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Extended conjugation in di- and tri-arylmethane dyes. Part 5. Vinylogues and ethynologues of Victoria Blue☆

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Dedicated to Dr. A.T. Peters in appreciation of his guidance and his significant contributions to dye chemistry

Abstract

Novel vinylogues and ethynologues of the naphthyldiphenylmethane dye system have been synthesised and their spectral parameters measured. The extended conjugation brings about red shifts of the absorption bands relative to the parent dyes. Although this effect is generally greater for the alkynyl derivatives, the vinylogue is better able to accommodate the *peri*-hindrance associated with the 4-dimethylamino-1-naphthyl group. © 2000 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Several cationic triarylmethane dyes have been shown to exhibit antimicrobial activity [2,3] and to be selective for tumours [4], features which have contributed to the recent interest in the use of the triarylmethane dye Victoria Blue BO as a photosensitizing compound in the experimental photodynamic therapy of cancer in vitro [5,6].

The part of the visible region in which triphenylmethane (TPM) dyes typically absorb is not optimum for photosensitizing compounds for clinical use against tumours, since tissue penetration is doubled between 600 nm and 700 nm [7]. In recent work, we have addressed this problem by increasing the planarity of the triarylmethane chromophore in the Victoria Blue series via the incorporation of a 9-fluorenyl moiety which results in significant red shifts though with a concomitant reduction in intensity [8]. The extension of the chromophoric system of triarylmethane dyes has also been achieved by the inclusion of an lunsaturated moiety between one of the aryl rings and the central carbon atom. The insertion of an acetylenic unit into the chromophoric system shifts the main absorption band of TPM dyes such as Malachite Green **1a** and Crystal Violet **1b** into the 660–700 nm region. Although the simple vinylogues **2** and ethynologues **3** of Malachite Green (Ar = Ph) and Crystal Violet (Ar = C_6H_4-NMe_2) were reported nearly fifty years ago [9,10], neither the actual synthesis nor the physical data of the vinylogues were reported. Recent interest in

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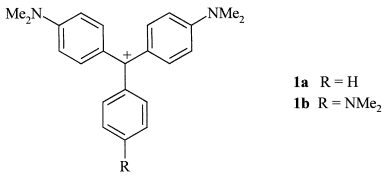
near-infrared absorbing dyes has prompted the synthesis and study of related ethynologues [11,12].



1a R = H
1b R = NMe_2

It is somewhat difficult to obtain accurate data concerning extinction coefficients from the earliest reports since these must be estimated from published absorption curves. Additionally, different values are given in the literature and such values should therefore be treated with care. Comparisons with more recent work in which the absorption characteristics have been obtained from solutions of the dye perchlorates in dichloromethane are also difficult. Nevertheless, the visible absorption of the ethynologue of Crystal Violet **3a** exhibits a large red shift (86 nm) relative to **1b** in the same solvent in line with the presence of an extended chromophore. It is as yet unclear whether the intensity of absorption decreases slightly [9] or increases a little [13] when compared to the parent dye, although the latter is favoured since the data quoted relate to measurements made under the same conditions. The absorption band (690 nm) of the corresponding vinylogue **2a** is shifted even further towards the red (106 nm), although the data are not strictly comparable since they were obtained in different solvents.

The symmetrical vinylogue of Malachite Green **2b** absorbs at a surprisingly lower wavelength (656 nm) than the corresponding ethynologue (688 nm) and its ϵ_{max} value is also low. The *y*-bands are almost identical, markedly bathochromically shifted (~60 nm) compared to Malachite Green, in good agreement with extended conjugation along the *y*-axis. Significant increases in $\epsilon_{max}(y)$ are observed such that the two absorption bands are of similar intensity unlike those of Malachite Green. The symmetrical ethynologue of Malachite Green **3b** responds in the same way as the parent compound towards substitution in the phenyl ring [13]. The *x*-band exhibits a hypsochromic shift and an intensity decrease, whilst the second band is shifted bathochromically with an increase in intensity when *para* electron-withdrawing groups are replaced by electron-donating groups.

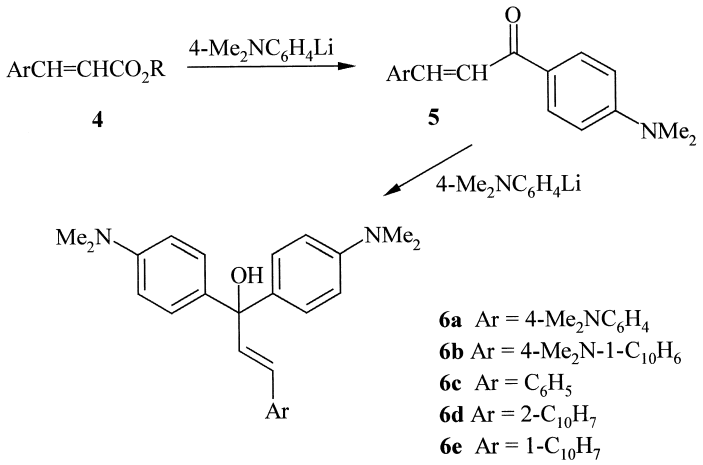
Large bathochromic shifts of the *x*-bands of the unsymmetrical vinyl and ethynyl derivatives of Malachite Green are observed (94 and 115 nm, respectively). Their y-bands, associated with delocalisation into the unsubstituted phenyl ring, are red-shifted by 34 and 50 nm respectively, probably because of the relief of steric crowding about the central carbon atom.

We have shown previously [14] that the expected electronic influence of the 1-naphthyl residue in the Victoria Blue dyes is moderated relative to a phenyl moiety because of increased steric crowding at the central carbon atom. Such crowding should be decreased by the incorporation of an unsaturated C_2 unit to link the two aromatic systems. We now report the synthesis and properties of vinyl and ethynyl analogues of the Victoria Blue system.

2. Results and discussion

There are a number of routes to the vinylogous TPM dyes. A study of the reaction of 4-dimethylaminobenzylideneacetophenone with various organometallic compounds established that phenyllithium gave the most efficient and selective 1,2-addition [15]. It seems likely that the earlier vinylogues and ethynologues of Malachite Green and Crystal Violet were synthesised by this route.

Benzylideneacetophenones are readily obtained, albeit in only moderate yields, from the reaction of benzaldehydes with acetophenones [16]. The reaction of a benzaldehyde with a phosphonate ester provides an alternative two-step synthesis [17] which is particularly suitable when vinylogous carbinols containing three different aryl groups or unsymmetrical diphenylmethanols are desired. However, since only symmetrical carbinols were required in this work, an alternative synthesis was chosen in which two molar equivalents of 4-dimethylaminophenyllithium are added to a cinnamic ester **4**. The initial product is a benzylideneacetophenone **5** (Scheme 1).



Scheme 1.

This reaction was found to be dependent on the solvent used, being extremely slow in THF but proceeding very satisfactorily in diethyl ether. The observation that a solid precipitated in large amounts in the latter solvent but not in the former may provide an explanation. The 1,2-addition of organolithium reagents to carbonyl compounds is an equilibrium between reactants and products and given the poorer solubilising properties of diethyl ether, the products precipitated shifting the equilibrium in favour of the reaction and leading to good yields ($\geqslant$ 45%)of the prop-2-enols **6a–e**.

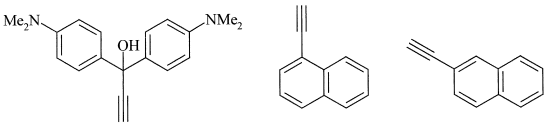
Of the α,β-unsaturated esters needed for the synthesis of the vinylogues, only ethyl cinnamate was commercially available. The methyl ester of the 1-naphthyl analogue was made in almost quantitative yield by esterification of 3-(1-naphthyl)propenoic acid in methanol and sulphuric acid. Although 4-dimethylaminocinnamic acid is commercially available, its methyl ester was preferably made by a Wittig reaction between 4-dimethylaminobenz aldehyde and the stable carbomethoxymethylene triphenylphosphorane in refluxing toluene [18]. The ^{1}H NMR spectrum of methyl 4-dimethylaminocinnamate showed only the *trans*-isomer ($J_{vinyl} = 14$ Hz); such stereoselectivity is a common feature of reactions involving stabilised phosphoranes [19].

Stabilised phosphoranes can be advantageously replaced by their corresponding phosphonate esters in the Wadsworth–Emmons–Horner (WEH) modification of the Wittig reaction [17,19,20]. The reaction of triethyl phosphonoacetate with sodium hydride and the 4-dimethylamino-1-naphthaldehyde gave an excellent yield of the cinnamate derivative; again only the *trans*-isomer ($J_{vinyl} = 16$ Hz) was isolated [19].

Several routes are available for the synthesis of the ethynologues of triphenylmethanol. The unsubstituted triphenyl compound has been made from benzoylphenylacetylene and phenyl magnesium bromide [21], whilst the ethynologues of Malachite Green carbinol 7 have been made by the reaction of Michler's ketone with lithium arylacetylides [13,22] or the corresponding Grignard reagent [22]. The organometallic species are generated in situ from the arylacetylene or from the corresponding 2-bromo- or 2-chlorostyrene [13,22].

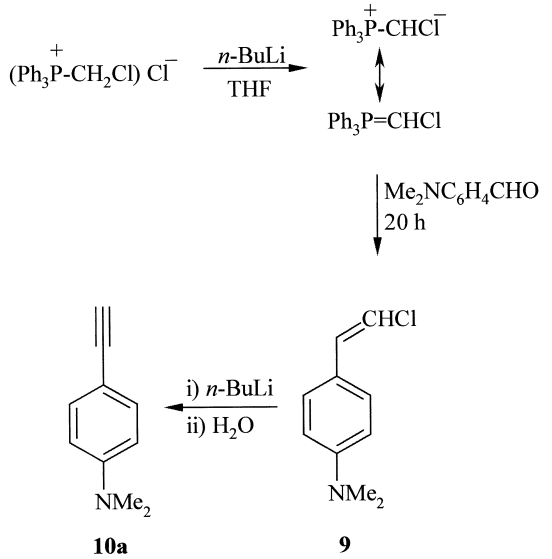
Cross-coupling reactions have more recently been used and the propynol **8**, made from Michler's ketone and the lithium acetylide-ethylenediamine complex, has been coupled with some aryl halides in moderate yields in the presence of a palladium(II) catalyst [23]. This latter route seemed attractive since the propynol **8** can be made on a large scale and aryl bromides are readily available. Unfortunately, several complications were encountered in practice. Thus monitoring the reaction by tlc was difficult since **8** and the product have very similar polarities. In many instances, significant quantities of unknown decomposition products formed rapidly and the reaction had to

be terminated before completion. In addition, it was observed that the reaction was slower when electron-releasing groups were present at active positions on the aryl halide. No improvement was noticed when palladium chloride was used as the coupling catalyst [24]. In fact, only the reaction of 1-bromonaphthalene and **8** gave a pure product (**7d**) and that in very low yield after a tedious series of chromatographic separations and recrystallisations.



8 **10b** **10c**

In view of these results, the arylacetylide route was considered. Phenylacetylene is the only arylacetylene commercially available, but its 4-dimethylamino analogue **10a** was synthesised via a Wittig reaction between 4-dimethylaminobenzaldehyde and chloromethylene triphenylphosphorane. The resulting 4-dimethylamino–chlorostyrene 9 was dehydrohalogenated to produce good yields of the alkyne **10a** (Scheme 2) [25]. This procedure was also used to make the naphthalene analogue **11** of the styrene in excellent yield.



10a **9**

Scheme 2.

Both **9** and **11** were obtained as mixtures of the *cis*- and *trans*-isomers which were not separated. The isomer ratios were determined from the ^{1}H NMR spectra and confirmed by gas chromatography as being, in both cases, of the order of 3:2 in favour of the *cis*-species, a result anticipated in view of previous work [25,26]. The presence of the two isomers makes the ^{1}H NMR spectrum of **11** quite complex, but it is readily explained after a study of the ^{1}H NMR spectrum of **9** (Fig. 1). The chlorine atom exerts a significant deshielding effect on the neighbouring protons and, therefore, H-2 appears further downfield in the *trans*-configuration than in the *cis*-isomer of **9**. Also, in the *trans*-isomer, H-1 experiences the additional deshielding effect of the phenyl ring. The effect of the halogen on H-3 is quite significant with *cis*-H-3 resonating at 7.64 ppm and its *trans* counterpart at 7.18 ppm. A similar pattern is encountered for the alkenic protons in the isomers of the naphthalene compound **11**. The difference in chemical shift of H-8 (0.1 ppm) in the isomers is attributed to rotation about the naphthyl-vinyl bond which brings H-8 in the *cis*-isomer into close proximity to the chlorine atom. Contrary to the situation in **9**, the adjacent protons H-3 and H-4 are well resolved in **11**. In practice, the triphenylphosphine oxide formed during the Wittig reaction was difficult to remove from the reaction mixture and another approach to the synthesis of the arylacetylenes was considered.

Trimethylsilyldiazomethane **12** has many uses in synthetic organic chemistry [27] and the reaction of its lithium derivative **13** with carbonyl compounds is known to give the homologous alkynes [28, 29]. The synthesis features the initial formation of an α-diazoalkoxide 14 which can be isolated as the corresponding alcohol by acidification [30]. Sequential elimination of trimethylsilanoate and nitrogen generates a carbene **16** which undergoes a Wolff rearrangement to give the alkyne **10** (Scheme 3). Good yields of 4-dimethylaminophenylacetylene **10a** and the naphthylacetylenes **10b** and **10c** were obtained in this way. Practically, this method is superior to the Wittig approach since the reaction is much faster and involves an easier work up because of the water solubility of the by-products. The reaction between the various

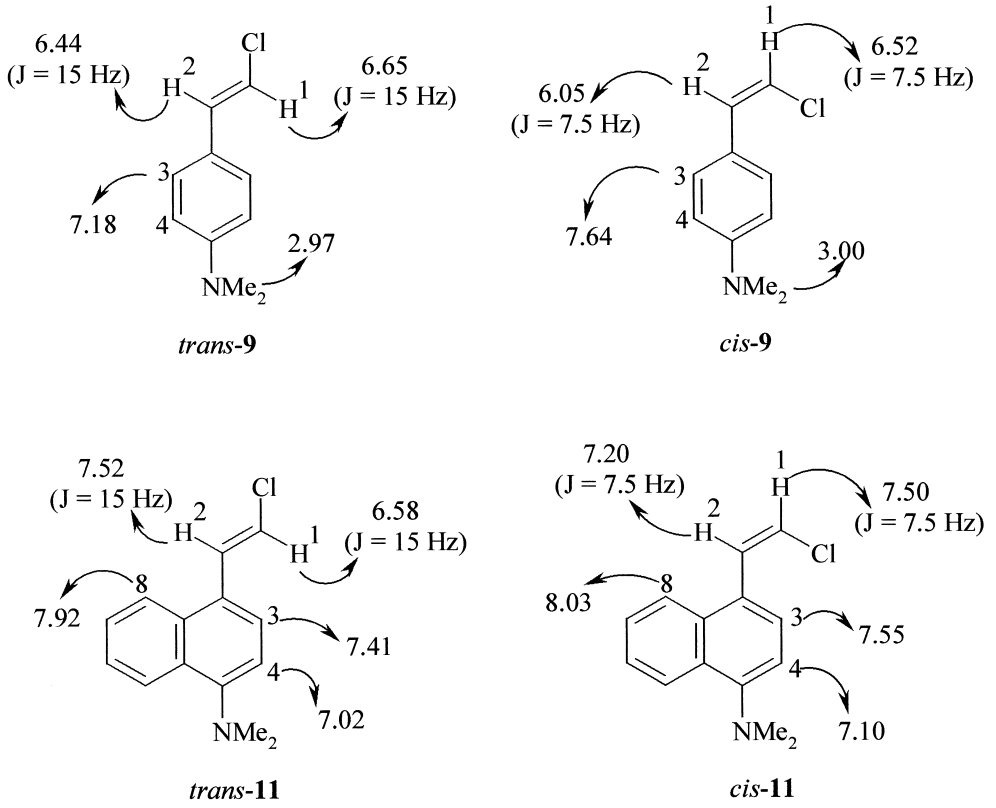
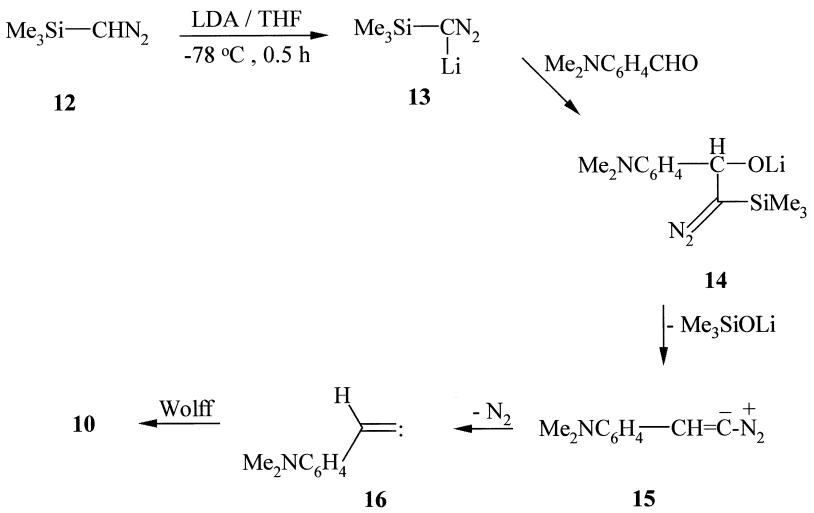
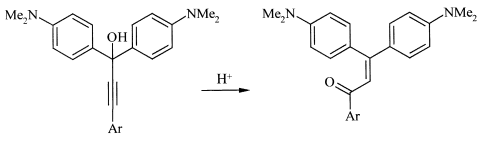


Fig. 1.



Scheme 3.

lithium arylacetylides and Michler's ketone occurred cleanly at room temperature and good yields of the propargyl alcohols **7a–e** were obtained (Scheme 4). Unfortunately, it seems that this route is limited to the least nucleophilic analogues of Michler's ketone, since 4,4′-dipyrrolidinobenzophenone reacted only partially with the lithium or potassium derivatives of 4-dimethylaminophenylacetylene under various reaction conditions.



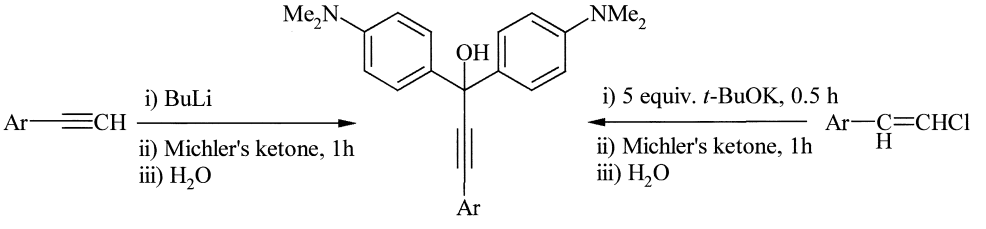
7e **17**

The spectral parameters of the dyes were derived from solutions of the dye bases in 98% acetic acid, a solvent system chosen to allow comparison with earlier work [8] and because its acidity is sufficient to promote the complete formation of the dye cation whilst minimising the possibility of forming other species such as dications [31]. The use of acetic acid also has the advantage of giving easy access to a wide range of solutions of different acid strengths as the addition of water promotes the ionisation of the acid, a feature which allows protonation of the dye cations to be studied.

The λ_{max} values of the vinylogues **2a** and **2b** of Crystal Violet and Malachite Green measured in this work (Table 1) closely match those reported by the earlier workers (690 nm for **2a** and 656 nm and 490 nm for **2b**), but the ϵ_{max} values now obtained are all higher than the published values [10]. Of course, the earlier data lack precision since they are extrapolated from absorption curves and also the nature of the solvent used was unspecified although it was probably glacial acetic acid.

Both the x- and y-bands of **2b** occur at significantly longer wavelengths than those of Malachite Green. The large bathochromic shift of the *y*-band which is accompanied by an increase in intensity is an indication of the extension of conjugation along the *y*-axis, although the shift is somewhat smaller than that observed on insertion of a vinyl unit into a cyanine chromogen (ca. 80–100 nm) [32].

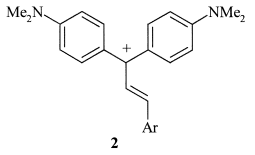
The red shift and significant decrease in intensity of the *x*-band are more difficult to explain. It is well known that a bathochromic shift of the *x*-band is observed when the phenyl ring of Malachite Green is forced out of conjugation, as for example in the 2,6-dimethyl derivative of Malachite Green [33], making the transition along the *x*-axis sterically favoured . Similarly, enforced bond rotation along the *x*-axis brought about by ortho substituents in the dimethylaminophenyl rings also results in a bathochromic shift of the *x*-band as in 2′-substituted Malachite Green dyes [33]. However, the latter situation is always accompanied by a large decrease in $\epsilon_{max}(x)$, whilst an increase in the extinction coefficient is observed when a substituent is introduced at an *ortho* position of the phenyl ring [34].



7a Ar = 4-$Me_2NC_6H_4$
7b Ar = C_6H_5
7c Ar = 1-$C_{10}H_7$
7d Ar = 2-$C_{10}H_7$
7e Ar = 4-Me_2N-1-$C_{10}H_6$

Scheme 4.

Table 1
Visible absorption spectra of the vinylogue dyes in 98% and 10% AcOH. Values in parentheses indicate a shoulder



2

	Ar	98% AcOH		10% AcOH	
		$\lambda_{max}(x)$ (nm) $\lambda_{max}(y)$ (nm)	$10^{-4}\epsilon_{max}(x)$ $10^{-4}\epsilon_{max}(y)$	$\lambda_{max}(x)$ (nm) $\lambda_{max}(y)$ (nm)	$10^{-}\epsilon_{max}(x)$ $10^{-4}\epsilon_{max}(y)$
2a	4-$Me_2NC_6H_4$	694 (610)	11.92 (5.13)	718 462	8.71 1.00
2b	C_6H_5	656 488	5.75 3.54	654 484	2.75 3.39
2c	4-Me_2N-1-$C_{10}H_6$	742 (656)	8.13 (5.37)	654 470	1.89 2.57
2d	1-$C_{10}H_7$	659 528	4.90 3.24	650 520	2.82 2.82

It thus appears that, instead of releasing steric crowding about the central carbon atom, the vinyl unit disrupts the electronic symmetry along the bisdimethylaminophenyl axis of **2b**, causing the $\epsilon_{max}(x)$ value to collapse. Examination of molecular models indicates that conjugation along the *y*-axis is unlikely to be seriously impeded in crowded configurations and this is substantiated by the high $\epsilon_{max}(y)$ value.

Replacement of the phenyl ring of **2b** by a naphthyl ring to give **2d** results in bathochromic shifts, especially of the y-band, as well as a reduction in intensity of both bands. The extended conjugation offered by the naphthyl ring accounts satisfactorily for the large (40 nm) shift of the *y*-band. The marginal reduction of $\epsilon_{max}(y)$ is in line with the increased electron-withdrawing effect of the polycyclic aromatic system [35]. This latter effect also explains the small red shift and decrease in intensity of the *x*-band, although it is likely that the naphthyl moiety may cause further steric congestion along the *x*-axis.

The spectrum of **2a** in 98% acetic acid displays an intense absorption at 694 nm with a pronounced shoulder at ca. 610 nm. The observed shift of about +100 nm compared to Crystal Violet is in line with that found on insertion of a vinyl unit into cyanine dyes [32]. This absorption spectrum is strongly modified in 10% acetic acid and a band at 462 nm ($\epsilon = 10^4$ dm^3 mol^{-1} cm^{-1}) indicates a fair degree of protonation, which is a surprising feature since all three rings would be expected to participate equally in the delocalisation of the positive charge. Furthermore, Crystal Violet is not protonated in 10% acetic acid. The main absorption band of **2a** in this solvent appears at 718 nm so that the overall aspect of the visible absorption spectrum is remarkably similar to that of the [1,3-bisdimethylaminophenyl-3-phenyl]propenyl cation, for which $\lambda_{max}(x)$ is 715 nm and $\lambda_{max}(y)$ is 462 nm [10]. The close similarity between these spectra is indicative of the presence of a quaternary ammonium substituent in the former species and it follows that the favoured transition of 2a is that which takes place along the dimethylaminophenyl–dimethylaminostyryl axis. The shoulder observed in 98% acetic acid may be attributable to the transition associated with the bisdimethylaminophenyl axis.

That such electronic asymmetry can be caused by a vinyl unit is rather surprising. It is probable that the advantageous electronic effects of the vinyl linkage are associated with a sterically enhanced ability to conjugate with the central

carbon atom. The flexibility of the propenyl unit may allow the styryl moiety to disrupt the bisdimethylaminophenyl axis sterically without significantly affecting its mesomeric activity.

The visible absorption spectrum of **2c** in 98% acetic acid is quite similar to that of **2a** although both the absorption band and its inflexion occur at longer wavelengths. The large red shift of λ_{max} (48 nm) is comparable to the difference between the y-bands of the Malachite Green derivatives **2b** and **2d** (+ 40 nm) and may therefore be ascribed to the enlarged chromophore. It is interesting to note that *peri* hindrance alone does not prevent the 4-dimethylamino-1-naphthyl ring from being a good component of the charge delocalisation system. It is nevertheless true that it has some effect and it is the naphthylamine moiety which undergoes protonation in 10% acetic acid. Partial deconjugation of this ring can also be held responsible for the reduced ϵ_{max} value of **2c** in 98% acetic acid compared to that of **2a**.

The shoulders observed in the spectrum of **2a** and **2c** have been assigned to the transition which takes place along the bisdimethylaminophenyl axis and the similarities between the x-bands of the two Green derivatives and the shoulder of **2c** are consistent with this. The hypsochromic shift of the shoulder of **2a** may be accounted for in terms of the reduced importance of the corresponding transition in this compound. This form of band-splitting may be the reason for the absence of any significant increase of the extinction coefficient which is usually associated with the insertion of a vinyl unit into a cyanine-type chromogen [32].

The absorption characteristics of the Violet dye **3a** (Table 2) are in good agreement with the published data [10] of λ_{max} 670 nm and ϵ_{max} 103,000 $dm^3\ mol^{-1}\ cm^{-1}$. On the other hand, whilst the λ_{max} values for the Green **3c** are identical, the published extinction coefficients [$\epsilon_{max}(x)$ 113,000 and $\epsilon_{max}(y)$ 55,000 $dm^3\ mol^{-1}\ cm^{-1}$] are larger than those measured here.

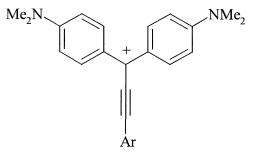
The $\lambda_{max}(y)$ values for **3b** and **3c** are very close to those of the corresponding vinylogues and the extinction coefficients are also comparable which suggests that the electronic effects of the vinylic and acetylenic units are similar. The *x*-bands of the two ethynologues absorb at much longer wavelengths (ca. + 35 nm) than those of the vinylogues. This observation, together with the much larger $\epsilon_{max}(x)$ values of **3b** and **3c**, can be explained by the different geometries of the two chromogens. It has been shown that insertion of an acetylenic linkage into a triphenylmethane structure significantly reduces steric crowding about the central carbon atom [23] and allows the dye molecule to achieve planarity [35] so that the large λ_{max} value of **3b** can be ascribed to an increase in the symmetry of the bisdimethylaminophenyl axis. The implications are that, whilst having apparently similar electronic effects, the double and triply bonded units have quite different steric consequences, both of which result in bathochromic shifts of the *x*-bands. The difference in nature of these two systems is apparent from the $\epsilon_{max}(x)$ values (Tables 1 and 2).

The *x*-band of **3d** exhibits a slight hypsochromic shift (3 nm) compared to that of **3c**, which presumably reflects the difference in the electron-withdrawing properties of 1- and 2-naphthyl substituents [36]. This shift confirms the 1-naphthyl ring as the stronger electron-withdrawing substituent since the introduction of electron-withdrawing groups in the 4-position of **3b** causes a red shift of the *x*-band [23,37]. The *y*-band of **3d** occurs at a shorter wavelength (−13.5 nm) than that of **3c** and the shift may indicate an increased ability of the 1-naphthyl ring to provide an extension of the chromophore.

The Violet dye **3e** absorbs at a longer wavelength but less strongly than **3a** (Table 2). As with the two related vinylogues, these differences probably originate in the extended conjugation and reduced electron-donating activity associated with the naphthyl ring. The close similarities in the spectra of **3c** and **3e** in 10% acetic acid (Table 2) confirm the 4-dimethylamino-1-naphthyl moiety of 3e as being the preferred site of protonation.

The situation is less straightforward with **3a** in the more acidic solvent. A small band appears at 480 nm which suggests that protonation occurs on the phenylethynyl moiety (Table 2). In this case, a band should also be present at 688 nm or above (the wavelength of maximum absorption of **3b**) instead of at 672 nm as observed. It seems that a relatively large amount of the monocation is still

Table 2
Visible absorption spectra of the ethynologue dyes in 98% and 10% AcOH. Values in parentheses indicate a shoulder



3

		98% AcOH		10% AcOH	
	Ar	$\lambda_{max}(x)$ (nm) $\lambda_{max}(y)$ (nm)	$10^{-4}\epsilon_{max}(x)$ $10^{-4}\epsilon_{max}(y)$	$\lambda_{max}(x)$ (nm) $\lambda_{max}(y)$ (nm)	$10^{-4}\epsilon_{max}(x)$ $10^{-4}\ \epsilon_{max}(y)$
3a	4-$Me_2NC_6H_5$	668 (624)	10.08 (7.59)	672 (614) 480	5.37 0.79
3b	C_6H_5	689.5 (644) 488	9.77 3.89	688 (649) 486	5.37 2.57
3c	1-$C_{10}H_7$	694 (644) 525	9.17 3.72	691 (650) 516	2.82 3.89
3d	2-$C_{10}H_7$	691 (644) 511.5	9.55 4.37	688 648	3.55 3.39
3e	4-Me_2N-1-$C_{10}H_6$	683 (640)	8.13 (5.89)	694 (632) 506	3.35 1.70

present in 10% acetic acid and is responsible for the intermediate value of 672 nm as well as for the rather low extinction coefficient of the 480 nm band. It may be recalled that the *x*- and *y*-bands of the (1,3-bisdimethylaminophenyl-3-phenyl)propynyl cation occur at 736 and 477.5 nm, respectively [10].

This apparent resistance of **3a** towards protonation contrasts with the behaviour of **2a** and is a good indication of the almost perfect electronic symmetry of the ethynologue. The same conclusion has been reached from PPP-MO calculations [37], which implies efficient involvement of the phenylalkynyl moiety of **3a** in the charge delocalisation system despite the implicated allene structure probably being energetically disfavoured [23].

Since the electronic effects of the two unsaturated linkages appear comparable, the difference in the electronic symmetries of **2a** and **3a** adds further evidence to the fact that the vinyl unit owes at least part of its effectiveness in the resonance system to its ability to force the dimethylaminophenyl rings out of conjugation. Accordingly, the combination of favourable steric and electronic effects allows the vinyl unit to compensate for the *peri* hindrance in **2c** to a larger extent than does the acetylenic linkage of **3e**. The overall influence of the 1-(4-dimethylamino)naphthyl ring on the absorption behaviour is consequently stronger in the vinylogue as shown by the much larger shift observed when moving from **2a** to **2c** (+ 48 nm) than from **3a** to **3e** (+13 nm).

An intriguing feature of the ethynologue series is the shoulder which is apparent at about 645 nm in all the Green derivatives. As this shoulder is absent in the corresponding vinylogues, it is reasonable to assume that it is the consequence of the presence of the acetylenic unit. A possible explanation is the formation of another species by reaction of the dye with the acidic solvent. This proposition is, however, not supported by the presence of a similar — albeit more marked — inflexion in the absorption spectrum of **3b** in dichloromethane [23]. Alternatively, it may be that the planar ethynologues are even more sensitive to solvent effects or association than the simple triarylmethane dyes [38,39]. Previous workers have not commented upon this apparent anomaly.

Nevertheless it is known that propargylic alcohols rearrange rapidly in acidic conditions to

α,β-unsaturated ketones via an allenic alcohol [10,40] and the present ethynologues rearrange extremely rapidly in warm glacial acetic acid (and also slowly at room temperature in 10% acetic acid) to give the α,β-unsaturated ketones (Scheme 5). The rearrangement of **7e** in sulphuric acid afforded the yellow 1-(4-dimethylamino-1-naphthyl)-3,3-bis(4′-dimethylaminophenyl)prop-2-en-1-one **17** in good yield but, after reduction to the unstable propenol, subsequent attempts at dehydration in acetic acid failed to produce the vinylogue **2c** although an intense blue solution was observed from which the impure methyl ether was isolated after treatment with sodium methoxide. The carbonyl group exerts a different deshielding effect on the dimethylaminophenyl rings of the crowded molecule **17** such that in the ^{1}H NMR spectrum the signals of the ortho protons of the two rings resonate at 7.05 and 7.35 ppm.

3. Experimental

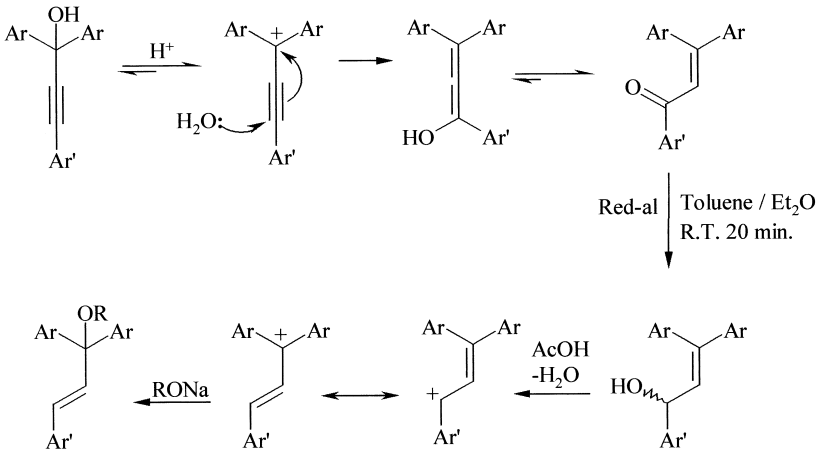
Visible spectra were measured on a Hewlett-Packard 8452A diode array spectrophotometer using 10^{-5} M solutions of the dye bases in glacial acetic acid containing 2% of water. The dyes were found to obey Beer's law in the concentration range 1–2.5 × 10^{-5} M, a range in which the maximum absorbance was between 0.5 and 0.9. Melting points were recorded in capillaries and are uncorrected. NMR spectra were recorded in $CDCl_3$ on a Bruker WM250 instrument; coupling constants are quoted in Hz. Flash chromatography was performed on silica gel (Sorbsil C60, MPD 60 Å, 40–60 μm) according to the published procedure [41].

3.1. Methyl 4-dimethylaminocinnamate

A mixture of 4-dimethylaminobenzaldehyde (4.47 g; 30 mmol), carbomethoxy-methylene-triphenylphosphorane (10.3 g; 30.8 mmol) and triethylamine (3 cm^3) was refluxed in toluene (150 cm^3) for 20 h. Removal of the solvent left a residue which was percolated through a short column of silica (30% ethyl acetate in hexane) and crystallised from ethyl acetate and hexane to afford pale yellow flakes of the product (5.12 g; 83%) m.p. 134–135°C ([42] quotes m.p. 132°C). δ_H 3.03 (6H, S, NMe_2), 3.79 (3H, S, CO_2CH_3), 6.21–6.27 (1H, d, *J* 14, *trans*-vinyl-H), 6.69 (2H, d, *J* 9, Ar-H), 7.43 (2H, d, *J* 9, Ar-H) and 7.61-7.68 (1H, d, *J* 14, *trans*-vinyl-H).

3.2. Ethyl 3-(4-dimethylamino-1-naphthyl)acrylate

Sodium hydride (4.01 g; 60% suspension in oil; 0.1 mmol) was washed 5 times with dry hexane under nitrogen and suspended in dry THF (40 cm^3) and the mixture was cooled to 0°C. Triethylphosphonoacetate (22.4 g; 0.1 mmol) was added and the slurry was stirred for 5 h at room temperature.



Scheme 5.

Solid 4-dimethylamino-1-naphthaldehyde (4 g; 20.1 mmol) was then added and the mixture was stirred overnight at room temperature. The addition of aqueous sodium hydroxide (50 cm^3; 2 M) was followed by extraction with ethyl acetate (4 × 50 cm^3) and the combined organic fractions were washed with water (3 × 50 cm^3), brine (50 cm^3) and dried (Na_2SO_4). Evaporation of the solvent and distillation of the dark orange residue (b.p. 120°C at 0.07 mmHg) afforded the product as a bright yellow oil (5.2 g; 96%). δ_H 1.36-1.42 (3H, t, CH_2CH_3), 7.95 (6H, s, NMe_2), 4.31–4.34 (2H, q, CH_2), 6.44–6.50 (1H, d, *J* 16, *trans*-vinyl-H), 7.06 (2H, d, *J* 8, Ar-H), 7.56 (2H, m, Ar-H), 8.24 (2H, m, Ar-H) and 8.47-8.54 (1H, d, *J* 16, *trans*-vinyl-H); MS (*m*/*z*) 269 (M^+).

3.3. Methyl 3-(1-naphthyl)acrylate

3-(1-Naphthyl)acrylic acid (10 g; 50.4 mmol) was refluxed in methanol (32 cm^3) in the presence of concentrated sulfuric acid (1.6 cm^3) for 4.5 h. The cooled solution was extracted with diethyl ether (2×200 cm^3) and the mixed organic extracts were washed with water (100 cm^3), aqueous sodium hydroxide (2 × 150 cm^3; 2M), water (100 cm^3) and brine (100 cm^3). Drying (Na_2SO_4) and removal of the solvent followed by distillation of the residue (b.p. 150 °C at 0.4 mm) yielded the product (10.1 g; 95%) as a colourless oil, MS (*m*/*z*) 212 (M^+).

3.4. 1,1-Bis(4-dimethylaminophenyl)-3-(4-dimethylamino-1-naphthyl)propen-1-ol **6b**

n-Butyllithium (9.12 cm^3; 2.5 M in hexane; 22.8 mmol) was added dropwise, under nitrogen and at room temperature to a solution of 4-bromo-*N,N*-dimethylaniline (4.68 g; 23.4 mmol) in dry diethyl ether (50 cm^3) and the mixture was stirred for 45 min before being added in a thin stream to a solution of ethyl 3-(4-dimethylamino-1-naphthyl)acrylate (3 g; 11.1 mmol) in dry diethyl ether (30 cm^3). The slurry which formed was stirred for 20 h and was then poured into water (200 cm^3). The aqueous layer was extracted with diethyl ether (100 cm^3) and the mixed organic phases were washed with water (2 × 150 cm^3), brine (100 cm^3), dried (Na_2SO_4/K_2CO_3) and the solvent was removed. The residue was purified by chromatography on silica using triethylamine/ethyl acetate/hexane (10/25/65) as eluent followed by recrystallisation from ethyl acetate to give colourless needles of the propenol (4.02 g; 78%), m.p. 144–147°C (decomp.) (Found: C, 79.9; H, 7.7; N, 8.9. $C_{31}H_{35}N_3O$ requires C, 80.0; H, 7.6; N, 9.0%).

The above method was used to produce the following compounds:

1,1,2-Tris(4-dimethylaminophenyl)propen-1-ol **6a**—(61%) from methyl 4-dimethylaminocinnamate as colourless micro-needles, m.p. 137–9°C (decomp.), after crystallisation from *tert*-butyl methyl ether and a second from acetone (Found: C, 78.3; H, 8.2; N, 10.0. $C_{27}H_{33}N_3O$ requires C, 78.03; H, 8.0; N, 10.1%).

1,1-Bis(4-dimethylaminophenyl)-3-phenylpropen-1-ol **6c**—(45%) from ethyl cinnamate as colourless needles, m.p. >143°C (decomp.) after repeated recrystallisation from acetone (Found: C, 80.4; H, 7.7; N, 7.3. $C_{25}H_{28}N_2O$ requires C, 80.6; H, 7.6; N, 7.5%).

1,1-Bis(4-dimethylaminophenyl)-3-(1-napthyl)-propen-1-ol **6e** — (69%) from methyl 3-(1-naphthyl)acrylate as colourless needles, m.p. 129–131°C (decomp.) after chromatography and recrystallisation from ethyl acetate/hexane (Found: C, 82.3; H, 7.1; N, 6.7. $C_{29}H_{30}N_2O$ requires C, 82.4; H, 7.2; N, 6.6%).

3.5. 4-Dimethylamino-cdb-chlorostyrene **9**

n-Butyllithum (4.3 cm^3; 2.3 M solution in hexane) was added dropwise and under nitrogen to a suspension of chloromethyltriphenyl phosphonium chloride (3.58 g; 10 mmol) in dry tetrahydrofuran (20 cm^3), maintaining the temperature below −10°C during the addition. After 30 min, finely powdered 4-dimethylaminobenzaldehyde (1.04 g, 7 mmol) was added and the mixture was stirred at room temperature for 20 h. The solid residue obtained by evaporation of the solvent was extracted with boiling petroleum ether (b.p. < 40°C) and recrystallised from diethyl ether to afford a mixture of the *cis*- and *trans*-isomers of the product (0.92 g, 72%), m.p. 41–43°C as a waxy solid [26] quotes 42–44°C).

3.6. 4-(2-Chloroethenyl)-dimethyl-l-naphthylamine **11**

4-*NN*-Dimethylamino-1-naphthaldehyde (0.6 g; 3 mmol) gave, by the above procedure, the title compound as a bright yellow fluorescent oil (0.68 g; 92%) as a mixture of isomers (Found: C, 72.7; H, 6.1; N, 6.1. $C_{14}H_{14}NC1$ requires C, 72.6; H, 6.1; N, 6.1%).

3.7. 4-Dimethylaminophenylacetylene **10a**

Trimethylsilyldiazomethane (2 cm^3; 2 M in hexane; 4 mmol) was added dropwise at −70°C and under nitrogen to a solution of LDA, [from *n*-butyllithium (2.5 M in hexane, 1.6 cm_3) and a solution of diisopropylamine (0.235 g; 4 mmol) in dry tetrahydrofuran (10 cm^3)]. After 30 min, a solution of 4-dimethylaminobenzaldehyde (0.56 g; 3.8 mmol) in dry THF (5 cm^3) was added and the mixture was stirred at −70°C for 1 h and at reflux for 3 h. The cooled solution was quenched with water (30 cm^3) and extracted with diethyl ether (3×100 cm^3). The combined ethereal layers were washed with water (3×100 cm^3), brine (50 cm^3) and dried (Na_2SO_4). Evaporation of the solvent gave a brown residue which was eluted from silica using 30% ethyl acetate in hexane to afford an oil which solidified to give pale yellow crystals of the product, (0.41 g; 75%), m.p. 53–54°C ([26] gives m.p. 53–54°C).

The following naphthylacetylenes were prepared by the same method.

1-Naphthylacetylene **10b**—(71%) from 1-naphthaldehyde (0.6 g; 3.8 mmol) as a pale, clear yellow oil, b.p. 70°C at 0.09 mmHg after chromatography on silica (20% ethyl acetate in hexane) and distillation ([43] gives b.p. 78°C at 1 mmHg).

2-Naphthylacetylene **10c**—(79%) from 2-naphthaldehyde (1.21 g; 3.8 mmol) as a colourless solid, m.p. 37–39°C, after elution from silica (20% ethyl acetate in hexane) and distillation, b.p. 111°C at 10 mmHg. ([44] quotes m.p. 36°C).

3.8. 1,1,3-Tris(4-dimethylaminophenyl)propyn-1-ol **7a**

Method (a). A solution of 4-dimethylaminophenylacetylene (0.41 g; 2.83 mmol) in dry THF (20 cm^3) was treated dropwise at room temperature and under nitrogen with *n*-butyllithium (1.1 cm^3; 2.5M in hexane; 2.75 mmol) and the resulting mixture was stirred for 30 minutes. Finely powdered Michler's ketone (0.72 g; 2.7 mmol) was added in one portion and the slurry was stirred for a further 45 min before the addition of water (300 cm^3). The solid which precipitated was collected, washed well with water and dried (Na_2SO_4). Recrystallisation from dichloromethane and light petroleum (b.p. 40–60°C) followed by a recrystallisation from ethyl acetate and hexane afforded the product as off-white micro-crystals, (0.70 g ; 63%) m.p. 144–145°C ([23] gives m.p. 143–145°C).

Method (b). Potassium *tert*-butoxide (2.8 g) was added as a single portion to a solution of 4-dimethylamino-β-chlorostyrene (0.51 g; 2.79 mmol) in dry THF (40 cm^3) and the slurry which formed was stirred at room temperature and under nitrogen for 25 min. Michler's ketone was then added as a fine powder (0.72 g) and the mixture was stirred for 40 min before being quenched with water (400 cm^3). The isolation and purification procedure described in method (a) gave the product (59%), m.p. 143-145°C.

1,1-Bis(4-dimethylaminophenyl)-3-(4-dimethylamino-1-naphthyl)propyn-1-ol **7e** — (60%) [by method b)] from 4-(2-chloroethenyl)-*N,N*-dimethyl-1-naphthylamine (0.36 g; 1.55 mmol), potassium *tert*-butoxide (1.16 g; 15 mmol) and Michler's ketone (0.32 g; 1.2 mmol). Quenching with water (300 cm^3) gave an oil which solidified in diethyl ether and was recrystallised from the same solvent to afford bright yellow granules of the product, m.p. 147–149 °C (Found: C, 80.5 ; H, 7.1; N, 9.1. $C_{31}H_{33}N_3O$ requires C, 80.4; H, 7.2; N, 9.1%).

1,1-Bis(4-dimethylaminophenyl)-3-phenylpropyn-1-ol **7b** — (78%) (by method a) from phenylacetylene (1.5 g; 14.7 mmol) and Michler's ketone (3.75 g; 14 mmol) as colourless micro-needles from ethyl acetate and acetone, m.p. 164–5°C ([24] quotes m.p. 163–164°C).

1,1-Bis(4-dimethylaminophenyl)-3-(2-naphthyl)-propyn-1-ol **7d** — (73%) [by method (a)] from 2-naphthylacetylene (0.3 g; 1.97 mmol) and Michler's ketone (0.5 g; 1.86 mmol) as colourless fine needles,

m.p. >123 °C (decomp.) from ethyl acetate/hexane (Found: C, 82.8; H, 6.8; N, 6.6. $C_{29}H_{28}N_2O$ requires C, 82.8; H, 6.7; N, 6.7%).

1,1-Bis(4-dimethylaminophenyl)-3-(1-naphthyl)-propyn-1-ol **7c** — a. (69%) [by method (a)] from 1-naphthylacetylene (0.3 g) and Michler's ketone (0.5 g) as fine colourless needles m.p. 129–135°C (decomp.) from ethyl acetate and hexane (Found: C, 82.6; H, 6.7; N, 6.5. $C_{29}H_{28}N_2O$ requires C, 82.8; H, 6.7; N, 6.7%).

b. A mixture of 1,1-bis(4-dimethylaminophenyl)propyn-1-ol [23] (2.0 g; 6.8 mmol), 1-bromonaphthalene (1.4 g; 6.8 mmol), palladium acetate (0.12 g; 0.56 mmol) and triphenylphosphine (0.23 g; 0.88 mmol) was refluxed in triethylamine (200 cm^3) for 5 h. The cooled mixture was filtered through celite and the removal of the solvent gave a brown paste which was eluted twice from silica with triethylamine/ethyl acetate/hexane (10/25/65) and recrystallised repeatedly from ethyl acetate and hexane to afford the product, (0.12 g; 4%) m.p. >130°C (decomp.).

3.9. 1-(4-Dimethylamino-1-naphthyl)-3,3-bis(4-dimethylaminophenyl)prop-2-en-1-one **17**

Concentrated sulphuric acid (2 cm^3) was cautiously added to a solution of 3-(4-dimethylamino-1-naphthyl)-1,1-bis(4-dimethylaminophenyl)propyn-1-ol (1.0 g; 2.16 mmol) in methanol (15 cm^3) and the mixture was refluxed for 20 min. The cooled dark brown solution was basified with aqueous sodium hydroxide solution and extracted with ethyl acetate (3×50 cm^3). The combined extracts were washed with water and brine, dried (Na_2SO_4) and evaporated to yield a brown solid. Elution from silica with ethyl acetate and hexane (1:2) and recrystallisation from ethyl acetate and hexane gave bright yellow needles of the ketone, (0.75 g; 75%) m.p. 163°C (Found: C, 80.7; H, 7.2; N, 9.0. $C_{31}H_{33}N_3O$ requires C, 80.4; H, 7.2; N, 9.1%).

3.10. Attempted synthesis of 1-(4-dimethylamino-1-naphthyl)-3,3-bis(4-dimethylaminophenyl)prop-2-en-1-ol.

1-(4-Dimethylamino-1-naphthyl)-3,3-bis(4-dimethylaminophenyl)prop-2-en-1-one (0.5 g; 1.08 mmol) was added to a solution of 70% sodium bis(2-methoxyethoxy) aluminium hydride (0.3 cm^3; 1.2 mmol) in dry toluene, further diluted with dry toluene (20 cm^3) and the mixture was stirred for 20 min. Water (20 cm^3) was cautiously added followed by ethyl acetate (50 cm^3) and the two layers were separated. The aqueous fraction was extracted with ethyl acetate (50 cm^3) and the combined organic layers were washed with water (2×30 cm^3), brine (20 cm^3) and dried (K_2CO_3). Evaporation of the solvent gave a semi-solid residue from which no pure product could be isolated and which slowly decomposed on standing. [λ_{max} (100% acetic acid) 742 (656) nm; $\epsilon_{max} > 50{,}000$ $dm^3\ mol^{-1}\ cm^{-1}$].

4. Conclusions

The incorporation of olefinic and acetylenic character into the Victoria Blue chromophore leads to dyes exhibiting significant bathochromic shifts compared to the parent triarylmethane system. Whereas the triple bond is responsible both sterically and electronically for the longer wavelength of the *x*-band in the naphthyl derivatives, the vinylogue is better able to accommodate the *peri*-hindrance associated with the 4-dimethylamino-1-naphthyl group, leading to a large bathochromic shift into the near infrared.

As candidate photosensitizers for photodynamic therapy, the longer wavelength absorption of both species is eminently suitable. However, the ethynologues are unlikely to be superior to the vinylogues, because of the instability of the former under acidic conditions. Propargyl alcohols are sensitive to acid, rearranging to unsaturated ketones. The ethynologues can also be expected to be more sensitive to basic conditions, since the reduced crowding at the central carbon atom may ease the approach of a hydroxide ion, leading to carbinol formation.

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