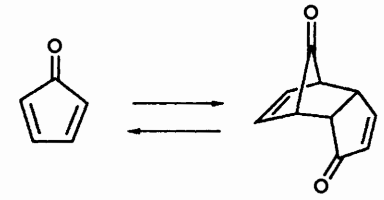
Steric Effects in the Dimerization of 2,5-Dialkyl-3,4-Diphenylcyclopentadienones

Hilton M. Weiss
Department of Chemistry, Bard College, Annandale-on-Hudson, NY 12504, USA

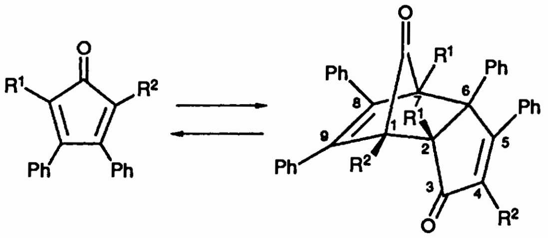
Some novel methyl- and ethyl-substituted dimers of 2,4-diphenylcyclopentadienones have been detected. Their enthalpies of dimerization have been determined and compared with values calculated by molecular mechanics. The steric demands of this dimerization have thus been clarified.

An on-going challenge of cyclopentadienone chemistry has been the understanding of the factors which control dimerization.[1] The parent compound **1** is known[2] to form the dimer **2** irreversibly above 77 K, while the tetraaryl derivatives are known only as the monomers.[1a]



1 **2**

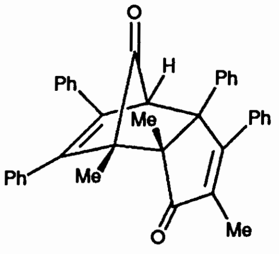
Other sterically-hindered derivatives are also reported to exist as monomers[3] while a very small number of cyclopentadienones have been reported to exist in a reversible equilibrium[1] at reasonable temperatures. The most heavily studied group of these are the 2,5-dialkyl-3,4-diphenyl derivatives (**3**) of which few dimers (**4**) have been reported. Equilibrium constants have not been determined for any of these dimerizations.



3 **4**

a $R^1 = R^2 = Me$
b $R^1 = R^2 = Et$
c $R^1 = Me$; $R^2 = Et$

The dimethyl derivative **3a** has been reported to exist as 95% dimer[4] at room temperature, while the diethylcyclopentadienone **3b** is reported to form no dimer under any conditions.[1b] This difference may seem surprising in the light of the similarity of the *A* values[5] for methyl (1.74) and ethyl (1.75) groups.* The known dissociating dimer **4c** exists in solution as similar amounts of monomer and dimer depending upon temperature and concentration. The structure of this dimer has been shown[4] to have the larger ethyl groups in the C(1) and C(4) positions, suggesting that steric congestion at C(7) is responsible for the inability of the tetraethyl dimer to form. In support of this idea Fuchs[6] has synthesized the trimethyl dimer **5**, and has shown that the single hydrogen resides in the C(7) position. Further, he has shown that this dimer does not dissociate into its constituent monomers and suggests that this stability results from the lack of an alkyl substituent in the C(7) position.



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In an effort to probe the situation further, we have synthesized the previously mentioned (di)cyclopentadienones **3** and **4** and have analysed their ^1H NMR spectra ($CDCl_3$; 400 MHz) over a range of temperatures and concentrations.

Results and Discussion

Tetramethyl Dimer **4a** (Me4D).—2,5-Dimethyl-3,4-diphenylcyclopentadienone (**3a**) was dissolved in $CDCl_3$ at a variety of concentrations and equilibrated at temperatures ranging from 4–70 °C. NMR spectra at these temperatures clearly showed five well-separated peaks that have been assigned[4] to the monomer and to the four different methyl groups of the dimer [Fig. 1(*a*)]. The relative concentrations of monomer and dimer were determined by comparing peak heights rather than peak areas because many subsequent analyses had to be made on minor peaks which could be discerned above the baseline, but whose integrals were too sensitive to the tailing of neighbouring peaks at high amplification. The heights of the four methyl peaks were, however, not identical to each other; this was traced to the low T_1 lifetimes of these resonances, especially the peak associated with the methyl group at C(2). Because of this, the relative concentrations of monomer and dimer were determined from the peak heights of the monomer methyl signal and the C(4) methyl signal. To confirm the validity of this method, equilibrium constants were also determined from peak areas as well as from spectral analysis. Results from all methods were comparable. Plotting ln K *vs.* $1/T$ provided ΔH^0 and ΔS^0 values for this equilibrium (see Fig. 2 and entry 1 in Table 1).

Tetraethyl Dimer **4b** (Et4D).—By equilibrating concentrated solutions (1–2 mol dm^{-3}) of 2,5-diethyl-3,4-diphenylcyclo-

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* *A* represents the steric bulk of a group, as measured by its (free energy) preference for the equatorial position on a cyclohexane ring. See *e.g.* N. Isaacs, *Physical Organic Chemistry*, Longman, Essex, 1987, p. 313.

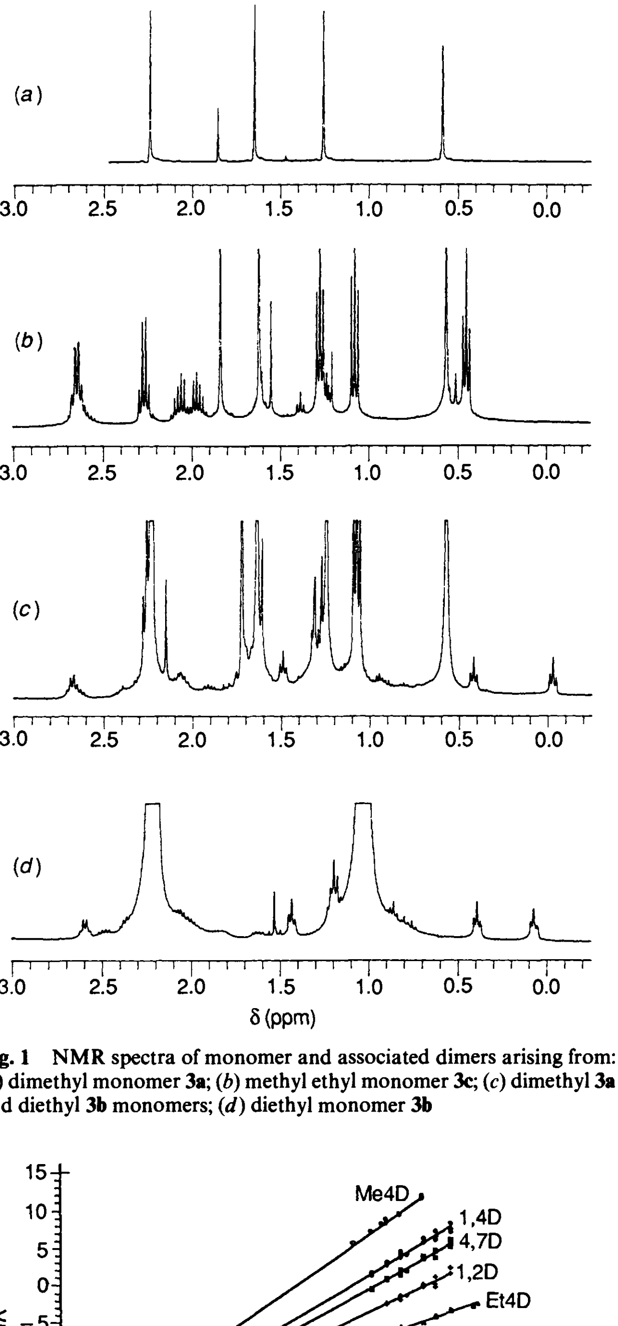


Fig. 1 NMR spectra of monomer and associated dimers arising from: (*a*) dimethyl monomer **3a**; (*b*) methyl ethyl monomer **3c**; (*c*) dimethyl **3a** and diethyl **3b** monomers; (*d*) diethyl monomer **3b**

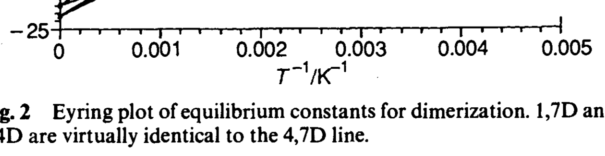
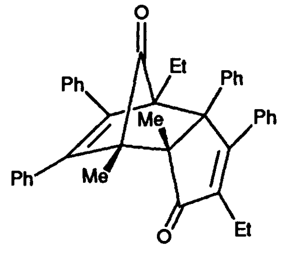


Fig. 2 Eyring plot of equilibrium constants for dimerization. 1,7D and 2,4D are virtually identical to the 4,7D line.

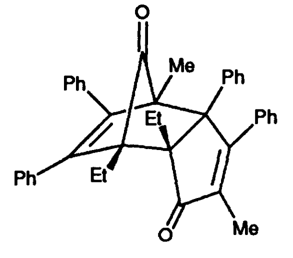
pentadienone (**3b**) in $CDCl_3$ at −30 °C and then quickly warming the solutions to 17 °C, we were able to obtain NMR spectra showing the elusive tetraethyl dimer as four clean triplets of similar size [Fig. 1(*d*)]. When these solutions were equilibrated at higher temperatures, the proportion of dimer decreased but could still be detected by increasing the signal amplitude. By comparing the average peak heights for these triplets [the triplet arising from the C(7) ethyl group was not included in this averaging because it was distorted by the methylene peak from the monomer] with the peak height for the ethyl triplet of the monomer, equilibrium constants were obtained over a range of temperatures. The triplet peaks were selected for analysis because they were clean, identifiable and of similar size. Many of these spectra were also amenable to peak area analysis and similar results were found from both methods. Analysis of the resulting data gave the value listed in Table 1 (entry 8). Since the entropies of dimerization for the tetraethyl and tetramethyl dimers were expected to be virtually identical, these values were averaged and used to define the intercepts for these plots.

When the NMR spectra of the tetraethyl derivatives were taken at their lower (equilibrated) temperatures, the ethyl triplets lost some resolution, presumably due to hindered rotation. This was particularly noticeable for the C(2) and C(7) triplets at −15 °C and reflects the greater steric constaints felt by these ethyl groups.

Diethyl Dimer.—When solutions of 2-ethyl-5-methyl-3,4-diphenylcyclopentadienone (**3c**) were equilibrated, it was easy to see [Fig. 1(*b*)] the triplets due to the monomer as well as those of the reported 1,4-diethyl dimer **4c** (1,4D). Also evident in the spectra was a clean triplet at 1.39 ppm which was assigned (*vide infra*) to an ethyl group occupying the C(7) position of the dimer. This result was surprising in that the C(7) position had been assumed to be the most sterically hindered. This peak was assumed to arise from the 4,7-diethyl dimer **6** present in the mixture. A similar size triplet could also be discerned just upfield of the major C(4) triplet peak and was notably absent from the region where a C(2) ethyl triplet would be expected. That these peaks came from a dimer was confirmed by their increased intensity at lower temperatures. The C(1) and C(2) methyl singlet peaks could also be seen at 1.2 and 0.5 ppm, respectively.



6 (4,7D)



7 (1,2D)

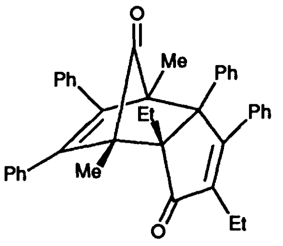
In an effort to find an ethyl group at C(2), the spectra were amplified and, in the colder, more concentrated solutions, the C(2) triplet could be seen at −0.1 ppm. This was taken as evidence for the 1,2-diethyl dimer **7** which was calculated by molecular mechanics (*vide infra*) to be 5.9 kJ mol^{-1} more stable than the alternately possible 2,7-diethyl isomer.

The relative peak heights for the monomer and the three dimers were used to determine the equilibrium constants for each of the dimers at different temperatures. From these data, ΔH^0 and ΔS^0 values were determined. Since each of these dimers arises from one of four possible combinations of the unsymmetrical monomer, it was assumed that each dimerization had the same ΔS^0 value and that this value was 11.5 J mol^{-1} K^{-1} more negative than that for the dimerization of the symmetrical monomers ($\Delta\Delta S^0 = R \ln \frac{1}{4} = -11.5$ J mol^{-1} K^{-1}). The experimental $\Delta\Delta S^0$ value was −14.2 J mol^{-1} K^{-1}. This assumption provided a more dependable comparison of the slopes of these lines than would otherwise be possible. Any errors from the correct intercepts would cause similar errors in all slopes and the differences in the slopes (and therefore the ΔH^0 values) would be minimal. Based on these assumptions, the ΔS^0 values were calculated to have errors of < 1% while the six ΔH^0 values

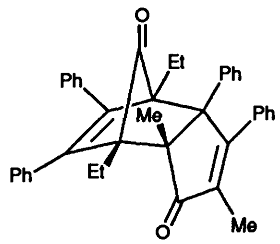
Table 1 Enthalpies of dimerization/kJ mol^{-1}

Entry	Dimer[b]	ΔH^0[c] (experimental)	$\Delta H^0 - \Delta H^0_{Me4D}$	ΔH^0 str[d] (calc.)	$\Delta H^0 - \Delta H^0_{Me4D}$ (calc.)
1	Me4D	−76.5	—	604.4	—
2	1,4D	−65.9	10.6	611.6	7.2
3	2,4D	−61.5	15.0	621.6	17.2
4	1,7D	−60.8	15.7	625.5	21.1
5	4,7D	−60.7	15.8	616.3	11.9
6	1,2D	−52.5	24.0	631.6	27.2
7	2,7D	—	—	637.4	33.0
8	Et4D	−38.2	38.3	644.5	40.1

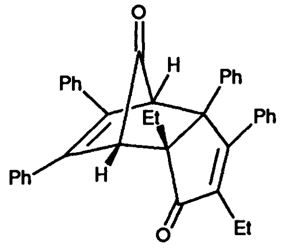
[a] Based on $\Delta S^0 = -178.4$ J mol^{-1} K^{-1} for both homosubstituted dimers and $\Delta S^0 = -190.0$ J mol^{-1} K^{-1} for all diethyl dimers. [b] Numbering system denotes positions of the two ethyl groups. [c] Calculated from the slopes in Fig. 2. [d] Strain energy calculated from molecular mechanics.



8 (2,4D)



9 (1,7D)



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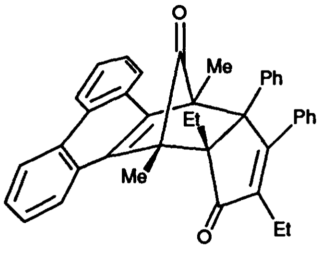

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had <5% errors. The results of these calculations are shown in Table 1 (entries 2, 5 and 6).

Other diethyl dimers could also be produced by preparing a concentrated solution of the dimethyl cyclopentadienone **3a** containing a smaller concentration of the diethyl cyclopentadienone **3b**. Since the concentration of the tetraethyl dimer was known to be very small in these solutions, the presence of ethyl triplets in the appropriate regions was ascribed to the cross dimers **8** and **9**. NMR spectra of these solutions showed triplet peaks of similar size in all four expected regions [Fig. 1(*c*)]. To show that these four signals were arising from similar amounts of the two cross dimers rather than the tetraethyl dimer **4b**, we calculated that the expected peak heights for the latter compound could not be more than 10% of the peak heights found experimentally. Furthermore, when these samples were analysed at −15 and −30 °C, there was, unlike the tetraethyl dimer, very little loss of resolution in the ethyl triplets. The most convincing evidence for this interpretation comes from the fact that, although these chemical shifts are somewhat temperature dependent, the C(2) ethyl triplet consistently appears at 0.1 ppm higher field in the 2,4-diethyl dimer than in the tetraethyl dimer. In addition, a small broadened peak for the C(2) triplet of the tetraethyl dimer could also be identified in the coldest cross-dimer mixtures. Equilibrium constants for the formation of each of these dimers were calculated and plotted. The extrapolated intercepts were averaged with the results from the other diethyl dimers because, here too, only one of four different combinations will lead to the dimer in question (one of two possible monomers acting as the diene and one of two possible monomers as the dienophile). The results are given as entries 3 and 4 of Table 1.

Assignment of the Triplet Peaks.—Cold, concentrated solutions of 2,5-diethyl-3,4-diphenylcyclopentadienone showed clear triplets at 1.43, 1.19, 0.39 and 0.07 ppm [Fig. 1(*d*)]. These could be assigned to specific ethyl groups by comparison with a variety of other dimers as follows.

The major dimer formed from 2-ethyl-5-methyl-3,4-diphenylcyclopentadienone (**4c**) showed its methyl group singlets in the C(2) and C(7) regions of the tetramethyl dimer and the strong ethyl triplets at 1.19 and 0.39 ppm could therefore be attributed to ethyl groups located at the C(1) and C(4) positions. This compound also had the allylic methylene hydrogens of the C(4) ethyl group appearing at 2.5 ppm. Irradiation of this quartet caused the collapse of the triplet at 1.39 ppm identifying it as the C(4) ethyl triplet. The triplet at 0.39 ppm was therefore assigned to the C(1) ethyl group. The non-dissociating 2,4-diethyl derivative **10** was synthesized and was also found to have its C(4) methylene at 2.5 ppm and its C(4) triplet at 1.19 ppm. The C(2) ethyl group, unfortunately, had its triplet at 0.9 ppm unlike any of the triplets seen for the tetraethyl dimer. This was presumably due to a unique conformation available to the C(2) ethyl group in the absence of an alkyl group at C(1). The C(2) methylene, however, could be seen as a pair of multiplets centred at 1.1 and 1.55 ppm. This proved useful in decoupling the C(2) ethyl triplets in other spectra. This could be done most clearly with the 2,4-diethyl derivative **8** present in the solution of dimethyl and diethyl cyclopentadienones. These solutions could be irradiated at 1.1 ppm and the high field triplet at −0.1 ppm could be seen to collapse. That we were irradiating the C(2) methylene resonance is supported by the fact that the C(2) methyl signal of the tetramethyl derivative is the only methyl group to appear upfield of 1.1 ppm. Thus the highest field triplets of the various dimers can be assigned to the C(2) ethyl group whose methyl is held directly over, and is shielded by, the C(6) phenyl ring (see Fig. 3). The 2,4-diethyl phenanthrene derivative **11** also showed its C(2) ethyl triplet at −0.20 ppm confirming this assignment. It might be noted that the C(4) ethyl triplet in this compound was also strongly shifted upfield (to 0.07 ppm) as a result of its proximity to the central ring of the phenanthrene fragment. Similar shifts have been reported by other authors.[7] The methyl singlets at C(1) and C(7) appeared at 2.05 and 2.20 ppm and require a reassignment of the peaks previously reported for the tetramethyl derivative.[8] The proximity of the C(2) methylene proton (2.3 ppm) to the C(1) methyl protons (2.05 ppm) was confirmed by an NOE experiment.

The remaining triplet at 1.43 ppm in the spectrum of the tetraethyl dimer could then be assigned to the C(7) ethyl group. Its low-field position is assumed to derive from the deshielding effect of the C(8) phenyl ring that it lies alongside. One of the C(7) methylene protons is similarly deshielded and can be detected at 2.5 ppm.

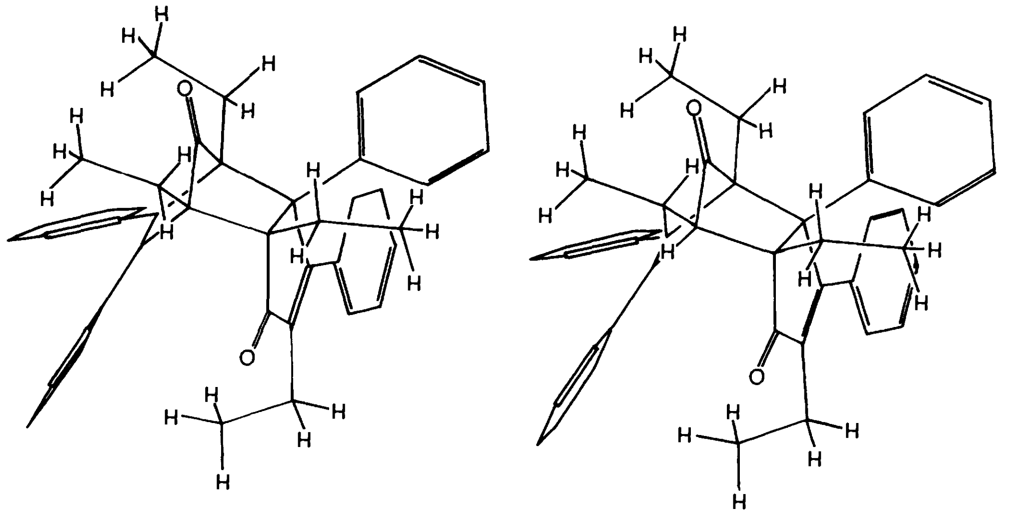

Fig. 3 Stereoplot of **4b** (Et4D) showing the preferred conformation for the ethyl groups

Calculations.—It was expected that molecular mechanics would be particularly suited to this study because very similar ground-state structures having few conformational possibilities are involved. Calculations were performed on each of the symmetrical dimers as well as the six possible diethyl dimers. The strain energies resulting from the introduction of the ethyl groups was calculated for each isomer by subtracting the strain energy of the tetramethyl dimer from each of the other results. These values were compared with the experimental increase in enthalpy of dimerization for each of the substituted dimers. The calculated strain energies of the dimers were within 20% of the experimental values (on average) including the tetraethyl dimer. When the steric strain of the monomers were included in these calculations, the results were less satisfying. The calculation of heats of dimerization from the heats of formation of monomer and dimer were off by an order of magnitude.

Conclusions

It is apparent that the (overrated) instability of the tetraethyl dimer comes as much from the crowding of the combined substitution at C(1) and C(2) as from the crowding at C(7). To wit, the enthalpy of dimerization for the 1,7-diethyl dimer is *ca.* 8 kJ more exothermic than that of the 1,2-diethyl dimer. If the small triplet arising from the C(2) ethyl group derives from the 2,7-diethyl dimer instead of the 1,2-diethyl isomer, the relative steric interference of the 1 and 2 positions would be even more pronounced. It might also be noted that the extra strain energy of the 1,2-diethyl dimer plus the extra strain energy of the 4,7-diethyl dimer approximates the extra strain energy of the 1,2,4,7-tetraethyl dimer and that the 1,2-diethyl compound contributes 60% of this strain.

The reason for the synergistic destabilization effect of the adjacent ethyl groups at C(1) and C(2) appears to come from their enforced *anti* conformation which drives both ethyl groups into the regions occupied by phenyl rings at C(6) and C(9). These steric constraints prevent the methylene groups from attaining the optimal conformations available to the methyl-substituted derivatives.

Experimental

M.p.s are uncorrected. IR spectra were recorded on a Perkin-Elmer 1600 FTIR spectrophotometer. NMR samples were sealed in 5 mm NMR tubes or in coaxial 0.02 cm^3 tubes and the spectra were obtained with a Varian XL-400 spectrometer operating at 400 MHz. Chemical shifts were measured relative to a methylene dichloride internal standard, and are reported as downfield relative to $(CH_3)_4Si$. Coupling constants are given in Hz. Equilibration of the mixed dimers at the coldest temperatures required two months and equilibrium was approached from higher and lower temperatures.

The various diphenylcyclopentadienones were synthesized according to published procedures.[1b,c] They were purified by fractional vacuum sublimation and, in the case of the diethyl monomer, by flash chromatography (elution with hexanes). This monomer was stored in a desiccator at −30 °C until ready for use.

Molecular mechanics calculations were performed with the program MMPM as supplied by Serena Software.[9] Energy minimizations were carried out using default values throughout. Structures were minimized until the energy differences between successive iterations were <0.13 kJ mol^{-1}. Calculations were performed on the three possible rotational conformations of each ethyl group [two conformations of the C(4) ethyl group] of monoethyl dimers and on many conformational combinations of the diethyl dimers. The ethyl groups at C(1), C(2) and C(7) showed a clear preference for one conformation (Fig. 3) whereas the C(4) ethyl group generally showed a slight preference for the *endo* position.

Cross Dimer **10**.—This non-dissociating diethyl dimer was prepared in a manner analogous to that reported[6] for the corresponding dimethyl derivative. M.p. 126–128 °C; ν_{max}(Nujol)/cm^{-1} 1774 and 1685 (C=O); $\delta(CDCl_3)$ 7.4–6.7 (m, 20 H, Ar), 4.35 [s, 1 H, C(7)], 3.67 [s, 1 H, C(1)], 2.45 (q, *J* 7.3, 2 H, 4-CH_2), 1.58 (m, 1 H, 2-CH_2), 1.09 (m, 1 H, 2-CH_2), 1.18 (t, *J* 7.3, 3 H, 4-Me) and 0.89 (t, *J* 7.1, 3 H, 2-Me).

Cross Dimer **11**.—This slightly dissociating phenanthrene dimer was prepared in a manner analogous to that reported[8] for the corresponding tetramethyl derivative. M.p. 190 °C (decomp.); ν_{max}(Nujol)/cm^{-1} 1765 and 1681 (C=O); $\delta(CDCl_3)$ 8.7–6.7 (m, 18 H, Ar), 2.31 (m, 1 H, 2-CH_2), 2.10 (s, 3 H, 7-Me), 2.06 (m, 1 H, 4-CH_2), 2.01 (s, 3 H, 1-Me), 1.88 (m, 1 H, 4-CH_2), 1.24 (m, 1 H, 2-CH_2), 0.05 (t, *J* 7.3, 3 H, 4-Me) and −0.20 (t, *J* 7.3, 3 H, 2-Me).

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