%.

After being heated at 65°C and 3 mmHg for 12 hr., the picrate melted at 119~120°C.

Found: N, 11.56. Calcd. for $C_{25}H_{22}O_7N_4$: N, 11.42%.

Polarographic Measurement.—The apparatus used for the measurement of the polarographic half-wave potential was a Yanagimoto pen-recording polarograph model P-B 4, while the pH values were measured on a Beckman pH meter model G.

The supporting electrolyte and buffer solution were that used by Huisgen and his co-workers[15]: 50% isopropanol containing potassium chloride (0.1 M), phosphoric acid (0.05 M) and acetic acid (0.05 M), the pH value was adjusted by the addition of 6 N ammonia in 50% isopropanol. The indolenine solution (ca. 10^{-4} M) was mixed with a gelatin solution, incuvated in a thermostat (26°C), and swept by a stream of nitrogen to replace the oxygen, which process took 30~90 min.

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39) K. Ziegler, H. Eberle and H. Ohlinger, *Ann.*, **504**, 123 (1933). See also the literature cited in footnote 14) for a more simplified apparatus.

40) Laboratoriums-Vibro-Mischer, Model El, AG. für Chemie-Apparatebau, Zürich.

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