# ARTICLES

## Competing Isomerizations: A Combined Experimental/Theoretical Study of Phenylpentenone Isomerism

**Zhongyi Wang,[†] Andrew G. H. Wee,* Steven S. Hepperle,[‡] Ron G. Treble, and Allan L. L. East***

*Department of Chemistry and Biochemistry, University of Regina, Regina, Saskatchewan S4S 0A2, Canada*

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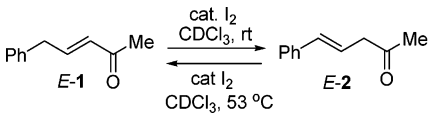
The possible competition of *Z*/*E* versus hydrogen-shift isomerization in (*E*)-5-phenyl-3-penten-2-one (*E*-**1**) and (*E*)-5-phenyl-4-penten-2-one (*E*-**2**) was studied, both experimentally and theoretically. Iodine-catalyzed isomerization experiments and computational modeling studies show that the equilibrated system consists predominantly of *E*-**1** and *E*-**2**, with *E*-**2** in moderate excess, and with no detectable amounts of the *Z* (cis) diastereoisomers. Density functional theory (DFT) calculations corroborated the free energy difference ($\Delta_r G^{298}_{expt}$ and $\Delta_r G^{298}_{theo}$ were −0.7 and −1.1 kcal mol$^{-1}$, respectively), and computations of Boltzmann-weighted $^1$H NMR spectra were found to be useful in confirming the assignment of the isomers. The relevance of this equilibrium to earlier work on double-bond stabilization is discussed.

### Introduction

The Wittig reaction[1] is one of the most widely used and versatile methods for the preparation of alkenes. It is well recognized that the *Z*/*E* stereoselectivity exhibited by the Wittig reaction is dependent on the nature of the substituent(s) and structure of the aldehyde and ketone, on the nature of the substituent(s) on the carbon unit and/or the phosphorus center of the organophosphorane reagent, and on the reaction conditions (solvent, temperature and base).[2] In general, it is found that stabilized Wittig reagents favor the *E*-alkene products whereas nonstabilized ones favor the *Z*-alkene products; however, exceptions to this general rule exist.[2]

Iodine is commonly used to speed the equilibration of *Z*/*E* products, to maximize the amount of the normally thermodynamically preferred *E* isomer: we cite, for example, the use of iodine in the preparations of stilbene[3] and its derivatives.[4] However, it has been known since the 1960s that iodine can also promote hydrogen-shift isomerization, as well as *Z*/*E* isomerization, in the gas phase[5] and in solution.[6] In this connection, we are interested in predicting which molecules might be more prone to undergo hydrogen-shift equilibration rather than the desired *Z*/*E* isomerization. In a previous computational study on *Z*/*E* isomerization,[7] many *Z*/*E* isomers had computed enthalpy differences of ∼1.5 kcal mol$^{-1}$; hence, we are interested in cases where hydrogen-shift isomerization energies differ by this amount or less.

Such small hydrogen-shift energies exist in situations such as eq 1, where the substituents X and Y have similar abilities to stabilize the alkene double bond. In 1973 Hine and Flachskam[8] published a nice summary of results for disubstituted alkenes (eq 1), but the acetyl group was not tested. In 1983 Hine and Linden[9] published another summary, based on a summary by Siroky and Prochazka,[10] in which one end of the alkene contained *gem*-dimethyl groups (eq 2). Hine and Linden added data from their own equilibration, with X as the acetyl group. Their results suggest that the double-bond stabilizing ability of the acetyl group should be similar to those of nitro and cyano groups (within 0.2 kcal mol$^{-1}$), and slightly less than that of a phenyl group (by 0.8−0.9 kcal mol$^{-1}$). Thus we would expect to see hydrogen-shift equilibria in 1,3-disubstituted propenes (eq 1) where the acetyl group is paired against any of the nitro, cyano, or phenyl groups. To test the prediction, we present results for the iodine-catalyzed equilibration of (*E*)-5-phenyl-3-penten-2-one (*E*-**1**)[11,12] and (*E*)-5-phenyl-4-penten-2-one (*E*-**2**),[13] as shown in eq 3.




(1)


(2)




(3)

The formation of the corresponding cis-isomers, *Z*-**1** and *Z*-**2**, were also potential possibilities, both from the direct synthesis of **1** and **2** and from the iodine-catalyzed equilibration. With four potential isomers, the opportunity was taken to test the usefulness of $^1$H NMR density functional theory (DFT) calcula-

* Corresponding authors. E-mail: A.L.L.E., Allan.East@uregina.ca; A.G.H.W., Andrew.Wee@uregina.ca.

† Current address: AstaTech Inc, 398 Laird Road, Guelph, ON, Canada N1G 3X7.

‡ Current address: Department of Chemistry, University of British Columbia, Vancouver, BC, Canada V6T 1Z1.

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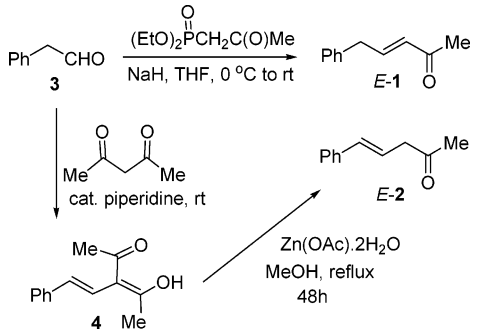
**SCHEME 1: Synthesis of 1 and 2**




tions for isomer identification. Applications of DFT NMR chemical shifts are more common with $^{13}C$ NMR or other nuclei, presumably because $^{1}H$ NMR chemical shifts are more prone to significant vibrational and internal-rotation averaging effects. The results of Boltzmann-averaged, computed $^{1}H$ NMR chemical shifts were indeed useful in isomer identification in this case. Hence, we wish to present these results in this article as well.

## Materials and Methods

**GC−MS Analysis.** All GC−MS analyses were performed on a quadrupole mass spectrometer interfaced via a heated transfer line/capillary to a GC. The GC was configured with a splitless injection port and a DB-5MS fused-silica capillary column coated with a 0.25 $\mu$m film of stationary phase (15 m, 0.25 mm i.d.). The mass spectrometer was operated in the electron-impact ionization mode with an electron energy of 70 eV. The ion source temperature was maintained at 180 °C for all analyses, and the capillary interface transfer line was held at 250 °C. All analyses were performed using a full scan mode resulting from 2 $\mu$L injections. To resolve the total ion chromatograms (TIC), variable temperature programming was employed on the GC.

**Synthesis of 1 and 2.** The enone *E*-**1** was prepared using the literature method[11] (phenylacetaldehyde (**3**) with 2-(oxopropylidene)triphenylphosphorane)[11] to give a 44% yield of **1**. A higher yielding route (Scheme 1), which involved the Horner−Wadsworth−Emmons condensation[14] of **3** and diethyl 2-(oxopropyl)phosphonate, yielded **1** in 68% yield. In both routes for the preparation of **1**, a "minor" isomer (**2**) that was inseparable (identical $R_f$ as judged by tlc) from **1** was also obtained.

**(*E*)-5-Phenyl-3-penten-2-one (1).** A solution of phenylacetaldehyde (118 mg, 0.98 mmol) in dry THF (3 mL) was added via cannula to a mixture of diethyl 2-(oxopropyl)phosphonate (291 mg, 1.5 mmol) and NaH (44 mg, 60% dispersion in paraffin oil) in dry THF (3 mL). The mixture was refluxed for 1 h, cooled to room temperature and water (2 mL) was added. The aqueous layer was extracted with ethyl acetate (15 mL) and the organic phase was washed with water, brine and dried ($Na_2SO_4$). The filtered solution was concentrated and the crude oil was purified by chromatography (5:1 v/v petroleum ether−$Et_2O$) to give the known[11] enone **1** and "minor" isomer **(2)** in a combined yield of 68% (106 mg). The "minor" isomer was identified as the $\beta,\gamma$-unsaturated enone **2** (vide infra).

The ratio of **1**:**2** based on the integration of the methylene doublets centered at $\delta$ 3.54 (**1**) and $\delta$ 3.33 (**2**) was 11:1. IR, $\nu_{max}$: 3061, 3028, 1696, 1672 cm$^{-1}$. $^{1}H$ NMR (200 MHz, signals for isomer **2** in square brackets), $\delta$: [2.19] and 2.24 (s, 3H), [3.33 (br d, $J$ = 6.0 Hz)] and 3.54 (dd, $J$ = 6.0, 1.5 Hz) (2H), 6.05 (d, $J$ = 16.0 Hz), [6.20−6.55 (m)] and 6.88 (ddd, $J$ = 15.0, 6.0, 6.0 Hz) (2H), 7.05−7.50 (m, 5H). GC−MS (GC, $t_R$ = 13.8 min), *m*/*z* (%): 160 ($M^+$, 7.2%), 145 ($M^+$ − Me, 3.9%), 117 ($M^+$ − MeC(O), 10.6%), 91 ($[PhCH_2]^+$, 7.1%), 43 (MeC(O), 10.3%).

**(*E*)-5-Phenyl-4-penten-2-one (2).**[13] A mixture of 2,4-pentanedione (4.8 g, 0.048 mol), phenylacetaldehyde (5.52 g, 0.046 mol) and piperidine (0.1 mL) was stirred for 48 h at room temperature. Then $CH_2Cl_2$ (50 mL) was added, and the mixture was washed with 5% aqueous HCl (40 mL), water (30 mL) and dried ($Na_2SO_4$). The filtered solution was concentrated and the crude oily mixture was purified by flash chromatography (15:1 v/v petroleum ether−$Et_2O$) to give **4**[13a] (0.895 g, 10%). IR, $\nu_{max}$: 3506−2507, 3026, 1701, 1596 cm$^{-1}$. $^{1}H$ NMR (200 MHz), $\delta$: 1.60 (s, 6H), 6.21 (d, 1H, $J$ = 16.2 Hz), 6.55 (d, 1H, $J$ = 16.2 Hz), 7.00−7.25 (m, 5H), 16.5 (s, 1H). GC−MS (GC, $t_R$ = 12.6 min), *m*/*z* (%): 202 ($M^+$, 7.4), 43 ($MeC^+$═O, 15.5).

Compound **4** (850 mg, 4.21 mmol) was dissolved in dry MeOH (7 mL) and $Zn(OAc)_2 \cdot 2H_2O$ (40 mg, 0.19 mmol) was added. The mixture was refluxed for 36 h. The cooled reaction mixture was concentrated and the residue taken into $CH_2Cl_2$; the solution was filtered, and the filtrate was concentrated. The crude oil was purified by flash chromatography (10:1 v/v and then 5:1 v/v petroleum ether−$Et_2O$) to give **2**[13] (386 mg, 57%). IR, $\nu_{max}$: 3020, 1715 cm$^{-1}$. $^{1}H$ NMR (200 MHz), $\delta$: 2.20 (s, 3H), 3.31 (d, 2H, $J$ = 6.0 Hz), 6.28 (ddd, 1H, $J$ = 16.0, 6.0, 6.0 Hz), 6.46 (d, 1H, $J$ = 16.0 Hz), 7.20−7.42 (m, 5H). GC−MS (GC, $t_R$ = 14.5 min), *m*/*z* (%): 160 ($M^+$, 5.6%), 145 ($M^+$ − Me, 2.2%), 117 ($M^+$ − MeC(O), 16.5%), 91 ($[PhCH_2]^+$, 6.0%), 43 ($MeC^+$═O, 16.6%).

**Iodine Equilibration Studies of Enones *E*-1 and *E*-2.** Isomerization of enone **1** and isomer **2** (eq 3) was followed by $^{1}H$ NMR spectroscopy. The forward equilibration (from **1**) was conducted at room temperature (23 °C) in $CDCl_3$, and in the presence of a catalytic amount of iodine. The $^{1}H$ NMR spectrum of the mixture was taken at set intervals over a 10 day period. For the reverse equilibration (from **2**), the $CDCl_3$ solution of **2** and a catalytic amount of iodine were heated in an oil bath (53 °C) and the$^{1}H$ NMR spectrum of the mixture was taken at set intervals over 33 h, followed by standing the mixture at room temperature in the dark for two additional weeks. By the principle of microscopic reversibility, the reverse equilibration should also have proceeded at room temperature, but in two trials we did not see any change in the NMR spectrum after 2 days.

**Theoretical Methods.** Most calculations were performed with the software package Gaussian98,[15] but the NMR calculations were performed with PQS 3.0.[16] Geometry optimizations and frequency calculations were performed at the B3LYP/cc-pVDZ level, i.e., density functional (B3LYP)[17,18] theory using the cc-pVDZ basis set.[19] Better electronic energies ($E_{elec}$) were computed at the B3LYP/cc-pVTZ level using the B3LYP/cc-pVDZ optimized geometries. Gibbs free energies ($G$) for each conformer of each isomer were built by beginning with the above computed $E$'s and adding zero-point, thermal, and entropy corrections calculated using the rigid-rotor/harmonic-oscillator approximation and B3LYP/cc-pVDZ molecular data.

For $^{1}H$ NMR calculations, several methods were tested against a catalogued experimental 2-butene spectrum; we settled on the isotropic (averaged) values from the gauge-independent atomic orbital (GIAO) method[20,21] at the B3LYP/cc-pVTZ level of theory. The zero-Kelvin calculations were performed on individual conformers at the geometries optimized as above. Chemical shifts (but not splittings) were calculated, relative to the shift for tetramethylsilane, whose absolute shift was computed to be 31.37 ppm. To account for thermal averaging

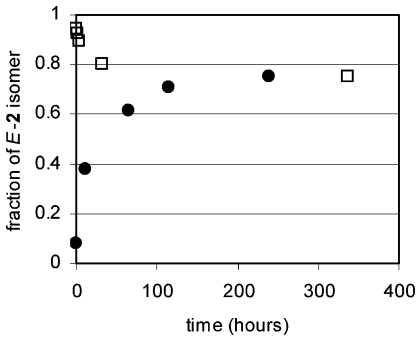



**Figure 1.** Results of forward (from **1**; ●) and reverse (from **2**; □) equilibration experiments. Initial mole fractions of **2** were 0.08 (forward run) and 0.94 (reverse run).

of the contributions from several zero-Kelvin conformers, the shift $S_i$ for the $i$th H-atom was computed as a Boltzmann average of its zero-Kelvin values $S_{ij}$ from each conformer $j$:

$$S_i = \frac{\sum_j^{N_j} W_j S_{ij}}{\sum_j^{N_j} W_j} \qquad W_j = e^{-(G_j - G_{lowest})/RT} \tag{4}$$

The Boltzmann factors $W_j$ used the 298 K Gibbs energies $G_j$ described above and were doubled for gauche conformers to account for their double degeneracy.

## Results and Discussion

**Equilibration Experiments.** In both the forward (from **1**) and reverse (from **2**) equilibrations, only two distinct isomers were detected in the $^1$H NMR spectra. The ratios of **1**:**2** were determined from the $^1$H NMR integrations of the methylene hydrogens. Figure 1 plots the mole fractions of *E*-**2** versus time, for both experimental runs, demonstrating an equilibrium mole fraction of 0.75. This corresponds to an equilibrium constant of K = 3.0 and a $\Delta_r G^{298}_{expt}$ of −0.7 kcal mol$^{-1}$.[22]

In 1977, Fayos et al. reported[13d] the preparation of *E*-**1** via the base-catalyzed elimination (DMF, $Na_2CO_3$) of *p*-toluenesulfinate from 5-phenyl-4-(*p*-toluenesulfonyl)-2-pentanone. Elimination at 60 °C resulted in a 3:1 ratio of *E*-**2**:*E*-**1**, the same ratio we observe above. Further, this ratio of *E*-**2**:*E*-**1** was not influenced by the type of solvent used in the reactions (DMF vs $CDCl_3$). Collectively, these results confirm the prediction in the Introduction of −0.8 to −0.9 kcal mol$^{-1}$ for the isomerization energy, attributed to the difference in double-bond stabilizing energy of the acetyl and phenyl groups.

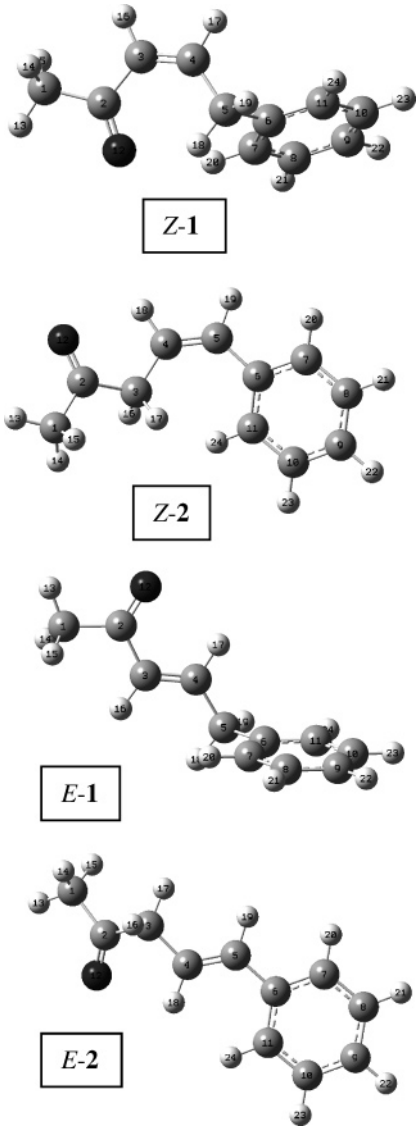



**Figure 2.** B3LYP/cc-pVDZ-optimized lowest-energy conformers (conformer I in Table 1) of the four isomers of interest. Dihedral angle ($\varphi$) definitions: for **1**, $\varphi_{Ac} = \varphi_{1234}$, $\varphi_{Bz} = \varphi_{3456}$, and for **2**, $\varphi_{Ac} = \varphi_{1234}$, $\varphi_{Sty} = \varphi_{2345}$.

**B3LYP Isomer Energies.** Geometry optimizations using B3LYP/cc-pVDZ resulted in one *Z*-**1**, two *Z*-**2**, four *E*-**1**, and four *E*-**2** conformers; results appear in Table 1. The lowest-energy conformer (conformer I) for each isomer is shown in Figure 2. To predict equilibrium ratios of isomers, we consider the Boltzmann factor for the lowest-energy conformer of each

**TABLE 1: Computed Relative Energies (kcal mol$^{-1}$) and Boltzmann Factors (Dimensionless) for Conformers of 1 and 2**

| isomer | conformer | $E_{elec}$ cc-pVDZ[a] | $E_{elec}$ cc-pVTZ[b] | $H^{298K}$ | $G^{298K}$ | Boltzmann factor |
|---|---|---|---|---|---|---|
| Z-**1** | I: $\{\varphi_{Ac},\varphi_{Bz}\} = \{167°,107°\}$ | 1.47 | 2.38 | 2.84 | 3.45 | 0.006[c] |
| Z-**2** | II: $\{\varphi_{Ac},\varphi_{Sty}\} = \{43°,126°\}$ | 4.58 | 4.14 | 4.31 | 4.51 | 0.001[c] |
| | I: $\{\varphi_{Ac},\varphi_{Sty}\} = \{-167°,155°\}$ | 2.23 | 2.29 | 2.38 | 2.76 | 0.010 |
| E-**1** | IV: $\{\varphi_{Ac},\varphi_{Bz}\} = \{0°,0°\}$ | 1.59 | 1.30 | 1.59 | 2.04 | 0.032 |
| | III: $\{\varphi_{Ac},\varphi_{Bz}\} = \{0°,121°\}$ | 0.94 | 0.63 | 0.97 | 1.25 | 0.243[c] |
| | II: $\{\varphi_{Ac},\varphi_{Bz}\} = \{180°,0°\}$ | 0.46 | 0.69 | 0.88 | 1.22 | 0.128 |
| | I: $\{\varphi_{Ac},\varphi_{Bz}\} = \{180°,123°\}$ | 0.48 | 0.71 | 0.98 | 1.07 | 0.326[c] |
| E-**2** | IV: $\{\varphi_{Ac},\varphi_{Sty}\} = \{167°,7°\}$ | 1.89 | 2.53 | 2.59 | 2.28 | 0.021 |
| | III: $\{\varphi_{Ac},\varphi_{Sty}\} = \{46°,110°\}$ | 1.10 | 0.76 | 0.90 | 0.82 | 0.502[c] |
| | II: $\{\varphi_{Ac},\varphi_{Sty}\} = \{-89°,117°\}$ | 0.56 | 0.16 | 0.40 | 0.15 | 1.562[c] |
| | I: $\{\varphi_{Ac},\varphi_{Sty}\} = \{-163°,138°\}$ | 0.00 | 0.00 | 0.00 | 0.00 | 2.000[c] |

[a] Smaller basis set. [b] Larger basis set; these values were used for calculations of the enthalpy (H) and Gibbs free energy (G). [c] Includes factor of 2 for ±gauche degeneracy (±∼120° possibilities for $\varphi_{Bz}$ and $\varphi_{Sty}$).

**TABLE 2: Computed Zero-Kelvin Chemical Shifts for Every Conformer of *E*-2, *Z*-2, *E*-1, *Z*-1, Using the GIAO Method and the B3LYP/cc-pVDZ Level of Electronic Structure Theory**

| atom[a] | *E*-**2**−IV | *E*-**2**−III | *E*-**2**−II | *E*-**2**−I | *Z*-**2**−II | *Z*-**2**−I | *E*-**1**−IV | *E*-**1**−III | *E*-**1**−II | *E*-**1**−I | *Z*-**1**−I |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $H_{ph-a}$ | 7.26 | 7.13 | 7.13 | 7.05 | 7.20 | 7.25 | 7.22 | 7.27 | 7.23 | 7.17 | 7.98 |
| $H_{ph-b}$ | 7.33 | 7.34 | 7.34 | 7.29 | 7.40 | 7.40 | 7.43 | 7.38 | 7.43 | 7.35 | 7.34 |
| $H_{ph-c}$ | 7.20 | 7.25 | 7.25 | 7.21 | 7.29 | 7.26 | 7.38 | 7.33 | 7.37 | 7.30 | 7.25 |
| $H_{ph-d}$ | 7.30 | 7.37 | 7.35 | 7.36 | 7.39 | 7.41 | 7.43 | 7.40 | 7.43 | 7.37 | 7.29 |
| $H_{ph-e}$ | 7.70 | 7.83 | 7.77 | 7.91 | 7.39 | 7.39 | 7.22 | 7.27 | 7.23 | 7.27 | 7.20 |
| **$H_{=a}$** | **6.23** | **6.76** | **6.39** | **7.14** | **6.07** | **6.68** | **7.05** | **6.62** | **7.64** | **7.21** | **6.35** |
| **$H_{=b}$** | **8.48** | **6.43** | **6.52** | **6.29** | **6.72** | **6.62** | **5.22** | **6.13** | **5.43** | **6.36** | **6.13** |
| $H_{m2-a}$ | 3.51 | 3.20 | 3.04 | 3.22 | 3.02 | 3.20 | 3.55 | 3.58 | 3.53 | 3.31 | 5.51 |
| $H_{m2-b}$ | 3.20 | 3.09 | 3.28 | 3.40 | 4.03 | 3.80 | 3.55 | 3.36 | 3.53 | 3.54 | 2.76 |
| $H_{m3-a}$ | 1.82 | 1.79 | 1.63 | 1.84 | 1.80 | 1.90 | 1.77 | 1.78 | 1.93 | 1.85 | 1.90 |
| $H_{m3-b}$ | 2.12 | 2.27 | 1.95 | 2.26 | 2.29 | 2.28 | 2.30 | 2.26 | 1.93 | 2.20 | 2.36 |
| $H_{m3-c}$ | 2.25 | 2.25 | 2.61 | 2.04 | 2.27 | 2.00 | 2.30 | 2.21 | 1.69 | 2.23 | 2.24 |
| $W_j$[b] | 0.021 | 0.502 | 1.562 | 2.000 | 0.001 | 0.010 | 0.032 | 0.243 | 0.128 | 0.326 | 0.006 |

[a] Notation: ph (phenyl), =a (C=C proton closest to methylene), =b (C=C proton furthest from methylene), m2 (methylene), m3 (methyl). [b] Boltzmann factors ($W_j$) from Table 1.

isomer. If the iodine catalyst were capable only of *Z*/*E* equilibration of **1**, the predicted equilibrium ratio of *E*-**1**:*Z*-**1** would be 0.163:0.003, or 50:1 in favor of *E*-**1**. If, however, all four of these isomers appeared in equilibrium, the equilibrium ratio for *E*-**2**:*E*-**1**:*Z*-**2**:*Z*-**1** would be 1.00:0.16:0.01:0.003, i.e., a 6:1 ratio of *E*-**2** to *E*-**1** with essentially no *Z*-isomers. Hence, the *Z* isomers were not seen in the equilibration because they are too high in energy (3.5 and 4.5 kcal mol$^{-1}$ for *Z*-**1** and *Z*-**2**, respectively).

From Table 1 the calculated isomer energies (based on B3LYP/cc-pVTZ electronic energies) give $\Delta_r E^{298}_{theo}$, $\Delta_r H^{298}_{theo}$, and $\Delta_r G^{298}_{theo}$ values of −0.7, −1.0, and −1.1 kcal mol$^{-1}$, respectively, for the reaction in eq 3. This is in good agreement with our experimental $\Delta_r G^{298}_{expt}$ value of −0.7 kcal mol$^{-1}$. This unexpectedly accurate computational estimate is partly fortuitous and likely benefits from excellent cancellation of errors upon taking the energy difference due to the structural similarities of *E*-**1** and *E*-**2**.

**B3LYP $^1$H NMR Spectra.** The salient features in the $^1$H NMR spectrum of conjugated enone *E*-**1** showed a set of olefin hydrogens centered at $\delta$ 6.05 (d) and at $\delta$ 6.88 (ddd), and the benzylic methylene double doublet centered at $\delta$ 3.54. For the minor deconjugated isomer *E*-**2**, the set of olefin hydrogens resonated in the range $\delta$ 6.28 (ddd) and $\delta$ 6.46 (d), and the α-methylene hydrogens appeared as a broad doublet at $\delta$ 3.31. The assignment of *E* stereochemistry of the double-bond in compounds **1** and **2** is supported by the large vicinal coupling constant observed for the olefin hydrogens; in *E*-**1**, $J_{vic}$ = 15.0 Hz and in *E*-**2**, $J_{vic}$ = 16.0 Hz.

We used spectral modeling to make the initial identification and peak assignments of **2**. Table 2 presents the zero-Kelvin chemical shifts, relative to that of $T_d$-symmetry tetramethylsilane, for the 11 conformers listed in Table 1. There are significant conformer effects on chemical shifts. Note that, even within one isomer like *E*-**2**, the H atoms directly attached to the C=C double bond (in bold) can be shifted up to 2 ppm depending on the particular conformation. Such effects are not seen in room-temperature spectra because of facile internal rotation. However, the data in Table 2 clearly demonstrate the sensitivity of chemical shifts to steric environment.

Boltzmann averaging over conformers resulted in four *effective* room-temperature stick spectra for each of the four isomers *E*-**1**, *Z*-**1**, *E*-**2**, and *Z*-**2**. These computed sets of Boltzmann-averaged proton chemical shifts, and the experimentally determined chemical shifts of the two observed isomers, *E*-**1** and *E*-**2**, are collected in Table 3. Inaccuracies of only 0.2 ppm are seen in the computed values for *E*-**1**, which is remarkable considering the variation of $H_{=a}$ and $H_{=b}$ with conformer (Table 2).

**TABLE 3: Experimental and Theoretical Chemical Shifts at 298 K**

| atom[a] | expt *E*-**1** | expt *E*-**2** | theo *Z*-**1** | theo *Z*-**2** | theo *E*-**1** | theo *E*-**2** |
|---|---|---|---|---|---|---|
| $H_{ph}$ | 7.2−7.4 | 7.2−7.4 | 7.20−7.98 | 7.26−7.43 | 7.22−7.40 | 7.09−7.85 |
| **$H_{=a}$** | **6.88** | **6.28** | **6.35** | **6.63** | **7.08** | **6.80** |
| **$H_{=b}$** | **6.05** | **6.46** | **6.13** | **6.63** | **6.07** | **6.41** |
| $H_{m2}$ | 3.54 | 3.31 | 4.13 | 3.50 | 3.46 | 3.23 |
| $H_{m3}$ | 2.24 | 2.20 | 2.17 | 2.07 | 2.05 | 2.06 |

[a] Notation: ph (phenyl), =a (C=C proton closest to methylene), =b (C=C proton furthest from methylene), m2 (methylene), m3 (methyl).

The agreement for *E*-**2** is not as good, due to the sensitive interaction between $H_{=a}$ and an H atom on the phenyl group ($H_{ph-e}$ in Table 2): the B3LYP optimization puts these too close, pushing up the chemical shifts of both these protons by roughly half a ppm. This steric problem is known in calculations on styrene: B3LYP optimizations suggest it is a planar molecule, but MP2 calculations and recent liquid-phase work[23] suggest it is nonplanar with a vinyl-phenyl torsion angle of roughly 18°. With a back-correction of 0.5 ppm to compensate, then all computed peaks again agree to within 0.2 ppm, and together with the computed energies this allowed a correct assignment of *E*-**2**. Hence, the spectrum modeling results in isomer assignments of *E*-**1** for the main isomer and *E*-**2** for the "growing isomer" of the forward equilibration, matching the ones suggested by the simple comparison of computed isomer energies, and ultimately confirmed by the synthesis and reverse equilibration of *E*-**2**.

## Conclusions

Iodine catalysis of the enone *E*-**1** resulted in the formation of the positional isomer *E*-**2**, and not a simple *Z*/*E* isomerization of **1**. Although enone *E*-**1** has been described in several reports, its facile isomerization to *E*-**2** has not been recognized until now. For enone *E*-**1**, the thermodynamic driving force for the isomerization of **1** to **2** can be attributed to the added benefit of conjugating the C=C bond to the phenyl ring rather than the carbonyl group. This benefit is experimentally determined to be $\Delta_r G^{298}_{expt}$ = −0.7 kcal mol$^{-1}$ for *E*-**1** → *E*-**2** in chloroform as solvent.

This confirms the hypothesis, based on Hine's tabulations,[8,9] that observable hydrogen-shift equilibria as depicted in eq 1 should be seen in systems where X and Y are nitro, phenyl, cyano, or acetyl groups. It also suggests that hydrogen-shift

isomerization will precede *Z/E* isomerism in attempts at the latter, via iodine catalysis, for these particular compounds.

Comparisons of computed $^1$H NMR spectra with the experimental ones demonstrate the importance of Boltzmann averaging in producing realistic computational predictions of room-temperature spectra. The fine quality of the computed $^1$H NMR spectra (chemical shifts within 0.2 ppm for 7 out of 8 peaks) and the computed isomerization energy ($-1.1$ kcal mol$^{-1}$) proved useful in this study and suggest that careful calculations with the B3LYP/cc-pVTZ level of theory could be useful in future isomerization investigations.

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**Supporting Information Available:** Cartesian coordinates for conformers. This material is available free of charge via the Internet at http://pubs.acs.org.

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