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Phase Transfer Wittig Reaction with 1,3-Dioxolan-2-yl-methyltriphenyl phosphonium Salts : an Efficient Method for Vinylogation of Aromatic Aldehydes

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Abstract : Aldehydes were efficiently transformed into allylic dioxolanes by a Wittig-type reaction, using 1,3-dioxolan-2-yl-methyltriphenylphosphonium bromide under phase transfer conditions. The substituent kinetic effects were studied, and related to Hammett values and electrochemical potentials.
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INTRODUCTION

Several methods have been described for 2-C homologation of aldehydes and ketones since direct condensation of acetaldehyde gives poor yields and complex mixtures.[1] Enol ethers,[2] ethyloxyvinyllithium[3] and trimethylsilyloxyvinyllithium[4] have been condensed on acetals or aldehydes with low to satisfying yields. Various anions next to imines,[1] hydrazones[5] and oxazines,[6] generated with strong bases, have been condensed in high yields on aldehydes and ketones. However, those methods require strong acidic treatments for complete dehydration in order to form the double bond, and their scope is limited to the synthesis of simple compounds. Condensation of formylmethylenephosphorane was shown to be very convenient for vinylogation of aliphatic aldehydes,[7] due to a great specificity and very mild reaction conditions, while iminomethylphosphonates led to satisfying results with most aromatic aldehydes and ketones.[8] Poorly stabilized ylides generated from hydrazinovinylphosphonium by *tert*-BuOK gave higher yields of condensation, with the release of α,β-unsaturated hydrazones as the protected form of α,β-unsaturated aldehyde.[9]

In our search for the development of a new synthesis of cinnamyl aldehydes and alcohols,[10] and their corresponding glucosides, we showed that aromatic aldehydes, substituted with electron-donating-groups are not reactive enough for standard condensation with iminomethylphosphonates, and lead to complex mixtures with formylmethylenephosphorane. Better results were obtained by condensation of α,α-bis(trimethylsilyl)-*tert*-butyl ketimine with aldehydes and ketones under acidic catalysis with $ZnCl_2$.[11] However, this method

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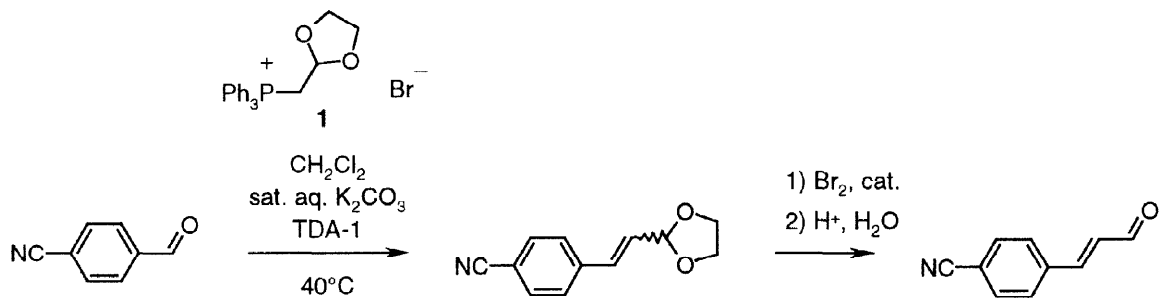
lacked selectivity and required drastic conditions for preparation of the reagent. A more powerful and highly selective method was thus necessary for facile vinylogation of aldehydes.

We report here on a far more efficient protocol, based on the use of phase transfer conditions at room temperature for a Wittig reaction with 1,3-dioxolan-2-yl-methyltriphenylphosphonium salts **1**. Our study was mainly focused on aromatic aldehydes, however good results were also obtained for the aliphatic aldehydes we studied, one of which is reported here.

RESULTS AND DISCUSSION

Mild conditions for the Wittig reaction with 1,3-Dioxolan-2-yl-methyltriphenylphosphonium salts 1



Scheme 1. Typical procedure for phase transfer vinylogation of aldehydes

The Wittig reaction with the ylide generated from **1** has been shown to be highly efficient,[12] but the conditions of use are until now not satisfactory. According to Cresp's reports,[12] standard deprotonation of diethoxymethyltriphenyl phosphonium salts by common strong bases (butyl lithium, LDA) leads to destruction of the reagent and very low yields of condensation. The same problems occur with **1**. Only *in situ* deprotonation by sodium methylate or lithium ethylate has led to good results.[12,13] However, 2.5 to 5 molar equivalents of **1** were used, generally in hot *N,N*-dimethylformamide (up to 85°C), leading to good yields only with simple aldehydes. The use of the parent tributylphosphonium salt improved the efficiency of this method, still under harsh conditions.[14]

Occasionally, some other bases have been used, giving satisfactory results : *tert*-BuOK for the synthesis of a potential Dopamine antagonist (**1** : 2 eq., DMF, r. t., 82 %),[15] butyl lithium for the synthesis of 1,4-dichloro-2,5-bis (2-formylethenyl)-3,6-dimethoxybenzene (**1** : 1.5 eq., THF, reflux, 52 %),[16] dimsylsodium for 2-C homologation of a glucose derivative (**1** : 3 eq., DMSO / THF 1 : 2, 10°C, 70 %),[17] and sodium hydride for the vinylogation of 2-(benzoyloxy)-hexanal (**1** : 1.8 eq., THF/HMPA 5 : 1, -78°C to r.t., 52 %).[18] None of these conditions can be considered general nor completely satisfactory. Conditions of use are harsh and not compatible with sensitive functions (e.g. ester groups are prohibited in Cresp's protocol). Large excesses of **1** are required and yields are rarely good.[19]

Though phase-transfer reactions have already been used for Wittig-type reactions with non-stabilized ylides, most authors have used sodium or potassium hydroxide and observed important hydrolysis side reactions. Only solid-liquid systems containing a small amount of water have led to satisfactory results, but often require high temperatures, except for one synthesis described by Le Bigot, in refluxing methylene chloride with a simple alkyltriphenylphosphonium salt.[20]

We observed that the Wittig reaction with 1,3-dioxolan-2-yl-methyltriphenylphosphonium salts **1** proceeds cleanly by use of a biphasic liquid medium composed of a saturated aqueous solution of potassium carbonate and methylene chloride, in the presence of TDA-1 (tris(methoxyethoxyethyl)amine).[21] This phase transfer catalyst strongly activates the base by chelation of the potassium cation. Owing to its simple structure and low cost, this reagent is used in stoechiometric amounts, and can be recovered by selective extraction.

The allylic dioxolane is hydrolysed neither in the reaction mixture, nor during the purification process. Thus, the aldehyde remains protected. The dioxolane function can also be used for further reactions such as double deprotonation for inverse polarity alkylation.[22]

*Reaction of aldehydes with **1** in stoechiometric ratio, substituent effects*

Reaction with variously substituted aromatic aldehydes with 1 eq. of **1** are reported below. All conditions are identical, reactions were stopped after 18 h (see experimental section for further details).

Table 1. Phase Transfer Wittig Reaction Yields under Stoechiometric Ratios

Entry[i]		Yield[ii] (%)		Z / E	Entry[i]		Yield[ii] (%)		Z / E
2	Benzaldehyde	95	(100)	66 : 34	**17**	4-OMe	29	(30)	63 : 37
3	2-NO_2	91	(97)	52 : 48	**18**	4-OAc	79	(97)	64 : 36
4	2-OMe	71	(72)	63 : 37	**19**	4-F	77	(95)	60 : 40
5	2-F	84	(100)	60 : 40	**20**	4-Cl	86	(96)	63 : 37
6	2-Cl	89	(98)	55 : 45	**21**	4-Br	86	(90)	61 : 39
7	2-Br	89	(97)	52 : 48	**22**	3,4-$(OMe)_2$	44	(54)	60 : 40
8	3-Me	76	(86)	64 : 36	**23**	3-OMe, 4-OAc	81	(97)	63 : 37
9	3-NO_2	90	(96)	58 : 42	**24**	4-COOMe	95	(96)	65 : 35
10	3-OMe	75	(84)	63 : 37	**25**	3-OMe, 4-$SCONMe_2$	83	(98)	60 : 40
11	3-F	100	(100)	62 : 38	**26**	3,4,5-$(OMe)_3$	51	(61)	69 : 31
12	3-Cl	97	(98)	61 : 39	**27**	3,5-$(OMe)_2$, 4-OAc,	82	(97)	63 : 37
13	3-Br	98	(100)	60 : 40	**28**	3,5-$(OMe)_2$,4-$SCONMe_2$	74	(100)	65 : 35
14	4-Me	78	(80)	66 : 34	**29**	Dodecanal	75	(76)	64 : 36
15	4-CN	100	(100)	72 : 28	**30**	2-naphtaldehyde	75	(79)	60 : 40
16	4-NO_2	88	(100)	60 : 40	**31**	4-CF_3	90	(96)	60 : 40

i) Reagent (full name) or benzaldehyde substituents ; ii) quantity of crude olefin; between parentheses : conversion percent as observed on NMR data after removal of TDA, triphenylphosphine oxide and eventually, other by-products.

Under these conditions, aromatic aldehydes bearing electron withdrawing groups lead to very high yields, only traces of starting material are observed. However, and as expected, yields decrease with compounds bearing electron donating substituents. We observe no side reaction, except a partial acetyl hydrolysis on 4-acetyloxybenzaldehydes, starting materials for **18**, **23** and **27** (about 3 %).

Besides, the course of the reaction is strongly inhibited by the presence of acidic groups (such as phenols or carboxyles), since they lead to the formation of salts that precipitate. Only 4-dimethylaminobenzaldehyde did not react at all. No reaction occurs on ketones and this protocol is thus selective for aldehydes toward ketones.

Hammett and electrochemical correlations

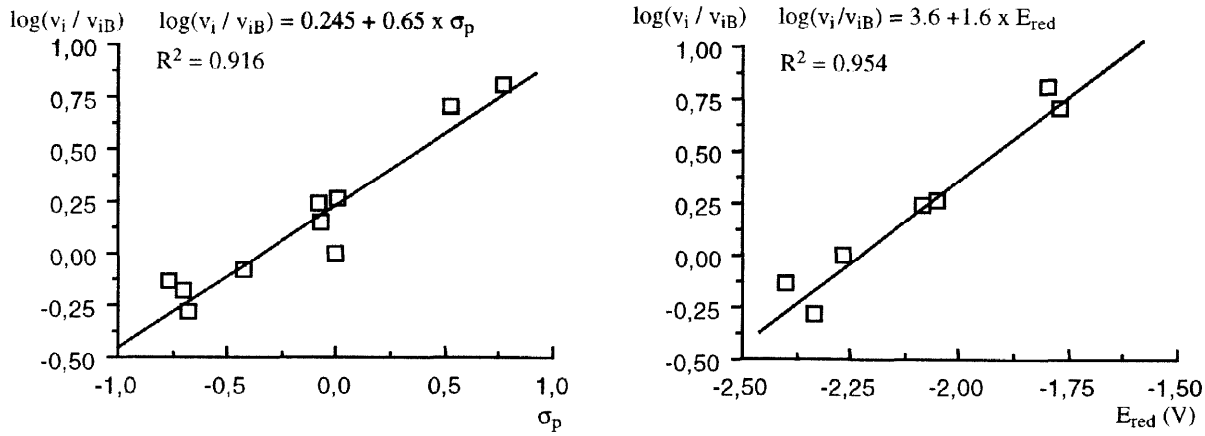
Since lower rates were observed for aldehydes bearing electron donating groups, we checked the correlations between rates and two standard parameters : redox potential and Hammett constants.

For kinetic measurements, the reaction was followed by NMR for various para substituted benzaldehydes. Ten to fifteen samples of the reaction mixture were successively collected (0.5 mL each), immediately passed through a short silica gel column and concentrated for direct NMR analysis. Data were fitted using a second order reaction profile. Initial rates prove related to Hammett constants and electrochemical reduction potentials[23] (Table 2, Scheme 2). A strong substituent effect is confirmed, corresponding to a Hammett reaction constant of 1.34. These data are interesting in order to optimise reaction conditions for further preparative syntheses.

Table 2. Reaction Rates v_i, Related to Hammett Constants and Reductive Potentials

Entry	Substituents on PhCHO	V_i (10^{-5}molL^{-1}s^{-1})	$T_{1/2}$ (mn)	σp [i]	E_{red} (V) [i, ii]
2	None	4.4 (v_{iB})	101	-	-2.267
16	4-NO_2	26.1	17	0.81	-1.797
15	4-CN	14.8	30	0.70	-1.773
21	4-Br	4.44	100	0.26	-2.055
19	4-F	3.75	118	0.15	
20	4-Cl	3.61	123	0.24	-2.088
26	3,4,5-$(OMe)_3$	1.64	271	- 0.08	
22	3,4-$(OMe)_2$	0.87	511	- 0.18	
17	4-OMe	0.91	488	- 0.28	-2.333
14	4-Me	0.76	585	- 0.14	-2.400

i) σp and E_{red} are from Arnett,[23] ii) E_{red} are related to silver electrode and were measured in acetonitrile.



Scheme 2. Initial reaction rates $(v_i)/v_{iB}$, related to Hammett σ_p (left) and reduction potentials E_{red} (right) for para substituted benzaldehydes

Optimisation for preparative syntheses

Lower yields with electron enriched are due to partial hydrolysis of **1**. A half-completion time of 4 h was measured for the hydrolysis of **1** in the biphasic medium.

However, benzaldehydes bearing electron donating groups, which previously did not react by use of any other methods, and aliphatic aldehydes give yields up to 75 % in stoechiometric conditions and no other side reaction occurs. As expected, for preparative synthesis, the use of **1** in excess allows completion of the reaction. Conditions and results are reported below for several relevant compounds. In all cases a total consumption of starting aldehydes was reached, even for **17** which required 8 equivalents of **1**.

Table 3 Preparative Wittig reactions with **1** in excess

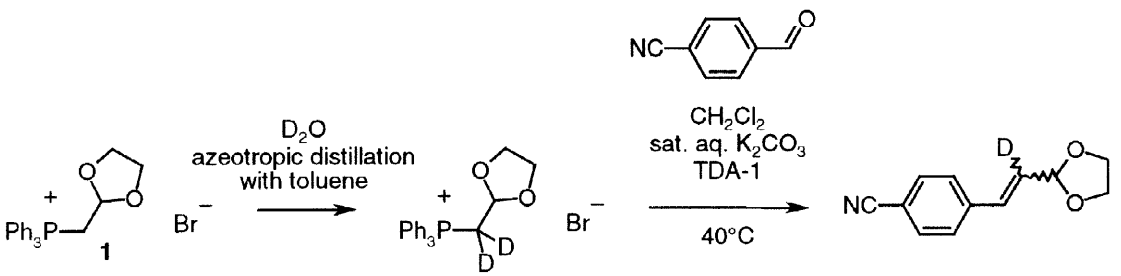
Entry [i]		**1**	Conversion (%)	Conversion (% with 1 eq.)	Isolated yield (%)
17	4-OMe	3 eq.	57	(30)	
		4 eq.	74		
		8 eq.	100		91
31	4-CF_3	3 eq.	100	(96)	88
18	4-OAc	1.5 eq.	100	(97)	60[ii]
23	3-OMe, 4-OAc	1.5 eq.	100	(97)	88[ii]
27	3-OMe, 4-OAc, 5-OMe	1.5 eq.	100	(97)	93[ii]
29	dodecanal	1.3 eq.	80	(76)	
		1.5 eq.	90		
		2 eq.	95		
		3 eq.	100		92

i) Reagent (full name) or benzaldehyde substituents ; ii) Yields of α,β-unsaturated aldehydes after isomerisation and cleavage of the dioxolane ring, see reference 10.

For benzaldehydes bearing electron-withdrawing groups also, we recommend the use of a slight excess of reagent during preparative syntheses. Shorter reaction times are usually sufficient, even if no other reaction occur. For example 30 mn are enough for 4-nitrobenzaldehyde **16** with 1.5 eq. of **1**.

Deuterium labelling

Another interesting aspect of this reaction is the easy incorporation of deuterium on the double-bond, during the Wittig reaction, by use of deuterated water. Completion of the deuterium enrichment was clearly demonstrated by a 1 mass unit shift in MS spectra and the disappearance of signal and corresponding couplings in NMR spectra.



Scheme 3. Deuterium labelling during PTC Wittig reaction

Stereochemistry and deprotection

With the methods previously described, the use of **1** for Wittig Reaction generally leads to an *Z/E* mixture, with a slight excess of the *Z* isomer[12,13]. Isomerisation into pure *E* isomer occurred in a second step, when using strong acidic conditions for cleavage of the dioxolane ring (10 % HCl, THF). Pure *Z* isomer could be obtained by use of butyl lithium[16] or sodium hydride[18] in THF, and large excess of the *E*-isomer was obtained with dimsyl sodium in a 1 : 2 DMSO / THF mixture.[17]

Here, the *Z/E* ratios, generally 60 : 40, are contained between 52 : 48 and 72 : 28 (Table 1). They are independent of substituent effects, but are slightly decreased by steric hindrance. A slightly acidic treatment (e. g. 1 : 2 : 2 acetic acid / THF / water solution) opens the dioxolane ring with almost no isomerisation. Alternatively, treatment with a catalytic amount of bromine (usually 0.05 eq.) in carbon tetrachloride leads to isomerisation of the double-bond with only very partial opening of the dioxolane ring. The same acidic treatment as above then releases pure *E* α,β-unsaturated aldehydes. Pure *E* isomers are directly obtained by the use of stronger acidic conditions (HCl 10 % / THF 1 : 1). The later method, is however not suitable for sensitive compounds.

CONCLUSIONS

The new procedure described herein provides a very mild and efficient method for the vinylogation of aromatic aldehydes suitable for highly functionalised molecules but also for poorly reactive substrates. The scope of application is wide and limited only by the solubility of starting materials in organic media in the presence of an aqueous basic phase. TDA-1 was used systematically in stoechiometric ratio in this study to provide comparable data. However, reactive aldehydes require smaller amounts of phase transfer catalyst and even no catalyst in the case of 4-nitrobenzaldehyde. Thus, the reagents ratio and reaction time can also be balanced to obtain better yields and optimum purification conditions. We would also like to stress that these reaction conditions, developed for a sensitive reagent, are also suitable for the use with other ylides. Accordingly, we have recently used the same reaction conditions for the use of triethylphosphonofluoroacetate during the preparation of α,β-unsaturated-α-fluoroesters.[24]

EXPERIMENTAL SECTION

General Methods

^{1}H NMR Spectra were recorded in $CDCl_3$ on a Bruker AM 250 spectrometer. Mass spectra were obtained on a Nermag R10-10C mass spectrometer. Elemental Analysis were performed by Service de Microanalyse de l'Université Pierre et Marie Curie. Chemicals were purchased from Aldrich and used as received. Dichloromethane was distilled over calcium hydride before use. Column chromatography was conducted on silica gel 60 (70-230 mesh) from Merck using a dichloromethane / ethyl acetate 85 : 15 mixture as the eluent.

4-(2-(1,3-dioxolane-2-yl)-ethenyl)-benzonitrile 15 : typical procedure for vinylogation test with 1 eq. of **1** (identical reaction conditions were used for compounds **2** to **30**) :

4-cyanobenzaldehyde (131 mg, 1 mmol) and TDA-1 (323 mg, 1 mmol) were diluted in dichloromethane (15 mL), under argon, at room temperature. The K_2CO_3 saturated aqueous solution (15 mL) and **1** were added (429 mg, 1 mmol), and the reactive solution was refluxed (40°C), for 18 h with vigorous stirring. Products were extracted with dichloromethane (2 x 15 mL), washed with water (15 mL) and dried over $MgSO_4$. **15**, TDA-1 and triphenylphosphine oxide were separated by chromatography on silica gel prepared from 30 g of silica. Yield : 200 mg, 100 %, white solide. ^{1}H NMR ($CDCl_3$) δ 7.36-7.61 (m, 4 H,), 6.80 (d, 0.28 H, ArC<u>H</u>CHCH *E*, *J* = 15.9 Hz), 6.80 (d, 0.72 H, ArC<u>H</u>CHCH *Z*, *J* = 11.9 Hz), 6.29 (dd, 0.28 H, ArCHC<u>H</u>CH *E*, *J* = 5.6 Hz, 15,9 Hz), 5.87 (dd, 0.72 H, ArCHC<u>H</u>CH *Z*, *J* = 7.4 Hz, 11.9 Hz), 5.46 (d, 0.28 H, ArCHCHC<u>H</u> *E*, *J* = 5.6 Hz), 5.43 (d, 0.72 H, ArCHCHC<u>H</u> *Z*, *J* = 7.4 Hz), 3.80-4.07 (m, 4 H, OCH_2CH_2O). Anal. Calcd for $C_{12}H_{11}NO_2$: C, 71.66; H, 5.51. Found C, 71.75; H, 5.49. MS (CI, NH_3) *m/z* : 219, 202 for *E* and *Z*. MS (EI, 70 eV) *m/z* (%) : *Z* : 201 (12), 200 (18), 156 (17), 140 (16), 129 (100), 102 (11), 101 (13), 99 (19), 73 (10). *E* : 201 (12), 200 (15), 156 (17), 140 (15), 129 (100), 102 (12), 101 (15), 99 (18).

For kinetic studies, the same procedure was used and small samples from the organic phase (0.5 mL) were purified by chromatography and analysed by NMR.

4-(2-(1,3-dioxolane-2-yl)-2-*d*-ethenyl)-benzonitrile

Without any treatment of solids, the percent of deuterated compound is about 88. With the following precautions, it increases to 96 %. K_2CO_3 (15 g) was stirred in of D_2O (15 mL), which, after one hour, were evaporated by heating under vacuum. This procedure was repeated twice. The phosphonium salt **1** (1 g) was also stirred one hour with D_2O (2 mL), which was eliminated by an azeotropic distillation with dry toluene. This procedure was also done three times.

1 (644 mg, 1.5 mmol) was mixed 60 min in the two-phase system (dichloromethane 15 mL, D_2O 10 mL, K_2CO_3, 15 g) with TDA-1 (323 mg, 1 mmol) at 40°C (reflux). 4-cyanobenzaldehyde (131 mg, 1 mmol) was added and the emulsion was mixed for 18 h. Products were extracted and purified as described for **15**, (eluent : dichloromethane). Yield : 172 mg, 85 %, white solid. ^{1}H NMR ($CDCl_3$) δ 7.36-7.61 (m, 4 H, aromatic H), 6.80 (s, 0.28 H, ArC<u>H</u>CDCH *E*), 6.80 (s, 0.72 H, ArC<u>H</u>CDCH *Z*), 5.46 (s, 0.28 H, ArCHCDC<u>H</u> *E*), 5.43 (s, 0.72 H, ArCHCDC<u>H</u> *Z*), 3.80-4.07 (m, 4 H, OCH_2CH_2O), ^{13}C NMR ($CDCl_3$) : 140.11 (CN), 140.05 (CN), 133.36 (CH= *Z*), 132.41 (CH= *E*), 132.30 (C_3 *E*), 131.91 (C_3 *Z*), 130.55 (CD *Z*), 130.30, 130.06, 129.44 (C_2 *Z*), 128.89 (CD *E*), 128.65, 128.41, 127.25 (C_2 *E*), 118.62 (C_4), 111.41 (C_1 *E*), 111.17 (C_1 *Z*), 102.79 (CHO_2 *E*), 98.98 (CHO_2 *Z*), 65.15 (CH_2O *Z*), 65.04 (CH_2O *E*). MS (CI, NH_3) *m/z* : 220, 203 for *E* and *Z*. MS (EI, 70 ev) *m/z* (%) : *Z* : 202 (18), 201 (27), 157 (29), 141 (25), 131 (10), 130 (100), 129 (61), 114 (13), 103 (13), 102 (21), 100 (16), 73 (13). *E* : 202 (14), 201 (18), 157 (21), 141 (21), 130 (100), 129 (24), 103 (10), 102 (18), 100 (17).

4-(3-oxo-propen-1-yl)-benzonitrile : typical procedure for isomerisation and hydrolysis :

4-(2-(1,3-dioxolane-2-yl)-ethenyl)-benzonitrile **15** (180 mg, 0.9 mmol) was dissolved in carbon tetrachloride (10 mL), and kept at 50°C. Bromine (7.2 mg, 0.045 mmol) in carbon tetrachloride (0.45 mL) was added and the mixture kept at 50°C for 2 h. Carbon tetrachloride was removed under vacuum, THF (10 mL), water (10 mL) and acetic acid (5 mL) were added. The mixture was stirred at room temperature for 4 h and concentrated under vacuum. The product was extracted with dichloromethane, washed with $NaHCO_3$ saturated aqueous solution, pure water, dried over $MgSO_4$ and purified by chromatography over silica gel. Yield : 127 mg, 90 %. mp = 130 °C. ^{1}H NMR ($CDCl_3$) δ 9.68 (d, 1 H, CHO, *J* = 7.5 Hz), 7.54-7.72 (m, 4 H, aromatic H), 7.43 (d, 1 H, ArC<u>H</u>CHCH *Z*, *J* = 16.1 Hz), 6.72 (dd, 1 H, ArCHC<u>H</u>CH, *J* = 16.1 Hz, 7.5 Hz). Anal. Calcd for $C_{10}H_7NO$: C, 76.42; H, 4.49. Found C, 76.75; H, 4.54.

2-[2-(4-trifluoromethylphenyl)-ethenyl]-1,3-dioxolane 31

Same procedure as **15** with 4-trifluoromethylbenzaldehyde (174 mg, 1 mmol) and **1** (1.29 g, 3 mmol).

Yield : 217 mg, 88 %, colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.41-7.58 (m, 4 H, aromatic H), 6.75 (d, 0.44 H, ArC<u>H</u>CHCH *E*, *J* = 16.4 Hz), 6.73 (d, 0.56 H, ArC<u>H</u>CHCH *Z*, *J* = 11.6 Hz), 6.18 (dd, 0.44 H, ArCHC<u>H</u>CH *E*, *J* = 5.6 Hz, 16.4 Hz), 5.75 (dd, 0.56 H, ArCHC<u>H</u>CH *Z*, *J* = 7.5 Hz, 11.6 Hz), 5.37 (d, 0.44 H, ArCHCHC<u>H</u> *E*, *J* = 5.6 Hz), 5.37 (d, 0.56 H, ArCHCHC<u>H</u> *Z*, *J* = 7.5 Hz), 3.80-4.07 (m, 4 H, OCH_2CH_2O). MS (EI, 70 eV) *m/z* (%) : *E* : 245 (11), 244 (84), 243 (21), 199 (21), 173 (17), 172 (100), 171 (17), 151 (26), 115 (21), 103 (13). *Z* : 245 (12), 244 (80), 243 (30), 225 (10), 199 (22), 175 (11), 173 (17), 172 (100), 171 (17), 151 (26), 133 (10), 115 (15), 103 (12), 73 (15).

2-[2-(4-methoxyphenyl)-ethenyl]-1,3-dioxolane 17

Same procedure as **15** with 4-methoxybenzaldehyde (136 mg, 1 mmol) and **1** (3.44 g, 8 mmol) in several portions (4 mmol, then twice 2 mmol separated by 90 mn).

Yield : 188 mg, 91 %, yellowish oil. ^{1}H NMR ($CDCl_3$) δ 7.24 (m, 2 H, aromatic H), 6.77 (m, 2H, aromatic H) 6.67 (d, 0.67 H, ArCHCHCH *Z*, *J* = 11.4 Hz), 6.64 (d, 0.33 H, ArCHCHCH *E*, *J* = 16.0 Hz), 5.95 (dd, 0.33 H, ArCHCHCH *E*, *J* = 6.2 Hz, 16.0 Hz), 5.55 (dd, 0.67 H, ArCHCHCH *Z*, *J* = 7.4 Hz, 11.4 Hz), 5.44 (d, 0.67 H, ArCHCHCH$_2$ *Z*, *J* = 7.4 Hz), 5.32 (d, 0.33 H, ArCHCHCH$_2$ *E*, *J* = 6.2 Hz), 3.78-4.02 (m, 4 H, OCH_2CH_2O), 3.73 (s, 0.66 H, OMe *Z*), 3.72 (s, 0.33 H, OMe *E*). MS (EI, 70 eV) *m/z* (%) : *Z* : 206 (31), 205 (10), 161 (16), 147 (25), 135 (12), 134 (100), 119 (18), 103 (11), 91 (11), 77 (10). *E* : 206 (27), 205 (10), 161 (15), 147 (25), 135 (11), 134 (100), 119 (18), 103 (12), 91 (11), 77 (11).

2-tridec-1-enyl-1,3-dioxolane 30

Same procedure as **15** with dodecanal (184 mg, 1 mmol) and **1** (1.29 g, 3 mmol).

Yield : 234 mg, 92 %, white solide. ^{1}H NMR ($CDCl_3$) δ 5.87 (dt, 0.35 H, $CH_2CHCHCH$ *E*, *J* = 6.5 Hz, 15.5 Hz), 5.69 (dt, 0.65 H, $CH_2CHCHCH$ *Z*, *J* = 7.5 Hz, 10.9 Hz), 5.47 (d, 0.65 H, $CH_2CHCHCH_2$ *Z*, *J* = 7.5 Hz), δ 5.37 (m, 1 H, $CH_2CHCHCH$ *E*+*Z*), 5.11 (d, 0.35 H, $CH_2CHCHCH_2$ *E*, *J* = 6.5 Hz), 3.90 (m, 4 H, OCH_2CH_2O), 2.10 (m, 1.3 H, $CH_2CHCHCH$ *Z*), 2.00 (m, 0.7 H, $CH_2CHCHCH$ *E*), 1.18-1.40 (m, 18 H, CH_2), 0.82 (t, 2 H, CH_3, *J* = 6.6 Hz). MS (EI, 70 eV) *m/z* (%) : *Z* : 253 (7), 225 (5), 211 (17), 197 (8), 183 (5), 169 (9), 155 (24), 141 (8), 125 (5), 113 (57), 99 (100), 73 (31), 55 (18). *E* : 253 (8), 225 (5), 211 (12), 197 (7), 183 (5), 169 (7), 155 (17), 141 (7), 125 (5), 113 (44), 99 (100), 73 (24), 55 (14).

2-[2-(4-*N*,*N* dimethylcarbamoylthioxy-3-methoxyphenyl)-ethenyl]-1,3-dioxolane 25

Thiovanillin *N*,*N* dimethylcarbamate[25] (1.87 g, 7.8 mmol), **1** (5.03 g, 11.7 mmol), TDA (2.53 g, 7.8 mmol) and dichloromethane (50 mL) were mixed. Saturated aqueous potassium carbonate (30 mL) was then added and the mixture was kept refluxing for 18 h. The products were extracted with dichloromethane (2 x 50 mL), washed with water with addition of 10 % HCl until neutral pH, and water. The organic layer was dried over $MgSO_4$ and concentrated under vacuum. Purification by chromatography afforded a viscous oil, 2,36 g, 98 %. ^{1}H NMR ($CDCl_3$) δ 7.44 (d, 0.6 H, aromatic H5, *Z*, *J* = 7.6 Hz).7.43 (d, 0.4 H, aromatic H5, *E*, *J* = 7.6 Hz), 6.94-7.06 (m, 2 H, aromatic H2,6, *Z* and *E*), 6.83 (d, 0.6 H, ArCH, *Z*, *J* = 11.6 Hz), 6.78 (d, 0.4 H, ArCH, *E*, *J* = 15.9 Hz), 6.20 (dd, 0.4 H, ArCHCH, *E*, *J* = 15.9 Hz, 6 Hz), 5.77 (dd, 0.6 H, ArCHCH, *Z*, *J* = 11.6 Hz, 7.3 Hz), 5.51 (d, 0.6 H, OCHO, *Z*, *J* = 7.3 Hz), 5.45 (d, 0.4 H, OCHO, *E*, *J* = 6 Hz), 3.9-4.1 (m, 4 H, OCH_2CH_2O),.3.89 (s, 3 H, MeO), 3.13 (br s, 3 H, MeN), 3.03 (br s, 3 H, MeN), Anal. Calcd for $C_{15}H_{19}NO_4S$: C, 58.23; H, 6.19. Found C, 58.09; H, 6.21

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