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HYDROGEN BONDING IN PHENOLS—III

ABNORMALLY PERSISTENT INTERMOLECULAR ASSOCIATION OF ETHYLCOUMARATE, *m*-HYDROXYACETOPHENONE AND BIS/1-HYDROXY-4-METHYLPHENYL/METHANE

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Abstract—IR, UV, NMR and osmometric measurements demonstrate the existence of an unusually strong self-association for ethyl coumarate, *m*-hydroxyacetophenone and bis(1-hydroxy-4-methylphenyl)methane in carbon tetrachloride and chloroform solutions. All measurements reveal that these compounds exist as "dimers" containing two H-bonds in the geometrically favourable 14- or 16-membered rings, respectively.

PHENOLS in non-polar solvents exhibit very weak intermolecular H-bonding, which usually does not persist down to a concentration 10^{-2} M[1,2]. Recently, unusually strong H-bonding in non-polar solvents was observed with some *m*-nitro- and *m*-methoxyphenols.[3] Although the self-association phenomenom is demonstrable by physical methods, these do not readily reveal the precise nature of the equilibrium involved.

In this work we have encountered several types of phenolic compounds where intermolecular association, presumably dimeric, is unusually persistent.

In the present study we have used, whenever possible, three spectral methods—IR, UV and NMR in conjunction with osmometric measurements of average molecular weight. The self-association of *m*-alkoxy carbonyl phenols reported[3] has been re-investigated in this manner. A new type of strongly associated phenolic compound–ethylcoumarate, is reported.

RESULTS AND DISCUSSION

As can be seen from the IR spectral data (Tables 1–4) that the strong self-association is observed only in compounds with strong proton-donor and proton-acceptor groups in the same molecule (**1**, **7** and **8**) and when a ring of H bonds is spatially favoured. With these molecules, which are capable of considerable freedom of rotation, self-association in solution down to very low concentrations (millimolar level) is observed when they can adopt energetically favourable conformations, i.e. meet requirements, like coplanarity of the aromatic ring and the electron system of the substituents and avoid steric hindrance. Four conformers of *m*-substituted phenols

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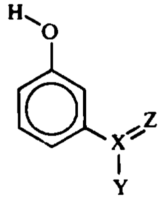
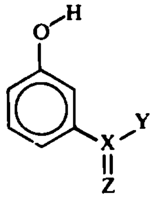
were studied (**a**, **b**, **c**, **d**) but only one (**d**) would permit dimeric association (Fig. a, b) by closure of the 14-membered ring through formation of twin H-bonds to the electron-donating groups (X=Z).



a



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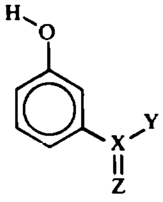

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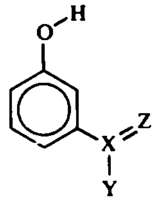


d

The Dreiding models show (Fig. 1a, b) that the interacting groups are within bonding distance, that is the O...O distance is ~3Å.

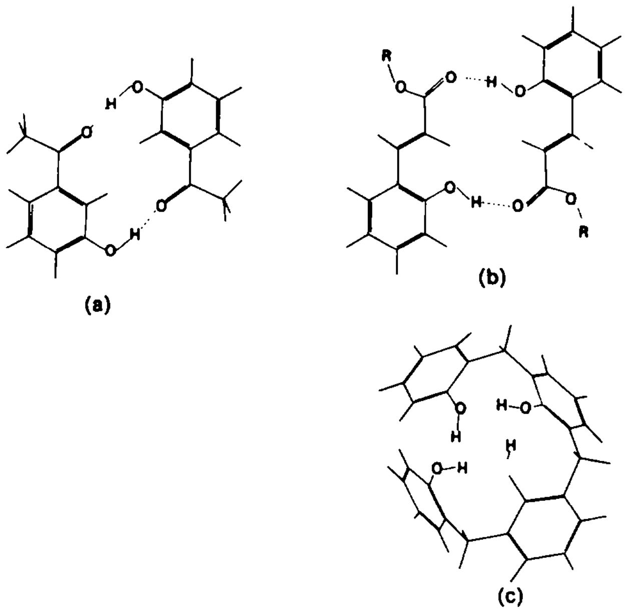
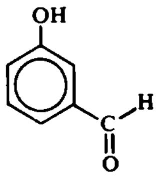


FIG. 1. Planar projection of the Dreiding molecular models of a—1; b—7 and c—9. The dotted lines indicate the H-bonds.

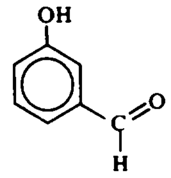
It is evident that steric requirements for H-bonding of the cyclic dimeric type are not fulfilled with *p*-substituted phenols which can associate only in a polymeric way (Table 1).

m-Hydroxyacetophenone (**1**), exists in carbon tetrachloride solution (0·228 mM) mainly as conformation **d**. This is confirmed by the presence of one absorption band, assigned to the carbonyl stretching vibrations. In the case of *m*-hydroxy-benzaldehyde (**2**) two bands (νC=O, 1719 and 1703 cm^{-1}) are observed which can be assigned to the two conformations (**e** and **f**).



$\nu C{=}O$, 1719 cm^{-1}

e



$\nu C{=}O$, 1703 cm^{-1}

f

Probably *m*-hydroxybenzaldehyde exists preferentially in a form (e) which can associate only in a polymeric way. It follows from the association constants (K) of the compounds investigated (Table 1; $K = (\text{dimer})/(\text{monomer})^2$ in 1/mole calculated from the Mecke–Kempter equation),[4] that *m*-hydroxyacetophenone ($K \sim 120$ l. $mole^{-1}$) associates more strongly than does *m*-hydroxybenzaldehyde ($K \sim 40$ l. $mole^{-1}$). This may be due to the stronger proton-acceptor character of the $COCH_3$ group in comparison with the CHO group and also by the presence of various conformations of *m*-hydroxybenzaldehyde as mentioned above. The asymmetrical shape of the band of the OH groups bonded at the concentration of 10 mM in carbon tetrachloride solution (higher frequency side of the band) points on polymeric association. The band at 3450 cm^{-1} can be assigned to the stretching vibrations of OH groups bonded in closed "dimer" (OH . . . O). In the carbonyl region also two concentration-dependent bands are observed in carbon tetrachloride solution of *m*-hydroxyacetophenone (1678 and 1691 cm^{-1}) and ethylcoumarate (1686 and 1715 cm^{-1}).

In the case of ethylcoumarate (7), despite the number of possibilities for conformational freedom inherent in the molecule, the H-bonding is very strong. The high association constant indicates that the s-transoid conformation, (Fig. 1b) is preferable for maintenance of conjugation in the system. In carbon tetrachloride this compound displays association down to 0·3 mM characterized by a broad band at 3298 (νOH bonded) and $\nu C{=}O$ (bonded) at $\sim$1687 cm^{-1}. The free species absorbs at 3607 and $\sim$1715 cm^{-1}. The strength of the association is comparable with that of *m*-hydroxy-acetophenone (1), but is higher ($K \sim 420$ l. $mole^{-1}$).

The bonding shifts in carbon tetrachloride [$\Delta\nu = \nu$OH (free) − OH (bonded) and $\nu C{=}O$ (free) − $\nu C{=}O$ (bonded)] are higher in ethylcoumarate than in *m*-hydroxyacetophenone ($\Delta\nu \sim 150$ cm^{-1} and 35 cm^{-1}). This stronger association in ethylcoumarate must be due to the stronger proton-acceptor nature of the CO_2Et group than the $COCH_3$ group of *m*-hydroxyacetophenone. Also the conjugated system in ethylcoumarate is extended by the H-bonding.

·Compound **8**, (Table 4) shows the presence of three OH absorptions in carbon tetrachloride solution (3609, $\sim$3470 and $\sim$3300 cm^{-1}). In accordance with previous results, the concentration-independent band at $\sim$3470 cm^{-1} has been assigned to an intramolecular OH · · · π-bond.

The band at 3609 cm^{-1} can be assigned to the stretching vibrations of the free OH group whilst the broad concentration-dependent band at $\sim$3300 cm^{-1} is assigned to the closed ring of H-bonds which results from dimeric association.

Compound **9**, (Table 4, Fig. 1c) shows only one concentration-independent band at 3255 cm^{-1} which we assigned to an intramolecular OH · · · OH-bond as illustrated in Fig. 1c. In accordance with the previous IR studies[1,2] this compound shows no tendency to associate, all four H atoms being involved in a closed ring of intramolecular H-bonds.

The strength of association of *m*-hydroxyacetophenone (1) and ethylcoumarate (7) in chloroform solution is reduced and some interaction with the solvent is to be expected (Tables 2 and 3) e.g. broadening and decrease in frequency. There is a marked change in the carbonyl absorptions on passing from carbon tetrachloride to chloroform solution and also the expected lowering in frequency by 4 cm^{-1} and the IR half band width by 6 cm^{-1} in *m*-hydroxyacetophenone (Table 2) and by 15 cm^{-1} in ethylcoumarate (Table 3), respectively. It is surprising that the self-association of ethylcoumarate still exists at the 10^{-4}M concentration in chloroform, although this solvent always solvates the more polar monomer. Ethylcoumarate was also examined in cyclohexane solution (Table 3) and the expected increase in the strength of association was observed.

Whilst the difference in association constant (ΔK) of ethylcoumarate (7) and *m*-hydroxyacetophenone (1) in carbon tetrachloride is relatively high ($\Delta K \sim 300$ l. mole^{-1}) only a small ΔK value in chloroform was observed ($\Delta K \sim 3$ l. mole^{-1}; Tables 2 and 3). A half-band width of bonded OH groups of ethylcoumarate in nujol is extremely small ($\Delta\nu_{\frac{1}{2}} \sim 40$ cm^{-1}; Table 3), which may indicate that in the solid state this compound exists only in the dimeric cyclic form with the two H- bonds in a 16-membered ring.

The UV spectral data of the compounds investigated (Table 5) show distinct changes in molar absorptivities of the bands with concentration, for example, the band with $\lambda_{max} = 325$ mμ, ε, 8400 → 4680 l. mole. cm^{-1}; with ethylcoumarate (10 → 0·016 mM) and the band with $\lambda_{max} = 260$ mμ, ε, 1600 → 190 l. mole^{-1}. cm^{-1}, (2 → 0·0158 mM) in cyclohexane.

Anet and Muchowski[3] observed marked NMR shifts for changing concentrations of methyl-3-hydroxy-4-isopropylbenzoate. In the present work the NMR spectrum

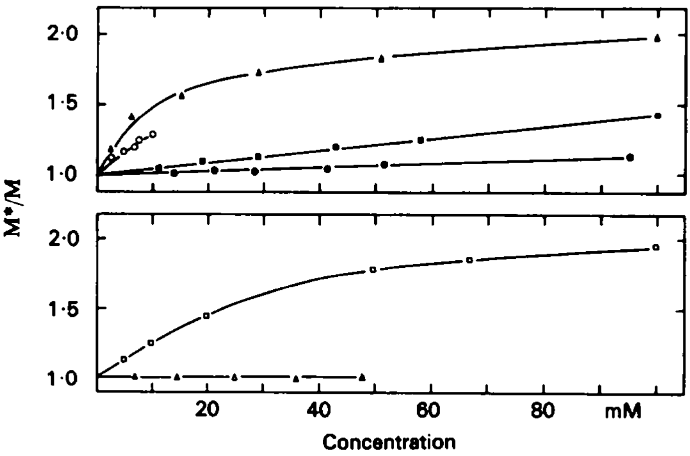


FIG. 2. Plot of the ratio (M*/M) of the apparent (M*) to true (M) molecular weight against molar concentration for solutions in carbon tetrachloride: ▲—7; ○—1; ■—5; □—8; △—9; ●—p-cresol.
In this figure *p*-cresol was included only for comparison.

TABLE 1. HYDROXYL AND CARBONYL ABSORPTIONS OF *m*- AND *p*-SUBSTITUTED PHENOLS IN CCl_4

Compound	Substituent		Conc (mM)	Cell paths (mm)	νOH						Cell paths (mm)	νCO						K 1/mole
					Free			Bonded				Free			Bonded			
	Position	X			ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a	τ	$\Delta\nu_{\frac{1}{2}a}$	ε_a		ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a	ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a	
1	*m*-	—$COCH_3$	10	5·0	3607	19	120	3450^a	89	85	1·0	1691	(12)	340	1678	(11)	200	120
			1	20·0	3607	20	180	3453	(85)	(20)	—	—	—	—	—	—	—	123
			0·228	60·0	3608	20	195	—	—	(5)	20·0	1692	12	535				114
2	*m*-	—CHO	5	5·0	3606	18	175	3480^b	65	25	2·0	1703	8	600				31
												1719	(8)	190				
			0·5	60·0	3607	19	195	(3475)	—	(5)	20·0	1703	8	610				40
												1719	(8)	200				
			0·1	60·0	3607	19	200					—	—	—				
3	*m*-	—OCH_3	100	0·5	3612	18	120	3451	160	20								43
			10	5·0	3612	18	145	3451	—	(5)								40
				20·0	3613	18	155											
4	*p*-	—NO_2	1	20·0	3596	24	230	(3377)	—	20								10
			0·1	60·0	3597	25	260											
5	*p*-	—OCH_3	100	0·5	3618	19	140	3455	180	30								7
			10	5·0	3619	18	170	(3455)	—	(10)								10
			1	20·0	3619	18												
6	*p*-	—CHO	1	20·0	3600	22	230				5·0	1703^c	15	500				

ν and $\Delta\nu_{\frac{1}{2}a}$ are in cm^{-1}; ^{a} overtone at 3365 cm^{-1}, $\varepsilon_a = 35$; ^{b} overtone at $\sim$3400 cm^{-1}; sh-shoulder at $\sim$1693 cm^{-1}; ^{c} asymetrical bands; Values in parenthesis are approximate; in all cases the highest possible concentration was used; *p*-Hydroxy-*o*-acetphenone was not included as it was only sparingly soluble in CCl_4.

Table 2. Hydroxyl and carbonyl absorptions of *m*-hydroxy acetophenone in $CHCl_3$

Conc (mM)	Cell paths (mm)	νOH						Cell paths (mm)	νCO			K
		Free			Bonded							
		ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a	ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a		ν	$\Delta\nu_{\frac{1}{2}}$	ε_a	
500	0·05	3595	41	65	(3385)[a]	262	105	0·05	1679	26	440	9
100	0·5	3594	36	105	3420[b]	235	55	0·11	1679	23	430	10
50	1·0	3595	32	130	3420[b]	236	40	0·11	1682	21	430	9
10	2·0	3595	31	155	3420[b]	—	10	1·0	1681	18	430	9
2	5·0	3596	32	175					—	—	—	

[a] assymetrical band; [b] shoulder at 3350 cm^{-1}.

— not measured; ν and $\Delta\nu_{\frac{1}{2}}$ are in cm^{-1}; Values in parenthesis are approximate.

of *m*-hydroxyacetophenone in $CDCl_3$ was too complicated to permit the small, but definite changes in the aromatic CH region, to be interpreted. However, in ethylcoumarate, it was possible to detect small, but significant changes with concentrations in the chemical shift values for the ethylenic protons (60 Mc/s spectrum; Table 6). In the range of concentrations (600 → 150 mM), the resonance signal of the OH proton in $CDCl_3$ was shifted from 2·43 to 3·17 τ and the same was observed for ethylenic protons/H_a from 1·88 to 1·92 τ and H_b from 3·24 to 3·25 τ. This is in accordance with the IR spectral data of this compound.

A plot of average molecular weight observed (M^*) over true molecular weight (M), (M^*/M) of the compounds investigated against molar concentration, determined by osmometry, reveals the dimeric association in the case of compounds **1**, **7** and **8**. Data on compound **5** indicate a polymeric association whilst the results obtained with compound **9** reveal intramolecular H-bonding. All these results are in accord with the spectral data of the compounds investigated. A similar graph is also observed by plotting the values of the molar absorptivities of (νOH) bonded against molar concentrations.

EXPERIMENTAL

IR spectra were recorded with a Unicam S.P.100 double beam infrared spectrophotometer equipped with an S.P.130 NaCl prism—grating double monochromator [3000 lines per inch (2150–3650 cm^{-1}) and 1500 lines per inch (650–2150 cm^{-1}] operated under vacuum. The calibration was checked against the spectrum of water after each group of measurements. The OH and CO absorptions were scanned at 4·6 and 8·0 cm^{-1} per min, respectively. Frequency measurements for the free and interbonded OH and CO bands are believed to be accurate to ±1 cm^{-1}. The intensities were measured on bands of not less than 0·05 absorbance. The theoretical spectral slit width—computed from tables supplied by Unicam Instruments Ltd., was 5·5 cm^{-1} at 3600 cm^{-1}, 4·5 cm^{-1} at 3350 cm^{-1} and 3·4 cm^{-1} at 1700 cm^{-1}. The apparent half-band widths, $\Delta\nu_{\frac{1}{2}a}$ are quoted to the nearest integer; where necessary they were determined by reflection of the undisturbed wings of the unsymmetrical bands. Intensities are given as apparent molar absorptivities, ε_a, (l. $mole^{-1}$ cm^{-1}) rounded to the nearest 5 units and measured from a solvent–solvent base line superimposed on the record of the spectrum of the solution.

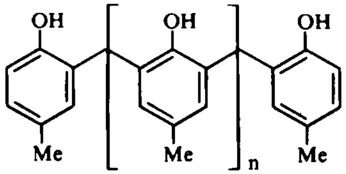
Association constants, K = (dimer)/(monomer)^2 in l./mole, were calculated from the Mecke–Kempter equation,[4] $K = 1/ac(1 - \sqrt{a})$, where a is the value of the ratio of the apparent molar absorptivity of the OH band at concentration c (mole/l.), to its value at infinite dilution. The values of K given by this equation are only very approximate as some of assumptions made in its derivation are not applicable in the present situation. Nevertheless, the given values of K serve as a guide to the degree of association.

TABLE 3. HYDROXYL AND CARBONYL ABSORPTIONS OF ETHYL COUMARATE (COMPOUND 7) IN VARIOUS SOLVENTS

Solvents	Conc (mM)	Cell paths (mm)	νOH						Cell paths (mm)	νCO						K[e]
			Free			Bonded				Free			Bonded			
			ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a	ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a		ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a	ν	$\Delta\nu_{\frac{1}{2}a}$	ε_a	
Cyclohexane	13	1·0	3614	(20)	40	3305	245	125	1·0	1724	18	160[a]	1689	18	565	
	6·5	1·0	3615	(20)	45	3305	240	120	1·0	1724	17	215[a]	1689	18	555	
	3·25	1·0	3615	(20)	60	(3305)	—	90	1·0	1725	17	245[a]	1688	18	520	
Carbon tetrachloride	107	0·5	3606	28	25	3300[b]	248	130	0·11	1714	(28)	140	1686[c]	22	590	420
	21·4	2·0	3607	22	50	3298[b]	245	110	0·5	1714	(25)	150	1687[c]	21	550	420
	2·14	20·0	3607	21	115	3295[b]	245	60	5·0	1715	(23)	390	1687[c]	22	330	437
	1·71	20·0	3606	22	125	3295[b]	245	50	5·0	1714	22	490	1687[c]	22	220	410
	0·355	60·0	3608	22	160	(3295[b])	—	20	20·0	1716	22	580	1686[c]	—	130	416
Chloroform	500	0·11	3592	42	55	3326	257	100								12
	100	0·5	3593	38	90	3326	284	60	0·11	1688[d]	42	525				13
	50	1·0	3592	37	110	3325	284	45	0·11	1702	38	520				13
	10	2·0	3593	38	140	3325	—	10	1·0	1704	31	520				12
	2	5·0	3593	38	160	—	—		2·0	1704	30	525				

ν and $\Delta\nu_{\frac{1}{2}a}$ are in cm^{-1}. Values in parenthesis are approximate. [a] shoulder at 1679 cm^{-1}, (ε_a = 333,339 and 333, respectively); [b] asymmetrical band, shoulder at 3390 cm^{-1}; [c] shoulder at 1676 cm^{-1}; [d] asymmetrical band. In Nujol $\nu_{(OH)(bonded)}$ = 3380 cm^{-1}, $\Delta\nu_{\frac{1}{2}}$ = 40 cm^{-1}. [e] K = [dimer]/[monomer]^2. l/mole.

TABLE 4. HYDROXYL ABSORPTIONS OF NOVOLAKS



Compound No.	n	Conc (mM)	Cell path (mm)	νOH Free ν	Free $\Delta\nu_{\frac{1}{2}a}$	Free ε_a	"Intra" bonded ν	"Intra" bonded $\Delta\nu_{\frac{1}{2}a}$	"Intra" bonded ε_a	"Inter" bonded ν	"Inter" bonded $\Delta\nu_{\frac{1}{2}a}$	"Inter" bonded ε_a
8	0	100	0·11	3609	—	(30)	(3468)	—	—	3292	272	240
		67	0·11	3609	—	(41)	(3468)		—	3292	270	208
		50	0·5	3609	—	65	(3463)	—	—	3292	270	178
		20	1·0	3609	—	88	(3468)	—	—	3298	270	160
		10	2·0	3608	—	120	(3468)	—	—	3315	270	126
		5	5·0	3608	26	138	3468	82	—	3322	—	84
		1	20·0	3608	27	180	3471	86	140	(3326)	—	42
		0·5	20·0	3608	27	210	3474	86	148	(3326)	—	30
9	2	48	0·11				3255	248	475			
		36	0·11				3255	248	475			
		14·4	0·5				3256	240	470			
		7·2	1·0				3255	242	470			
		3·6	2·0				3255	245	470			
		0·36	20·0				3256	245	470			

ν and $\Delta\nu_{\frac{1}{2}a}$ are in cm^{-1}, values in parenthesis are approximate, — not measured.

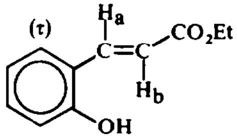
TABLE 5. UV ABSORPTION SPECTRAL DATA FOR ETHYL COUMARATE AND *m*-HYDROXYACETOPHENONE (IN CYCLOHEXANE)

Compound	Conc. (mM)		λ(mμ) 267	280	307	317	325
Ethyl coumarate[a]	10·0	ε	16300	16200			8400
	1·0		15500	14300	6300	8000	6800
	0·2		15100	13800	6700	8000	5500
	0·1		15000	13600	6900	8100	5000
	0·016		14800	12800	7600	8640	4680
			244	250	260	300	
m-Hydroxyacetophenone[b]	2·0	ε	6600	7200	1600	2100	
	1·0		8000	7000	1300	2100	
	0·1		8800	6800	400	2100	
	0·0158		9280	5900	190	2080	

[a] cell paths (in mm): 0·1, 1·0, 5·0, 10·0 and 60·0.

[b] cell paths (in mm): 0·5, 1·0, 10·0 and 60·0.

TABLE 6. NMR DATA FOR ETHYLCOUMARATE



Solvent	Conc. (mM)	H_a		$CHCl_3$	H_b		OH	Ar-H
$CDCl_3$	600	1·74	2·02	2·74	3·21	3·48	2·43	2·4 → 3·2
	300	1·76	2·04	2·75	3·23	3·49	2·80	2·4 → 3·2
	150	1·78	2·06	2·74	3·25	3·51	3·17	2·4 → 3·2
$CDCl_3 + D_2O$	600	1·76	2·02	2·73	3·24	3·51	5·34	2·4 → 3·2
	300	1·78	2·04	2·73	3·24	3·51	5·36	2·4 → 3·2
	150	1·79	2·06	2·73	3·25	3·52	5·37	2·4 → 3·2
	75	1·81	2·08	2·73	3·26	3·53	5·38	2·4 → 3·2

$J_{ab} \sim 16$ c/s; $-O-\underset{\substack{5\cdot7\\ \text{Quartet}}}{\underline{C}H_2}-\underset{\substack{8\cdot7\\ \text{triplet}}}{\underline{C}H_3}$ $J \sim 8$ c/s

U V spectra of compounds 1 and 7 were recorded with a Unicam S.P. 800 double beam spectrophotometer over a wide range of concentrations in cyclohexane.

NMR spectra were obtained with a Perkin–Elmer, model R-10 spectrometer (60 Mc/s) with TMS as internal standard in $CDCl_3$.

Osmometry. The mol wt measurements were made with a Mechrolab, model 301 A vapour pressure osmometer precalibrated with benzil in CCl_4 over a wide range of concentrations in CCl_4.

Materials. Analar CCl_4 and cyclohexane (spectroscopic grade) were used without further purification. Analar $CHCl_3$ was dried several times by passage through a column of blue silica gel before direct use.

Compound 7 was kindly supplied by Dr. D. Austin and contained less than 1% of *cis*-isomer. Other samples were of analytical purity, and the physical constants agreed well with those in the literature.

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