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Bond Rotation Dynamics of Enamides: The Effect of the Acyl Group and Potential for Chirality Transfer during 5-Endo Trig Radical Cyclizations

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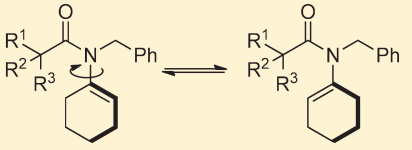
Supporting Information

ABSTRACT: Barriers to rotation of the *N*-alkenyl bond in a series of *N*-cycloalkenyl-*N*-benzyl acetamide derivatives have been measured in different solvents by variable-temperature NMR experiments. The barriers range from 9.7 to 14.2 kcal/mol, depending on substituents on the acetamide acyl group. Polar solvents such as chloroform and methanol increase the barrier to rotation compared to nonpolar solvents such as toluene. The barrier to rotation of "mimics" for acetamide-based radicals are estimated. The relative order of the values of k_{rot} for different acyl groups parallels their reported Taft E_s paramaters. For successful chirality transfer in 5-*endo trig* radical cyclization, it is evident that rotations would need to be significantly slower than those reported here.



Rotation barriers 10-14 kcal/mol depending upon R groups.

INTRODUCTION

We recently reported that *N*-cycloalkenyl-*N*-benzyl α-haloacetamide derivatives **1a**−**c** and the radical derived from them, **2**, are axially chiral due to restricted rotation around the C−N bond of the enamide functionality (Figure 1).[1] For example, a torsion angle of 74° is observed for the *N*-alkenyl bond (CHC−NC(O)) in the X-ray crystal structure of *N*-cyclohexenyl-α-chloroacetamide **1a** (X = Cl).[2] Radicals derived from homolysis of the C−X bond **2** have been shown to undergo 5-*endo* radical cyclization to give **3**.[2−6] Most 5-*endo* radical cyclization reactions employ α-haloenamides as starting materials and alternate 4-*exo* cyclization modes are also possible depending upon the substitution pattern of the enamide.[2−6]

It is evident that radicals like **2** can only cyclize as the *E*-rotamer of the amide N−C═O bond.[2] In the *Z*-rotamer, the radical cannot reach the alkene. Fortunately, enamides typically prefer the *E*-rotamer,[7] so their radicals are formed in a geometry that is predisposed to cyclize. Variable temperature NMR studies of **1a**−**c** confirmed the existence of largely a single *E*-amide rotamer in $CDCl_3$ but more importantly also indicated a relatively slow bond rotation ($\sim 10^4\ s^{-1}$) of the *N*-cyclohexenyl (enamide) bond (*E,P*-**1**→ *E,M*-**1** $\Delta G = 11.7-12.1$ kcal mol^{-1}).[1] Depending on whether cyclization (**2**→**3**) is faster than *N*-alkenyl bond rotation in the radicals (*E,P*-**2**→ *E,M*-**2**) then the axial chirality of suitable enamides (*E,P*-**1** or *E,M*-**1**) (if separated) could be retained or transferred in 5-*endo* radical cyclization reactions.[8]

To better contemplate the prospects of chirality transfer in radical (**2**→**3**) or other reactions of enamides,[9] a basic understanding of their rotation dynamics is needed. In particular, an ability to estimate the value of k_{rot} for the radicals *E,P*-**2**→ *E,M*-**2** themselves is crucial when considering the prospects of high levels of chirality transfer. We previously reported how the size of the ring in which the enamide was constrained effected the barrier to rotation. With the rate of bond rotation observed being

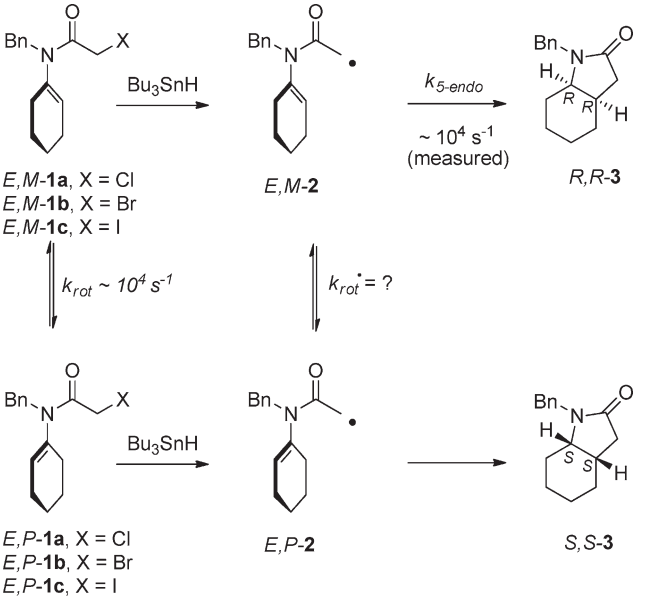


Figure 1. Rotamers of radical precursor **1a**−**c** and cyclizations of derived radical **2**.

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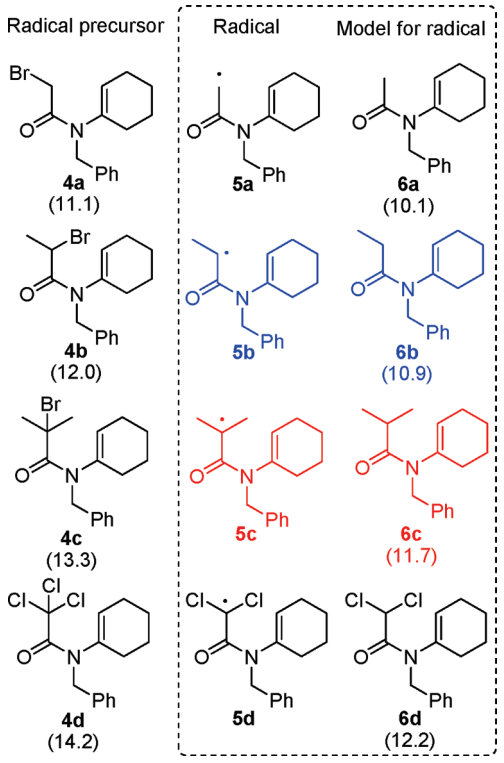

Figure 2. Radical precursors **4a**−**d** and models for the corresponding radicals **6a**−**d** with measured $\Delta G^{\ddagger}_{298}$ barrier to rotation in kcal/mol in paranthesis.

cyclopentene ≪ cyclododecene < cyclooctene < cyclohexene ≈ cycloheptene.[1] Here we report variable temperature NMR experiments that provide rotation barriers of a complementary series of *N*-cyclohexene derived enamides in which the size of the acyl group has been steadily increased. To estimate the barrier to rotation in radicals such as **2**, we have prepared analogues where the bromine atom has been replaced by a hydrogen atom. These results provide a quantitative footing for estimation of rotation barriers that can be used to design axially chiral enamides that could be resolved at ambient temperatures and that could undergo onward reactions that are faster (or slower) than bond rotations.

RESULTS AND DISCUSSION

The experiments were initiated by preparing the series of enamides **4**−**6**[1] to determine the effect of additional methyl groups and halogen atoms attached to the acyl group on the rotation barrier. Compounds **4a**−**c** were prepared to determine the effect of sequential replacement of H atoms with methyl groups in the radical precursors, while compounds **6a**−**c** were prepared to determine the same effect in analogues where the bromine atoms have been replaced by hydrogen atoms and were studied as potential models for the reactive radicals (Figure 2). The tri- and dihalo substrates **4d** and **6d** were also prepared because these substrates have often been utilized in atom transfer radical cyclizations (ATRC) reactions[10] as well as organostannane mediated radical reactions,[11] where the additional halogen substituents have been reported to facilitate cyclization. In addition, **6d** would act as a model for the radical **5d** obtained from the trichloroacetyl radical precursor **4d**.

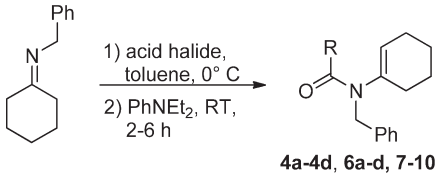

Figure 3. Synthesis of enamides **4a**−**d**, **6a**−**d**, **7**−**10**.

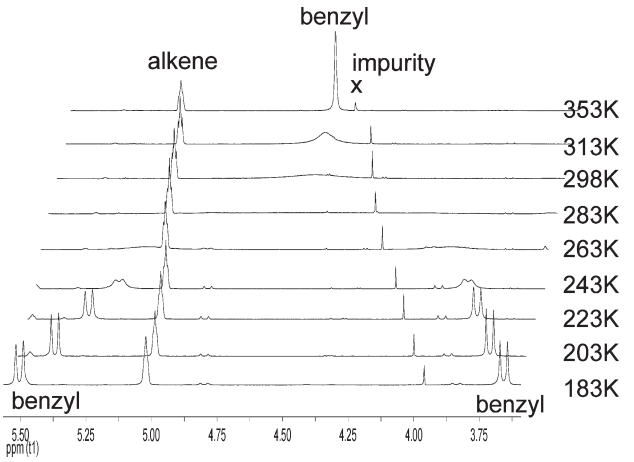

Figure 4. Expansion of the ^{1}H NMR spectra of **6c** at 183−353 K.

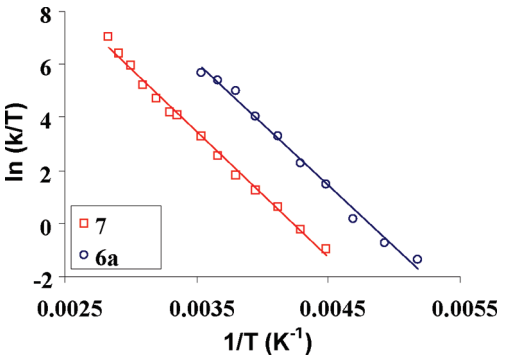

Figure 5. Erying plot of VT NMR data of **7** (□) and **6a** (○).

The compounds were prepared by acylation with the appropriate acid chloride or acid bromide of the imine formed from cyclohexanone and benzylamine, Figure 3.[1] Compounds **4a**−**d** and **6a**−**d** were dissolved in d_8-toluene with a small amount of tetramethylsilane for use as a chemical shift and line width standard. ^{1}H NMR spectra were recorded at temperature intervals in the range of 183−353 K. Portions of these spectra for compound **6c** are shown in Figure 4.

Consistent with expectation as the samples were cooled, decoalescence of the benzyl proton resonances occurred giving rise to mutually coupled doublets as seen in our previously reported work. This behavior is consistent with the existence of largely a single *E*-amide rotamer in solution where decoalescences are caused by slowing of the *N*-cyclohexenyl bond rotation, which reveals the diastereotopicity of the pairs of geminal protons. Enamide **4b** has an additional stereocenter, so its rotamers are diastereomers, not enantiomers. The equilibrium constant for the two diastereomers **4b** is about 1.

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Table 1. *N*-Alkenyl Bond Rotation Rates and Activation Parameters from Variable Temperature NMR Experiments

entry	comp.	R group	k_{rot} 298 K[a] (s^{-1})	$\Delta H^{\ddagger}$[a](kcal/mol)	$\Delta S^{\ddagger}$[a](cal/molK)	$\Delta G^{\ddagger}_{298}$[a] (kcal/mol)
1	**4a**	CH_2Br[b]	4.39×10^4	7.9	−10.9	11.1
2	**4b**	CH(Me)Br[c]	4.55×10^3	7.9	−13.9	12.0
			4.55×10^3	7.9	−13.9	12.0
3	**4c**	$C(Me)_2Br$	1.06×10^3	11.3	−6.6	13.3
4	**4d**	CCl_3	2.52×10^2	14.8	2.0	14.2
5	**6a**	Me	2.51×10^5	9.2	−2.9	10.1
6	**6b**	Et	7.46×10^4	6.4	−14.7	10.9
7	**6c**	*i*-Pr	1.80×10^4	8.5	−10.6	11.7
8	**6d**	$CHCl_2$	6.66×10^3	10.0	−7.4	12.2
9	**7**	*t*-Bu	6.43×10^3	12.5	0.9	12.3
10	**8**	$CH{=}CH_2$	7.45×10^4	7.5	−11.1	10.8
11	**9**	C_6H_5	4.89×10^5	6.0	−12.2	9.7
12	**10**	CH_2Ph	2.29×10^4	7.8	−12.4	11.5

[a] Estimated errors k_{rot} 298 K ± 13%, $\Delta H^{\ddagger}$ = ± 0.3 kcal/mol, $\Delta S^{\ddagger}$ = ± 1.0 cal/(mol K), $\Delta G^{\ddagger}_{298}$ = ± 0.2 kcal/mol, these are in-line with related work.[7] [b] Values taken from ref 1. [c] The rotamers are diastereomers, so forward and reverse rates were determined.

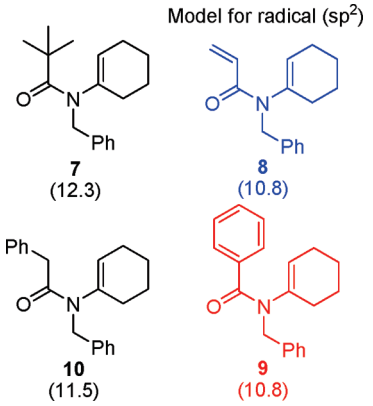

Figure 6. Radical precursors **7**−**10** with measured $\Delta G^{\ddagger}_{298}$ barrier to rotation in kcal/mol in paranthesis.

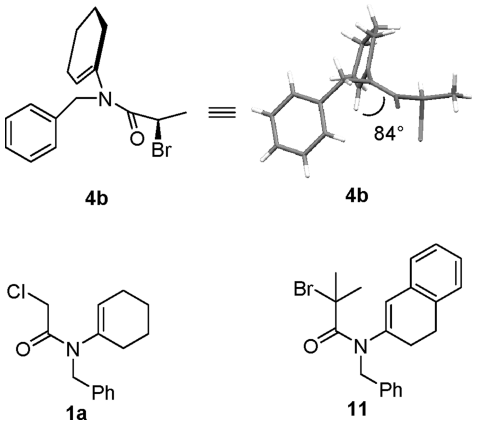

Figure 7. X-ray crystal structure of one diastereomer of **4b**.

Using the WINDNMR 7.1 line-shape analysis program[12] to analyze the benzyl peaks of **4a**−**d** and **6a**−**d**, we determined the rotational rate constant k_{rot} at each temperature T. The standard Erying plots for the **6a** and **7** are shown in Figure 5. The activation enthalpies and entropies were calculated in the standard way and are shown in Table 1. The benzylic protons were well resolved from other resonances in every case, so these were made the focal points of the line shape analyses.

The 400 MHz NMR spectra of **4a**−**c** and **6a**−**c** at room temperature were simple, and peak broadening and decoalescence were observed upon cooling. It can be seen from comparing **6a**−**c** in Table 1 that the sequential addition of methyl groups imparts a steady increase of 0.8 kcal/mol in the $\Delta G^{\ddagger}_{298}$ values (**6a**→**6b** $\delta\Delta G^{\ddagger}_{298}$ = 0.8 kcal/mol, **6b**→**6c** $\delta\Delta G^{\ddagger}_{298}$ = 0.8 kcal/mol). For completeness, we prepared the pivaloyl analogue **7** and found a similar increase (**6c**→**7** $\delta\Delta G^{\ddagger}_{298}$ = 0.6 kcal/mol). A similar but marginally larger trend was observed in the bromide series **4a**−**c** (**4a**→**4b** $\delta\Delta G^{\ddagger}_{298}$ = 0.9 kcal/mol, **4b**→**4c** $\delta\Delta G^{\ddagger}_{298}$ = 1.3 kcal/mol). More importantly, when comparing the bromides **4a**−**c** with their "radical models" **6a**−**c** where we have replaced the bromine atom with a hydrogen atom a decrease of between 1.0 and 1.6 kcal/mol in the $\Delta G^{\ddagger}_{298}$ value is observed (**4a**→**6a** $\delta\Delta G^{\ddagger}_{298}$ = 1.0 kcal/mol, **4b**→**6b** $\delta\Delta G^{\ddagger}_{298}$ = 1.1 kcal/mol, **4c**→**6c** $\delta\Delta G^{\ddagger}_{298}$ = 1.6 kcal/mol). A greater difference was observed upon comparison of the trichloracetyl derivative **4d** with the dichloroacetyl "radical model" **6d**, (**4d**→**6d** $\delta\Delta G^{\ddagger}_{298}$ = 2.0 kcal/mol). Thus, a drop of $\Delta G^{\ddagger}_{298}$ between 1.0 and 2.0 kcal/mol correlates to a 5−26 times increase in the k_{rot} 298 K value on going from the radical presursors to the "radical models".

Arguably a better model for the sp^2 hybridized radicals **5b**−**c** are the vinyl **8** and the aryl **9** derivatives containing an sp^2 carbon center where the radical would be situated, Figure 6.[13] While the barrier for rotation of "sp^2 radical model" **8** ($\Delta G^{\ddagger}_{298}$ = 10.8 kcal/mol) is similar to the "sp^3 radical model" **6b** ($\Delta G^{\ddagger}_{298}$ = 10.9 kcal/mol) the measured barriers for **6c** ($\Delta G^{\ddagger}_{298}$ = 11.7 kcal/mol) and the benzoyl derivative **9** ($\Delta G^{\ddagger}_{298}$ = 9.7 kcal/mol) were significantly different. The decreased value for the benzoyl analog **9** is consistent with related observations in anilides.[14] The phenyl ring of **9** is likely twisted out of the plane of the C=O in the ground state and can twist even more as the C−N bond rotates. So it can get out of the way relatively easier than corresponding sp^3 groups. On the other hand the vinyl compound **8**, while it looks less hindered than **9**, is conjugated s-*cis*, so in order to twist this group out of the way during C−N bond rotation this conjugation must be broken. Finally, we measured the barrier to rotation of the benzylic derivative **10**. This was found to be

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Table 2. *N*-Alkenyl Bond Rotation Rates and Activation Parameters from Variable Temperature NMR Experiments for 4a and 4c in Different Solvents

compound	solvent	k_{rot} 298 K[a] (s^{-1})	$\Delta H^{\ddagger a}$ (kcal/mol)	$\Delta S^{\ddagger a}$ (cal/mol K)	$\Delta G^{\ddagger}_{298}{}^{a}$ (kcal/mol)
4a	d_8-toluene[b]	4.54×10^3	8.1	−10.0	11.1
4a	CD_3OD[b]	1.96×10^3	8.2	−11.3	11.6
4a	$CDCl_3$[b]	1.58×10^3	8.5	−10.6	11.7
4c	d_8-toluene	1.06×10^3	11.3	−6.6	13.3
4c	CD_3OD	326.1	12.7	−4.3	14.0
4c	$CDCl_3$	251.4	15.4	4.2	14.2
4c	CD_3NO_2	245.3	12.5	−5.7	14.2

[a] Estimated errors k_{rot} 298 K ± 13%, $\Delta H^{\ddagger}$ = ±0.3 kcal/mol, $\Delta S^{\ddagger}$ = ±1.0 cal/(mol K), $\Delta G^{\ddagger}_{298}$ = ±0.2 kcal/mol, these are in-line with related work.[7] [b] Value taken from ref 1.

greater than the primary bromide **4a** and similar to the isopropyl derivative **6c**.

It was possible to solve the X-ray structure for **4b**. The torsional angle of the key *N*-alkenyl bond for one of the isomers is 84°, this is similar to that observed for anilides[1,15] and is slightly larger than the reported value of 74° for the primary chlorine analogue **1a**[1] and significantly larger than the 2-tetralone derivative **11** (56°), Figure 7.[2] Unlike the 2-tetralone derivative **11**, where the amide nitrogen exhibited partial sp^3 hybridization with the sum of bond angles to nitrogen being 356.9° and the torsion angle of the amide C−N bond being around 152.0°, for **4b** the amide nitrogen shows sp^2 character as expected (with the sum of bond angles to nitrogen being 359.9° and the torsion angle of the amide C−N bond 179.1°).

We briefly explored the effect of solvent on the rotation barrier of both enamide **4c** and **4a** (Table 2). Radical cyclizations of related enamides have been mediated by organostannane reagents[11] and with copper complexes under ATRC conditions.[10] The former reactions tend to be carried out in nonpolar solvents (such as cyclohexane, toluene or benzene) while the latter tend to be carried out in polar solvents (such as dichloromethane, acetonitrile or methanol). The data shows that in general more polar solvents increase the barrier to rotation, although this difference is slight (0.5−0.9 ± 0.2 kcal/mol) and there seems to be no correlation with dielectric constant ε, dipole moment μ, or viscosity η. Focusing on the solvents used in Bu_3SnH (toluene) and in ATRC (chlorinated, alcohol) reactions, the trend with **4c** was identical with **4a**, namely $\Delta G^{\ddagger}_{298}$ = toluene < MeOH ≈ $CDCl_3$. This corresponds to a decrease in the rate of C−N bond rotation upon changing the solvent from d_8-toluene to $CDCl_3$ of approximately 2.9 and 4.2 times for **4a** and **4c**.

CONCLUSIONS

A range of radical precursors **4a**−**d**, radical "mimics" **6a**−**d**, and **8** have been prepared to measure the rate of bond rotation around their C−N bonds. The relative order of rotation parallels the size of the acyl substituents and their reported Taft E_s parameters,[16] notably **6a** (0.00) < **6b** (0.07) < **4a** (0.27) < **6c** (0.47) < **4b** (0.93) < **6d** (1.54) ≈ **7** (1.54) < **4c** (1.77)[17] < **4d** (2.06). For efficient chirality transfer to occur in 5-*endo trig* cyclizations, the rate of C−N bond rotation must be significantly slower than the rate of cyclization (1×10^4 s^{-1}). Increased steric hindrance at the acyl center lowers the rate of rotation as expected (**4a** = 43 900 s^{-1}, **4b** = 9000 s^{-1}, **4c** = 1060 s^{-1}, **4d** = 252 s^{-1}) but more importantly replacing the large halogen atom with a hydrogen atom to 'mimic' the radical interemediates **5a**−**d** increases the rate of rotation only between 5 and 26 times. Unfortunately, for radical mimic **6a** this corresponds to the rate of C−N bond rotation being approximately 25 times faster than cyclization at room temperature indicating that while chirality transfer in radicals such as **5a** is not practical, transfer from radical **5d** should occur, but be relatively low. For successful chirality transfer in 5-*endo* cyclizations, it is evident that rotations would need to be significantly slower than those reported here.

EXPERIMENTAL SECTION

***N*-Cyclohex-1-enyl-*N*-benzyl-2-bromopropionamide (4a).** The literature procedure[3a] was followed using benzylamine (1.07 g, 10 mmol), cyclohexanone (2.94 g, 10 mmol), bromoacetyl bromide (2.20 g, 11.0 mmol) and triethylamine (2.97 g 30 mmol) to give the product **4a** (925 mg, 30%).[3a] Spectroscopic data (^{1}H NMR and ^{13}C NMR) was consistent with previously reported results. R_f (3:1 pet ether: EtOAc) 0.6; υ_{max} (film)/cm^{-1} 2934, 1646; δ_H ($CDCl_3$, 400 MHz) 7.28 (5H, m), 5.50 (1H, s), 4.62 (2H, br s), 3.95 (2H, s), 2.07 (4H, m), 1.69 (2H, m), 1.40 (2H, m); δ_C (100 MHz, $CDCl_3$) 166.1, 137.8, 137.4, 129.2, 128.7, 128.4, 127.4, 49.8, 41.9, 27.4, 25.3, 24.7, 21.4; *m*/*z* (ESI) 330 ($[M]^+$Na); [Found: ($[M]^+$Na) 330.0464, $C_{15}H_{18}BrNO$ requires ($[M]^+$Na) 330.0469].

General procedure for the formation of compounds **4b**−**d**, **6a**−**d**, **7**−**10**: Cyclohexanone (1 equiv) and benzylamine (1 equiv) were added to dry toluene at room temperature. The reaction mixture was heated at reflux, using Dean−Stark apparatus, overnight. The crude reaction mixture was allowed to cool to room temperature, then cooled further to 0 °C, before addition of the appropriate acyl halide (1 equiv), followed by diethylaniline (1 equiv). The reaction was allowed to reach room temperature and stirred for 4 h. The reaction mixture was washed with 2 M HCl. The organic layer was dried over $MgSO_4$, filtered and concentrated in *vacuo* to yield a crude product purified via flash chromatography using 3:1 pet ether/EtOAc. For compounds **7** and **8**, the enamide alkene quaternary carbon and the aromatic quaternary carbon are coincident in the ^{13}C NMR spectra. For **4c**, the gem dimethyl group exhibits a very broad ^{13}C NMR resonance.

***N*-Cyclohex-1-enyl-*N*-benzyl-2-bromopropionamide (4b).** Yield (70%); Cream solid mp 86−87 °C; R_f (3:1 pet ether/EtOAc) 0.8; υ_{max} (film)/cm^{-1} 2922, 1651; δ_H ($CDCl_3$, 400 MHz) 7.20 (5H, m), 5.48 (1H, m), 4.75−4.50 (3H, m), 2.16 (1H, m), 2.00 (3H, m), 1.79 (3H, d, J 6.8 Hz), 1.64 (2H, m), 1.53 (2H, m); δ_C (100 MHz, $CDCl_3$) 169.7, 138.0, 137.8, 129.4, 129.0, 128.7, 128.7, 50.4, 39.9, 28.4, 25.1, 23.1, 22.7, 21.7; *m*/*z* (ESI) 344.1 ($[M]^+$Na) 322.1 $[M]^+$; [Found: ($[M]^+$Na) 344.0620, $C_{16}H_{20}BrNO$ requires ($[M]^+$Na) 344.0626]; [Found: C, 59.6; H, 6.2; N, 4.4. $C_{16}H_{20}BrNO$ requires C, 59.6; H, 6.3; N, 4.35].

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***N*-Cyclohex-1-enyl-*N*-benzyl-2-bromo-2-methylpropionamide (4c)**[1]. Yield (69%); clear oil; R_f (3:1 pet ether/EtOAc) 0.80; υ_{max} (film)/cm^{-1} 2931, 2859, 1630, 1495, 1449, 1390, 1364, 1257, 1171, 1107, 920, 726, 697; δ_H (300 MHz $CDCl_3$) 7.21 (5H, m), 5.53 (1H, m), 4.90 (1H app br s), 4.19 (1H, app br s), 2.12 (2H, br s), 1.96 (8H, app br s), 1.63 (2H, m), 1.47 (2H, m); δ_C (75.5 MHz, $CDCl_3$) 170.2, 137.4 (x 2), 129.3 (broad), 128.2, 128.0, 126.9, 58.2, 52.2, 34.0 (broad), 27.8, 24.4, 22.4, 21.0; *m*/*z* (ESI) 358 ([M]$^+$Na) 336; [Found: ([M]$^+$Na), 358.0777, $C_{17}H_{22}BrNO$ requires ([M]$^+$Na), 358.0782]; [Found: C, 60.7; H, 6.7; N, 4.1. $C_{17}H_{22}BrNO$ requires C, 60.7; H, 6.6; N, 4.2].

***N*-Cyclohex-1-enyl-*N*-benzyltrichloroacetamide (4d)**[18]. Yield (20%); dark yellow oil; R_f (3:1 pet ether/EtOAc) 0.78; υ_{max} (film)/cm^{-1} 3032, 2928, 2859, 1665, 1496, 1438, 1389, 1246, 1175, 848, 808, 697; δ_H (300 MHz $CDCl_3$) 7.34−7.28 (5H, m), 5.59 (1H, m), 5.05 (1H, br d, J 13.0 Hz), 4.26 (1H, br s), 2.22 (2H, br), 2.01 (2H, br), 1.68−1.51 (4H, br); δ_C (75 MHz $CDCl_3$) 178.7, 142.0, 128.8, 128.4, 128.3, 127.7, 74.6, 53.3, 27.5, 24.6, 22.4, 21.1; *m*/*z* (ESI) 354 ([M]$^+$Na); *m*/*z* [Found: ([M]$^+$Na) 354.0193, $C_{15}H_{16}Cl_3NNaO$ requires 354.0195].

***N*-Cyclohex-1-enyl-*N*-benzylacetamide (6a)**.[3a] Yield (33%); Pale yellow oil; R_f (3:1 pet ether/EtOAc) 0.6; υ_{max} (film)/cm^{-1} 2928, 1644; δ_H ($CDCl_3$, 300 MHz) 7.22 (5H, m), 5.37 (1H, m), 4.60 (2H,s), 2.06 (3H,s), 1.95 (4H,m), 1.62 (2H, m), 1.49 (2H, m); δ_C ($CDCl_3$, 75.5 MHz) 170.0, 138.9, 138.1, 128.7, 128.2, 128.1, 127.1, 49.4, 28.0, 24.7, 22.7, 21.6, 21.5; *m*/*z* (ESI) 252 ([M]$^+$Na), 231 [M]$^+$; [Found: ([M]$^+$Na) 252.1359, $C_{15}H_{19}NO$ requires ([M]$^+$Na) 252.1364].

***N*-Cyclohex-1-enyl-*N*-benzylpropionamide (6b).** Yield (20%); Cream solid mp 72−73 °C; R_f (3:1 pet ether/EtOAc) 0.6; υ_{max} (film)/cm^{-1} 2935, 1634; δ_H ($CDCl_3$, 300 MHz) 7.28 (5H, m), 5.38, (1H, s), 4.60 (2H, s), 2.33 (2H, q, J 7.5 Hz), 2.00 (4H, m), 1.64 (2H, m) 1.53 (2H, m), 1.12 (3H, t, J 7.5 Hz); δ_C ($CDCl_3$, 75.5 MHz) 173.4, 138.4, 138.3, 128.7, 128.2, 128.0, 127.0, 49.6, 28.2, 26.8, 24.8, 22.8, 21.5, 10.1; *m*/*z* (ESI) 266 ([M]$^+$Na); [Found: ([M]$^+$Na) 266.1515, $C_{16}H_{21}NO$ requires ([M]$^+$Na) 266.1521].

***N*-Cyclohex-1-enyl-*N*-benzyl-2-methylpropionamide (6c).** Yield (18%); Pale yellow solid mp 78−80 °C; R_f (3:1 pet ether/EtOAc) 0.8; υ_{max} (film)/cm^{-1} 2929, 1634; δ_H ($CDCl_3$, 400 MHz) 7.24 (5H, m), 5.40 (1H, s), 4.59 (2H, s), 2.81 (1H, sept, J 6.7 Hz), 1.99 (4H, m), 1.68 (2H, m), 1.52 (2H, m), 1.12 (6H, d, J 6.5 Hz); δ_C ($CDCl_3$, 75.5 MHz) 177.0, 138.6, 138.5, 128.7, 128.2, 127.5, 127.0, 49.7, 31.4 (broad), 28.8, 24.7, 22.9, 21.5, 20.2; *m*/*z* (ESI) 280.2 ([M]$^+$Na) 258.1 [M]$^+$; [Found: ([M]$^+$Na) 280.1672, $C_{17}H_{23}NO$ requires ([M]$^+$Na) 280.1677].

***N*-Cyclohex-1-enyl-*N*-benzyldichloroacetamide (6d)**.[18] Yield (31%); Off-white solid mp 41−42 °C; R_f (3:1 pet ether/EtOAc) 0.67; υ_{max} (film)/cm^{-1} 3030, 2927, 1673, 1495, 1440, 1403, 1210, 1177, 1078, 922, 803, 744, 670; δ_H (300 MHz $CDCl_3$) 7.34−7.24 (5H, m), 6.39 (1H, s), 5.53 (1H, br m), 4.65 (2H, br s), 2.06 (4H, m), 1.74−1.52 (4H, m); δ_C (75 MHz $CDCl_3$) 163.8, 136.9, 136.5, 130.4, 128.8, 128.5, 127.7, 64.1, 50.4, 27.9, 24.7, 22.5, 21.2; *m*/*z* (ESI) 320 ([M]$^+$Na); *m*/*z* [Found: ([M]$^+$Na) 320.0579, $C_{15}H_{17}Cl_2NNaO$ requires 320.0585].

***N*-Cyclohex-1-enyl-*N*-benzyl-2-dimethylpropionamide (7).** Yield (6%); Yellow oil; R_f (3:1 pet ether/EtOAc) 0.9; υ_{max} (film)/cm^{-1} 2928, 1625; δ_H ($CDCl_3$, 400 MHz) 7.23 (5H, m), 5.28 (1H, m), 4.42 (2H, br s), 2.07 (4H, m), 1.67 (2H, m), 1.54 (2H, m), 1.25 (9H, s); δ_C ($CDCl_3$, 75.5 MHz) 178.0, 138.7 (x 2), 128.4, 128.2, 128.1, 126.8, 51.7, 40.9, 29.3, 28.4, 24.6, 22.6, 21.3; *m*/*z* (ESI) 294.2 ([M]$^+$Na) 272.2 [M]$^+$; [Found: ([M]$^+$Na) 294.1828, $C_{18}H_{25}NO$ requires ([M]$^+$Na) 294.1834].

***N*-Cyclohex-1-enyl-*N*-benzylprop-2-enamide (8)**.[19] Yield (46%); Yellow oil; R_f (3:1 pet ether/EtOAc) 0.41; υ_{max} (film)/cm^{-1} 2926, 1648, 1408, 1350, 1236, 1138, 1079, 980, 698; δ_H (300 MHz, $CDCl_3$) 7.29−7.18 (5H, m), 6.54−6,45 (1H, dd, J 17.0, 9.7 Hz), 6.42−6.35 (1H, dd, J 17.0, 2.8), 5.63−5.59 (1H, dd, J 9.7, 2.8), 5.39 (1H, br s), 4.67 (2H, s), 2.06−1.92 (4H, m), 1.68−1.48 (4H, m); δ_C (75.5 MHz $CDCl_3$) 165.2, 137.9 (x 2), 136.6, 128.7, 128.6 (x 2), 128.3, 128.2, 127.1, 49.8, 28.7, 24.7, 22.7, 21.5; *m*/*z* (ESI) 264 ([M]$^+$Na) 242 [M]$^+$; [Found: ([M]$^+$Na) 264.1359, $C_{16}H_{19}NNaO$ requires 264.1364].

***N*-Cyclohex-1-enyl-*N*-benzamide (9)**.[20] Yield (32%); Dark yellow oil; R_f (3:1 pet ether/EtOAc) 0.54; υ_{max} (film)/cm^{-1} 3061, 3029, 2929, 2858, 2837, 1632, 1576, 1495, 1446, 1436, 1388; δ_H (300 MHz, $CDCl_3$) 7.44−7.40 (2H, m), 7.29−7.15 (8H, m), 5.18 (1H, br t, J 3.5 Hz), 4.73 (2H, s), 1.84−1.66 (4H, m), 1.40−1.19 (4H, m); δ_C (75.5 MHz $CDCl_3$) 170.6, 139.0, 138.1, 137.3, 129.7, 128.6, 128.4, 128.2, 127.9, 127.6, 127.3, 50.7, 28.9, 24.8, 22.6, 21.4; *m*/*z* (ESI) 314 ([M]$^+$Na), 292 [M]$^+$; [Found: [M]$^+$ 292.1696, $C_{20}H_{22}NO$ requires 292.1701]; [Found: ([M]$^+$Na) 314.1515, $C_{20}H_2NNaO$ requires 314.1521]; [Found: C, 81.9; H, 7.3; N, 4.5, $C_{20}H_{21}NO$ requires C, 82.4; H, 7.3; N, 4.8].

***N*-Cyclohex-1-enyl-*N*-benzyl-2-phenylacetamide (10).** Yield 23%; Off-white solid mp 146−147 °C; R_f (3:1 pet ether/EtOAc) 0.56; υ_{max} (film)/cm^{-1} 3028, 2937, 1632, 1581, 1451, 1427, 1399, 1248, 1166, 1026, 702; δ_H (300 MHz, $CDCl_3$) 7.33−7.19 (10H, m), 5.29 (1H, br s), 4.61 (2H, s), 3.70 (2H, s), 2.03−1.86 (4H, m), 1.67−1.49 (4H, m); δ_C (75.5 MHz $CDCl_3$) 170.6, 138.3, 138.2, 136.3, 129.2, 129.0, 128.9, 128.5, 128.3, 127.3, 126.7, 49.7, 41.0, 28.3, 24.9, 22.9, 21.6; *m*/*z* (ESI) 328 ([M]$^+$Na); 306 [M]$^+$; [Found: ([M]$^+$Na) 328.1672, $C_{21}H_{23}NNaO$ requires 328.1677]; [Found: C, 82.4; H, 7.5; N, 4.5, $C_{21}H_{23}NO$ requires C, 82.6; H, 7.6; N, 4.6].

■ ASSOCIATED CONTENT

Supporting Information. Contains VT NMR experiments, rotational data, Eyring plots and copies of ^{1}H NMR and ^{13}C NMR spectra spectra for **4a**−**d**, **6a**−**d**, **7**−**10** and X-ray data for **4b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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