A Novel Route to 1,3-Diphenyl Substituted Isoindoles, Isobenzofurans and Isobenzothiophens

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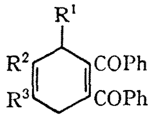
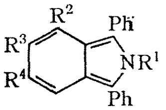
IN a search for a more versatile synthesis of stable isoindole derivatives, we have developed a general approach which leads to 1,3-diphenylisoindoles, and which can be adapted to preparation of the corresponding isobenzofurans and isobenzothiophens.



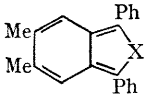
(II)

	R^1	R^2	R^3
a;	H	H	H
b;	Me	H	H
c;	H	Me	H
d;	H	Me	Me



(III)

	R^1	R^2	R^3	R^4
a;	Me	H	H	H
b;	Me	Me	H	H
c;	Me	H	Me	H
d;	Me	H	Me	Me
e;	Ph	Me	H	H
f;	Ph	H	Me	H
g;	Ph	H	Me	Me
h;	H	H	Me	H



(IV) X=O (V) X=S

Diels–Alder addition of butadiene to dibenzoylacetylene (I) in toluene at 150—160° gave 1,2-dibenzoylcyclohexa-1,4-diene (IIa), which readily underwent condensation with 40% aqueous methylamine to yield the previously reported 2-methyl-1,3-diphenylisoindole (IIIa).[1] Similarly, the adduct (IIb) of piperylene and (I), as well as the known Diels–Alder products (IIc, d)[2] of isoprene and 2,3-dimethylbutadiene with (I), afforded the corresponding *N*-methylisoindoles (IIIb—d) upon treatment with methylamine.†

Condensation of dibenzoylcyclohexadienes (IIb—d) with aniline led to the respective *N*-phenylisoindoles (IIIe—g), and (IIc), with ammonium acetate as condensing agent, gave an *N*-unsubstituted isoindole (IIIh). The reactions involving methylamine were carried out in refluxing methanol as solvent, whereas those with aniline took place in hot glacial acetic acid. The isoindole was filtered in a high state of purity from the cooled reaction mixture and, in each case, the structure of the product was verified by means of u.v., n.m.r., and mass spectral data.‡

Ried and Boeminghausen have reported that dehydration of 1,2-dibenzoyl-3,6-diphenylcyclohexa-1,4-diene with acetic anhydride in acetic acid leads to 1,3,4,7-tetraphenylisobenzofuran.[3] Similar treatment of (IId) gave 5,6-dimethyl-1,3-diphenyl isobenzofuran (IV), m.p. 194—195° (lit.[3] 193—195°) (76%), whereas condensation of (IId) with phosphorous pentasulphide in refluxing toluene gave the analogous sulphur heterocycle (V), m.p. 182·5—183° (90%).

Isoindole		Yield (%)	M.p. (degrees)
(IIIa)	..	68	148—150[a]
(IIIb)	..	74	144—145·5
(IIIc)	..	92	171·5—172·5
(IIId)	..	87	254—255
(IIIe)	..	58	191·5—192·5
(IIIf)	..	57	179—180
(IIIg)	..	65	193—194·5
(IIIh)	..	48	99—100

[a] lit.[1] 149·5—150°.

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† Satisfactory elemental analyses and spectral data were obtained for all new compounds.

‡ The mass spectra of these isoindoles showed an intense peak for the molecular ion.

[1] J. C. Emmett, D. F. Veber, and W. Lwowski, *Chem. Comm.*, 1965, 272; J. C. Emmett and W. Lwowski, *Tetrahedron*, 1966, **22**, 1011.

[2] G. Dupont and C. Paquot, *Compt. rend.*, 1937, **205**, 805.

[3] W. Ried and K. H. Boeminghausen, *Annalen*, 1961, **639**, 61.