Further Heterocyclic Analogs of Polyaryls

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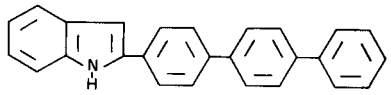
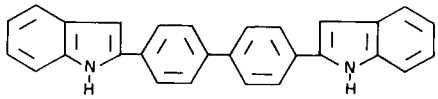
A series of indoles, indolizines, imidazo[1,2-*a*]pyridines, and quinolines, all of them heterocyclic analogs of polyaryls, have been prepared from diacetyl derivatives of aromatic hydrocarbons.

In continuation of earlier work on the physico-chemical and biological properties of polyaryls (1) and their nitrogen heterocyclic analogs (2), we have now investigated a new series of polycyclic mono- and di-heteryl derivatives of benzene, biphenyl, *p*-terphenyl, naphthalene, acenaphthene, and fluorene; these compounds contain from five to seven rings, and their heteryl component is an indole, indolizine, imidazo[1,2-*a*]pyridine, or a quinoline group.

Indolization of 4′-acetyl-*p*-terphenyl phenylhydrazone by means of polyphosphoric acid afforded 4′-(2-indolyl)-*p*-terphenyl (I). The same procedure was successful to achieve double Fischer cyclizations of the bis-phenylhydrazones of 4,4′-diacetylbiphenyl, 3,6-diacetylacenaphthene, and 2,7-diacetylfluorene, to give 4,4′-di(2-indolyl)-biphenyl (II), 3,6-di(2-indolyl)acenaphthene (III), and 2,7-di(2-indolyl)fluorene (IV) respectively. These four indoles were high-melting, pale yellow to bright yellow compounds, which formed black picrates.



I



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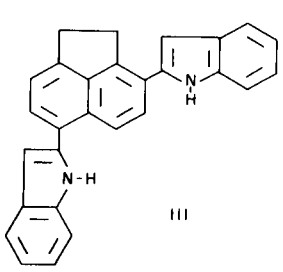
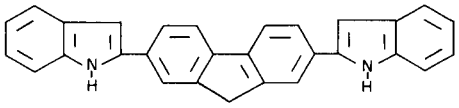
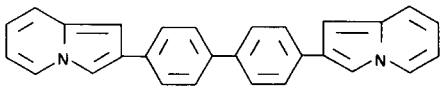


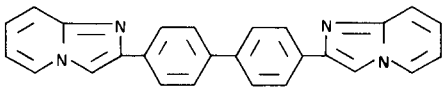
III



IV



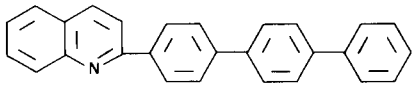
V



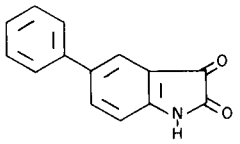
VI

4,4′-Di(2-indolizinyl)biphenyl (V) was prepared by a double Tschitschibabin cyclization (3) of the bis-quarternary salt obtained in the reaction of 2-methylpyridine with 4,4′-bis(bromoacetyl)biphenyl; the reaction of this bis-bromoacetyl derivative with 2-aminopyridine furnished 4,4′-di(2-imidazo[1,2-*a*]pyridyl)biphenyl (VI). Compounds V and VI showed extremely high melting points and reacted with sodium nitrite and hydrochloric acid to give red precipitates, probably the hydrochlorides of the 2-nitrosation products (1).

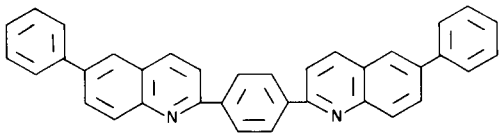
4′-(2-Quinolyl)-*p*-terphenyl (VII) was prepared by thermal decarboxylation of the cinchoninic acid obtained in the Pfitzinger reaction of isatin and 4′-acetyl-*p*-terphenyl. A double Pfitzinger reaction using 5-phenylisatin (VIII) and 1,4-diacetylbenzene, followed by copper chromite-catalyzed thermal decarboxylation of the ensuing bis-cinchoninic acid, afforded 1,4-(6-phenyl-2-quinolyl)benzene (IX); 4,4′-di(2-quinolyl)biphenyl (X) was similarly prepared from isatin and 4,4′-diacetylbiphenyl. 3,6-Di(2-quinolyl)acenaphthene (XI) and 2,7-di(2-quinolyl)fluorene (XII) were obtained from isatin and, respectively, 3,6-diacetylacenaphthene and 2,7-diacetylfluorene.



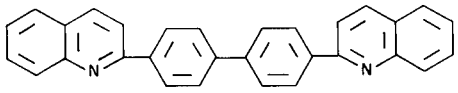
VII



VIII

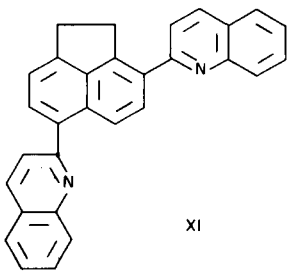


IX

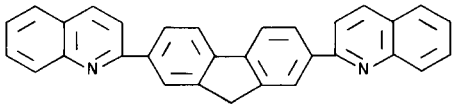


X

The various substances reported here might be of value as scintillators for liquid scintillation counters; they are being investigated both in this respect and for potential carcinogenic activity. It is interesting that none of them showed a propensity to give addition-products with cyclic hydrocarbons, whereas we noted that several compounds in the group of polyaryls themselves formed extremely stable addition-complexes with one molecule of the cyclic hydrocarbon used for their crystallization: for instance, 1,3,5-tri(5-acenaphthyl)benzene (XIII) gave an addition-compound with cyclohexane that was still stable at $> 80°$, and 1,3,5-tri(2-phenanthryl)benzene (XIV) formed a 1:1 complex with *m*-xylene.



XI



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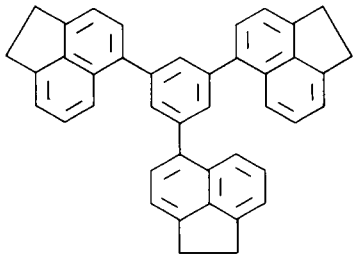
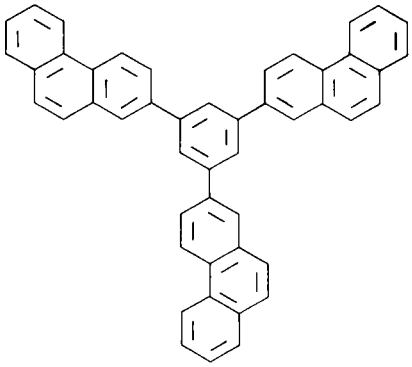
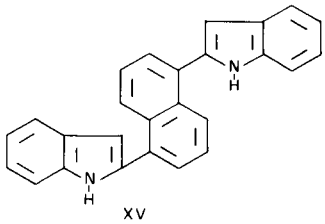


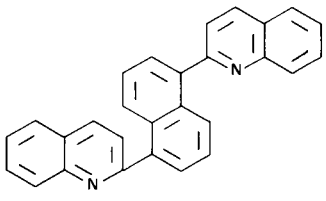
XIII



XIV



XV



XVI

In the one case (*i.e.* XV) where the di-indole formed a stable, well-defined addition-compound with picric acid, this was found to be a dipicrate; likewise, in the quinoline series, the addition-compound given by picric acid and 1,5-di(2-quinolyl)naphthalene (XVI) was a dipicrate.

EXPERIMENTAL

All melting points are uncorrected.

4′-(2-Indolyl)-*p*-terphenyl (I).*

4′-Acetyl-*p*-terphenyl Phenylhydrazone.

This compound, prepared by heating at 120° the ketone (1 part) with phenylhydrazine (1 part) and 1 drop of acetic acid until steam ceased to evolve, crystallized from benzene in pale yellow needles, m.p. 242°; yield: 95%.

Anal. Calcd. for $C_{26}H_{22}N_2$: C, 86.2; H, 6.1. Found: C, 85.9; H, 6.4.

Indolization was effected by heating 1 g. of the above hydrazone with 10 g. of polyphosphoric acid (prepared from 1 part of phosphorus pentoxide and 1 part of phosphoric acid) at 150° for 15 minutes. After cooling and decomposition with ice, the solid precipitate obtained was collected, washed with water, and crystallized from xylene to give, in 70% yield, the *indole* (I) as faintly yellow prisms, m.p. 386°, which sublimed above 300°, and whose yellow solutions in sulfuric acid showed a green fluorescence.

Anal. Calcd. for $C_{26}H_{19}N$: C, 90.4; H, 5.5; N, 4.1. Found: C, 90.2; H, 5.4; N, 4.0.

4,4′-Di(2-indolyl)biphenyl (II).

The bis-phenylhydrazone of 4,4′-diacetylbiphenyl, prepared as above from 1.2 g. of the diketone, 1.2 g. of phenylhydrazine, and 1 drop of acetic acid, crystallized from benzene in yellow prisms, m.p. 296°. Cyclization with polyphosphoric acid afforded, in 70% yield, the *di-indole* (II), which, after vacuum-sublimation, formed yellow needles, m.p. 482-484°, giving a yellow halochromism and a green fluorescence in sulfuric acid.

Anal. Calcd. for $C_{28}H_{20}N_2$: C, 87.5; H, 5.2; N, 7.3. Found: C, 87.5; H, 5.3; N, 7.4.

1,5-Diacetylnaphthalene bis-Phenylhydrazone.

The diketone (4) was prepared by treating a mixture of 120 g. of aluminum chloride and 400 ml. of carbon disulfide with 26 g. of naphthalene (during 1 hour), then with 40 g. of acetyl chloride (during 2 hours), with stirring; the mixture was kept for 12 hours at room temperature, then refluxed for 10 hours and decomposed with ice. After the usual treatment, the diketone portion boiling at 225-230°/18 mm. was crystallized from cyclohexane, giving 12 g. of 1,5-diacetylnaphthalene, m.p. 131° [lit. (4, 5), m.p. 132°], whose two-dimensional chromatogram on silica showed it to be free from isomers. The bis-phenylhydrazone crystallized from butanol as colorless needles, m.p. 209-210° (dec. >145°).

Anal. Calcd. for $C_{26}H_{24}N_4$: N, 14.3. Found: N, 14.3.

1,5-Di(2-indolyl)naphthalene (XV).

A mixture of 1 g. of the foregoing bis-phenylhydrazone and 10 g. of polyphosphoric acid was stirred at 150° for 15 minutes and the green solution obtained was poured on ice after cooling; the precipitate was washed with water, dried, and purified by vacuum-sublimation, giving the *di-indole* (XV) as faintly yellow needles, m.p. 312° (sublim. >190°).

Anal. Calcd. for $C_{26}H_{18}N_2$: C, 87.1; H, 5.1; N, 7.8. Found: C, 86.8; H, 5.0; N, 7.8.

The *dipicrate* crystallized from butanol in orange-red needles, m.p. 195° (dec. >155°).

Anal. Calcd. for $C_{38}H_{24}N_8O_{14}$: N, 13.7. Found: N, 13.9.

3,6-Di(2-indolyl)acenaphthene (III).

3,6-Diacetylacenaphthene, prepared according to the literature (6), was converted into its bis-phenylhydrazone in the usual way, and the latter compound was then indolized without further purification; the *di-indole* (III) crystallized from toluene in pale yellow prisms, m.p. 276°, which, with picric acid in toluene solution, gave a brown-black complex that could not be recrystallized.

Anal. Calcd. for $C_{28}H_{20}N_2$: C, 87.5; H, 5.2; N, 7.3. Found: C, 87.3; H, 5.3; N, 7.5.

2,7-Diacetylfluorene bis-Phenylhydrazone.

Prepared from 2.5 g. of 2,7-diacetylfluorene, 2.5 g. of phenylhydrazine, and 2 drops of acetic acid, this compound crystallized from toluene in yellow leaflets, m.p. 255°.

Anal. Calcd. for $C_{29}H_{26}N_4$: C, 80.9; H, 6.1; N, 13.0. Found: C, 80.7; H, 6.3; N, 12.8.

2,7-Di(2-indolyl)fluorene (IV).

Obtained in 50% yield from 2 g. of the previous bis-phenylhydrazone and 20 g. of polyphosphoric acid, this *di-indole* was purified by vacuum-sublimation, and formed pale yellow needles, m.p. 423-424° (dec. >280°).

Anal. Calcd. for $C_{29}H_{20}N_2$: C, 87.8; H, 5.1; N, 7.1. Found: C, 87.4; H, 5.3; N, 7.0.

This compound gave a lemon yellow halochromism in sulfuric acid, and with picric acid a brown-black complex which could not be purified.

4,4′-Di(2-indolizinyl)biphenyl (V).

A mixture of 2 g. of 4,4′-bis(ω-bromoacetyl)biphenyl and 1 g. of 2-methylpyridine in 100 ml. of absolute ethanol was refluxed until a clear solution was obtained, and the pale yellow precipitate formed on cooling was collected, and dissolved in boiling water: to this solution, sodium carbonate was added in small portions, and heating was continued for a few minutes. The flocky precipitate obtained was washed with water, dried, and purified by vacuum-sublimation, to give yellowish prisms, m.p. 468-470° (sublim. > 390°); yield: 80%.

Anal. Calcd. for $C_{28}H_{20}N_2$: C, 87.5; H, 5.2; N, 7.3. Found: C, 87.4; H, 5.2; N, 7.4.

This compound, treated with sodium nitrite in the presence of hydrochloric acid, gave a red, chlorine-containing precipitate, probably the hydrochloride of a nitroso derivative (basification with aqueous ammonia produced the free base, a green solid which could not be recrystallized).

4,4′-Di(2-imidazo[1,2-*a*]pyridyl)biphenyl (VI).

A solution of 1 g. of 4,4′-bis(ω-bromoacetyl)biphenyl and 0.5 g. of 2-aminopyridine in 100 ml. of 2-propanol was refluxed for 7 hours; after cooling, aqueous ammonia was added, and the precipitate formed in quantitative yield was washed with water, dried, and purified by vacuum-sublimation, to give compound VI as faintly yellow needles, m.p. 409-410° (sublim. >380°).

Anal. Calcd. for $C_{26}H_{18}N_4$: C, 80.8; H, 4.7; N, 14.5. Found: C, 80.3; H, 4.7; N, 14.1.

*Recently, several derivatives of 2-phenylindole have been found to be excellent scintillators in the supercooled molten state [D. L. Horrocks and H. O. Wirth, *J. Chem. Phys.*, 47, 3241 (1967)].

This compound, treated with sodium nitrite in the presence of sulfuric acid, gave a red precipitate (probably the sulfate of a nitroso derivative), which turned green on basification with ammonia.

1,4-(6-Phenyl-2-quinolyl)benzene (IX).

5-Phenylisatin (VIII), m.p. 208-210°, was prepared from ethyl oxomalonate and 4-aminobiphenyl, according to the literature (7). A mixture of 2.2 g. of this isatin, 1.6 g. of potassium hydroxide, and 0.8 g. of 1,4-diacetylbenzene in 10 ml. of ethanol was refluxed for 24 hours; after dilution with water and acidification with acetic acid, the yellow bis-cinchoninic acid which precipitated (80% yield) was collected, washed with water, and dried at 120°. Decarboxylation was effected by heating an intimate mixture of this product above its melting point with powdered copper chromite, and the black mass obtained was then extracted repeatedly with hot acetone. The insoluble residue yielded, on vacuum-sublimation, the *di-quinoline* (IX) as faintly yellow leaflets, m.p. 368°, giving an orange-yellow halochromism in sulfuric acid.

Anal. Calcd. for $C_{36}H_{24}N_2$: C, 89.2; H, 5.0; N, 5.8. Found: C, 89.1; H, 4.8; N, 5.5.

4′(2-Quinolyl)-*p*-terphenyl (VII).

Similarly prepared by condensation of isatin (1 mole) with 4′-acetyl-*p*-terphenyl (1 mole) in the presence of potassium hydroxide (3 moles) in 1-butanol, followed by thermal decarboxylation of the cinchoninic acid formed in almost quantitative yield, the *quinoline* (VII) crystallized from xylene in colorless needles, m.p. 275°.

Anal. Calcd. for $C_{27}H_{19}N$: C, 90.7; H, 5.4; N, 3.9. Found: C, 90.9; H, 5.5; N, 4.1.

4,4′-Di(2-quinolyl)biphenyl (X).

This compound, obtained from the corresponding bis-cinchoninic acid (8) by thermal decarboxylation with copper chromite, crystallized as faintly yellow leaflets, m.p. 323°, from tetralin; Steinkopff and Petersdorff (8) gave m.p. 314-315° for their less pure compound. The *di-quinoline* (X) gave a pale yellow halochromism and a blue fluorescence in sulfuric acid.

Anal. Calcd. for $C_{30}H_{20}N_2$: N, 6.9. Found: N, 6.9.

3,6-Di(2-quinolyl)acenaphthene (XI).

The corresponding pale yellow bis-cinchoninic acid, prepared in 80% yield from 3 g. of isatin, 2.8 g. of potassium hydroxide, and 2.8 g. of 3,6-diacetylacenaphthene, afforded, on thermal decarboxylation, the *diquinoline* (XI), which crystallized from benzene in faintly yellow needles, m.p. 234°; the benzene solutions of this compound showed a green fluorescence, and the halochromism in sulfuric acid was yellow. An ochre yellow addition-compound, m.p. 198° (dec. > 132°) was obtained with picric acid in 2-propanol, but did not give satisfactory analyses for either a mono- or a dipicrate.

Anal. Calcd. for $C_{30}H_{20}N_2$: C, 88.2; H, 4.9; N, 6.9. Found: C, 87.9; H, 5.0; N, 7.0.

1,5-Di(2-quinolyl)naphthalene (XVI).

Prepared as above from 2 g. of 1,5-diacetylnaphthalene, 2.9 g. of isatin, and 3 g. of potassium hydroxide in 35 ml. of ethanol, with a 50% overall yield, this *diquinoline* crystallized in colorless leaflets, m.p. 252°, from benzene, giving practically no coloration in sulfuric acid.

Anal. Calcd. for $C_{28}H_{18}N_2$: C, 87.9; H, 4.7; N, 7.3. Found: C, 87.7; H, 4.7; N, 7.3.

The *dipicrate* crystallized from benzene in yellow prisms, m.p. 262° (dec. >240°).

Anal. Calcd. for $C_{40}H_{24}N_8O_{14}$: N, 13.3. Found: N, 13.4.

2,7-Di(2-quinolyl)fluorene (XII).

Obtained in 50% overall yield from 2.5 g. of 2,7-diacetylfluorene, 2.8 g. of potassium hydroxide, and 3 g. of isatin in 30 ml. of ethanol, this compound crystallized from xylene in pale yellow leaflets, m.p. 173°, whose solutions in sulfuric acid were yellow and showed a strong green fluorescence. Here again, the orange-yellow addition-complex, m.p. 234° (dec. >190°) obtained with picric acid in xylene, did not analyze either for a mono- or for a dipicrate.

Anal. Calcd. for $C_{31}H_{20}N_2$: C, 88.5; H, 4.8; N, 6.7. Found: C, 88.2; H, 4.8; N, 6.7.

1,3,5-Tri(5-acenaphthyl)benzene (XIII).

This hydrocarbon was prepared in 60% yield by bubbling hydrogen chloride for an hour at room temperature, into a solution of 2 g. of 5-acetylacenaphthene and 3 g. of ethyl orthoformate (9) in 20 ml. of anhydrous benzene; the precipitate formed was collected, washed with aqueous ammonia, then with water, dried, and recrystallized from cyclohexane, to give fine colorless needles of a 1:1 addition-compound of XIII with cyclohexane, which resisted heating at 100° (the hydrocarbon XIII melted at 308°).

Anal. Calcd. for $C_{42}H_{30} + C_6H_{12}$: C, 93.2; H, 6.8. Found: C, 92.8; H, 7.0.

Tri(2-phenanthryl)benzene (XIV).

This hydrocarbon, which had been mentioned briefly in an earlier paper (1), was prepared in 60% yield as above from 2-acetylphenanthrene (2.2 g.) and ethyl orthoformate (3 g.) in benzene; crystallization from xylene afforded a 1:1 addition-complex with xylene, in the form of colorless prisms which did not lose xylene on heating in an oven at 120° (the hydrocarbon XIV melted at 329°).

Anal. Calcd. for $C_{48}H_{30} + C_8H_{10}$: C, 94.3; H, 5.7. Found: C, 94.6; H, 5.5.

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REFERENCES

(1) N. P. Buu-Hoi, P. Jacquignon, F. Périn and M. Delcey, *Compt. Rend.*, **263**, 1237 (1966).

(2) N. P. Buu-Hoi, F. Périn and P. Jacquignon, *J. Heterocyclic Chem.*, **2**, 7 (1965).

(3) A. Tschitschibabin, *Ber.*, **58**, 1704 (1925); *ibid.*, **59**, 2048 (1926); *ibid.*, **60**, 1607 (1927); see also N. P. Buu-Hoi and N. Hoán, *Rec. Trav. Chim.*, **68**, 441 (1949).

(4) R. Stephan, *Chem. Ber.*, **90**, 296 (1957).

(5) G. Lock, *Monatsh. Chem.*, **81**, 850 (1930).

(6) M. M. Dashevskii and E. M. Shamis, *Zh. Obshch. Khim.*, **33**, 1573 (1963).

(7) W. Langenbeck, K. Rüthmann, H. H. Reif and F. Stolze, *J. Prakt. Chem.*, **4** [4], 136 (1956).

(8) W. Steinkopff and V. Petersdorff, *Ann. Chem.*, **543**, 119 (1940).

(9) According to a general method reported by H. O. Wirth, W. Kern and E. Schmitz, *Die Makromolekulare Chimie*, **68**, 69 (1963).

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