

SYNTHESIS OF NEW BIS(INDAZOL-1-YL)PHENYLMETHANES

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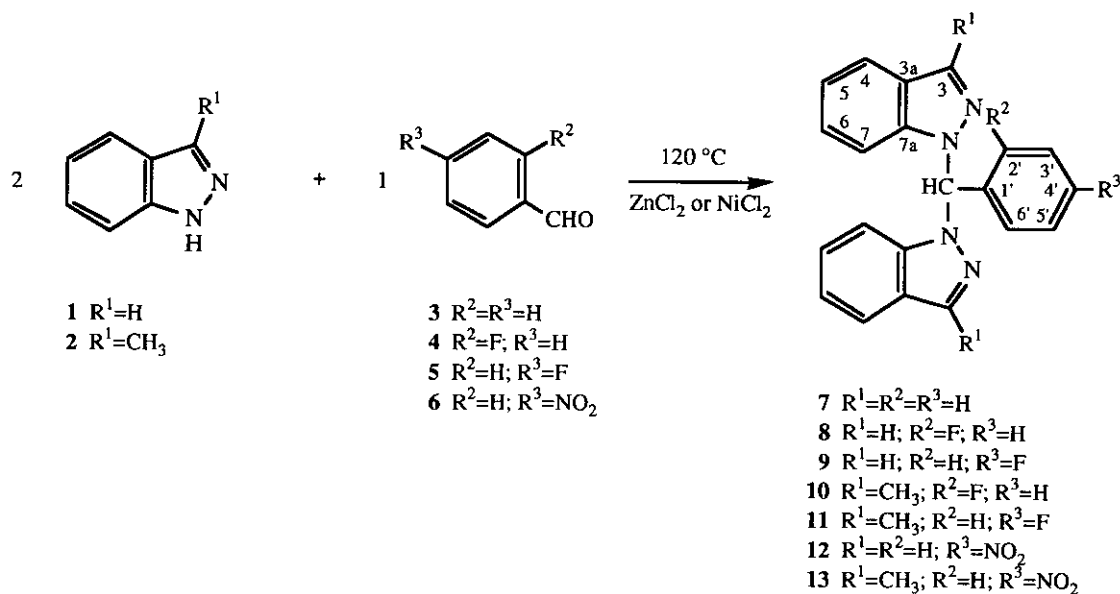
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Abstract -Synthesis and spectroscopic characterization of new bis(indazol-1-yl)fluoro- or nitrophenylmethanes are reported. They have been prepared by reaction of indazole and 3-methylindazole with *ortho*-fluoro-, *para*-fluoro- and *para*-nitrobenzaldehydes in the presence of ZnCl₂ and NiCl₂.

Bis(indazol-1-yl)phenylmethanes behave as nitrogen-donor neutral ligands^{1,2} with capability to chelate heavy metals such as rhodium and iridium. The complexes are able to present similar properties to those reported for bis(pyrazol-1-yl)phenylmethanes, bis(pyrazol-1-yl)methanes and tris(pirazol-1-yl)methanes complexes.³⁻⁵ Recently we have described a pentacoordinate rhodium (I) complex derived from bis(indazol-1-yl)pyridin-2'-ylmethane.⁶ Some bis(indazol-1-yl)aryl-methanes have been easily prepared by thermal reaction of indazole with the corresponding aromatic or heteroaromatic aldehyde in the presence of ZnCl₂.^{6,7} In this work we extend the procedure to fluoro- and nitrobenzaldehydes using as well NiCl₂ as an alternative Lewis acid catalyst.

Synthesis of bis(indazol-1-yl)phenylmethanes (**7-13**) has been performed by condensation at 120 °C of indazole with the corresponding benzaldehyde in the presence of ZnCl₂ or NiCl₂ (Scheme I). The reaction proceeds regioselectively to give the thermodynamically more stable 1,1-isomer as we demonstrated previously.⁸ According to the yields shown in Table I, the use of NiCl₂ seems to be more adequate for the reaction of indazole and *ortho*-fluorobenzaldehyde, but no significant improvement with the other aldehydes was obtained.



Scheme I

New compounds (**8-13**) were fully characterized by ^1H and ^{13}C nmr spectroscopy (Tables II and III). Assignments of all protons and carbons were made on the basis of previous data^{7,8} and with the help of 2D homonuclear and heteronuclear correlations. The bis(indazol-1-yl) isomer was easily recognized by the characteristic chemical shift (see table III) of the carbon atom at the position 3 (ca. 135 ppm for indazole nucleus and ca. 143 for 3-methylindazole nucleus) and at the position 7 (ca. 110 ppm for both nucleus). The chemical shift values of these carbon atoms in compounds (**8-13**) were in agreement with those found in other 1-substituted indazoles.⁹ Another significant feature was that proton H-7 of the indazole ring resonates in all compounds at higher field than proton H-4. This behaviour is also found in unsubstituted indazole. However, in aliphatic series such as bis(indazol-1-yl)alkanes, proton H-7 always resonates at lower field than proton H-4.⁸

EXPERIMENTAL

Melting points were obtained on a Gallenkamp MFB-595 and are uncorrected. Elemental analyses were performed with a Perkin Elmer 240 apparatus. Mass spectra were determined on a VG-12-250

Table I. Isolated yields, melting points and elemental analyses of compounds (8-13).

Compound	Lewis acid	Yields %	mp °C	Formula	Elemental Analyses					
					Calculated		N	Found		N
					C	H		C	H	
7	ZnCl ₂	64 ^a	136-138 (Ethanol)							
	NiCl ₂	26								
8	ZnCl ₂	30	138-140 (Ethanol)	C ₂₁ H ₁₅ N ₄ F	73.65	4.42	16.37	73.38	4.75	16.60
	NiCl ₂	51								
9	ZnCl ₂	59	119-121 (Ethanol)	C ₂₁ H ₁₅ N ₄ F	73.65	4.42	16.37	73.90	4.32	16.45
	NiCl ₂	52								
10	ZnCl ₂	73	155-157 (Hexane-Ethanol)	C ₂₃ H ₁₉ N ₄ F	74.57	5.17	15.12	74.48	5.14	14.92
11	ZnCl ₂	42	168-169 (Ethanol)	C ₂₃ H ₁₉ N ₄ F	74.57	5.17	15.12	74.20	5.25	15.17
12	ZnCl ₂	58	154-156 (Ethanol)	C ₂₁ H ₁₅ N ₅ O ₂	68.28	4.10	18.66	68.01	4.27	18.75
13	ZnCl ₂	62	187-189 (Ethanol)	C ₂₃ H ₁₉ N ₅ O ₂	69.51	4.82	17.62	69.21	4.76	17.65

a: From reference 7.

Table II. ¹H Nmr chemical shifts (δ) and coupling constants (Hz) of compounds (8-13) in CDCl₃ at 200.13 MHz.

Compound	H ₃	H ₄	H ₅	H ₆	H ₇	CH(sp ³)	H ₂	H ₃	H ₄	H ₅	H ₆	CH ₃
8	8.09(d)	7.70(ddd)	7.17-7.09(m)	7.17-7.09(m)	7.37(ddd)	8.55(s)	7.33-7.09(m)	7.33-7.09(m)	7.33-7.09(m)	7.15-6.99(m)	7.15-6.99(m)	7.33-7.09(m)
9	8.07(d)	7.70(ddd)	7.16(ddd)	7.33(ddd)	7.51(ddd)	8.44(s)	7.15-6.99(m)	7.15-6.99(m)	7.15-6.99(m)	7.15-6.99(m)	7.15-6.99(m)	7.15-6.99(m)
10	7.61(ddd)	7.36-7.20(m)	7.36-7.20(m)	7.36-7.20(m)	8.40(s)	7.15-7.02(m)	7.15-7.02(m)	7.15-7.02(m)	7.15-7.02(m)	7.15-7.02(m)	7.15-7.02(m)	2.55(s)
11	7.60(ddd)	7.11(ddd)	7.29(ddd)	7.49(ddd)	8.29(s)	7.05-6.95(m)	7.05-6.95(m)	7.05-6.95(m)	7.05-6.95(m)	7.05-6.95(m)	7.05-6.95(m)	2.53(s)
12	8.10(d)	7.73(ddd)	7.18(ddd)	7.34(ddd)	7.54(ddd)	8.51(s)	8.21(d)	7.30(d)	8.21(d)	7.30(d)	7.30(d)	7.30(d)
13	7.63(ddd)	7.14(ddd)	7.32(ddd)	7.52(ddd)	8.34(s)	7.27(d)	8.18(d)	7.27(d)	8.18(d)	7.27(d)	7.27(d)	2.55(s)

s, singlet; d, doublet; t, triplet; m, multiplet.

Table III. ¹³C Chemical shifts (δ) of compounds (8-13) in CDCl₃ at 50.33 MHz.

Compound	C ₃	C _{3a}	C ₄	C ₅	C ₆	C ₇	C _{7a}	CH(sp ³)	C ₁	C ₂	C ₃	C ₄	C ₅	C ₆	CH ₃
8	134.7	124.8	121.2	121.6	127.1	109.8	139.6	70.0	123.1	160.0	115.7	128.9	124.2	131.1	
9	134.8	124.7	121.0	121.5	126.8	110.6	139.6	74.0	130.8	129.3	115.5	162.7	115.5	129.3	
10	142.9	124.3	120.3	120.6	126.8	109.9	140.4	69.9	123.7	160.1	115.5	128.9	124.0	130.6	12.0
11	143.0	124.3	120.1	120.5	126.5	110.8	140.5	73.5	131.5	129.3	115.3	162.6	115.3	129.3	11.9
12	135.2	124.8	121.2	121.8	127.2	110.3	139.5	73.7	142.0	128.6	123.6	147.9	123.6	128.6	
13	143.6	124.4	120.3	120.9	126.9	110.5	140.5	73.3	142.9	128.7	123.5	147.8	123.5	128.7	12.0

spectrometer at 70 eV. Nmr spectra were recorded with a Bruker AC-200 (200.13 MHz for ^1H , and 50.33 MHz for ^{13}C). ^1H and ^{13}C chemical shifts (δ) are given from internal tetramethylsilane with an accuracy of ± 0.01 and ± 0.1 ppm respectively. Coupling constants (J) are accurate to ± 0.2 Hz for ^1H nmr spectra and ± 0.6 Hz for ^{13}C nmr spectra. Homonuclear ^1H - ^1H COSY-90 and heteronuclear ^1H - ^{13}C correlations were performed in the usual manner.^{10,11} Tlc chromatography was performed on DC-Alufolien/Kieselgel 60 F₂₅₄ (Merck, 0.2 mm) and column chromatography through silica gel Merck 60 (70-230 mesh). Products were purchased from commercial sources. ZnCl_2 and NiCl_2 were stored in a vacuum desiccator prior to use. 3-Methylindazole was prepared by a described procedure.¹² Isolated yields, melting points and elemental analyses of the new bis(indazol-1-yl)phenylmethanes (**8-13**) are given in Table I.

Reaction of Indazoles (1-2) with Benzaldehydes (3-6). General method. A one-necked round-bottomed flask was fitted with a reflux condenser attached to drying tube (CaCl_2) and with a magnetic stirrer. The flask was charged with the indazole (10 mmol), the corresponding aldehyde (5 mmol) and ZnCl_2 or NiCl_2 (0.25 mmol) (2:1: 1/20 molar ratio). The mixture was heated with stirring in an oil bath at 120-125 °C for 16 to 20 h. After cooling to room temperature the reaction mixture was purified by silica gel column chromatography using methylene chloride as eluent.

Bis(indazol-1-yl)-ortho-fluorophenylmethane (8) $R_f = 0.32$. Ir (KBr) 3120, 3080, 1615, 1490, 1450, 1415, 1370, 1330, 1310, 1285, 1225, 1185, 1160, 1095, 900, 850, 790, 740 cm^{-1} . Ms m/z (%) 342 (M^+ , 27), 328 (9), 327 (3), 226 (26), 225 (100), 224 (3), 205 (3), 196 (5), 170 (4).

Bis(indazol-1-yl)-para-fluorophenylmethane (9) $R_f = 0.38$. Ir (KBr) 3200, 2930, 2840, 1620, 1500, 1470, 1415, 1370, 1320, 1225, 1160, 1120, 1025, 900, 800, 760 cm^{-1} . Ms m/z (%) 342 (M^+ , 9), 226 (16), 225 (100), 224 (2), 196 (4), 170 (3).

Bis(3-methyl-indazol-1-yl)-ortho-fluorophenylmethane (10) $R_f = 0.22$. Ir (KBr) 3060, 2920, 1600, 1505, 1480, 1440, 1395, 1350, 1290, 1230, 1200, 1165, 1070, 1030, 1015, 880, 805, 770, 735 cm^{-1} . Ms m/z (%) 370 (M^+ , 3), 240 (19), 239 (100), 219 (5), 170 (2), 102 (2).

Bis(3-methyl-indazol-1-yl)-para-fluorophenylmethane (11) $R_f = 0.26$. Ir (KBr) 3070, 2925, 1610, 1505, 1430, 1330, 1280, 1260, 1170, 1150, 1130, 1075, 1035, 1020, 850, 825, 800, 760, 740 cm^{-1} . Ms m/z (%) 370 (M^+ , 2), 240 (20), 239 (100), 238 (1), 237 (2), 223 (1), 170 (2).

Bis(indazol-1-yl)-para-nitrophenylmethane (12) $R_f = 0.32$. Ir (KBr) 3100, 3075, 2970, 1600, 1510, 1330, 1300, 1275, 1250, 1190, 1160, 1140, 1100, 1025, 910, 860, 840, 825, 760, 740 cm^{-1} . Ms m/z (%) 370 (12), 369 (M^+ , 12), 253 (16), 252 (100), 225 (3), 206 (15), 205 (12), 178 (3).

Bis(3-methyl-indazol-1-yl)-para-nitrophenylmethane (13) $R_f = 0.24$. Ir (KBr) 3080, 3050, 2920, 1605, 1595, 1505, 1440, 1390, 1290, 1200, 1175, 1080, 1010, 830, 800, 750, 740, 725 cm^{-1} . Ms m/z (%) 397 (M^+ , 2), 267 (20), 266 (100), 220 (16), 219 (14), 144 (6), 77 (10).

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