J. Org. Chem. **2000,** *65,* 6791−6794 **6791**

The "No Reaction" Reaction of 1-Vinylnortricyclene to Tricyclo[4.2.1.0^{3,7}]non-3-ene

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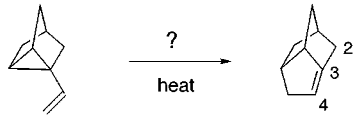
Received June 19, 2000

In 1962, just before the advent of orbital symmetry theory provided influential theoretical generalizations for pericyclic transformations, thermally activated cyclic reorganizations such as Diels−Alder additions and Cope rearrangements were dubbed, "half in jest, half in desperation", "no mechanism" reactions.[1,2] Classical tools for defining mechanistic characteristics seemed ill-suited for delineating these types of conversions: acidic or basic catalysts were not required, intermediates could not be detected or trapped, and reaction rates proved relatively insensitive to solvent or substituent effects. The reactions were elusive, enigmatic, to be categorized as "neither fish nor fowl", reactions of the "twilight zone".[3] The "no mechanism" terminology and concept introduced by Doering and Roth[1,2] served most usefully as intended, as "a humorous way of calling attention to the serious predicament organic chemists are in when the classical criteria of mechanism are not fulfilled".[3]

A complementary innovative coinage soon followed, in 1965: reactions "which surely occur but which there is no way of detecting" were recognized by Berson and Willcott as "no reaction" reactions.[4] The specific instance prompting this original concept was the attempted conversion of 1-vinylnortricyclene (**1**) by a thermal vinylcyclopropane-to-cyclopentene isomerization to tricyclo[4.2.1.0^{3,7}]non-3-ene (**2**).[4] The starting material was recovered essentially unchanged after prolonged heating above 350 °C; even after 25 min at 475 °C, some 90% of **1** could be recovered.



1 **2**

Formation of the hypothetical product **2**, which could be thought of either as a strained Bredt-rule-contradicting olefin or perhaps as a "1,2-diradical", appeared to be interdicted. It might have been formed, or possibly not formed: in any event, it was not detected. Had **1** isomerized to **2** it would have reverted swiftly to starting material; its relatively high heat of formation would correspond to a negligibly small relative concentration at equilibrium.

Though the conceptual ramifications of the "no reaction" reaction formulation have not been fully developed, the essential question—how might one detect reactions that generate a much higher energy product which reverts at once back to starting material?—remains challenging today. Joining **1** → **2** in the "no reaction" reaction category, other reactions which may well occur but which seem intrinsically undetectable, or at least have so far not been detected, are such isomerizations as the thermal conversions of 4-phenyl-1-butene to 1-methylene-6-allylcyclohexa-2,4-diene[5] and of hexa-1,5-diene to bicyclo[2.2.0]hexane.[6]

For many degenerate isomerizations, isotopic labeling techniques serve to expose the reactions in question, which then no longer fall in the "no reaction" category. The 1,5-hydrogen shifts in monodeuterio *cis,cis*-cycloocta-1,3-dienes[7] and the Cope rearrangement of 1,1-d_2-hexa-1,5-diene[8] exemplify the point. In these and similar cases the reactions cause isotopic labels to relocate to different positions, thus making the reactions detectable and kinetic investigations feasible.

Progress since 1965 permits a more optimistic consideration of the "no reaction" reaction **1** → **2.** The olefin **2** would now be considered strained but not excessively distorted; our calculations at the Hartree−Fock level using a 6-31G* basis set[9] have placed the anti-Bredt rule olefin **2** only 15.5 kcal/mol above 1-vinylnortricyclene (**1**). The olefinic unit in **2** is nonplanar, but not drastically distorted: the dihedral angles in **2** (the (7*S*) enantiomer of **2**) for C5−C4−C3−C7 and for H−C4−C3−C7 are calculated to be +11.8° and +170.4°.

Further, one now knows that the vinylcyclopropane rearrangement takes place in system after system with both suprafacial and antarafacial utilization of the allylic unit.[10,11] This stereochemical fact has been given prominence in the synthetic community through the example used by Corey and Cheng to illustrate the vinylcyclopropane−cyclopentene rearrangement transform,[12] for it

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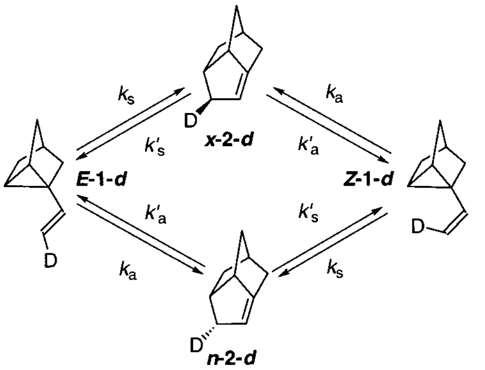
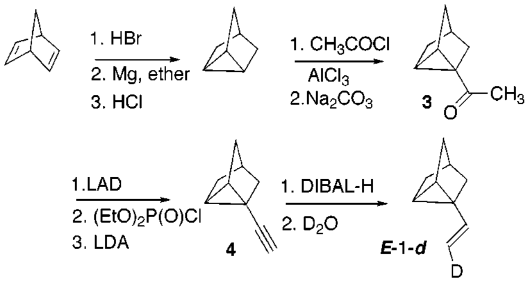
Scheme 1



Scheme 2



involves [1,3] carbon migrations in both *suprafacial,retention* and *antarafacial,retention* modes.[13]

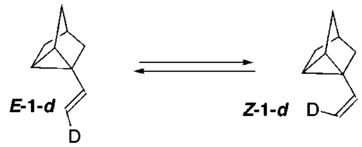
This facet of vinylcyclopropane-to-cyclopentene reaction stereochemistry can be exploited to devise a novel experimental test for the original “no reaction” reaction. A deuterium label stereoselectively positioned in the vinyl group of starting material, as in ***E*-1-*d***, might serve to bring the “undetectable” reaction to light, for *E* and *Z* isomers of the starting material could be interconverted by passage through the racemic tricyclic isomers ***x*-2-*d*** and ***n*-2-*d***, as formulated in Scheme 1.

The 1,3-shifts proceeding both suprafacially and antarafacially lead to equilibration of ***E*-1-*d*** and ***Z*-1-*d***, however great the k'_s:k_s and k'_a:k_a ratio, provided that $k_s k_a \neq 0$.

The test substrate ***E*-1-*d*** was readily prepared as outlined in Scheme 2. Acetylnortricyclene (**3**) was prepared in four steps from norbornadiene following good precedents in the literature.[14,15] The conversion of **3** to 1-ethynylnortricyclene (**4**) was accomplished at first through a four-step sequence: oxidation to the acid (Br_2, NaOH),[15] reduction to 1-(hydroxymethyl)nortricyclene ($LiAlH_4$),[15] oxidation (PCC),[15] and application of Corey–Fuchs chemistry (CBr_4, PPh_3, then BuLi).[16] The alternative one-pot conversion shown in Scheme 2[17] proved more efficient.

Reduction of the triple bond of **4** with diisobutylaluminum hydride followed by hydrolysis of the intermediate vinylaluminum compound[18] with D_2O gave ***E*-1-*d*** with high (but not always complete) incorporation of label and high stereochemical integrity. The ^{1}H NMR spectrum in the olefinic region showed the two vinyl hydrogens as a classic AM two-spin system, with a trans coupling constant of 17 Hz (Figure 1), along with minor absorptions for unlabeled **1**.

Heating ***E*-1-*d*** in the gas phase at 412.9 °C gave a clean first-order approach to ***E*-1-*d***:***Z*-1-*d*** equilibrium with rate constant $k_{obs} = 1.1 \times 10^{-5}$ s^{-1}. The NMR resonances at δ 4.95 and 5.01 characteristic of ***E*-1-*d*** were joined by new peaks at 4.85 and 4.885 ($J = 10.5$ Hz) attributable to the ***Z*-1-*d*** isomer (Figure 1).



The NMR spectra of reaction mixtures confirmed that no significant loss of label occurred during the thermal isomerizations, for the NMR signals in the olefinic region appropriate to unlabeled **1** did not grow more prominent. This point is critical, for it rules out an alternative mechanism for the *E*:*Z* isomerization: a surface-catalyzed protonation of *E* olefin to give a cyclopropylcarbinyl cation which could shed a proton (or deuteron) to give ***E*-1-*d***, ***Z*-1-*d***, or unlabeled **1**.

At 445.9 °C, k_{obs} is 3.5×10^{-5} s^{-1}, only modestly larger than the $k_{obs} = 1.1 \times 10^{-5}$ s^{-1} measured at 412.9 °C. These two rate constants are inconsistent with expectations for either a direct thermal *E:Z* equilibration of olefins ***E*-1-*d*** and ***Z*-1-*d*** or an *E:Z* isomerization about the allylic unit in diradicals formed from ***E*-1-*d*** or ***Z*-1-*d*** through cleavage of a cyclopropane C–C bond, kinetically simple processes which would involve activation energies of about 60–65 kcal/mol. A two-point Arrhenius plot for the k_{obs} values leads to “E_a” = 34 kcal/mol.

For the kinetic situation inherent in reaction Scheme 1, k_{obs} would depend on both ($k_s + k_a$) and the k_s:k_a ratio. Values of $k_{obs}(T)$ would show linear Arrhenius behavior reflective of E_a for ($k_s + k_a$) only if k_s:k_a were independent of temperature, an unwarranted supposition at this stage. Further kinetic work, with careful attention to possible surface-catalyzed but deuterium-label-conservative processes or low-pressure rate falloff effects, as well as studies at higher temperatures using shock-tube techniques,[19] will be required to sort out the temperature dependencies of the unimolecular rate constants which together dictate k_{obs}.

The experimental approach used here, which depends on detecting a stereochemical rather than a positional redisposition of label, could well be applied to some other “no reaction” reactions. The tactic could be utilized whenever the hypothetical reaction might, like the isomerization $\mathbf{1} \rightarrow \mathbf{2}$, give experimental results plausibly interpretable as an indication that the reaction does indeed occur.

Experimental Section

1-Acetylnortricyclene (**3**) was prepared from bicyclo[2.2.1]-heptadiene in four steps, by way of 3-bromotricyclo[2.2.1.0^{2,6}]-heptane and tricyclo[2.2.1.0^{2,6}]heptane (nortricyclene).[14,15] The

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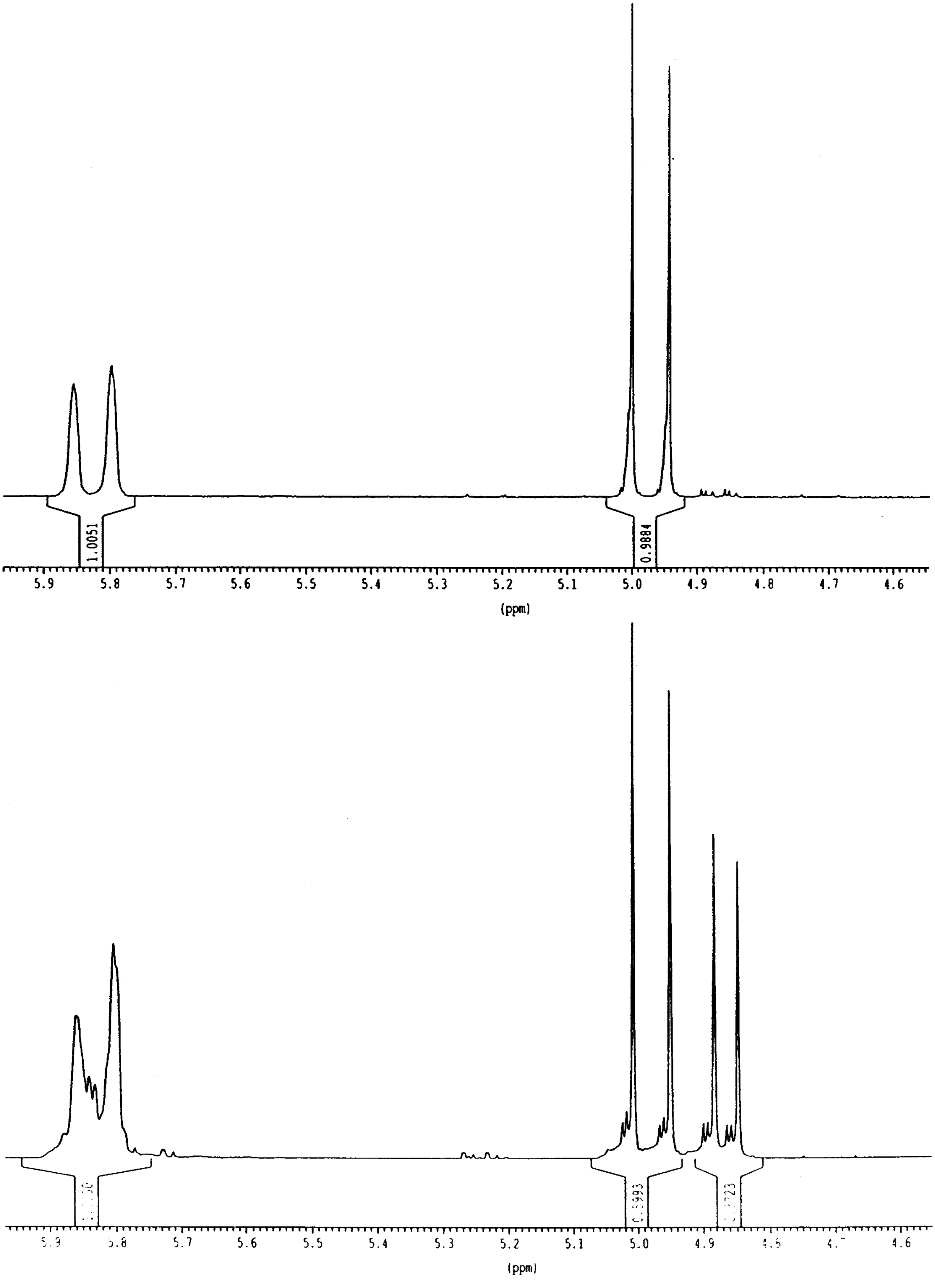

Figure 1. ^{1}H NMR spectra for vinyl hydrogens in ***E*-1-*d*** (above) and in a 61:39 mixture of ***E*-1-*d*** and ***Z*-1-*d*** formed through thermal gas-phase isomerization of ***E*-1-*d*** for 38.4 h at 412.9 °C (below).

ketone had bp 56−62 °C (2−3 mm) (lit.[15] bp 50−52 °C (2 mm)); ^{1}H NMR δ 20.8 (m, 1 H), 2.03 (s, 3 H), 1.94 (br, 2 H),1.49 (d, $J = 1.6$ Hz, 2 H), 1.417, 1.381, 1.361, 1.325 (AB pattern, $J = 10.8$ Hz, 4 H). ^{13}C NMR δ 207.9, 36.7, 33.6, 33.1, 31.1, 27.2, 25.5.

1-Ethynylnortricyclene (4).[17] To an oven-dried 250-mL three-necked round-bottomed flask under argon was added 100 mL of THF (dried over Na and benzophenone). Diisopropylamine (4.1 g, 40 mmol, 1.1 equiv) was added at 0 °C, followed by 25 mL of 1.6 M BuLi (40 mmol, 1.1 equiv) in hexanes. The reaction mixture was stirred 30 min and cooled to −78 °C, and then 5.0 g (37 mmol, 1.0 equiv) of **3** was added. After 1 h at −78 °C, the reaction mixture was treated with 6.3 g (37 mmol, 1.0 equiv) of diethyl chlorophosphate. It was removed from the cold bath and allowed to warm to 0 °C over a 3-h period.

In a separate flask a solution of LDA was prepared from diisopropylamine (8.0 g, 82 mmol, 2.1 equiv) in THF and BuLi in hexanes at 0 °C. This solution was added by cannulation to the reaction mixture containing the diethylalkenyl phosphate at −78 °C. The mixture was allowed to warm to room temperature and was stirred for 12 h. Water was added, the organic layer was separated, and the aqueous phase was extracted with pentane (2 × 75 mL). The combined organic material was washed with 1 N HCl (2 × 75 mL), twice with brine, twice with aqueous $NaHCO_3$, and once with H_2O. It was dried ($MgSO_4$), filtered, and concentrated by distillation. The residue was purified by simple distillation (bp 130−131 °C; 3.2 g, 74%); ^{1}H NMR δ 2.01 (m, 1 H), 1.96 (s, 1 H), 1.52 (br, 2 H), 1.44 (d, $J = 1.6$ Hz, 2 H), 1.429, 1.393, 1.297, 1.266 (AB pattern, $J = 10$ Hz, 4 H); ^{13}C NMR δ 126.6, 65.8, 37.5, 33.3, 30.5, 21.2.

(*E*)-(*d*-Ethenyl)nortricyclene (*E*-1-*d*).[18] To a solution of 3.2 g (27 mmol) of **4** in 100 mL of pentane was added 5.0 mL (28 mmol, 1.04 equiv) of DIBAL-H. The reaction mixture was stirred at room temperature for 27 h and then cooled to −78 °C and treated with 1.7 mL of D_2O. The mixture was allowed to warm to room temperature and was combined with 100 mL of saturated aqueous sodium potassium tartarate. The biphasic mixture was stirred 1 h; the organic layer was separated, washed with water, and dried over $MgSO_4$. Filtration and concentration by distillation gave crude ***E*-1-*d*** (2.3 g, 72%), which was purified by preparative GC; ^{1}H NMR δ 5.83 (d, $J = 17$ Hz, 1 H), 4.97 (d, $J = 17$ Hz, 1 H), 2.02 (br, 1 H), 1.32 (d, $J = 1.3$ Hz, 2 H), 1.427, 1.394, 1.324, 1.290 (AB pattern, $J = 10$ Hz, 4 H), 1.24 (s, 2 H); ^{13}C NMR δ 139.7, 109.8 (t), 34.5, 33.96, 33.41, 30.8, 20.4.

Thermal Isomerizations. The 300-mL quartz bulb static kinetic reactor and associated equipment used have been detailed elsewhere.[20] Samples of ***E*-1-*d*** (20 μL) were injected into the evacuated bulb at a given temperature and heated for a given time and then transferred to an evacuated U-tube cooled in liquid nitrogen. A further transfer to an NMR tube and dilution with $CDCl_3$ gave samples giving very clean spectra indicative of mixtures of ***E*-1-*d*** and ***Z*-1-*d***; signals appropriate to unlabeled **1** or of significant amounts of other thermal products were not evident (Figure 1). At 412.9 °C, the reaction times and *E*:*Z* ratios found were 8 h (85:15), 16 h (70:30, and 38.4 h (61:39). At 445.9 °C, the times and ratios were 2 h (86:14), 4.1 (79:21), and 8.4 (67:33).

Acknowledgment. We thank Professor Gabriel Chuchani of the Instituto Venezolando de Investigaciones Cientificas, Caracas, for invaluable suggestions regarding gas phase static reactors, and the National Science Foundation for supporting this work through grants CHE-9532016 and CHE-9902184.

Supporting Information Available: NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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