ONE-POT SYNTHESIS OF NEW UNSYMMETRICAL β-HETEROARYL-o-DIVINYLBENZENES

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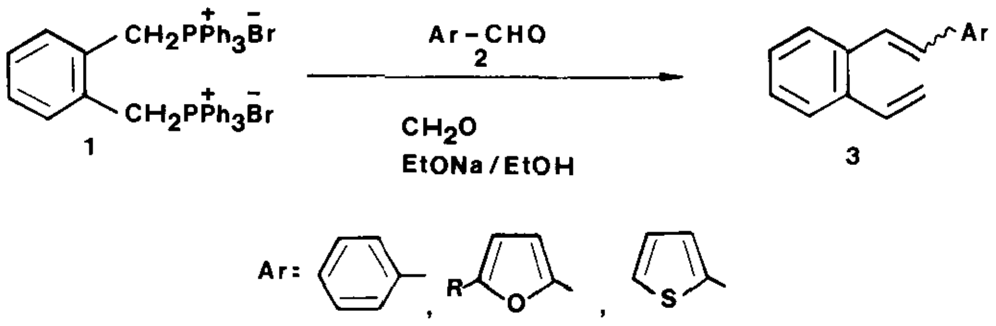
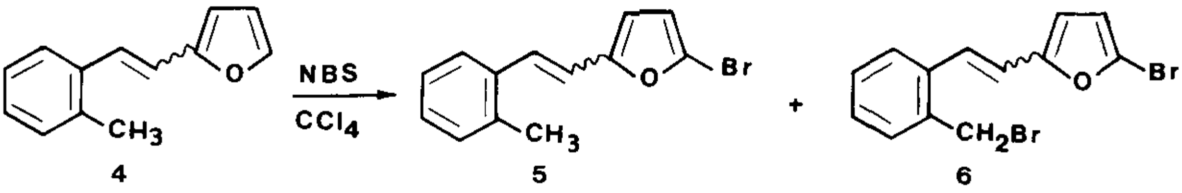
Abstract - By Wittig reaction of *o*-xylylenebis(triphenylphosphonium bromide) (1) with aldehydes (2) and formaldehyde in the presence of base, unsymmetrically substituted *o*-divinylbenzenes (3) have been prepared in one pot.

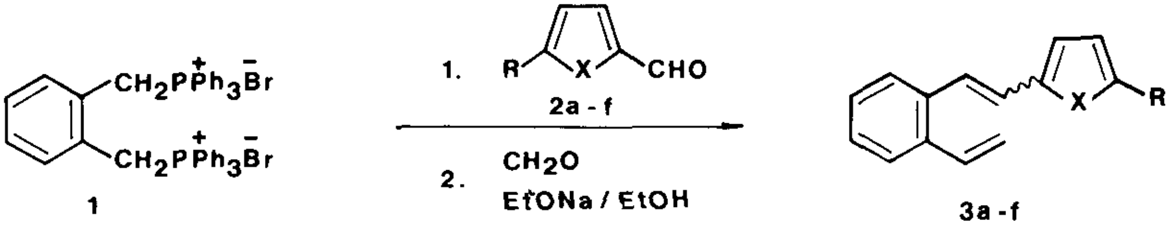
Our interest in photochemical behaviour of aryl[1] and furyl[2] substituted *o*-divinylbenzenes prompted us to develop the synthesis of β-(2-heteroaryl) derivatives (3) and to investigate their spectral properties. The β-phenyl substituted *o*-divinylbenzene, *o*-vinylstilbene, has been prepared earlier.[1] Attempts to apply a similar route to the furan analogs were unsuccessful due to the reactive furan ring. Wittig reaction using diphosphonium salt (1), corresponding aldehydes (2) and formaldehyde seemed to us to be particularly attractive because of its simplicity and good yields.



RESULTS AND DISCUSSION

The initial approach to these compounds (3) was to introduce the vinyl group via 1-(*o*-tolyl)-2-(2-furyl)ethene (4)[3] transforming the methyl group into the bromomethyl group and subsequently into the phosphonium salt followed by Wittig reaction with formaldehyde. However, by the bromination with N-bromosuccinimide (NBS) the substitution in the furan ring primarily took place and only in case of two equivalents of NBS, beside compound (5) and tarry material, some bromomethyl derivative (6) was identified (less than 20%). In order to expand the furyl analogues of *o*-vinylstilbene we have developed the syntetic method from diphosphonium salt (1) and proved it to be versatile for preparation of various heterocyclic compounds (3) only by changing reagents (2) without altering synthetic route. Thus, to obtain the desired products with as little as possible byproducts, the key matter was the sequence of addition as well as the equivalent quantity, first of aldehydes (2) and then formaldehyde, both under the basic conditions. After work-up, the products (3a-f, mixture of cis- and trans-isomers) were isolated by chromatography on the silica gel column (Table 1). The small quantities of the formed *o*-divinylbenzene were easily separated in first fractions whereas β,β'-disubstituted impurities remained on the column. The pure isomers were separated by repeated column chromatography and the structures were determined by their uv, ^1H and ^{13}C nmr spectra (Tables 2,3 and 4).





3a: X=O, R=H ; b: X=O, R=Me , c: X=O, R=Br ;
d: X=O, R=p-MePh ; e: X=O, R=p-ClPh ; f: X=S, R=H

Table 1. Preparation and Properties of New cis- and trans-1-(2-Heteroaryl)-2-(o-vinylphenyl)ethenes (3a-f)

Compd	Isomer	X	R	mp	Ratio (%)[a]	Yield	Ms	Analysis Found(Calcd)	
				°C	cis:trans	(%)	m/z(M^+,%)	C	H
3a	cis	O	H	oil				$C_{14}H_{12}O$	
	trans	O	H	oil	30:70	85	196(30)	85.80	6.08
								(85.68)	(6.17)
3b	cis	O	Me	oil				$C_{15}H_{14}O$	
	trans	O	Me	oil	20:80	74	210(73)	85.79	6.60
								(85.68)	(6.71)
3c	cis	O	Br	oil				$C_{14}H_{11}OBr$	
	trans	O	Br	oil	20:80	86	274,276(60)	61.20	4.08
								(61.11)	(4.03)
3d	cis	O	p-MePh	59-60				$C_{21}H_{18}O$	
	trans	O	p-MePh	44-45	45:55	70	286(100)	87.99	6.44
								(88.08)	(6.33)
3e	cis	O	p-ClPh	85-86				$C_{20}H_{15}ClO$	
	trans	O	p-ClPh	74-75	30:70	82	306(100)	78.53	4.99
								(78.30)	(4.93)
3f	cis	S	H	oil				$C_{14}H_{12}S$	
	trans	S	H	oil	40:60	76	212(29)	79.29	5.61
								(79.20)	(5.70)
3g[b]		o-vinylstilbene			40:60	75			

[a] Based on ^1H nmr spectrum. [b] o-Vinylstilbene is known from the lit.[1].

The uv spectra (Table 2) of obtained 1-(2-heteroaryl)-2-(o-vinylphenyl)ethenes (3a-f) have showed the great resemblance with their o-tolyl analogues.[3] The substituted derivatives show effects which depend on electron donating

Table 2. Uv Spectral Data of cis- and trans-Isomers (3a-f)

Compd	λ_{max} (log ε) in ethanol	
	cis	trans
3a	255 (4.13), 280(3.99), 305(3.96)	256(4.15), 310(4.30), 322(4.29), 340(4.00)
3b	222(4.13), 254(4.16), 294(4.06), 305(3.95)	222(3.99), 260(4.07), 326(4.34), 345(Sh, 4.15)
3c	225(4.12), 263(4.13), 288(4.13)	225(4.08),258(4.22), 322(4.58)
3d	232(4.32), 332(4.33)	233(4.29), 268(4.29), 362(4.57)
3e	235(4.40), 330(4.43)	238(4.10), 269(4.15), 348(4.48), 362(4.47)
3f	233(4.20), 252(4.25), 286(4.00)	225(4.03), 258(4.14), 322(4.35)

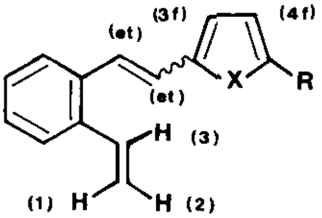


Table 3. ^1H nmr Spectra of cis- and trans-Compounds (3a-f) (in $CDCl_3$,δ,TMS)

Compd		H_{ar}	H_{et}	H_{fur}	H(1)[a]	H(2)[a]	H(3)[a]
3a	cis	7.1-7.6	6.52(s,2H)	5.90(dd), 6.21(dd)	5.61	5.22	6.89
	trans	7.1-7.6	6.76(d,1H)	6.33(dd), 6.41(dd)	5.63	5.35	7.10
3b[b]	cis	7.1-7.7	6.44(s,2H)	5.78(s,2H)	5.66	5.21	6.90
	trans	7.0-7.5	6.69(d,1H)	5.99(dq), 6.22(d)	5.63	5.34	
3c	cis	7.1-7.7	6.41,6.57 (AB,2H)	5.77(d), 6.10(d)	5.66	5.23	6.86
	trans	7.1-7.5	6.64(d,1H)	6.27(d), 6.33(d)	5.63	5.37	7.10
3d[c]	cis	6.9-7.6	6.52(s,2H)	6.10(d), 6.45(d)	5.65	5.21	
	trans	7.0-7.7	6.76(d,1H)	6.39(d), 6.61(d)	5.65	5.38	
3e	cis	7.1-7.7	6.50, 6.60 (AB,2H)	6.12(d), 6.50(d)	5.66	5.22	6.93
	trans	7.2-7.7	6.78(d,1H)	6.43(d), 6.67(d)	5.67	5.40	7.14
3f	cis	6.9-7.7			5.67	5.22	
	trans	6.9-7.7			5.62	5.37	

Coupling constants (Hz): $J_{1,2}$=1.4; $J_{1,3}$=17.5; $J_{2,3}$=10.9; $J_{3f,4f}$=3.4; $J_{3f,5f}$=0.5; $J_{4f,5f}$=2.0; $J_{4f,Me}$=0.9; J_{et}=12.2(cis), 16.1(trans).

[a] Characteristic signals of the vinyl protons appear as dd.

[b] δ_{Me}=2.17(cis), 2.34(trans); [c] δ_{Me}=2.31(cis), 2.35(trans).

or withdrawing substituents. Especially pronounced bathochromic effect is seen in trans-3d compound due to the extended conjugation by *p*-chlorophenyl group.

The ^1H nmr spectra of the vinyl compounds, presented in Table 3, show well resolved patterns of aromatic, ethylenic, vinylic and furanic hydrogens (3f excluded). Specially noticeable are the terminal protons which appear as two doublets of doublets. It is important to mention that the position of cis-H(2) is always at higher field than that of trans-isomer. The chemical shifts for the ethylenic hydrogens are close to those found for their *o*-tolyl analogues,[3] stilbene[4] and 1,2-difurylethenes.[5] The furan protons,[6-9] H_{3f}

and H_{4f}, are readily distinguished by their chemical shifts from the other aromatic hydrogens.

Carbon-13 nmr spectra of 3a-f are recorded and shown in Table 4. Based on the literature data[10-16] and the data obtained by the off-resonance technique many carbons are unambigously assigned.

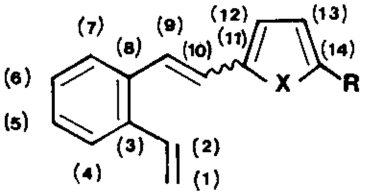


Table 4. Carbon-13 Chemical Shifts of Compounds 3a - f (ppm, $CDCl_3$,TMS)

Compd		C-1 (t)	C-3 C-8 (s)	C-11 C-14 (s)	C-12 C-13 (d)	C-2,4,5,6,7,9,10, C-phenyl (d)
3a	cis	115.2	136.4 135.9	152.1 141.5	111.2 109.5	134.9, 129.2, 127.6, 126.7, 125.3, 119.8
	trans	116.5	136.5 135.2	153.4 142.2	111.6 108.6	135.0, 127.8, 127.6, 126.7, 125.8, 124.8, 118.6
3b[a]	cis	114.8	136.4 135.7	151.2 150.4	107.3 110.4	134.8, 129.1, 127.3, 125.0, 119.7
	trans	116.1	136.2 135.4	152.2 151.9	107.9 110.2	135.0, 127.8, 127.3, 126.3, 125.4, 122,9, 118.8
3c	cis	115.2	135.7 135.7	153.9 120.8	111.5 112.8	134.5, 128.7, 127.7, 127.4, 127.3, 125.2, 118.9
	trans	116.4	136.4 134.5	155.1 121.6	110.6 113.2	134.5, 127.6, 127.6, 126.5, 125.6, 125.0, 117,3
3d[b]	cis	115.1	137.1 136.9	153.4 151.4	112.3 105.9	135.9, 135.1, 129.8, 129.2, 127.9, 127.4, 126.1, 125.3, 123.7, 119.4
	trans	116.4	137.3 136.4	153.9 152.7	111.1 106.5	135.3, 135.0, 129.3, 128.0, 127.8, 126.7, 125.8, 124.2, 123,9, 118.6
3e	cis	115.1	136.6 135.8	151.9 151.9	112.4 106.9	128.8, 132.8, 134.9, 129.1, 128.6, 127.4, 126.9, 125.2, 124.7, 119.1
	trans	116.5	136.4 134.9	153.2 152.3	111.1 107.7	128.8, 133.0, 134.8, 129.08 128.8, 127.8, 127.6, 126.6, 125.5, 124.9, 124.8, 118.2
3f	cis	115.0	136.2 135.9	139.7		134.6, 129.6, 128.2, 127.9(2), 125.9 126.1(2), 125.3, 124.5
	trans	116.5	136.2 134.9	142.8		134.7, 127.7, 127.4, 126.5, 126.0, 125.9, 124.3, 123.8

[a] δMe=13.3(cis), 13.7(trans); [b] δMe=21.16(cis), 21.22(trans).

EXPERIMENTAL

All melting points are uncorrected. The ^1H and ^{13}C nmr spectra were recorded on a JEOL FX-90 Q instrument using $SiMe_4$ as internal standard in $CDCl_3$. Mass spectral data were obtained on a Varian MAT CH-7 (70 eV) instrument. Uv spectra were measured on a Perkin-Elmer double beam spectrophotometer 124. Silica gel (Merck 0.05-0.2 mm) was used for chromatographic separations. Aryl substituted furancarboxaldehydes were prepared according to the procedure described in literature.[17]

General Procedure for the Synthesis of β-Aryl/Heteroaryl-*o*-divinylbenzenes

A solution of sodium ethoxide (obtained by dissolving 0.01 mol of sodium in 10 ml of absolute ethanol) was added dropwise to a stirred solution of *o*-xylylenebis(triphenylphosphonium bromide) (1) (7.88g, 0.01 mol, prepared from α,α'-di-bromo-*o*-xylene and triphenylphosphine in dimethylformamide) and the corresponding aldehyde (2) (0.01 mol) in absolute ethanol (ca. 300 ml, dried over molecular sieves 3A). The stirring was continued at room temperature for 0.5 h. Under the stream of dry nitrogen gaseous formaldehyde (obtained by decomposition of paraformaldehyde taken in excess, 1.5 g) was introduced and the next quantity of sodium ethoxide (0.012 mol in 10 ml of absolute ethanol) was added dropwise. The reaction was completed within 3-4 h (usually was left to stand overnight). After removal of the solvent under reduced pressure, the residue was worked up by adding water and then extracting with benzene. The benzene extracts were dried (anhydrous $MgSO_4$) and concentrated. The resulting residue was purified and separated by repeated column chromatography on silica gel using petroleum ether as eluent. The first fractions yielded cis- and the last fractions trans-isomer. Characterizational data of new compounds is provided in Table 1.

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REFERENCES

1. M. Sindler-Kulyk and W. H. Laarhoven, J. Am. Chem. Soc., 1976, 98, 1052; ibid., 1978, 100, 3819; Recl. Trav. Chim. Pays-Bas, 1979, 98, 187, 452.
2. M. Sindler-Kulyk, L. Spoljaric, and Z. Marinic, Heterocycles, 1989, 29, 679.
3. M. Sindler-Kulyk, Z. Stiplosek, and B.Metelko, Croat. Chem. Acta, 1989, 62, 81.
4. L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", Pergamon Press, London, 1959.
5. M. H. Gianni, E. L. Stogryn, and C. M. Orlando Jr., J. Phys. Chem., 1963, 67, 1385.
6. T. J. Batterham,"NMR Spectra of Simple Heterocycles", John Wiley, 1973.
7. F. Fringuelli, S. Gronowitz, A. B. Hornfeldt, I. Johnson, and A.Taticchi, Acta Chim. Scand., 1974, B28, 175.
8. W. J. E. Parr, R. E. Wasylichen, and T. Shaefer, Can. J. Chem., 1976, 54, 3216.
9. M. Dandarova, J. Kovac, D. Vegh, and V. Zvak, Coll. Czech. Chem. Comm., 1982, 47, 3412.
10. H.-O. Kalinowski, S. Berger, and S.Braun,"^{13}C-NMR-Spektroskopie", Georg Thieme Verlag, Stuttgart, New York, 1984.
11. S. Gronowitz, I. Johnson, and A. B. Hornfeldt, Chem. Scr., 1975, 7, 211.
12. M. T. W. Hearn, Aust. J. Chem., 1976, 29, 107.
13. I. Stibor, P. Trska, J. Strogl, and M. Janda, Coll. Czech. Chem .Comm., 1978, 43, 2170.
14. E. Pretsch, T. Clerc, J. Seibl, and W. Simon, "Tabellen zur Strukturaufklarung organischer Verbindungen mit spaktroskopischen Methoden", Springer Verlag, Berlin, 1981.
15. A. R. Katritzky and K. W. Law, Magn. Res., 1988, 26, 129.
16. C. E. Aun, T. J. Clarkson, and D. A. R. Happer, J. Chem. Soc., Perkin Trans. 2, 1990, 635, 645.
17. L. Janda and Z. Voticky, Chem. Zvesty, 1984, 38, 507.

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