FURAN COMPOUNDS

XLIV.* SYNTHESIS OF 2-ARYL DERIVATIVES OF 4,7-DIHYDRO- AND 4,5,6,7-TETRAHYDROISOINDOLES

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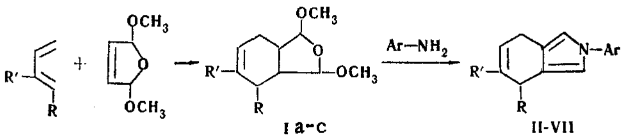
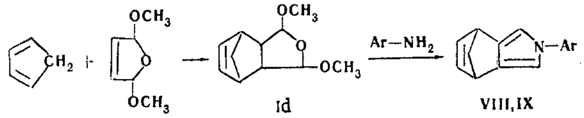
A method for obtaining 2-aryl derivatives of 4,7-dihydro- and 4,5,6,7-tetrahydroisoindoles from the products of the diene synthesis of 2,5-dimethoxy-2,5-dihydrofuran with aliphatic and cylic dienes is described.

The existing methods for the synthesis of 2-substituted isoindoles and their derivatives involve many steps or the use of starting materials that are difficult to obtain [2-6].

We have developed a convenient method for obtaining 2-aryl-substituted 4,7-dihydro- and 4,5,6,7-tetrahydroisoindoles from the products of the diene synthesis of 2,5-dimethoxy-2,5-dihydrofuran with aliphatic and cyclic dienes:



I a $R=R'=H$; b $R=H$, $R'=CH_3$; c $R=R'=CH_3$; II $R=R'=H$, $Ar=C_6H_5$; III $R=H$, $R'=CH_3$, $Ar=C_6H_5$; IV $R=R'=CH_3$, $Ar=C_6H_5$; V $R=R'=H$ $Ar=p\text{-}CH_3C_6H_4$; VI $R=H$, $R'=CH_3$ $Ar=p\text{-}CH_3C_6H_4$; VII $R=R'=CH_3$, $Ar=p\text{-}CH_3C_6H_4$



VIII $Ar=C_6H_5$; IX $Ar=p\text{-}CH_3C_6H_4$

The reaction was carried out by heating the adducts with primary aromatic amines in glacial acetic acid; in propionic acid the yields decrease by a factor of almost two.

4,5,6,7-Tetrahydroisoindoles are formed by the reaction of the saturated adducts, obtained by hydrogenation of Ia, b, and d, with primary aromatic amines under similar conditions.

A number of intense bands, which correspond to the valence vibrations of the double bonds of the aromatic and pyrrole rings [7], are observed in the IR spectra of II-XIII at 1490-1610 cm^{-1}. The absorption band at 1021-1067 cm^{-1} attests to the presence of a tertiary nitrogen [8]. A strong band at 750 cm^{-1}, due to out-of-plane deformation vibrations of the C—H group of monosubstituted benzene, is noted in the spectra of II-IV, VIII, and XI. An intense band at 804-822 cm^{-1} (1,4-disubstituted benzene [7]) is characteristic for V-VII, IX, X, XII, and XIII.

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*See [1] for Communication XLIII.

† Deceased.

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TABLE 1. 2-Aryl-Substituted 4,7-Dihydro- and 4,5,6,7-Tetrahydroisoindoles

Compound	Name	Mp, °C	M		Empirical formula	Found %			Calc. %			IR spectra, cm^{-1}			Yield, %
			found	calc		C	H	N	C	H	N	$\nu_{C=C}$	$\gamma_{=CH}$	ν_{C-N}	
II	2-Phenyl-4,7-dihydroisoindole	123	173 179	195	$C_{14}H_{13}N$	86,07 86,45	6,82 6,92	7,35 7,39	86,14	6,71	7,18	1490, 1518 1590	754	1047	53,8
III	5-Methyl-2-phenyl-4,7-dihydroisoindole	103—104	204,5 208,5	209	$C_{15}H_{15}N$	85,98 86,12	7,72 7,58	6,51 6,52	86,09	7,23	6,70	1505, 1533 1595	695 750	1055	91
IV	4,5-Dimethyl-2-phenyl-4,7-dihydroisoindole	70	231 224	223	$C_{16}H_{17}N$	86,06 85,78	7,84 7,91	6,31 6,32	86,05	7,67	6,27	1500, 1521 1595	759	1046	60,5
V	2-(p-Tolyl)-4,7-dihydroisoindole	127	211,7 207,7	209	$C_{15}H_{15}N$	86,54 86,29	7,30 7,35	6,58 6,65	86,08	7,22	6,69	1517, 1534 1613	822	1051	73
VI	5-Methyl-2-(p-tolyl)-4,7-dihydroisoindole	108—109	219 223	223	$C_{16}H_{17}N$	86,30 85,88	7,81 7,73	6,40 6,11	86,06	7,67	6,27	1515, 1535 1612	825	1050	81
VII	4,5-Dimethyl-2-(p-tolyl)-4,7-dihydroisoindole	72	238 234	237	$C_{17}H_{19}N$	86,36 86,34	8,36 7,91	6,39 6,47	86,07	8,07	5,90	1527, 1610	812	1050	62
VIII	2-Phenyl-4,7-dihydro-4,7-methanoisoindole	277 (dec.)	—	—	$C_{15}H_{13}N$	86,71 86,56	5,92 5,98	6,92 6,98	86,91	6,32	6,75	1497, 1597	750	1035	60
IX	2-(p-Tolyl)-4,7-dihydro-4,7-methanoisoindole	213 (dec.)	—	—	$C_{16}H_{15}N$	85,25 85,85	7,49 7,70	5,98 6,11	86,84	6,83	6,33	1507, 1610	804	1021	68
X	2-(p-Tolyl)-4,5,6,7-tetrahydroisoindole	115	209,9 210,8	211	$C_{15}H_{17}N$	84,99 84,92	8,20 8,52	6,58 6,46	85,26	8,11	6,63	1531, 1610	814	1043	67
XI	5-Methyl-2-phenyl-4,5,6,7-tetrahydroisoindole	51—52	209 212	211	$C_{15}H_{17}N$	85,14 85,14	8,32 8,20	6,46 6,47	85,26	8,11	6,63	1505, 1528 1599	690 750	1047	88
XII	5-Methyl-2-(p-Tolyl)-4,5,6,7-tetrahydroisoindole	97—98	229 219	225	$C_{16}H_{19}N$	85,22 85,26	8,42 8,88	5,96 6,20	85,28	8,50	6,22	1528, 1607	815	1050	91
XIII	2-(p-Tolyl)-4,5,6,7-tetrahydro-4,7-methanoisoindole	238 (dec.)	—	—	$C_{16}H_{17}N$	85,22 85,05	7,83 7,40	6,32 6,52	86,06	7,67	6,27	1509, 1569 1610	813	1067	87

EXPERIMENTAL

Adducts Ia-d were obtained by a previously described method [9] by condensation of 2,5-dimethoxy-2,5-dihydrofuran with butadiene, isoprene, 1,2-dimethyl-1,3-butadiene, and cyclopentadiene. Hydrogenation of Ia, b, and d yielded saturated products Ie-g [9].

2-Phenyl-4,7-dihydroisoindole (II). Compound Ia (0.01 mole), 0.01 mole of freshly distilled aniline, and 5 ml of glacial acetic acid were placed in a round-bottom flask equipped with a reflux condenser, and the mixture was heated on a water bath (70°C) for 25 min. The crystals that precipitated on cooling the reaction mixture were removed, washed several times with water, and recrystallized from alcohol. The yield was 53.8%.

5-Methyl-2-phenyl-4,7-dihydroisoindole (III). This compound was obtained by heating 0.01 mole of Ib, 0.01 mole of aniline, and 10 ml of glacial acetic acid on a boiling water bath for 1.5 h. The crystals that precipitated on cooling were isolated. Another aliquot of product was additionally precipitated from the mother liquor with cold water. The crystals were washed with hot water and recrystallized from alcohol. The yield was 91%.

4,5-Dimethyl-2-phenyl-4,7-dihydroisoindole (IV). This compound was obtained by heating a mixture of equimolecular amounts of Ic and aniline and 5 ml of glacial acetic acid on a boiling water bath for 1.5 h. After cooling, the reaction mixture was poured over crushed ice. An oil separated and crystallized on standing. The crystals were washed with water and methanol and recrystallized from alcohol. The yield was 60.5%.

2-(p-Tolyl)-4,7-dihydroisoindole (V) and 5-Methyl-2-(p-tolyl)-4,7-dihydroisoindole (VI). These were obtained, like III, from Ia and b and p-toluidine.

4,5-Dimethyl-2-(p-tolyl)-4,7-dihydroisoindole (VII) and 2-(p-Tolyl)-4,7-dihydro-4,7-methanoisoindole (IX). These were obtained, in a manner similar to that used to obtain IV, from Ic and d and p-toluidine.

2-Phenyl-4,7-dihydro-4,7-methanoisoindole (VIII). This was obtained in the same way as II from Id and aniline. The product was washed several times with ether and methanol.

2-(p-Tolyl)-4,5,6,7-tetrahydroisoindole (X), 5-Methyl-2-phenyl-4,5,6,7-tetrahydroisoindole (XI), 5-Methyl-2-(p-tolyl)-4,5,6,7-tetrahydroisoindole (XII), and 2-(p-tolyl)-4,5,6,7-tetrahydro-4,7-methanoisoindole (XIII). These were obtained in the same way as III from Ie, f, and g and the appropriate amine.

Compounds II-VII and X-XII are white or slightly yellowish crystals that are quite soluble in most organic solvents and insoluble in water. Compounds VIII, IX, and XIII are yellow powders that are insoluble in water, slightly soluble in organic solvents, and melt with decomposition. Compound XIII is quite soluble in ether. A qualitative confirmation of the structures of these compounds is the fact that alcohol solutions of them give a raspberry color with Erlich's reagent that gradually turns dark red on standing.

The IR spectra were recorded with a UR-10 double-beam spectrophotometer from 700-2000 cm^{-1}. The compounds were investigated in the form of mulls in mineral oil.

LITERATURE CITED

1. A. A. Ponomarev, I. A. Markushina, and N. V. Shulyakovskaya, Khim. Geterotsikl. Soedin., 1155 (1970).
2. G. Wittig, H. Tenhaeff, W. Schoh, and G. Koenig, Ann., 572, 1 (1951).
3. W. Theilacker and H. Kalenda, Ann., 584, 87 (1953).
4. W. Theilacker and W. Schmidt, Ann., 605, 43 (1957).
5. R. Kreher and J. Schubert, Angew. Chem., 76, 682 (1964).
6. R. Jan Fryer, J. V. Earley, and L. H. Sternbach, J. Am. Chem. Soc., 88, 3173 (1966).
7. L. Bellamy, Infrared Spectra of Complex Molecules, Methuen (1958).
8. R. Alan Jones, Austral. J. Chem., 19, 289 (1966).
9. A. A. Ponomarev, I. A. Markushina, and G. E. Marinicheva, Author's Certificate No. 253,806; Byull. Izobr., No. 31, 30 (1969).