

Tetravinylethylene**

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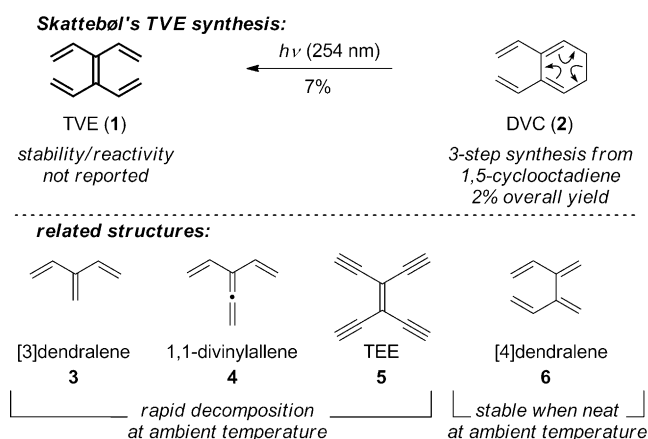
Abstract: The first four-fold cross coupling reaction involving alkenic partners leads to the title hydrocarbon on multi-gram scale in one step from commercially available precursors. In stark contrast to its close structural relatives, tetravinylethylene is a remarkably robust, bench-stable compound. 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

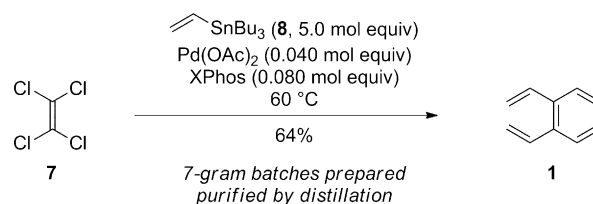
analogues. The closest structural relatives of TVEs—namely the linear polyenes,^[1] [n]dendralenes,^[2] and tetraethynylethylenes^[3]—have been studied extensively and their value in efficient complex molecule synthesis and new materials has been established. In contrast, there is a conspicuous absence 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 6 π -electrocyclic ring opening of 2,3-divinyl-1,3-cyclohexadiene (DVC, **2**) as a key step.

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,



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



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

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.

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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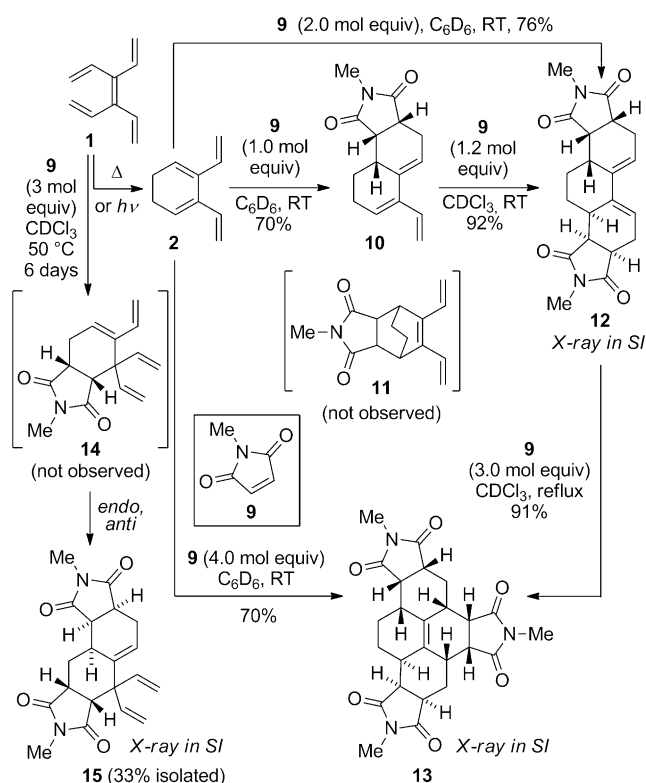
[**] This work was supported by the Australian Research Council.
M.N.P.-R. acknowledges that the computational component of this research was undertaken with the assistance of resources provided at the NCI National Facility through the National Computational Merit Allocation Scheme supported by the Australian Government.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.201402840>.

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 6 π -electrocyclization.^[14] This 6 π -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



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

a substituted [4]dendralene,^[2] specifically, one in which the two central alkenes are linked through a $-\text{CH}_2\text{CH}_2-$ 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.

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 ^1H 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 6 π -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**),

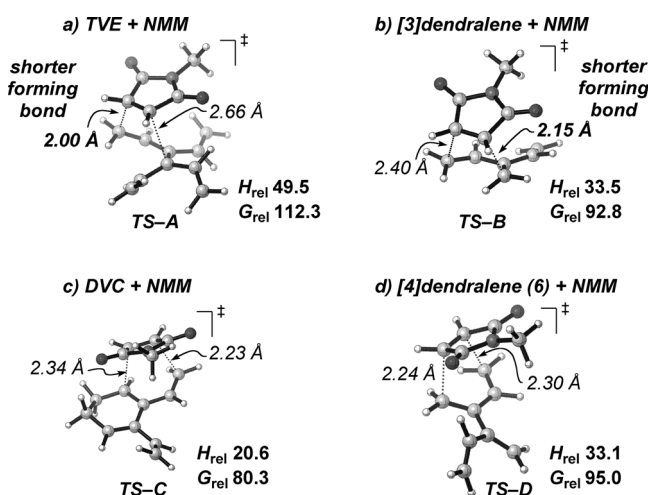


Figure 1. B3LYP/6-31G(2df,p) geometries, G4(MP2) relative enthalpies and free energies (kJ mol⁻¹) of the most stable TS for the Diels–Alder reactions between NMM (**9**) and a) [3]dendralene (**3**); b) TVE (**1**); c) DVC (**2**); and d) [4]dendralene (**6**).

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

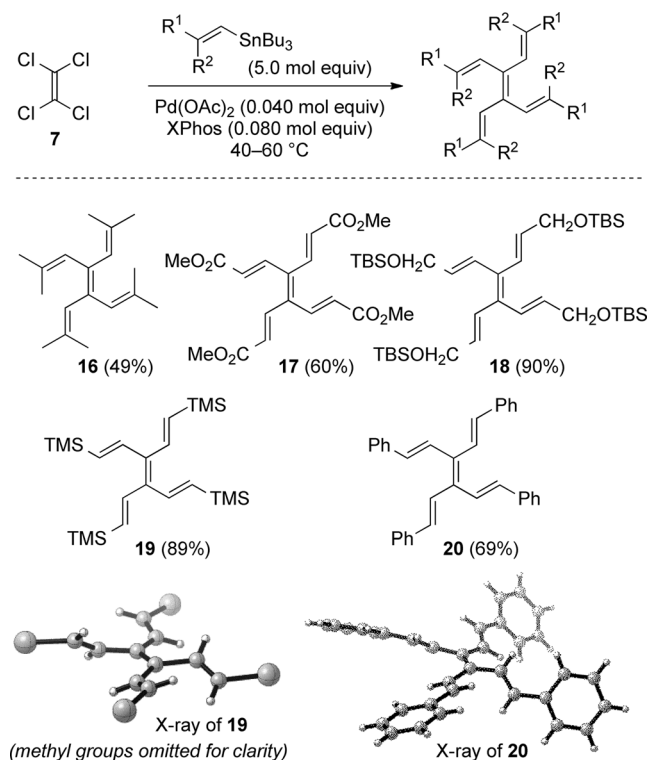
Of the ten TSs located for the first DA addition of NMM to TVE (**1**), the lowest energy one was found to be **TS-A**, in which *endo* addition takes place (Figure 1 a). This TS displays marked bond-forming asynchronicity, as evidenced by forming bond lengths of 2.003 Å and 2.663 Å ($\Delta r = 0.66$ 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 kJ mol^{−1}) is markedly larger than that for the corresponding DA reaction involving [3]dendralene (**3**) (33.5 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 $\Delta G^\ddagger = 80.3$ 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 $\Delta G^\ddagger = 92.8$ 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 $\Delta G^\ddagger = 95.0$ 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 $-\text{CH}_2\text{CH}_2-$ group in DVC, which, through a combination of hyperconjugative and $+I$ effects, raises the HOMO of DVC, thereby narrowing the HOMO_{DVC}–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 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 $-\text{CH}_2\text{CH}_2-$ 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 pre-catalyst/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.

Received: February 27, 2014

Published online: April 24, 2014

Keywords: cycloaddition · Diels–Alder reaction · hydrocarbons · one-pot reactions · tetravinylethylene

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