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Synthesis of Photochromic Spiroindolinopyrans with Extended Conjugation

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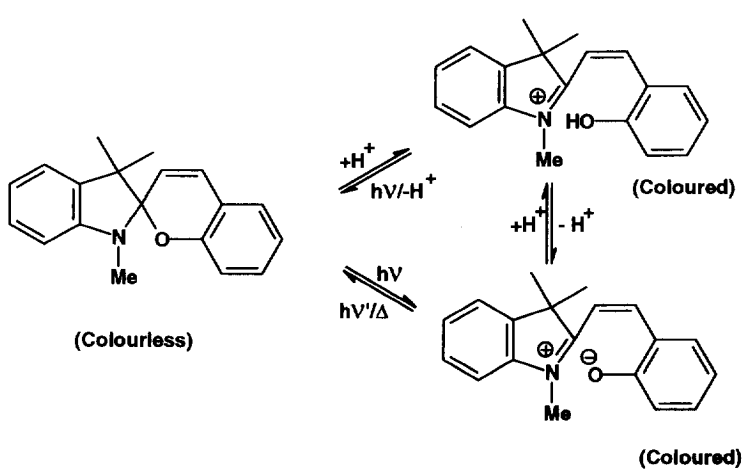
Abstract : Unsaturated side chains have been introduced in benzopyran site of parent indolinospiropyran moiety using Wittig reaction under conditions of Phase Transfer Catalysis in a one pot synthesis. The resultant unsaturated photochromic indolinospirobenzopyrans show significant bathochromic shift in the uv region of absorption spectra.

In past, Wittig reactions with photochromic indolinospirobenzopyrans have been carried out using either NaOEt[1] or NaOH in DMSO[2]. Since indolinospirobenzopyrans exhibit thermochromism as well as reverse photochromism[3] in presence of even mild organic acids, like malonic acid or Lewis acids, like $SnCl_4$, reaction conditions eliminating the use of acid and thermal conditions were envisaged. [Scheme - 1]

SCHEME 1.



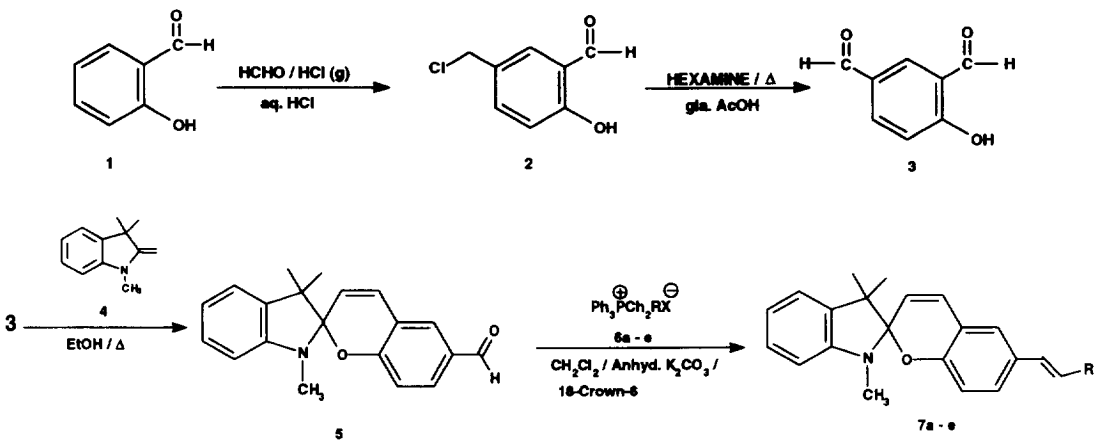
Phase Transfer Catalysis (PTC) which satisfies these requirements was adopted, and is being reported for the first time for this class. Quaternary ammonium salts using bases like KOH, NaOH, K_2CO_3, Na_2CO_3 have been used, but these reaction conditions need refluxing and during work-up procedure use of acid is essential.

We now report a method using phase transfer catalyst, namely 18-Crown-6 for Wittig olefination of indolinospirobenzopyrans. This method is of significance as reactions are carried out at room temperature in a

one pot synthesis. The Wittig olefination was successfully attempted using two different routes. Both the routes gave comparable yields (25 - 28%).

In the first approach 1',3',-dihydro-6-formyl-1',3',3'-trimethylspiro[2H-1-benzopyran-2,2'[1H]indoline] i.e. 6 - formyl BIPS (**5**) was prepared by reacting Fischer base (**4**) and 5-formyl salicylaldehyde (**3**). It was then treated with phosphonium salt of alkyl halide in presence of anhydrous K_2CO_3 and 18-Crown-6 at room temperature. [Scheme - 2]

SCHEME 2.



In the second methodology, 5-chloromethyl salicylaldehyde (**2**) on reaction with triphenyl phosphine gave corresponding phosphonium salt (**8**). The latter on condensation with Fischer base (**4**) gave a spiro phosphonium salt (**9**). Without isolating this intermediate further reaction with different substituted aldehydes in presence of anhydrous K_2CO_3 and 18-Crown-6 in CH_2Cl_2 was carried out. [Scheme - 3]

SCHEME 3.

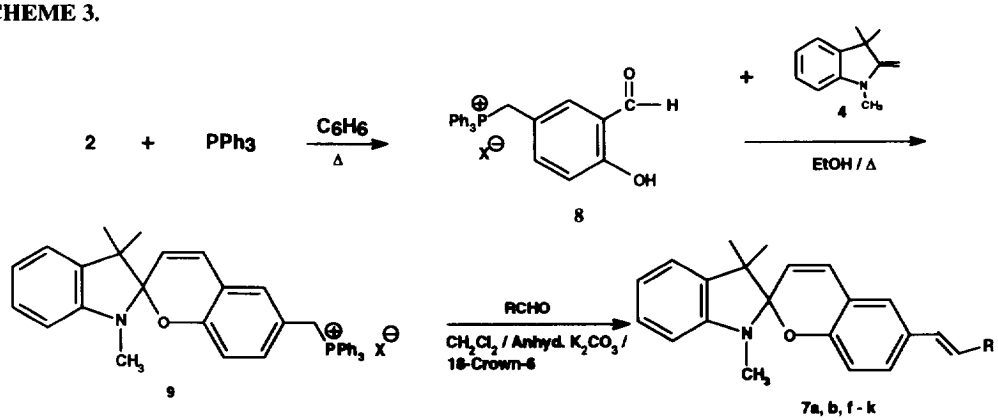
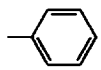
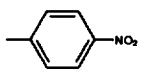
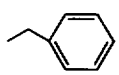
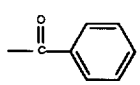


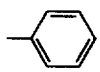
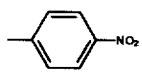
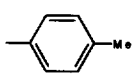
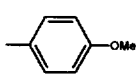
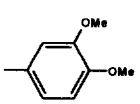
Table 1

6,7	R	^{1}H NMR ($CDCl_3$) δ ppm	IR (KBr) cm^{-1}	UV (EtOH) λ_{max} nm
a		1.2 (s, 3H, Me); 1.3 (s, 3H, Me) ; 2.8 (s, 3H, N-Me); 5.8 (d,1H,C_4-H); 6.4 - 7.8 (m, 15H, Ar-H & C= C-H)	960 cm^{-1} (C_{spiro} - O), 1650 cm^{-1} (C = C-Ar)	316nm (Ɛ 33620)
b		1.2 (s, 3H, Me); 1.3 (s, 3H, Me) ; 2.8 (s, 3H, N-Me); 5.8 (d,1H,C_4-H); 6.4 - 8.0 (m, 14H, Ar-H & C = C-H)	960 cm^{-1} (C_{spiro} - O), 1520 cm^{-1} (-NO_2), 1650 cm^{-1} (C = C-Ar)	386nm (Ɛ 33000)
c		1.2 (s, 3H, Me); 1.3 (s, 3H, Me) ; 2.8 (s, 2H, CH_2-Ar); 2.8 (s, 3H, N-Me); 5.7 (d,1H, C_4-H); 6.2 - 7.6 (m, 15H, Ar-H, C_3-H and HC = CH)	960 cm^{-1} (Cspiro - O)	294nm (Ɛ 13880)
d		1.2 - 1.6 (m, 9H, Me); 2.8 (s, 3H, N-Me); 4.2 - 4.3 (q, 2H, -O-CH_2); 5.8 (d,1H, C_4-H); 6.2 - 7.8 (m, 10H, Ar-H, C_3-H and C = C-H)	970 cm^{-1} (Cspiro - O), 1250 cm^{-1} (O-C), 1720 cm^{-1} (for ester)	317nm (Ɛ 25000)
e		1.2 (s, 3H, Me); 1.3 (s, 3H, Me); 2.8 (s, 3H, N-Me); 5.8 (d,1H, C_4-H); 6.4 - 7.8 (m, 15H, Ar-H, C_3-H and C = C-H)	960 cm^{-1} (C_{spiro} - O), 1660 cm^{-1} (C = O of keto)	331nm (Ɛ 39300)

Compounds **7a** and **7b** were synthesized by this pathway using phosphonium salt (**9**) and benzaldenyde and 4-nitrobenzaldehyde respectively and they were found to be identical with those obtained by first route.

Further experimental studies on photochromic properties of newly synthesised spiro compounds are under investigations.

Table 2

7	R	^{1}H NMR ($CDCl_3$) δ ppm	IR (KBr) cm^{-1}	UV (EtOH) λ_{max} nm
a		1.2 (s, 3H, Me); 1.3 (s, 3H, Me) ; 2.8 (s, 3H, N-Me); 5.8 (d,1H,C_4-H); 6.4 - 7.8 (m, 15H, Ar-H & C= C-H)	960 cm^{-1} (C_{spiro} - O), 1650 cm^{-1} (C = C-Ar)	316nm (Ɛ 33620)
b		1.2 (s, 3H, Me); 1.3 (s, 3H, Me) : 2.8 (s, 3H, N-Me); 5.8 (d,1H,C_4-H); 6.4 - 8.0 (m, 14H, Ar-H & C = C-H)	960 cm^{-1} (C_{spiro} - O), 1520 cm^{-1} (-NO_2), 1650 cm^{-1} (C = C-Ar)	386nm (Ɛ 33000)
f		1.17 (s, 3H, Me); 1.29 (s, 3H, Me); 2.3 (s, 3H, Ar-Me); 2.7 (s, 3H, N-Me); 5.7 (d, 1H, C_4-H), 6.4 - 7.7 (m, 14H, Ar-H, C_3-H & C = C-H)	----------	317nm (Ɛ 36140)
g		1.2 (s, 3H, Me); 1.3 (s, 3H, Me); 2.7 (s, 3H, N-Me); 3.8 (s, 3H, OMe); 5.6 (d,1H, C_4-H) 6.4 - 8.0 (m, 14H, Ar-H, C_3-H & C = C-H).	960 cm^{-1} (Cspiro - O), 1260 cm^{-1} (-O-Me), 1650 cm^{-1} (>C = O of keto)	319nm (Ɛ 37660)
h		1.14 (s, 3H, Me); 1.27 (s, 3H, Me); 2.7 (s, 3H, N-Me); 3.6 (s, 3H, O-Me); 3.8 (s, 3H, O-Me); 5.6 (d,1H, C_4-H); 6.4 - 7.2 (m, 13H, Ar-H, C_3-H & C = C-H).	960 cm^{-1} (Cspiro - O), 1260 cm^{-1} (-O-Me), 1650 cm^{-1} (>C = O of keto)	302nm (Ɛ 20200)

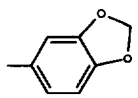
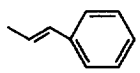
i		1.19 (s, 3H, Me); 1.28 (s, 3H, Me); 2.8 (s, 3H, N-Me); 5.8 (d,1H, C_4-H); 6.0 (s, 2H, -O-CH_2-O); 6.4 - 7.6 (m, 13H, Ar-H, C_3-H & C = C-H).	960 cm^{-1} (Cspiro - O), 1260 cm^{-1} (-O-CH_2-O), 1650 cm^{-1} (>C = O of keto)	363nm (ε 23520)
j		1.19 (s, 3H, Me); 1.28 (s, 3H, Me); 2.7 (s, 3H, N-Me); 5.7 (d,1H, C_4-H); and 6.5 - 7.4 (m, 17H, Ar-H)	960 cm^{-1} (Cspiro - O), 1660 cm^{-1} (>C = O of keto)	342nm (ε 31360)
k		1.19 (s, 3H, Me); 1.28 (s, 3H, Me); 2.1 (s, 3H, Me); 2.8 (s, 3H, N-Me); 5.8 (d,1H, C_4-H) and 6.5 - 7.8 (m, 12H, Ar-H).	960 cm^{-1} (Cspiro - O), 1660 cm^{-1} (>C = O of keto)	295nm (ε 21700)

Table 3

7	M. P. ^oC	YIELD
a	120 ^oC (lit[1] 120 - 1^oC)	25% (lit[1] 26%)
b	153 ^oC (lit[1] 152 ^oC)	25% (lit[1] 24%)
c	oil	22%
d	oil	22%
e	106 - 8 ^oC	24%
f	126 - 8 ^oC	24%
g	166 ^oC	24%
h	oil	22.8%
i	120 - 1 ^oC	26%
j	126 ^oC	28%
k	oil	22%

EXPERIMENTAL

The compounds were identified by ^1H NMR, IR and uv spectroscopy. Satisfactory, microanalyses were also obtained (C, H, N analysis match with ± 0.4%). Following chemicals used were prepared according to

literature methods; 5-chloromethylsalicylaldehyde[4], 5-formylsalicylaldehyde[4], phosphonium salts[5]. Fischer base, 18-Crown-6 used were commercially available products from Fluka. ^{1}H NMR spectra were scanned in $CDCl_3$ on FT Brucker (80 MHz) and JEOL Fx 90 Q (90 MHz). The IR spectra were recorded on Shimadzu FTIR 4200, UV spectra were recorded using Shimadzu UV-160A. All the melting points are uncorrected.

Condensation of Fischer base with 5-formyl salicylaldehyde: 6-formyl-1',3',3'-trimethylspiro[2H-1-benzopyran-2,2'-[1H]-indole] i.e. 6-Formyl BIPS (5). Equimolar quantities of 5-formyl salicylaldeyde (**3**) and Fischer base (**4**) in ethanol (dry) gave the condensed product. The reaction mixture after refluxing for 5hrs on water bath was decomposed in ice. The solid separating out was filtered, dried and further purified by crystallization from pet ether (bp 40 - 60^{o}C) mp 128 ^{o}C (lit[6] mp128 - 9 ^{o}C)

IR (KBr) showed absorption at 970 cm^{-1} for (Cspiro-O) 1680 cm^{-1} for -CHO group.

^{1}H NMR in $CDCl_3$ showed signals at δ 1.19 (s, 3H, Me); δ 1.28 (s, 3H, Me); δ 2.85(s, 3H, N-Me); δ 5.7 (d,1H,C4-H); δ 6.4-7.8 (m, 8H, Ar-H) and δ 9.83 (s,1H, H of ).

GENERAL PROCEDURE FOR COMPOUNDS 7a-e USING METHOD-1

Equimolar quantities of triphenyl phosphine and alkyl halide were refluxed in dry benzene for about 8 hours. The solid separating out was filtered, washed with benzene and dried.

11 mmoles of phosphonium salt prepared as above were dissolved in 25ml CH_2Cl_2. To this 11 mmoles of anh. K_2CO_3, was added followed by 10 mmoles of 6-Formyl BIPS. To this 30 mgms of 18-Crown-6 was added and reaction mixture was monitored at time intervals with TLC (Pet.ether: ethyl acetate 95:5). The reaction mixture was filtered, residue was washed with dichloromethane; washings and the filtrate were combined and concentrated. From the residual oil the desired product was isolated using silica gel column chromatography with pet ether : ethyl acetate (98:2) as mixed solvent for elution.

Synthesis of 6-styryl BIPS (7a). 6-Formyl BIPS (**5**) was reacted with triphenyl phosphonium salt of benzyl chloride (**6a**) as described in general procedure given above. The pure product obtained was crystallised from pet ether (40 - 60 ^{o}C) white crystals mp 120 ^{o}C (lit[1] 120 - 1 ^{o}C) yield ~ 25%.

6-(4-nitrostyryl) BIPS (7b). Reaction of 6-Formyl BIPS (**5**) with triphenyl phosphonium salt of 4-nitrobenzyl bromide (**6b**) gave compound **7b**. Yellow crystals, mp 153 ^{o}C (lit[1] 152 ^{o}C) yield 25%

6-(3-phenylprop-1-enyl) BIPS (7c). Reaction of 6-formyl BIPS (**5**) with triphenyl phosphonium salt of phenethyl bromide (**6c**) gave compound **7c**. Oil, yield 22%.

6-[2- ethyl carboxy vinyl] BIPS (7d). Reaction of 6-formyl BIPS (**5**) with triphenyl phosphonium salt of Bromo ethyl acetate (**6d**) gave compound **7d**. Light pink Oil, Yield 22%.

6-[3-oxo-3-phenyl-prop-1-enyl] BIPS (7e). Reaction of 6-formyl BIPS (**5**) with triphenyl phosphonium salt of phenacyl chloride (**6e**) gave compound **7e**. Yellow needles mp 106-8 ^{o}C. Yield 24%

GENERAL PROCEDURE FOR COMPOUNDS 7f-k USING METHOD-2

Equimolar quantities of triphenyl phosphine and 5-chloromethylsalicylaldehyde[4] were refluxed in benzene for 8 hrs. The solid separating out was filtered washed with benzene and dried. 11 mmoles of above phosphonium salt (**7**) and Fischer base (**1**) were condensed in dry ethanol by refluxing for 6 hrs on water bath. After condensation ethanol was removed completely by distillation and phosphonium salt (**8**) was used as such for further reaction. 11 mmoles of this spiro phosphonium salt (**8**) were taken in CH_2Cl_2 (50ml). To this 11 mmoles of anhyd. K_2CO_3 was added followed by addition of 10 mmoles of aldehyde and 30mgms of 18-Crown-6. The reaction mixture was stirred at room temperature and monitored at time intervals by TLC (pet ether : ethyl acetate 95:5). The reaction was worked up following procedure similar to that in Method-1. After isolation from silica gel column, further purification was done by crystallisation from pet ether.

6-styryl BIPS (7a). Reaction of phosphonium salt (**9**) with benzaldehyde according to above proedure gave a product with mp 120 ^{o}C (lit[1] 120 -1 ^{o}C). Yield 25%. Spectral analysis of this showed that it was 6-styryl BIPS (**7a**) as all data was in agreement with that of **7a** obtained from Method-1.

6- (4-nitro styryl) BIPS (7b). Reaction of **9** with 4-nitrobenzaldehyde gave compound which was found to be identical to **7b** obtained via Method-1. mp 153 ^{o}C (lit[1] 152 ^{o}C) (Yield 25%)

6 - (4-methyl styryl) BIPS (7f). Reaction of **9** with p-tolulaldehyde gave compound **7f**. White-pale yellow crystals. mp 126 - 8 ^{o}C, Yield 24%.

6-(4 methoxy styryl) BIPS (7g). Reaction of phosphonium salt (**9**) with anisaldehyde gave compound **7g**. Yellow needles mp 166 ^{o}C Yield 24%.

6-(3,4-dimethoxy styryl) BIPS (7h). Compound **7h** was obtained by reaction of phosphonium salt **9** with veratraldehyde. Yield 22.8%.

6(3,4-methylenedioxy styryl) BIPS (7i). Phosphonium salt (**9**) and piperonal gave compound (**7i**). White crystals mp 120 - 1 ^{o}C. Yield 26%.

6-(4-phenyl-but-1,3-dienyl) BIPS (7j). Compound (**7j**) was obtained from reaction of **9** with cinnamaldehyde. White crystals, mp 126 ^{o}C. Yield 28%.

6-(penta-1,3-dienyl) BIPS (7k). **7k** was obtained by reaction of **9** with Crotonaldehyde, as an oil. Yield 22%.

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* Dedicated to Prof. A. B. Kulkarni on his seventyfifth birthday

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