NMR spectral studies of dimedone–aldehyde adducts. Part 3. A re-investigation of the reaction with cinnamaldehyde, ^{1}H and ^{13}C NMR studies of the products

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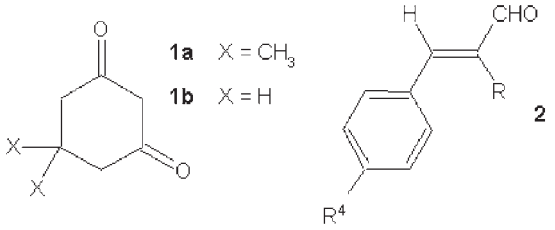
The reaction between some substituted cinnamaldehydes with dimedone and cyclohexane-1,3-dione under neutral, acidic and basic conditions have been investigated. The structures of the adducts obtained have been studied by ^{1}H and ^{13}C NMR spectroscopy.

Keywords: dimedone–aldehyde adducts, cyclohexane-1,3-done, cinnamaldehyde, ^{1}H NMR, ^{13}C NMR

In previous papers we have presented ^{1}H and ^{13}C NMR spectral studies of dimedone[1] (5,5-dimethylcyclohexane-1,3-dione, methone, **1a**) and of some dimedone–aldehyde adducts.[2]

Under the standard base reaction conditions (piperidine/boiling ethanol)[3] it has now been established that, depending upon the structure of the aldehyde component, four classes of adduct can be obtained which we have termed types A–D.[2] Whereas aliphatic α,β-unsaturated aldehydes (*e.g. trans*-crotonaldehyde) always lead to a dehydrated cyclic benzopyrone adduct (type D), there has been considerable controversy in the literature[4-7] concerning the nature of the products obtained from the corresponding parent α,β-unsaturated aromatic aldehyde, cinnamaldehyde, **2a**.



	R	R4
a	H	H
b	H	NO_2
c	Me	H
d	H	NMe_2
e	H	OMe

Nagarajan and Shenoy[8] have performed an excellent investigation of the reaction between **1a** and **2a** and their results are summarised in Schemes 1 and 2.

In contrast, reaction with the *para*-substituted aldehyde **2d** gave the type D adduct under both neutral and basic conditions. In our previous study,[2] we reported that **2e** gave the type D adduct under basic conditions. However, with α-methyl-cinnamaldehyde **2c**, due to steric effects, the initial product was the normal type A adduct **3c** which could be readily dehydrated[9] to the "anhydride" **5c**. Nagarajan and Shenoy[8] did not perform a comprehensive spectroscopic study on their products and we have subsequently discovered[2] that several of their assignments are in need of correction. Accordingly, we have undertaken a more thorough study of the reaction of dimedone **1a** and the associated reagent cyclohexane-1,3-dione **1b** with some substituted cinnamaldehyde derivatives, under varying experimental conditions, and have examined all of the products by ^{1}H and ^{13}C NMR spectroscopy.

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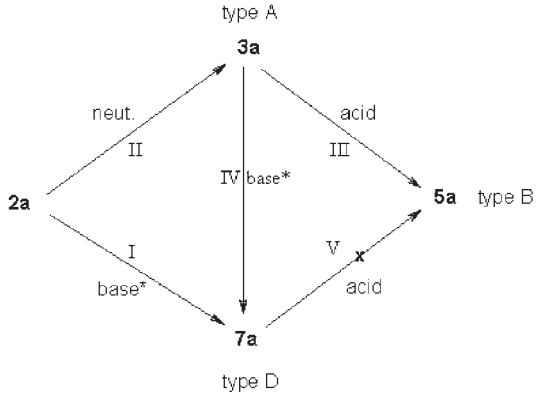


Scheme 1 Reaction sequences from cinnamaldehyde **2a** and dimedone **1a**
base* : piperidine/ethanol[3]
I–V : pathway identification letters.

Results and discussion

Synthetic studies

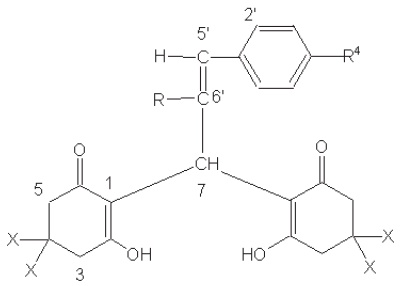
Experiments were initially conducted to determine the preferred technique for sample isolation. After boiling under reflux, if water was added to induce crystallisation then the isolated products, although obtained in superior yield, were always less pure. The preferred method of isolation was therefore to allow the products to crystallise after standing, which generally required a minimum of about one week. However, isolation of the adducts from reactions with **1b** always proved more problematic. The reaction pathways involved have been identified as I–V as shown in Scheme 1, the results from each pathway will now be discussed in turn.

Pathway I (standard base conditions)

The reactions with dimedone **1a** proceeded as previously reported.[2,4] Aldehydes **2a**, **2b** and **2e** each gave the appropriate type D adducts. The corresponding reactions with cyclohexane-1,3-dione **1b** were less successful. Although **8a** was obtained from **2a** (see also later discussion) no crystalline products could be isolated from the reactions with **2b** and **2c**.

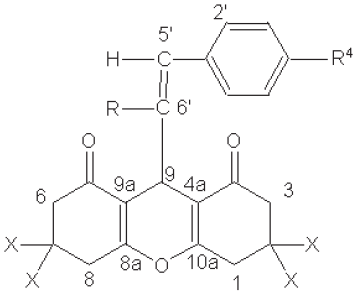
Pathway II (neutral conditions)

The reactions of **1a** with **2a**[4] and **2b** gave the normal type A adducts **3a** and **3b** respectively. With **1b**, however, although **2a** successfully gave **4a**, the reaction with **2b** failed. The course of the reactions with **2c** were of interest, since due to steric constraints, the type D adduct (**7c**) could not form.[2] Under neutral conditions no product could be isolated. However, the normal type A adduct **3c** could be obtained under basic conditions (Pathway II) as reported previously.[2] With **1b** the results reversed, the normal type A adduct **4c** only being obtained when neutral conditions were employed.



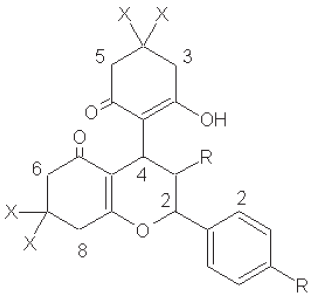
Type A adducts (normal bis-methone) **3** & **4**

No.	R	R^4	X
3a	H	H	Me
3b	H	NO_2	Me
3c	Me	H	Me
4a	H	H	H
4b	H	NO_2	H
4c	Me	H	H



Type B adducts ("anhydrides")[5] 5 & 6

No.	R	R^4	X
5a	H	H	Me
5b	H	NO_2	Me
5c	Me	H	Me
6a	H	H	H
6b	H	NO_2	H
6c	Me	H	H



Type D adducts (benzopyrone")[5] 7 & 8

No.	R	R^4	X
7a	H	H	Me
7b	H	NO_2	Me
7c	Me	H	Me
7e	H	OMe	Me
8a	H	H	H
8b	H	NO_2	H

Scheme 2 Structure and spectral numbering of the adducts[1]

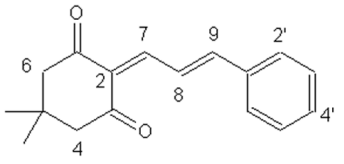
Pathway III (acid conversion of type A into type B)
These reactions all proceeded in accordance with the literature[4] to give the pure "anhydrides" **5a–5c**, **6a** and **6c**. Nagarajan and Shenoy[8] quoted the melting point of **5a** as 166–168 °C (148-150 °C) with the value in parentheses referred to as "another crystalline form". In the present work the crystalline phase changes were viewed using a Kofler hot stage microscope. At 160–161 °C part of the carefully recrystallised sample melted and then re-formed into a second crystalline phase, which melted completely at 175-176 °C. It would therefore appear that this compound exists in two distinct polymorphic forms, with m.p.s about 15 °C apart. That the values reported previously[8] were somewhat lower and of a wider range suggests that their product still contained some impurities. As recommended by Horning and Horning[3] these were the preferred derivatives for characterisation purposes.

Pathway IV (base conversion of type A into type D)
These conversions were only successful with **3a**, **3b** and **4a**; no products could be isolated from the other reactions. It is interesting that the type D products synthesised via type A (pathways II and IV) were obtained in a much purer state that those prepared directly (pathway I) (see Scheme 1).

Pathway V (interadduct conversion)
An attempt was made to ascertain whether interadduct conversion from type D (**7a**) to the type B (**5a**) might conceivably be possible to provide an alternative route to this final product. Although the conversion failed, the process did, nevertheless, provide an unexpected means of purification of **7a**.

King and Felton[10] introduced cyclohexane-1,3-dione 1b as an alternative cost-effective aldehyde specific derivatisation reagent.[11a] However, only a few melting points of derivatives are available.[10,11c] The products were all considered to be the *bis*-adducts (type A) with "anhydrides" (type B) only being obtained in two instances after further acid treatment. However, their cinnamaldehyde adduct, m.p. 216 °C, would now appear to be the benzopyrone type D adduct, **8a**. Moreover, through the use of appropriate reaction conditions the full range of **1b** adducts, *viz* type A, m.p. 143–145 °C; type B, m.p. 182–184 °C and type D, m.p. 214–216 °C (see Table 10) may be prepared.

During the course of their studies Nagarajan and Shenoy[8] noted that their prepared samples of **3a** and **7a** were contaminated with orange cinnamylidenedimedones, such as **9a**, which could be isolated by chromatography. Our products were similarly contaminated. (see Table 7).



a X = CH_3
b X = H

9

Table 1 ^{1}H NMR chemical shifts (δ) of series A adducts[a,b,c]

Proton	**3a**[d]	**3a**[e]	**3b**	**3c**[f]	**3c**	**4a**[d]	**4c**
	D	C	C	C	D	D	C
H-7	5.27	4.93	4.94	4.83	5.20	5.10	4.79
H-2'/H-4'[g]	7.18		7.44[h]	7.14	7.11	7.18	7.14
	7.29			7.20	7.17	7.28	7.20
H-3'[g]	[j]		8.14	7.26	7.28	[j]	7.26
				7.33	7.34		7.32
H-5'	6.14	6.23	6.36	6.25	6.25	[k]	6.23
H-6'	6.36	6.57	6.63	–	–	[k]	–
CH_3-6'	–	–	–	1.72	1.72	–	1.68

[a]For numbering see Scheme 2; [b]C : in $CDCl_3$ D : in DMSO-d_6; [c]for spectral data of dionyl substituent (DS) groups, see Table 8; [d]see also Table 7; [e]data from ref. 8; [f]data from ref. 2; [g]range of multiplet given; [h]signal for H-2' only; [j]included in H-2'/H-4' multiplet; [k]peak obscured.

Table 2 ^{1}H NMR chemical shifts (δ) of series B adducts[a,b]

Proton	**5a**	**5a**[c]	**5b**	**5c**[d]	**6a**	**6c**
	D	C	C	C	D	C
H-1a	2.51	2.40	2.47	2.43	2.58[f]	2.48[f]
H-1b	2.51	2.40	2.47	2.46	2.58[f]	2.48[f]
CH_3-2a	1.04	1.10	1.12	1.08	1.97[e,f]	2.03[e,f]
CH_3-2b	1.05	1.10	1.14	1.11	1.97[e,f]	2.03[e,f]
H-3a	2.24	2.27	2.32	2.27	2.36[f]	2.48[f]
H-3b	2.31	2.27	2.32	2.27	2.36[f]	2.48[f]
H-9	4.15	4.40	4.44	4.18	4.19	4.33
H-2'/H-4'[g]	7.18	7.2	7.40[h]	7.09	7.18	7.13
	7.28			7.16	7.33	7.29
H-3'[g]	[j]	7.2	8.10	7.23	[j]	[j]
				7.28		
H-5'	6.20	6.27	6.36	6.31	6.13	6.37
H-6'	6.22	6.27	6.50	–	6.19	–
CH_3-6'	–	–	–	2.05		1.93

[a]For numbering see Scheme 2; [b]C : in $CDCl_3$ D : in DMSO-d_6; [c]data from ref. 8; [d]data from ref. 2; [e]signals for H-2a/H-2b; [f]centre of multiplet; [g]range of multiplet given; [h]signal for H-2' only; [j]included in H-2'/H-4' multiplet.

Spectroscopic studies

The spectroscopic results are shown in Tables 1–7. A full discussion of the assignments of the ^{1}H and ^{13}C NMR spectra of the type A–D adducts and of the dionyl substituent (DS) and dionyl ring (DR) residue portions has been presented in our earlier study.[2]

Due to solubility restrictions samples have been examined in both $CDCl_3$ and DMSO-d_6 solutions. In this paper we therefore propose only to highlight those variations caused by solvent effects, and also to mention any further chemical shift correlation changes consequent upon the additional substituents introduced in the wider range of compounds studied.

^{1}H NMR spectroscopy

For the type A adducts (see Table 1), the characteristic signal for H-7 in both the dimedonyl (**3**) and cyclohexanedionyl (**4**) series appeared in the 4.1–5.2 δ region; chemical shifts in DMSO-d_6 being subject to a *ca* 0.3 p.p.m. downfield solvent shift.

For the type B adducts (see Table 2), the characteristic H-9 resonances all appeared in the narrow 4.1–4.4 δ region and were generally unaffected by change of solvent or structural variation.

All the series D adducts were examined in DMSO-d_6 solution. We have previously proposed[2] that **7a** exists in a half-chair conformation with a pseudo-axial dimedone substituent. Since the chemical shifts and coupling constants of the pyrone ring protons (see Table 3) were very similar in all of the compounds studied, it may be concluded that all exhibit similar conformations and that the observed signals are particularly characteristic for these adducts.

The spectra of the dimedonyl and cyclohexanedionyl (dionyl) substituent (DS) groups in adduct types A and D have been collected in Table 8 to facilitate comparison. The methyl signals were always equivalent in DMSO-d_6. However, they were marginally different in $CDCl_3$; likewise H-4a/H-4b in **4c**. Although the dimedonyl 3-CH_2 and 5-CH_2 signals were isochronous in DMSO-d_6, in the cyclohexanedionyl derivative **4a** they were non-equivalent. In $CDCl_3$ the situation was variable, with only a single methylene signal seen in **3b**, whilst four separate resonances were observed in both **3c** and **4a**. Unfortunately the complex methylene multiplet of **8a** proved too complex to analyse with certainty.

The spectra of the dimedone and cyclohexanedione (dionyl) ring (DR) residue portions contained in adduct types B and D (see Tables 2 and 3) will now be considered. Individual signals for the axial and equatorial methyl groups (at positions 2 and 7 respectively) were always observed in each solvent. However, the corresponding methylene proton patterns in **6a** and **6c** proved difficult to analyse. The methylene groups of series D were always isochronous in DMSO-d_6, whilst for series B there was no obvious trend. The methylene protons situated *peri* to the oxygen heteroatom (H-1a/1b in B; H-8a/8b in D) were always the most downfield.

The chemical shift separation between the cinnamyl side chain protons (types A and B : H-5' and H-6') was quite minimal and did not appear to be susceptible to solvent effects. The shift separations were increased in the *para*-nitro derivatives **3b** and **5b** due to a conjugative effect.

Table 3 ^{1}H NMR spectra of series D adducts[a,b] in DMSO-d_6

Chemical shifts (δ)					
Proton	**7a**[c]	**7a**[d]	**7b**	**7e**[c]	**8a**
H-2	5.04	5.03	5.00	5.02	4.98
H-3a	2.84	2.83	2.94	2.78	2.84
H-3e	1.55	1.55	1.62	1.51	1.56
H-4	3.91	3.90	4.06	3.84	3.90
H-6a	2.14	2.14	2.16	2.13	m
H-6b	2.21	2.20	2.38	2.20	m
CH3-7a	1.03	1.04	1.04	1.02	m[e]
CH3-7b	1.09	1.10	1.10	1.08	m[e]
H-8a	2.32	2.32	2.14	2.31	m
H-8b	2.40	2.46	2.41	2.38	m
Ar-2/4[f]	7.11	7.12	7.44[g]	6.95[g]	7.10
	7.18	7.15			7.17
Ar-3[f]	7.25	7.27	8.17	6.83	7.24
	7.30				7.29
OCH_3-4				3.71	
Coupling constants (Hz)					
$J_{2.3a}$	12.3	12.3	12.3	12.3	12.3
$J_{2.3e}$	2.3	2	2.3	2.3	2.3
$J_{3a.3e}$	13.4	14	13.7	13.4	13.7
$J_{3a.4}$	5.1	5.5	5.2	5.3	5.2

[a]For numbering see Scheme 2; [b]for spectral data of dionyl substituent (DS) groups, see Table 8; [c]data from ref. 2; [d]data from ref. 8; [e]signals for H-7a/H-7b; [f] range of multiplet given; [g]signal for Ar-2 only.

^{13}C NMR spectroscopy

The discussion will focus on those carbons which were particularly characteristic[2] for each adduct series.

For the type A adducts (see Table 4) the characteristic C-7 signals appeared in the 27-35 δ region in each of the solvents with no obvious trend. Note that for the methylcinnamyl derivatives **3c** and **4c**, all the shifts were particularly consistent.

Table 4 ^{13}C NMR chemical shifts (δ) of series A adducts[a,b,c]

Carbon	**3a**	**3b**	**3c**[d]	**3c**	**4a**	**4c**
	D	C	C	D	D	C
C-7	27.8	31.6	36.4	35.4	[e]	36.5
C-1'	137.1	143.8	138.5	138.1	137.5	138.6
C-2'	125.7	126.7	129.0	128.5	125.6	128.9
C-3'	128.4	123.9	127.9	128.0	128.4	127.9
C-4'	126.8	146.6	126.0	125.7	126.6	126.0
C-5'	130.7*	134.2	125.7	122.8	132.6*	125.3
C-6'	128.3*	128.3	133.5	136.2	128.3*	133.4
CH_3-6'	–	–	17.9	17.6	–	17.2
CO-a	197.3[f]				195.6[g]	
CO-b	198.9[f]				196.0[f]	

[a]For numbering see Scheme 2; [b]C : in $CDCl_3$ D : in DMSO-d_6; [c]for spectral data of dionyl substituent (DS) groups, see Table 9; [d]data from ref. 2; [e]sample impure, precise assignments uncertain; [f]CO signals of **9a**; [g]CO signals of **9b**. *Assignments could be interchanged.

Table 5 ^{13}C NMR chemical shifts (δ) of series B adducts[a,b]

Carbon	**5a**	**5b**	**5c (c)**	**6a**	**6c**
	D	C	C	D	C
C-1	39.4	40.9	40.8	27.5	27.2
C-2	31.5	32.2	32.1	19.9	20.4
CH_3-2a	27.1	27.6	27.1	–	–
CH_3-2b	28.2	29.2	29.4	–	–
C-3	49.7	50.8	50.9	36.4	37.1
C-4	195.9	196.6	196.8	196.4	196.9
C-4a	112.8	113.7	115.5	113.9	116.2
C-8a	163.2	163.5	162.4	165.3	164.3
C-9	26.4	28.5	34.6	26.5	34.8
C-1'	136.2	143.9	138.2	136.6	138.2
C-2'	125.6	126.8	128.8	126.1	128.9
C-3'	128.2	123.8	127.8	128.4	127.8
C-4'	127.0	146.6	125.9	127.2	126.0
C-5'	131.0*	136.3	128.1	130.9*	128.1
C-6'	129.2*	128.6	143.2	129.0*	141.1
CH_3-6'			18.4		18.1

[a]For numbering see Scheme 2; [b]C : in $CDCl_3$ D : in DMSO-d_6; [c]data from ref. 2. *Assignments could be interchanged.

In the B series adducts, C-9 absorbed near 26 δ for the cinnamyl and near 34 δ for the methylcinnamyl derivatives. The structural change from dimedonyl to cyclohexanedionyl (**5a** to **6a** in DMSO-d_6; **5c** to **6c** in $CDCl_3$) only produced a very minimal effect.

The pyrone ring ^{13}C chemical shifts for the type D adducts were very consistent throughout; these, together with the ^{1}H NMR spectroscopic study, indicated that all the compounds exhibited similar conformations.

The spectra of the dionyl substituent (DS) groups in adduct types A and D have been collected in Table 9 to facilitate comparison. In our previous studies[1,2] the assignments of the ring methylene carbons were rigorously examined and it was observed that some signals were considerably broadened. In this further study, all of the series D adducts in DMSO-d_6 exhibited similar broad signals that for C-3/C-5 of the cyclohexanedionyl example **8a** appearing *ca* 14 δ upfield from the **7** series compounds. The only other signals requiring comment are those for C-1, which exhibit characteristic solvent effects, and that the methyl signals were always equivalent in DMSO-d_6 but isochronous in $CDCl_3$.

The spectra of the dionyl ring (DR) residue portions contained in adduct types B and D (see Tables 5 and 6) will now be considered. The methyl groups were always non-equivalent in both solvents. The quaternary carbons adjacent to the oxygen heteroatom (C-8a) showed a consistent *ca* 6 p.p.m. downfield shift between the series B and D adducts, a useful diagnostic tool. Looking at the methylene resonances, those adjacent to the carbonyl function (C-6) absorbed the furthest downfield. All of the cyclohexanedione adducts showed a consistent *ca* 11 p.p.m. upfield shift at the site of demethylation (A : C-4 ; B : C-2 ; C-7).

Table 6 ^{13}C NMR chemical shifts (δ) of series D adducts[a,b] in DMSO-d_6

Carbon	**7a**[c,d]	**7b**	**7e**[c]	**8a**
C-2	66.6	66.7	66.6	66.6
C-3	32.3	32.1	32.5	32.5
C-4	33.5	34.0	32.6	33.5
C-4a	109.6	109.0	109.9	111.9
C-5	195.4	196.0	195.4	195.7
C-6	50.2	50.1	50.2	36.5
C-7	31.7	31.8	31.7	20.0*
CH_3-7a	27.8	27.7	27.8	–
CH_3-7b	28.2	28.5	28.1	–
C-8	41.8	41.8	41.8	28.3
C-8a	171.2	172.0	171.0	173.1
Ar-1	145.4	163.8	137.3	145.3
Ar-2	127.6	128.3	128.5	127.6
Ar-3	127.9	123.2	113.3	127.9
Ar-4	125.6	145.8	157.2	125.6
Ar-4'			54.8	

[a]For numbering see Scheme 2; [b]for spectral data of dionyl substituent (DS) groups, see Table 9; [c]data from ref. 2; [d]original assignments of ref. 8 as later revised[2]. *assignments could be interchanged.

In DMSO-d_6 there was only a minimal separation between the cinnamyl olefinic carbons (C-5' and C-6') in the dimedone adducts **3a** and **5a** which made their assignments difficult.[2] The separations were increased in the corresponding cyclohexanedione derivatives **4a** and **6a** and further increased in the *para*-nitro compounds **3b** and **5b** due to a conjugative effect. For the methylcinnamyl compounds only minimal changes ensued following the dimedonyl to cyclohexanedionyl structural change (**3c** to **4c**, **5c** to **6c**).

Impurities

The ^{1}H NMR spectra of the cinnamylidenedimedone impurities, first identified by Nagarajan and Shenoy[8] are shown in Table 7. There is a close correspondence between their data for the compounds isolated after chromatography and our spectroscopic determination in DMSO-d_6 of the isolated adducts.

In this paper we have presented a study of the reactions of cinnamaldehydes with dimedone under a variety of conditions and have presented ^{1}H and ^{13}C NMR spectroscopic data from which the isolated compounds may be definitively identified.

Table 7 ^{1}H NMR spectrum of cinnamylidenedimedone **9a**[a]

Chemical shifts (δ)		
Proton(s)	This work[b]	Lit.[c]
H-4/H-6	2.57[d]	2.55
CH_3-5	0.99	1.09
H-7	7.70	7.78
H-8	8.26[e]	8.38
H-9	7.23	7.34
Ar-2'/3'/4'	[f]	[g]
Coupling constants (Hz)		
J_{78}	12.1	12
J_{79}	15.7	15

[a]For ^{13}C NMR spectrum, see Table 4; [b]in DMSO-d_6, in admixture with **3a**; [c]in $CDCl_3$, ref. 8; [d]centre of multiplet; [e]also 8.226 δ for **9b**; [f]definitive assignment uncertain, within 7.16–7.48 δ multiplet region; [g]not reported.

Table 8 ^{1}H NMR chemical shifts (δ) of dimedonyl and cyclohexanedionyl (dionyl) substituent (DS) groups[a,b]

Series	Compd.	Solv.[c]	CH		CH		CH_3	
			3a	**3b**	**5a**	**5b**	**4a**	**4b**
A	**3a**	D	2.30	2.30	2.30	2.30	1.10	1.10
	3a[d]	C	2.30	2.30	2.30	2.30	1.10	1.10
	3b	C	2.36	2.36	2.36	2.36	1.09	1.14
	3c[e]	C	2.34	2.37	2.30	2.40	1.08	1.16
	4a	D	2.59	2.59	2.22	2.22	1.86[f]	1.86[f]
	4c	C	2.55	2.56	2.33	2.41	1.94[f]	1.91[f]
D	**7a**[e]	D	2.21	2.21	2.21	2.21	0.94	0.94
	7a[d]	D	2.2	2.2	2.2	2.2	0.95	0.95
	7b	D	2.23	2.23	2.23	2.23	0.95	0.95
	7e[e]	D	2.21	2.21	2.21	2.21	0.95	0.95
	8a	D	[m]	[m]	[m]	[m]	[m]	[m]

[a]For numbering see Scheme 2; [b]see also Tables 1 and 3; [c]C : in $CDCl_3$ D : in DMSO-d_6; [d]data from ref. 8; [e]data from ref. 2; [f]H-4a/H-4b; [m]multiplet.

Table 9 ^{13}C NMR chemical shifts (δ) of dimedonyl and cyclohexanedionyl (dionyl) substituent (DS) groups[a,b]

Series	Compd.	Solv.[c]	C-1	C-2	C-3	C-4	C-5	C-6	CH_3-4a	CH_3-4b
A	**3a**	D	114.9	187.2	46.2	31.2	46.2	187.2	27.5	
	3b	C	115.9	189.4	46.3	31.5	46.8	190.0	27.0	29.6
	3c[d]	C	115.3	189.3*	46.4	31.4	47.0*	190.5*	27.5	29.6
	3c	D	113.8	187.0	46.4	31.2	46.4	187.0	27.6	
	4a	D	116.3	189.4	[e]	[e]	[e]	189.4	–	
	4c	C	116.3	191.0	32.9	20.1	33.3	191.8	–	
D	**7a**	D	110.8	~175	~47	31.2	~47	~193	27.6	
	7b	D	110.5	~175	~47	31.3	~47	~193	27.5	
	7e	D	110.9	~175	~47	31.2	~47	193	27.6	
	8a	D	110.8	[f]	~33	20.7	~33	[f]	–	

[a]For numbering see Scheme 2; [b]see also Tables 4 and 6; [c]C : in $CDCl_3$ D : in DMSO-d_6; [d]data from ref. 2; [e]sample impure, precise assignment uncertain; [f]very broad signal, precise location indefinite. *Assignments may be interchanged.

Experimental

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Elemental analyses were performed in house. NMR spectra were recorded, for dilute (5%) solutions in chloroform-d or dimethylsulphoxide-d_6 at 37 °C on a Jeol EX270 instrument as described previously.[1]

Synthesis of adducts

1. *Pathway I – standard base conditions (ref. 3)*
   A mixture of dione **1a** or **1b** (0.02 mol) and the appropriate cinnamaldehyde (0.01 mol) in ethanol (50 ml) containing piperidine (six drops) was boiled under reflux for 30 min, allowed to cool and then set aside at room temperature.

   Isolation procedures
   (i) After 2 days, if no product had begun to crystallise out, a little water was added and the isolated product later filtered off, examined by ^1H NMR spectroscopy, and then recrystallised from ethanol. This procedure gave impure products and was subsequently abandoned.
   (ii) The reaction mixture was allowed to stand for a minimum of 7 days, any separated product was then filtered off, examined by ^1H NMR spectroscopy and then recrystallised several times from ethanol. If no product had separated after 28 days, the reaction was abandoned. The products obtained are shown in Table 10.

2. *Pathway II – neutral conditions*
   The procedure described above for pathway I was used, except that piperidine was omitted. Products were isolated and examined using isolation procedure (ii). The products obtained are shown in Table 10.

3. *Pathway III – preparation of "anhydrides" (ref. 3)*
   The adduct A (2 g) was dissolved in ethanol (30 ml) and concentrated hydrochloric acid (six drops) was added. The solution was warmed on the steam bath for 30 min and then allowed to cool. After 24 h

Table 10 Synthesis of cinnamaldehyde adducts

Pathway	Dione or adduct	Aldehyde	Series	Adduct no.	% Yield	m.p./ºC (lit.)
I	**1a**	**2a**	D	**7a**	83	214–216 (220–222)(8)
	1a	**2b**	D	**7b**	64	190–192 (a)
	1a	**2c**	A	**3c**	44	148 (141–142)(2)
	1a	**2d**	D	**7d**	[b]	(192–194)(8)
	1a	**2e**	D	**7e**	[c]	(198)(2)
	1b	**2a**	D	**8a**	56	209–211 (216)(10)
	1b	**2b**	–	[d]		
	1b	**2c**	–	[d]		
II	**1a**	**2a**	A	**3a**	74[e]	162–164 (162–164)(8)
	1a	**2b**	A	**3b**	68[e]	192–194 (a)
	1a	**2c**	–	d		
	1b	**2a**	A	**4a**	59[e]	143–145 (a)
	1b	**2b**	–	[d]		
	1b	**2c**	A	**4c**	66[e]	160–162 (a)
III	**3a**	–	B	**5a**	69	(f)
	3b	–	B	**5b**	71	217–220 (a)
	3c	–	B	**5c**	68	188–189 (185)(2)
	4a	–	B	**6a**	70	182–184 (a)
	4c	–	B	**6c**	62	154–155 (a)
IV	**3a**	–	D	**7a**	55	216–218 (220–222)(8)
	3b	–	D	**7b**	47	190–192 (a)
	3c	–	–	[d]		
	4a	–	D	**8a**	59[g]	214–216 (a) (216)(10)
	4c	–	–	[d]		
V	**7a**	–	D	**7a**	63[h]	220–221 (220–222)(8) (219)(11c)

[a]For elemental analysis, see Table 11; [b]data ex ref. 8; [c]data ex ref. 2; [d]no product isolated; [e]crude samples were contaminated with cinnamylidenedione impurities, see Table 7; [f]m.p. 174–176 (160–161), lit.8 m.p. 166–168 (148–150); see text for discussion; [g]the sample of **8a** from pathway IV was purer than that from pathway I; [h]The recovered sample of **7a** from pathway V was purer than samples from pathways I or IV.

Table 11 Elemental analyses of adducts

Compound	Formula	Elemental analysis/%[a]		
		C	H	N
3b	$C_{25}H_{29}NO_6$	68.3	6.5	3.1
		68.3	*6.6*	*3.2*
4a	$C_{21}H_{22}O_4$	74.7	6.5	
		74.5	*6.6*	
4c	$C_{22}H_{24}O_4$	74.9	6.8	
		75.0	*6.9*	
5b	$C_{25}H_{27}NO_5$	73.1	4.1	3.4
		73.0	*4.2*	*3.4*
6a	$C_{21}H_{20}O_3$	78.9	6.3	
		78.7	*6.3*	
6c	$C_{22}H_{22}O_3$	78.9	6.6	
		79.0	*6.6*	
7b	$C_{25}H_{29}NO_6$	68.4	6.5	3.1
		68.3	*6.6*	*3.2*
8a	$C_{21}H_{22}O_4$	74.6	6.4	
		74.5	*6.6*	

[a]Calculated values shown in italics.

the separated product was collected and recrystallised from ethanol. The products obtained are shown in Table 10.

4. *Pathway IV – reaction of type A adduct with base*
The procedure described above for pathway I was used, except that **1a** or **1b** was replaced by the type A adduct. Isolation procedure (ii) was used, which often required an extended period of standing to effect separation. The products obtained are shown in Table 10.

5. *Pathway V – reaction of type D adduct with acid*
The procedure described above for pathway III was used, except that adduct **7a** was used in place of adduct A. The product isolated (63% recovery) was a purified sample of **7a** as colourless microcrystalline needles, m.p. 220–221 °C, lit.[8] m.p. 220-222 °C. (see also Table 10)

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