Hydrocarbons

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Tetravinylethylene**

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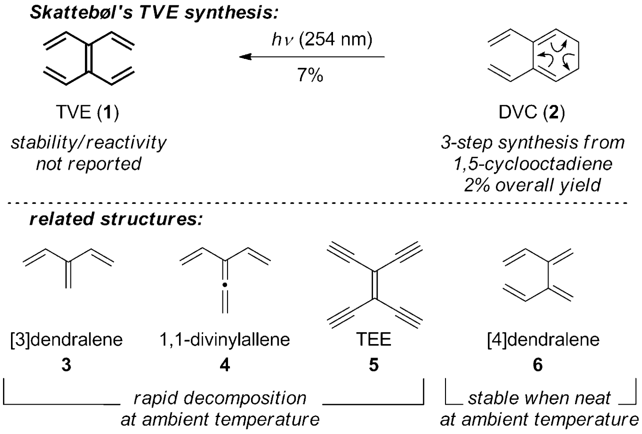
Abstract: *The first four-fold cross coupling reaction involving alkenic partners leads to the title hydrocarbon on multi-gram scale in one step from commercially available precursors. In stark contrast to its close structural relatives, tetravinylethylene is a remarkably robust, bench-stable compound. The π-bond rich hydrocarbon is shown to undergo one-pot sequences of pericyclic reactions leading to the formation of complex systems with four new rings, seven C–C bonds and ten stereocenters with a very high level of stereoselectivity. Insights into the reactivity of this and related systems is provided using the accurate composite ab initio MO G4(MP2) method.*

Tetravinylethylene (TVE, **1**, Scheme 1) is the smallest symmetrical alkene-based structure containing both through-conjugation and cross-conjugation. Very little is known about the structure, stability and reactivity of TVE (**1**) or its analogues. The closest structural relatives of TVEs—namely the linear polyenes,[1] [*n*]dendralenes,[2] and tetraethynylethylenes[3]—have been studied extensively and their value in efficient complex molecule synthesis and new materials has been established. In contrast, there is a conspicuous absence of studies involving TVEs. There exists only one reported synthesis of the parent hydrocarbon, an ingenious approach by Skattebøl and co-workers that allows access to the hydrocarbon in a 0.1% overall yield through a linear sequence of four steps from 1,5-cyclooctadiene.[4] The synthesis features the photolytic 6π-electrocyclic ring opening of 2,3-divinyl-1,3-cyclohexadiene (DVC, **2**) as a key step.



stability/reactivity not reported

3-step synthesis from 1,5-cyclooctadiene 2% overall yield

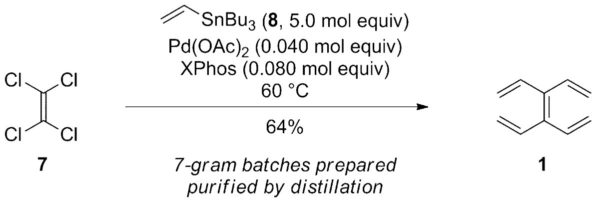
rapid decomposition at ambient temperature

stable when neat at ambient temperature

Scheme 1. TVE (**1**): reported synthesis and related structures.

No group has reported a duplication—or extension—of Skattebøl's 1966 synthesis, a fact that we attribute to the perception that the synthesis is not practically viable. Perhaps TVE (**1**) is also assumed to be unstable and therefore difficult to handle. While the Skattebøl publications offer no information on the stability of the hydrocarbon, several closely related structures, for example [3]dendralene **3**,[5] 1,1-divinylallene **4**,[6] and tetraethynylethylene (TEE, **5**)[7] cannot be stored neat at ambient temperature. On the other hand, [4]dendralene **6**[8] shows no sign of decomposition under these conditions.

Our experience with dendralenes[9] gave us the confidence to adopt a bold synthetic approach. Our optimized, one-step synthesis of tetravinylethylene (TVE, **1**), commencing with commercially available starting materials **7** and **8**, and allowing access to the hydrocarbon in multi-gram quantities, is depicted in Scheme 2. This represents, to our knowledge, the first four-fold cross-coupling reaction involving alkenic partners.[10,11] We also witnessed the formation of TVE (**1**) with Suzuki–Miyaura and Kumada couplings but a four-fold Stille coupling employing Buchwald's XPhos ligand[12] was superior.



Scheme 2. Four-fold cross-coupling approach to TVE (**1**).

The four-fold Stille coupling shown in Scheme 2 is best performed solvent-free, which allows the product to be isolated by reduced pressure distillation directly from the reaction mixture, without recourse to work-up. Tri-*n*-butyltin chloride is easily recycled by simply exposing the residue from the distillation to vinylmagnesium bromide, thereby re-

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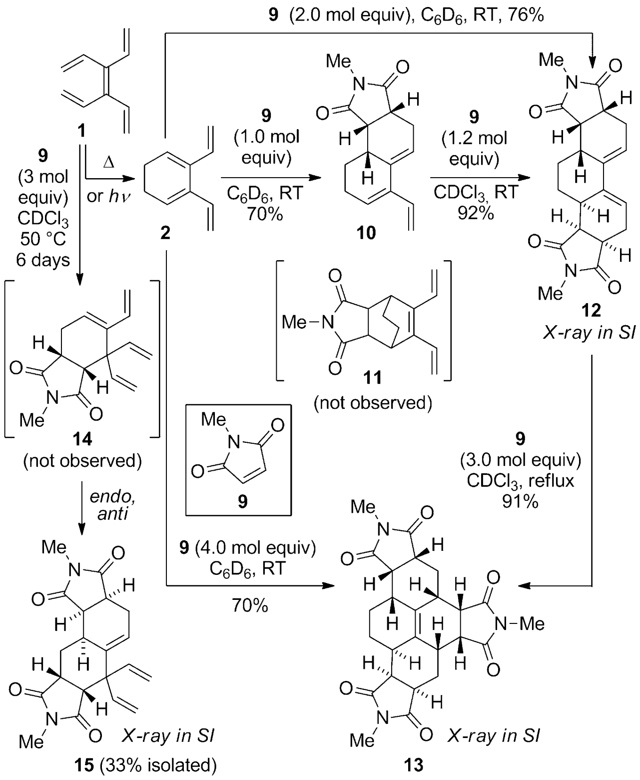
generating vinyltri-*n*-butylstannane (**8**) for use in a subsequent reaction. This four-fold Stille coupling reaction has been performed to generate batches of TVE (**1**) on scales of up to 7 g.[13]

We were delighted to find that TVE (**1**) is stable as a neat liquid at ambient temperature, in light and in air. We have stored samples for weeks in this way without appreciable decomposition.

The reaction temperature for the four-fold cross-coupling reaction is of critical importance for the generation of a clean product: progressively higher temperatures lead to the co-formation of increasing amounts of DVC (**2**), formed through heat-promoted 6π-electrocyclization.[14] This 6π-electrocyclization can be performed under both thermal and photochemical activation to generate DVC (**2**) cleanly (Scheme 3).[15] The DVC structure **2** can be viewed as a substituted [4]dendralene,[2] specifically, one in which the two central alkenes are linked through a $-CH_2CH_2-$ tether. Unlike bench-stable [4]dendralene (**6**), however, DVC (**2**) rapidly decomposes when neat[16] and we find that this hydrocarbon is best generated and handled in solution and used directly.



Scheme 3. Conversion of TVE (**1**) into DVC (**2**) and Diels–Alder sequences with NMM (**9**).

Irrespective of their divergent stabilities, hydrocarbons **1** and **2** are both participants in sequences of diene-transmissive[17] Diels–Alder (DA) reactions, which allow the rapid construction of fused bi-, tri- and tetracyclic systems. Thus, on exposure to 1.0 molar equivalent of the dienophile *N*-methylmaleimide (NMM, **9**), DVC (**2**) was converted cleanly into single terminal DA adduct **10** (Scheme 3). None of the regioisomeric internal product **11** was observed.

Exposure of adduct **10** to 1 molar equivalent of NMM (**9**) led to a single diastereomer (within the limits of ^{1}H NMR detection) of double DA adduct **12**. Double adduct **12** could also be obtained directly from DVC (**5**) in one pot with 2.0 molar equivalents of NMM (**9**). In turn, double adduct **12** reacted with NMM (**9**) stereoselectively to form triple DA adduct **13** as a single diastereoisomer. Finally, starting from TVE (**1**), the electrocyclization–triple DA sequence was conducted in one pot to generate product **13**, in the process forming seven new C–C bonds and four new rings with complete regio- and diastereoselectivity, and avoiding the isolation of unstable DVC (**2**).[18]

When the reaction temperature was kept below 60 °C to minimize the thermal 6π-electrocyclization of TVE (**1**), a direct DA cycloaddition with NMM (**9**) occurred (Scheme 3). In the event, the product of a diene-transmissive double DA reaction, substituted decalin **15**, was the isolated product, with only traces of mono-adduct **14** detected, even when stoichiometric amounts of NMM were used.

The DA reactions depicted in Scheme 3 provide markedly different outcomes to those that might be anticipated based upon precedent with the parent dendralenes. Thus, whereas TVE (**1**) undergoes a diene-transmissive double DA sequence to form **15**, the related [3]dendralene (**3**) undergoes high-yielding single DA additions with dienophiles.[5] Furthermore, the very high levels of chemo-, regio- and stereoselectivity exhibited by DVC (**2**) in its DA reactions with NMM are dramatically different to the very poor selectivities seen with [4]dendralene (**6**).[8]

Computational studies were employed to offer insights into the origins of these differences in reactivity. The accurate composite ab initio MO G4(MP2) method was employed throughout, in which a series of CCSD(T), MP2 and HF calculations are carried out on B3LYP/6-31G(2df,p) equilibrium geometries.[19,20] The lowest-energy transition structures (TSs) located for reactions of NMM with the dienes TVE (**1**),

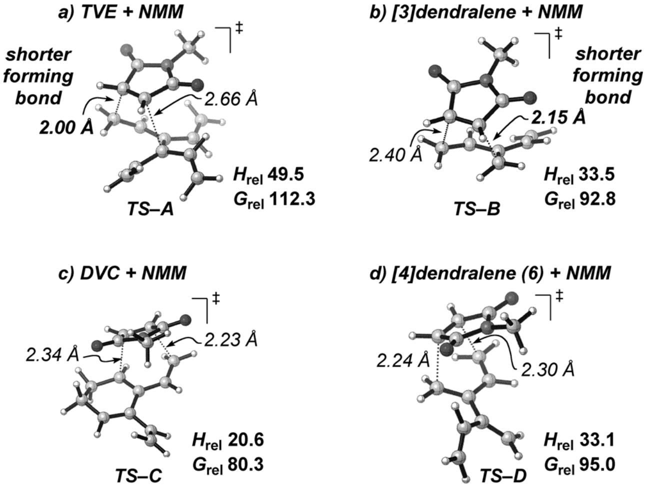


Figure 1. B3LYP/6-31G(2df,p) geometries, G4(MP2) relative enthalpies and free energies (kJ mol^{-1}) of the most stable TS for the Diels–Alder reactions between NMM (**9**) and a) [3]dendralene (**3**); b) TVE (**1**); c) DVC (**2**); and d) [4]dendralene (**6**).

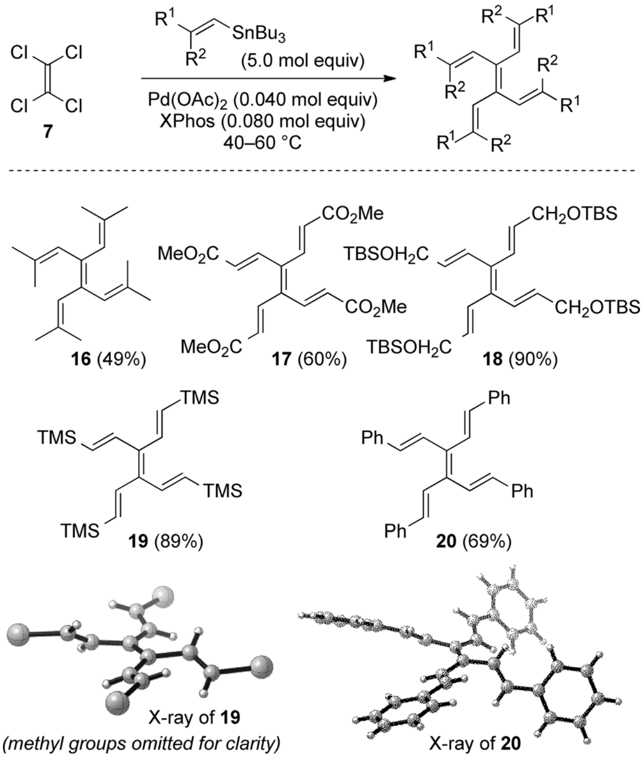
DVC (**2**), [3]dendralene (**3**) and [4]dendralene (**6**) are depicted in Figure 1.

Of the ten TSs located for the first DA addition of NMM to TVE (**1**), the lowest energy one was found to be **TS-A**, in which *endo* addition takes place (Figure 1 a). This TS displays marked bond-forming asynchronicity, as evidenced by forming bond lengths of 2.003 Å and 2.663 Å ($\Delta r = 0.66$ Å). The shorter forming bond involves C1 of TVE (**1**). The most stable TS for the addition of NMM to [3]dendralene (**3**), **TS-B** (Figure 1 b), unsurprisingly also has the *endo* stereochemistry. However, the TS geometry differs from that of **TS-A**, involving TVE (**1**), in that the bond-forming asynchronicity in **TS-B** (2.403 Å, 2.154 Å; $\Delta r = 0.25$ Å) is less than one half of that for **TS-A**. Also, the shorter forming bond in **TS-B** involves C4, rather than C1, in the case of **TS-A**. This arrangement of creating a short forming bond at C4 in **TS-B** serves to produce a TS that is stabilized by pentadienyl delocalization of charge in the dendralene unit.[21] The different character of asynchronicity in the TS for the TVE (**1**) reaction is most likely due to adverse steric interactions between the *Z*-4-vinyl substituent with C1, which would be significant in an idealized planar reacting diene component of the DA TS. This steric strain is relieved through substantial twisting about the C3−C4 bond in the TS, which results in the *Z*-4-vinyl group being rotated by 37° (= value of the dihedral angle C2-C3-C4-C5) away from both C1 and the incoming dienophile. The forming bond at C4 is weaker and, therefore, longer because of reduced dienophile-C4 orbital overlap and increased steric interaction between the dienophile and the *E*-4-vinyl groups brought about by this twisting. The hindrance to partial C4 bond formation in the TS is partially compensated through generation of a sterically unencumbered very short forming bond length of 2 Å at C1. This highly asynchronous TS, with a pair of long and very short forming bonds, should possess substantial closed-shell biradicaloid character, the closed-shell configuration arising from strong through-bond coupling between the short NMM-C1 forming bond and the NMM and TVE partial radicals.[21] The presence of a (vinyl substituted) trivinylmethyl functionality in the TVE component should further stabilize **TS-A**. Steric factors also explain why the activation enthalpy for **TS-A** ($49.5\ \mathrm{kJ\,mol^{-1}}$) is markedly larger than that for the corresponding DA reaction involving [3]dendralene (**3**) ($33.5\ \mathrm{kJ\,mol^{-1}}$). Evidently, the rate of the first NMM cycloaddition to TVE (**1**) is retarded by this steric effect sufficiently that the subsequent addition to the transmitted diene **14** is faster.

In line with experimental observations, calculations identify the *endo*-TS leading to the terminal addition product, **TS-C** (Figure 1 c), as the most stable in the reaction between NMM and DVC (**2**). It is interesting that the activation enthalpy and activation free energy for this mode of addition ($\Delta H^{\ddagger} = 20.6$ and $\Delta G^{\ddagger} = 80.3\ \mathrm{kJ\,mol^{-1}}$) are remarkably small and are even significantly smaller than those for DA addition of NMM to [3]dendralene (**3**) ($\Delta H^{\ddagger} = 33.5$ and $\Delta G^{\ddagger} = 92.8\ \mathrm{kJ\,mol^{-1}}$; Figure 1 b). The calculated activation parameters for the reaction of the parent [4]dendralene (**6**) with NMM through **TS-D**[22] (Figure 1 d) are $\Delta H^{\ddagger} = 33.1$ and $\Delta G^{\ddagger} = 95.0\ \mathrm{kJ\,mol^{-1}}$, values which are almost identical with those for [3]dendralene (**3**). We conclude, therefore, that the additional spectator vinyl group in DVC is not responsible for the enhanced DA reactivity of this structure, compared to [3]dendralene. Instead, we attribute this exalted reactivity to the electronic effect of the $-CH_2CH_2-$ group in DVC, which, through a combination of hyperconjugative and $+I$ effects, raises the HOMO of DVC, thereby narrowing the $\mathrm{HOMO_{DVC}}$–$\mathrm{LUMO_{NMM}}$ energy gap. Within the context of second-order PMO theory, this narrowing will lead to enhanced reactivity. Indeed, B3LYP/6-31G(d) calculations reveal a substantial 0.7 eV elevation of the HOMO energy of DVC relative to both [3]dendralene and [4]dendralene.

Terminal addition of NMM to DVC is predicted to be favored over internal addition by about $5\ \mathrm{kJ\,mol^{-1}}$, a preference that may be due to steric interactions in the internal TS.[13] The lack of predicted terminal vs. internal selectivity in the DA reaction of NMM with [4]dendralene is consistent both with experimental observations[8] and with our explanation for terminal selectivity in the corresponding DA reaction with DVC, in terms of moderate steric interactions involving the $-CH_2CH_2-$ group.

These powerful and highly selective, multi-bond forming domino reactions of TVE invite application in complex molecule synthesis. We also believe that TVE is worthy of further scrutiny in materials-based research, considering the importance of close relatives TEE (**5**) and substituted 1,3-butadienes in this field. Substitution on the TVE framework is likely to be important in such work. Gratifyingly, the four-fold cross-coupling reaction of alkenyl stannanes with tetrachloroethylene is one of useful scope, as evidenced by the formation of substituted TVEs **16**–**20** (Scheme 4), all of which are



Scheme 4. Four-fold cross-couplings to substituted TVEs.

"bench-stable" compounds. The high yields and low precatalyst/ligand loadings are notable, considering that four C−C bonds are formed in each synthesis. Both known[23] and new compounds are accessible in this way and this general, four-fold coupling offers significant advantages over existing approaches to substituted TVEs. For example, the tetraethyl ester analogue of **17**—prepared here in one step—was previously prepared in 4% overall yield through a linear synthetic sequence of nine steps.[23c] The first X-ray crystal structures[24] of tetravinylethylenes both confirm the identity of these compounds and reveal the presence of a largely in-plane (dihedral angles within ca. 20°) *E*,*E*-1,3,5-hexatriene moiety, which presumably maximizes conjugative stabilization.

In summary, the first four-fold cross-coupling reactions involving alkenic partners has allowed the one-step synthesis of TVE (**1**) and substituted analogues. Not only are TVE (**1**) and its substituted analogues easy to prepare using standard laboratory methods and equipment, they are also bench-stable and easy to handle. These findings pave the way for wider applications of tetravinylethylenes.

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[13] See the Supporting Information for full details.

[14] This finding is consistent with a note in one of Skattebøl's publications (see reference [4c]). No experimental details or yields were reported in this earlier study.

[15] The thermal reaction proceeds in quantitative yield at 120°C in 10 mM $CDCl_3$ solution, as measured by ^1H NMR spectroscopic analysis employing an internal standard. The practicality of the thermal process is limited, however, by the propensity of DVC (**5**) to oligomerize at higher concentrations. The transformation is more conveniently carried out photochemically at ambient temperature. In this way, much higher concentration solutions of **5** (0.2 M) can be prepared. See the Supporting Information for details.

[16] Upon rotary evaporation of the solvent (benzene, diethyl ether, petrol, or acetonitrile) from solutions of DVC (**5**) at ambient temperature, a solid residue remained. ^1H NMR spectra of the solid contained only broad and ill-defined peaks. Addition of the antioxidant BHT did not inhibit this decomposition, the mechanism of which remains unclear.

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[22] The most stable reference [4]dendralene (**6**) reactant is not appropriate for comparing activation energies for the DA reactions of [3]dendralene (**3**) and [4]dendralene (**6**) because the most stable conformation of [4]dendralene (**6**) consists of two nearly planar *s-trans* 1,3-butadiene units twisted 78° with respect to each other, whereas the reactive diene components in [3]dendralene (**3**) and DVC (**2**) have a *gauche* relationship. See the Supporting Information for details.

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[24] CCDC 985422–985427 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.