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# Spectroscopic and X-ray Crystallographic Evidence for Electrostatic Effects in 4-Substituted Cyclohexanone-Derived Hydrazones, Imines, and Corresponding Salts

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Supporting Information

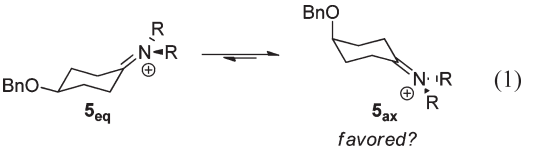
**ABSTRACT:** The axial conformer of several 4-substituted cyclohexanone hydrazone salts was found to predominate in solution. Changes in the charge of the molecule and the polarity of the solvent led to changes in the conformational preference of each molecule that were consistent with electrostatic stabilization of the axial conformer. $^1$H NMR spectroscopic analysis was utilized to determine the structure of cyclohexanone-derived substrates by comparison to conformationally restricted *trans*-decalone derivatives and computational models. X-ray crystallography demonstrated that the axial configuration of a pendant benzyloxy group is the preferred conformation of an iminium ion in the solid state. The structure of a neutral hydrazone was also determined to favor the axial configuration for a pendant benzyloxy group in the solid state.

## INTRODUCTION

Iminium ions are important intermediates in the bond-forming steps of many organic reactions. Transformations such as the Mannich reaction,[1,2] reductive amination,[3,4] and amine-catalyzed Michael reactions[5] utilize iminium ion intermediates in key bond-forming steps. The conformation adopted by iminium ion intermediates in these reactions are important in determining the stereochemical outcomes of these processes.[6,7]

Electrostatic effects should strongly influence the conformational preferences of iminium ion intermediates. In general, electrostatic effects play an important role in defining the conformational preferences of charged intermediates.[8−12] For example, cyclic oxocarbenium ion intermediates adopt conformations that minimize the distance between partially negatively charged substituents and the positively charged oxocarbenium ion center.[8−14] Nucleophilic substitution reactions of 4-substituted cyclohexanone acetals illustrate this phenomenon (Scheme 1).[14] The stereochemical courses of nucleophilic addition reactions to oxocarbenium ions bearing alkyl groups (**1**, Scheme 1) suggest that an alkyl substituent resides in the equatorial position but alkoxy groups reside in axial orientations (**3**, Scheme 1).[14] Evidence for the conformational preferences of these cations was provided by studies of related dioxocarbenium ions, which are air-sensitive.[15,16]

Iminium ions should exhibit similar electronically controlled conformational preferences (eq 1).[17] This hypothesis could be tested using spectroscopic methods. In contrast to oxocarbenium ions, which are highly reactive compounds[18,19] that have been observed spectroscopically in only a few cases,[20−22] iminium ions are much more stable. Alkyl iminium salts are commercially available,[23] and simple protonated imines have been isolated and are amenable to X-ray crystallographic analysis.[24] Similar ions can be formed from hydrazones, which are typically protonated at the double-bonded nitrogen atom to form stable cations.[25]

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In this article, we describe the preparation and conformational analysis of cations derived from cyclohexanone hydrazones and an imine. Comparing spectral parameters to those obtained for appropriate model compounds revealed that electrostatic effects can strongly influence the conformational preferences of hydrazonium ions. X-ray crystallography provided supporting evidence for the conformational preferences determined in solution.

## RESULTS AND DISCUSSION

**General Approach to Determination of Conformational Preference by NMR Spectroscopy.** $^1$H NMR spectroscopy can be used to determine the conformational equilibrium of molecules in solution.[26−28] Examination of $^1$H NMR signal bandwidths can be used to determine the ratios of axial to equatorial conformers in substituted cyclohexanes and cyclohexanones.[29−34] The bandwidth of a multiplet is defined as the peak width at quarter height. Alternatively, it can be represented as the outer peak-to-peak distance of the multiplet, which is the sum of the coupling constants for that resonance.[26,27] The latter

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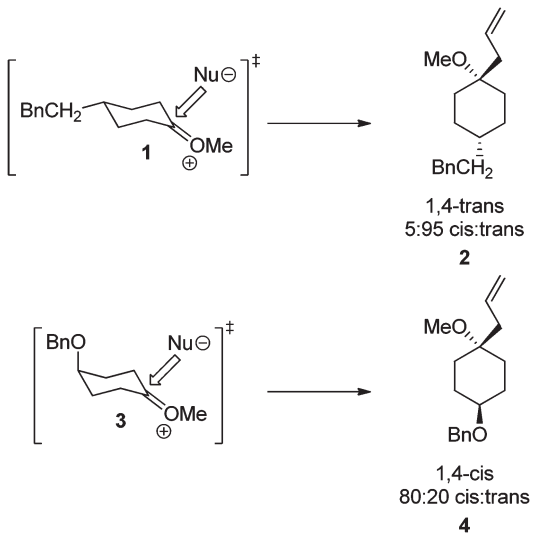
**Scheme 1. Preferred Conformation of a 4-Benzyloxycyclohexanone-Derived Oxocarbenium Ion and Products of Nucleophilic Addition**




definition is used in this article. In a rapidly equilibrating cyclohexane system, the bandwidth of each multiplet ($W_{obs}$) is equal to the weighted average of the bandwidths of axial ($W_{ax}$) and equatorial ($W_{eq}$) conformers as shown in eq 2, assuming that these two states dominate the conformational equilibrium.

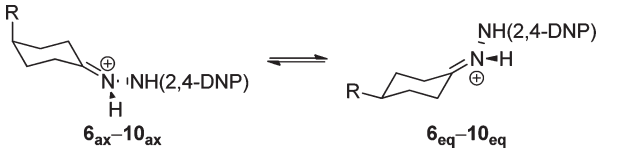
$$W_{obs} = \chi_{ax} W_{ax} + (1 - \chi_{ax}) W_{eq} \quad (2)$$

Synthetic studies and computer modeling were used to determine the predicted bandwidth benchmark values ($W_{ax}$ and $W_{eq}$) for each conformer. Both techniques were compared to previous literature results and to each other. Computer modeling of bandwidth values allows for examination of compounds for which there are no model compounds.

**Substrate Choice.** The conformational preferences of several hydrazonium ions derived from 4-substituted cyclohexanones were examined computationally to determine which ones might have unusual conformational preferences. Hydrazonium ions were chosen for study because of their relative ease of synthesis and purification of their precursors.[35] Using the Gaussian 03 package,[36] we determined the minimum energy structures of the axial and equatorial conformers by systematically rotating about each degree of freedom at the 4-position of the ring. Only standard chair conformations were considered and optimized using the Hartree−Fock method. Each conformer was initially examined using the 3-21g basis set and further optimized using the 6-311g** basis set. The lowest energy conformers from the 6-311g** basis set optimization were then analyzed using a single-point calculation with the DFT/B3LYP method and the 6-311g(3df,3pd) basis set. The cutoff for inclusion in each round of calculation was 2.5 kcal/mol above the lowest energy conformer. The conformational energy differences determined from structure calculations in the following discussion were determined without solvent and were used as a guide to direct synthetic efforts.

These computational studies revealed an axial preference for several functional groups in the hydrazonium ions. All of the substrates are predicted to favor an axial conformation when the hydrazone is protonated (Table 1). By comparison, the neutral

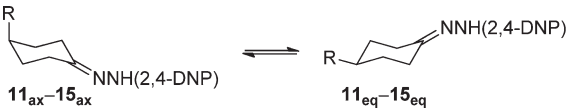
**Table 1. Computer Modeling of Charged Hydrazones (2,4-DNP = 2,4-Dinitrophenyl)**




| compd | R | $\Delta E^a$ (kcal/mol) |
|---|---|---|
| **6** | OBn | +6.3 |
| **7** | OMe | +3.5 |
| **8** | OC(O)OMe | +2.3 |
| **9** | NHC(O)OMe | +0.8 |
| **10** | $CF_3$ | +1.0 |

[a] As determined at the DFT/B3LYP level using 6-311g(3df,3pd).

**Table 2. Computer Modeling of Neutral Hydrazones**




| compd | R | $\Delta E^a$ (kcal/mol) |
|---|---|---|
| **11** | OBn | +0.7 |
| **12** | OMe | +0.8 |
| **13** | OC(O)OMe | +0.4 |
| **14** | NHC(O)OMe | −1.3 |
| **15** | $CF_3$ | −1.4 |

[a] As determined at the DFT/B3LYP level using 6-311g(3df,3pd).

hydrazones either slightly preferred the axial conformer or favored the equatorial one (Table 2). These studies indicate that significant preferences for the axial conformer can only be anticipated for the cation, not for the neutral species. Consequently, both the neutral hydrazones and their conjugate acids were examined to evaluate the validity of these computational predictions.

Further examination of the low-energy conformers validated the premise that the distance between charged groups in the axial conformation is less than the distance measured in the equatorial conformation. The distance between the partially negatively charged functional groups and positively charged carbon of the hydrazone decreased by an average of 23% for the protonated hydrazones.[37] The neutral hydrazones decreased the distance by an average of 17%. An examination of the Cremer−Pople parameters suggests that all of the conformers adopted slightly flattened rings close to the $^1C_4$ conformation.[38,39] The largest deviation seen was for a conformation of the axial carbamate salt, which had a $Q$ value of 0.443, a $\theta$ value of 18.6°, and a $\phi$ value of 188.2°.

**Substrate Synthesis.** The cyclohexanone-derived substrates required for this study were prepared in several steps. 4-Benzyloxy- and 4-methoxy-substituted cyclohexanones **19** and **21** were prepared from the protected dione **16** (Scheme 2). The carbonate **24** and carbamate **27** were synthesized from the diol **22** and amino alcohol **25**, respectively (Scheme 3). The trifluoromethyl ketone substrate **29** was prepared by following a general procedure developed by Qing and co-workers (Scheme 4).[40] Elimination of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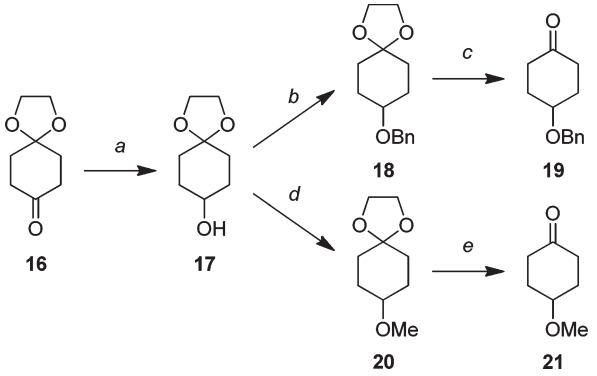
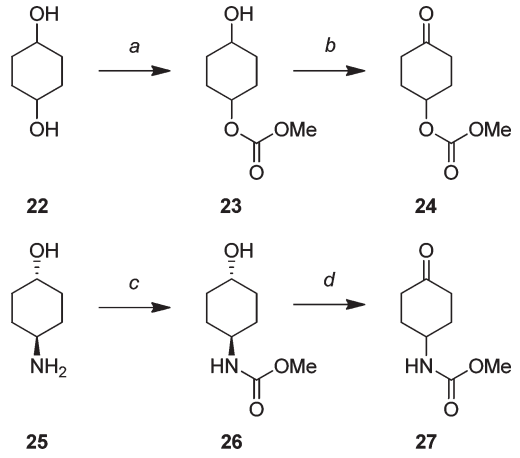
**Scheme 2. Synthesis of Hydrazone Precursors**[a]



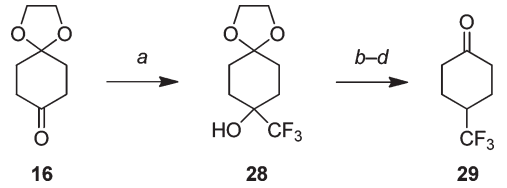

[a] Reagents: (*a*) $NaBH_4$, MeOH, 97%; (*b*) BnBr, KH, 67%; (*c*) HCl, THF, $H_2O$, 93%; (*d*) MeI, KH, 82%; (*e*) HCl, THF, $H_2O$, 100%.

**Scheme 3. Synthesis of Carbonate 24 and Carbamate 27**[a]




[a] Reagents: (*a*) ClC(O)OMe, DMAP, pyridine, 47%; (*b*) Dess−Martin periodinane, 98%; (*c*) ClC(O)OMe, DMAP, pyridine, 33%; (*d*) Dess−Martin periodinane, 70%.

**Scheme 4. Synthesis of Trifluoromethyl-Substituted Ketone 29**[a]

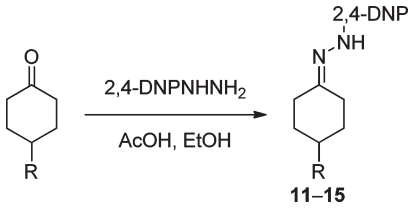



[a] Reagents: (*a*) $Me_3Si$-$CF_3$, TBAF, 77%; (*b*) $SOCl_2$, DMAP, pyridine, THF, Δ, 31%; (*c*) Pt/C, $H_2$; (*d*) HCl, $H_2O$, 60% over two steps.

the tertiary hydroxyl group from compound **28** was performed by following a procedure by Diter and co-workers.[41]

The substituted ketones were converted to the corresponding 2,4-dinitrophenyl hydrazones **11**−**15** (Table 3). The syntheses of the hydrazones were clean, and the products were typically purified by crystallization from the reaction mixture. Chromatography was required when conversion to the hydrazone was incomplete and hydrazine remained in the reaction mixture. An alkyl imine (**30**) was produced from 4-benzyloxycyclohexanone

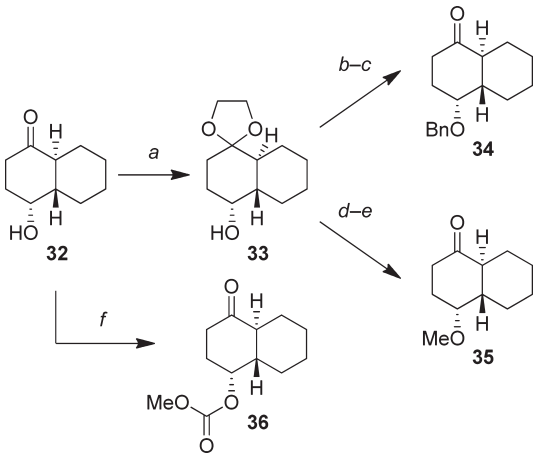
**Table 3. Synthesis of Hydrazones**




| compd | R | yield (%)[a] |
|---|---|---|
| **11** | OBn | 80 |
| **12** | OMe | 82 |
| **13** | OC(O)OMe | 71 |
| **14** | NHC(O)OMe | 84 |
| **15** | $CF_3$ | 38 |

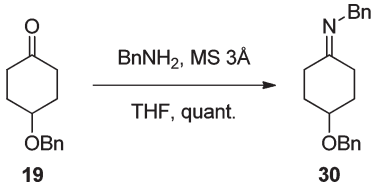
[a] Isolated yield of purified product.

**Scheme 5. Elaboration of the Core Axial Diastereomer**[a]




[a] Reagents: (*a*) $HO(CH_2)_2OH$, PTSA, Δ, 87%; (*b*) BnBr, NaH, Δ, 97%; (*c*) HCl, THF, $H_2O$, 88%; (*d*) MeI, NaH, Δ, 91%; (*e*) HCl, THF, $H_2O$, 91%; (*f*) ClC(O)OMe, DMAP, pyridine, 13%.

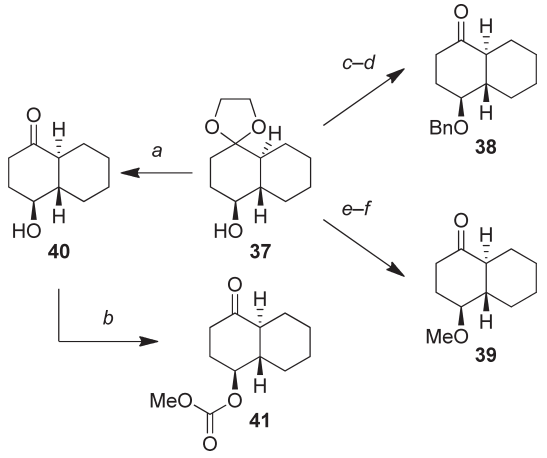
and benzylamine, as shown in eq 3. No purification of the product was attempted. Protonation of the hydrazones at the more basic nitrogen atom[25] gave sensitive hydrazonium ions that could be examined spectroscopically, but they hydrolyzed upon attempted purification by crystallization or chromatography.




(3)

**Synthesis of Conformationally Restricted Substrates.** A series of conformationally restricted hydrazones were prepared so that coupling constants and bandwidths of peaks could be determined for the axial and equatorial conformers of the simple cyclohexanone derivatives. Although 2,6-dimethylcyclohexanones could be used as constrained models,[33,34] the resulting imines and hydrazones could be destabilized by interactions between the substituents on the nitrogen atom and the nearby methyl groups. These interactions could lead to distortion of the

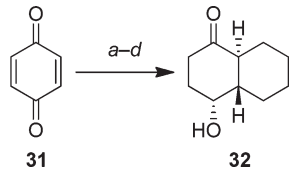
**Scheme 6. Elaboration of the Core Equatorial Diastereomer**[a]




[a] Reagents: (*a*) HCl, THF, $H_2O$, 65%; (*b*) ClC(O)OMe, DMAP, pyridine, 74%; (*c*) BnBr, NaH, Δ, 97%; (*d*) HCl, MeOH, $H_2O$, 63%; (*e*) MeI, NaH, Δ, 91%; (*f*) HCl, THF, $H_2O$, 22%.

ring and therefore perturbations in the coupling constants. A *trans*-decalone is unlikely to be similarly distorted.

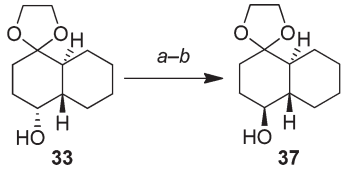
Hydroxy ketone **32** served as the key intermediate for the synthesis of all decalone substrates. It was obtained in four steps from benzoquinone (eq 4).[42] The axially substituted *trans*-decalones were prepared from this ketone by the transformations shown in Scheme 5.




(4)

Reagents: (*a*) 1,3-butadiene, $BF_3 \cdot OEt_2$, 95%; (*b*) $NaBH_4$, $NH_4Cl$, 92%; (*c*) Rh / $Al_2O_3$, $H_2$, 95%; (*d*) KOH, EtOH, Δ, 76%.

The equatorially substituted *trans*-decalones were produced by following a procedure reported by Johnson and co-workers.[43] Oxidation of hydroxyl ketal **33** followed by reduction gave the desired equatorial diastereomer **37** (eq 5). Hydroxy ketal **37** was elaborated using the synthetic sequence shown in Scheme 6. These decalones, along with their axially substituted stereoisomers, were converted into the corresponding hydrazones **42**–**47** (Table 4) and ultimately to the hydrazonium ions. Only a single stereoisomer appears to be present in $^1$H NMR spectra of hydrazones **42**–**47**. It is likely that all of the hydrazones (**43**–**47**) adopt the same *E* configuration as hydrazone **42**, on the basis of the results obtained from X-ray crystallography (vide infra).

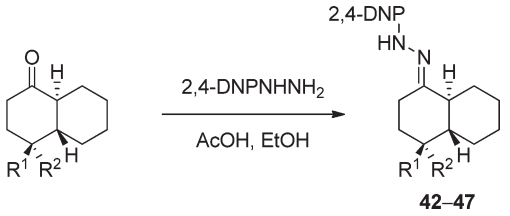



(5)

Reagents: (*a*) Dess–Martin periodinane, 88%; (*b*) $LiAlH_4$, 66%.

**Experimental Determination of Conformational Preference.** The conformational preferences of hydrazones and hydrazonium ions were determined by calculating the sum of all $^3J_{HH}$ coupling constants in each multiplet of the heteroatom-bearing

**Table 4. Synthesis of Decalone Hydrazones**




| compd | $R^1$ | $R^2$ | yield (%)[a] |
|---|---|---|---|
| **42** | H | OBn | 50 |
| **43** | OBn | H | 92 |
| **44** | H | OMe | 85 |
| **45** | OMe | H | 67 |
| **46** | H | OC(O)OMe | 43 |
| **47** | OC(O)OMe | H | 69 |

[a] Isolated yield of purified product.

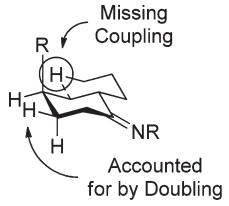



**Figure 1.** Accounting for the missing coupling in the bandwidth of decalones.

methine peak.[44] The location of all peaks in each multiplet were determined by curve-fitting the multiplet to a linear combination of Gaussian and Lorentzian line shapes (Voigt) according to a procedure by Marshall and co-workers.[45,46] Microsoft Excel was used to perform the least-squares curve fits.[47] The error in the bandwidth value for each multiplet was determined from the error in each averaged $^3J_{HH}$ coupling constant composing the multiplet. Extraneous peaks and baseline errors due to shimming were accounted for by adding additional Voigt functions to the multiplet in question. Narrow-band $^{19}$F decoupling was used on the trifluoromethyl-substituted compounds to remove extraneous coupling to fluorine and to simplify the analysis. Narrow-band $^1$H decoupling was used on the carbamate hydrazones to remove line broadening due to coupling to the proton on the nitrogen atom. The bandwidth values were converted into mole fractions of the axial conformation for each compound using eq 2. Error bars are included on all data when they could be established.

Further analysis was required to determine bandwidth values for the decalone model compounds. The methine group at the bridgehead carbon atom in the decalone model system is missing a coupling relationship present in the monocyclic system. The bandwidth was calculated assuming that the missing coupling is equivalent to the coupling with the equatorial methylene proton at the 3-position of the ring and doubling this coupling constant (Figure 1).

**Computational Determination of Conformational Preferences.** Coupling constant calculations were performed on all systems. The minimum energy structures from the single-point calculations were analyzed to determine the $^3J_{HH}$ coupling constants using CP-DFT/B3LYP methodology with a mixed aug-cc-pVDZ/EPRIII basis set.[48,49] Solvent was accounted for

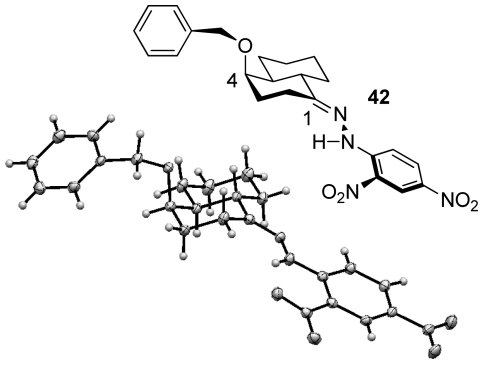



**Figure 2.** Neutral hydrazone X-ray analysis.

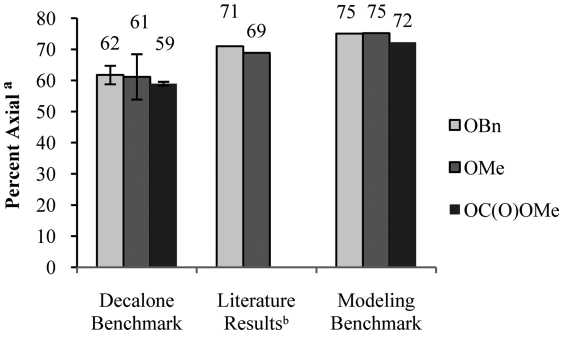



**Figure 3.** Conformational preference method for 4-substituted cyclohexanones. Error bars for the decalone benchmark were determined from averaged $^3J_{HH}$ values (vide supra). Methoxy results were taken from Robinson et al.[54] and benzyloxy results from Nagao et al.[33]

using the integral-equation-formalism polarizable continuum model (IEFPCM).[50] A nondistorted chair was used in the $^3J_{HH}$ coupling constant calculations for the carbamate hydrazone salt. The theoretical bandwidth was determined by summing the $^3J_{HH}$ coupling constants as discussed above.

**Determination of Conformational Preferences.** Initial experiments were aimed to test the validity of key assumptions. If the *trans*-decalone systems **42**–**47** were to provide suitable models of $^3J_{HH}$ coupling constants for the conformationally mobile systems, then they should be free of distortion. To verify this hypothesis, a crystal of axial benzyloxy hydrazone **42** was grown and subjected to X-ray crystallographic analysis (Figure 2). The mean dihedral angle between atoms 1 and 4 in compound **42** was 54.3°. The mean dihedral angle between atoms 1 and 4 in cyclohexanone is 52.0°.[51] The good agreement between the structures of cyclohexanone and compound **42** indicates that decalones should provide good models for $^1$H NMR spectroscopic analysis.

Central to our evaluation of the conformational preferences were the assumptions that the bandwidth of peaks could be attributed to a two-state model of axial and equatorial conformers[52,53] and that the aggregated coupling constants of these conformers could be determined accurately. To verify that these assumptions would yield meaningful results, we re-examined the reported[33,54] conformational preferences of 4-alkoxycyclohexanones **19** and **21** using two methods (Figure 3). Carbonate ketone **24** is included in the comparison as well. In the first method, the conformational preferences of ketones **7** and **9** were determined using the benchmark bandwidth values

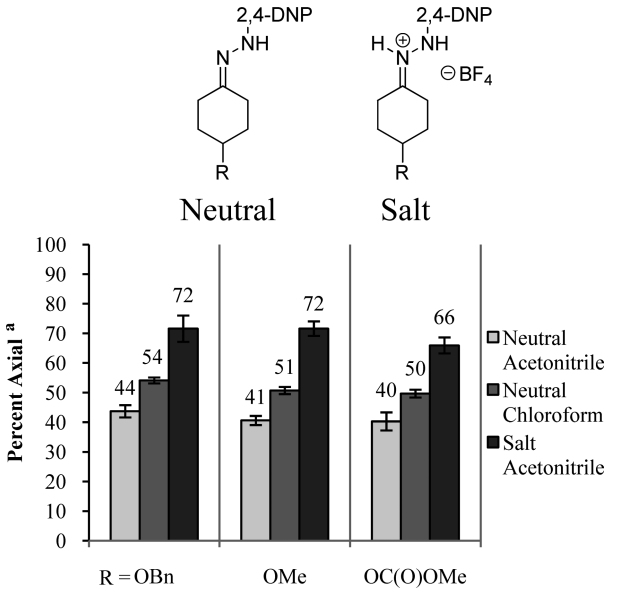



**Figure 4.** Hydrazone results with the decalone $^1$H NMR benchmark. Error bars were determined from averaged $^3J_{HH}$ values (vide supra).

derived from decalones **38**, **39**, **41** and **34**–**36**. The second method used bandwidth values derived from computational studies of the axial and equatorial conformers of **19**, **21**, and **27**. The results obtained using the decalone benchmark method provided lower values for the axial preference of ketones **19** and **21** in comparison to literature results.[33,54] The conformational preferences determined using benchmark bandwidth values derived from computer modeling gave higher axial preferences of ketones **19** and **21** in comparison to literature results.[33,54] Although neither method agrees quantitatively with the previous studies,[33,54] all three methods predict that the axial conformer should be favored. It should be noted that previous studies,[33,54] like ours, were made by comparison to benchmark values (in the earlier case, from 2,6-dimethylcyclohexanone derivatives); therefore, all of these studies depend upon assumptions to determine equilibrium populations.

Using the decalone data as benchmarks, we determined that the conjugate acids of hydrazones have even higher axial preferences than ketones. The neutral hydrazones, in three cases, favored the equatorial conformer with acetonitrile as solvent, but the axial conformer became more prevalent in the less polar solvent, as observed previously (Figure 4).[34,54] The importance of solvent in the conformational preferences of 2-substituted cyclohexanones has been discovered by other authors as well.[55] The observed solvent-dependent shift in the conformational preference is consistent with decreased shielding of the charged centers of the molecule and an increase in electrostatic attraction.[56] The preference for the axial conformer, however, was lower for the neutral hydrazone than for the ketone. The protonated hydrazones,[57] however, exhibited a strong preference for the axial conformer even in $CD_3CN$ (they were only sparingly soluble in $CDCl_3$).

Other heteroatom-containing hydrazones show similar preferences for axial conformers. The conformational preferences were established using the computer modeling benchmark data because not all synthetic benchmarks were prepared. As shown in Figure 3, the computational results likely overestimate the amount of the axial conformer, but they establish trends for

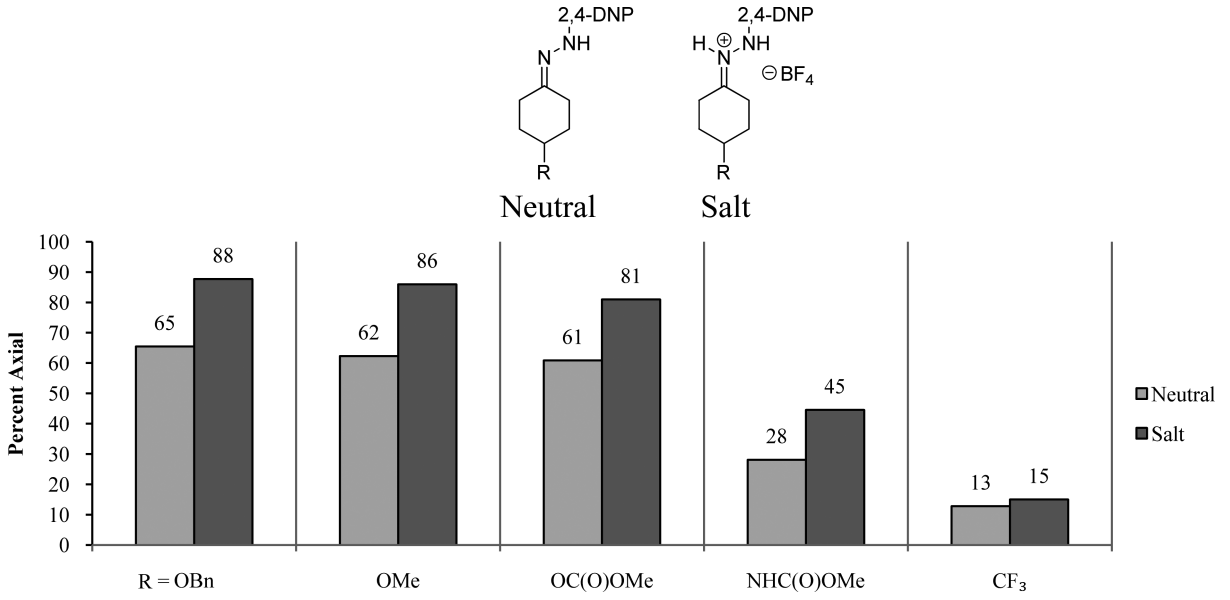



**Figure 5.** Hydrazone results with computer modeling benchmark.

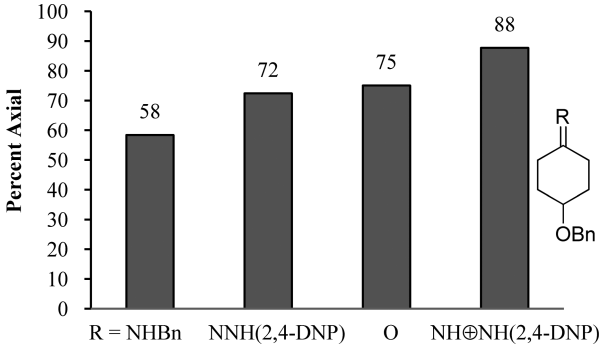


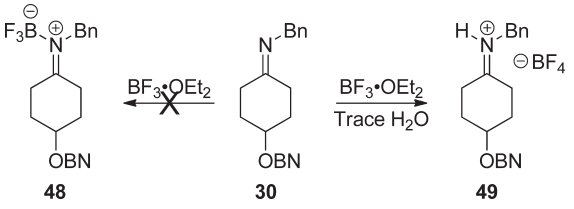

**Figure 6.** Trend of axial preferences (using the computer modeling benchmark).

oxygen-substituted systems (Figure 5). In contrast, both the 4-carbamoyl- and 4-trifluoromethyl-substituted hydrazones **14** and **15** preferred the equatorial conformer. Just as observed for the oxygen-substituted systems, the hydrazone salts of both compounds preferred the equatorial conformer less than the neutral hydrazones did.

The above results establish a clear trend, illustrated by the 4-benzyloxy-substituted derivative in Figure 6. The neutral imine showed the smallest axial preference, followed in increasing order by the neutral hydrazone, the ketone, and, finally, the hydrazonium salt. These results parallel the electrophilicities of these species.[58] The difference in the axial preference of the neutral hydrazone with respect to the corresponding imine provides a calibration point for the use of hydrazones as a model for alkyl imines. This study shows that the conformation of the positively charged nitrogen species is not determined by steric effects. Instead, electrostatic effects contribute significantly to the conformational preferences, as determined in solution for the hydrazonium ion.[59]

**X-ray Crystallographic Data in Support of the Solution-Phase Structures.** Crystallographic studies indicated that the conformational preferences adopted in solution can also be

**Scheme 7. Attempted Imine Complex Formation**




favored in the solid state. The analysis of crystal structure data to determine the minimum energy structure of interacting functional groups is well-known.[60] Initially, we attempted to determine the conformational preference of the zwitterionic complex of imine **30** with $BF_3$ (**48**) in analogy to the work of Collum and co-workers with other imines (Scheme 7).[61] Instead of complex **48**, the conjugate acid **49** was formed. It is likely that adventitious water hydrolyzed some of the $BF_3 \cdot OEt_2$ to form $HBF_4$[62] and that the iminium ion (**49**) formed crystals more readily than complex **48**.

The X-ray crystal structure of **49** revealed that the iminium ion adopted the conformer with the benzyloxy group in the axial arrangement (Figure 7).[63] The axial conformer observed is consistent with the expected electrostatic stabilization of this cation by the axial alkoxy group, as seen in solution for hydrazonium ions (Figure 5). This result also agrees with studies of dioxocarbenium ions bearing alkoxy groups, which adopt conformations that place the substituent near the cationic center.[15,64]

Even neutral hydrazones can reside in axial conformers in the solid state. The 4-benzyloxy hydrazone **11** was subjected to X-ray crystallographic analysis, and the pendant benzyloxy group was found to be in an axial arrangement (Figure 8). The preference for the axial arrangement of the benzyloxy group on the neutral hydrazone in the solid state diverges from the observation made for the solution-phase data obtained with the decalone benchmark (vide supra). The role solvent plays in shielding the charged centers of the molecule may explain the difference observed.[55] The structures of hydrazone **11** and iminium ion **49**, like that of

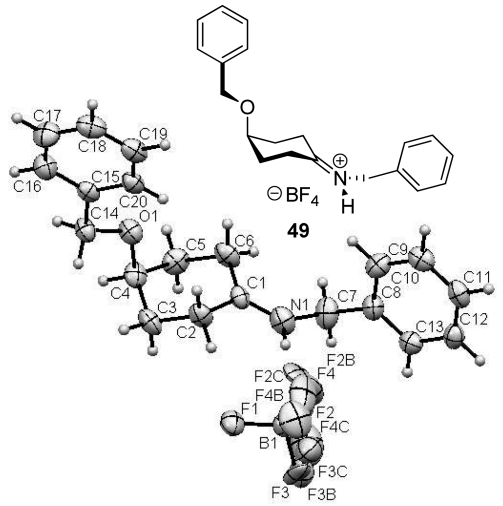



**Figure 7.** X-ray crystal structure of conjugate acid **49**.

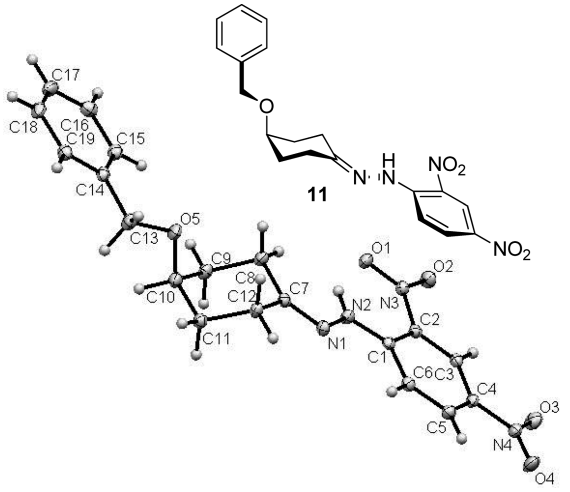



**Figure 8.** X-ray crystal structure of neutral hydrazone **11**.

the decalone-derived hydrazone **42**, do not appear to be distorted: the average dihedral angles between the 1- and 4-carbon atoms are 51.1 and 54.4° for **11** and **49**, respectively, as compared to 52.0° in cyclohexanone.[51]

## CONCLUSION

The strong influence of electrostatic effects on conformational preferences was demonstrated in several hydrazones, protonated hydrazones, ketones, and an iminium ion. Upon formation of the salts of the hydrazones, the axial preference increased, consistent with increased electrostatic attraction between the charged centers of the hydrazones and pendant partially negatively charged functional groups. The neutral hydrazones demonstrated an increase in the axial preference in less polar solvent, which is consistent with decreased shielding of the charged centers of the molecule and an increase in electrostatic attraction.[56] The results from the X-ray crystallographic studies show the presence of an electrostatic effect in an iminium ion and provide supporting evidence for the solution-phase structure of the hydrazones. On the basis of the results of this study, electrostatic effects on the conformational preferences of charged nitrogen intermediates should be considered when designing or analyzing reactions involving species such as iminium ions.[17,58,65−71]

## EXPERIMENTAL SECTION

**4-Hydroxycyclohexanone Ethylene Ketal (17).** The procedure was adapted from the synthesis performed by Noland and coworkers.[72] To a cooled (0 °C) solution of 1,4-dioxaspiro[4.5]decan-8-one (**16**; 10.0 g, 64.0 mmol) in methanol (150 mL) was added sodium borohydride (2.56 g, 67.8 mmol). The reaction mixture was warmed to room temperature. After 3 h, the reaction mixture was neutralized with 1 N aqueous HCl and extracted with dichloromethane (3 × 200 mL). The organic phases were poured through a cotton plug, and the solvent was removed in vacuo to yield the crude product, which was used directly in the next steps (9.78 g, 97%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.91 (m, 4H), 3.76 (m, 1H), 1.90−1.73 (m, 5H), 1.68−1.49 (m, 4H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 108.5, 68.3, 64.45, 64.42, 32.2, 31.7 ($^1$H NMR and $^{13}$C NMR spectroscopic data match those previously reported);[73,74] IR ($CHCl_3$) 3422, 3016, 2953, 2888 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_8H_{14}NaO_3$ $(M + Na)^+$ 181.0841, found 181.0839.

**4-Benzyloxycyclohexanone Ethylene Ketal (18).** KH (35% in mineral oil, 5.80 g, 50.6 mmol) was washed with pentane (3 × 200 mL) and suspended in still-dried tetrahydrofuran (60 mL). The suspension was cooled to −16 °C, and a solution of 4-hydroxycyclohexanone ethylene ketal (**17**; 2.00 g, 12.6 mmol) in tetrahydrofuran (60 mL) was added to the mixture over 1 min. The reaction mixture was warmed to room temperature over 30 min, and then benzyl bromide (4.32 g, 25.3 mmol) was added. After 48 h at room temperature, saturated aqueous ammonium chloride (100 mL) was added and the mixture was extracted with dichloromethane (3 × 200 mL). The organic phases were filtered through a cotton plug, and the solvent was removed in vacuo. The product was purified by flash chromatography (3/7 ethyl acetate/hexanes) to yield the product as a colorless oil. Evacuation at vacuum (0.1 mmHg) for 24 h removed residual benzyl bromide to form the product (2.11 g, 67%): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.37−7.29 (m, 4H), 7.28−7.23 (m, 1H), 4.52 (s, 2H), 3.96−3.89 (m, 4H), 3.51 (m, 1H), 1.91−1.74 (m, 6H), 1.59−1.50 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 139.2, 128.5, 127.52, 127.49, 108.7, 74.3, 70.0, 64.4, 31.5, 28.7 cm$^{-1}$ (NMR spectroscopic data match those previously reported);[74] HRMS (ESI) $m/z$ calcd for $C_{15}H_{20}NaO_3$ $(M + Na)^+$ 271.1310, found 271.1315.

**4-Benzyloxycyclohexanone (19).** To a solution of 4-benzyloxycyclohexanone ethylene ketal (**18**; 1.49 g, 6.00 mmol) in tetrahydrofuran (24 mL) was added 1 N aqueous HCl (24 mL). The solution was heated to reflux, and after 30 min the reaction mixture was cooled and poured into aqueous saturated sodium bicarbonate (100 mL). The mixture was extracted with dichloromethane (3 × 100 mL). The organic phases were dried with anhydrous sodium sulfate and then filtered through a cotton plug, and the solvent was removed in vacuo. Kugelrohr distillation under vacuum (0.1 mmHg) at 250 °C gave the product as a colorless oil (1.14 g, 93%): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.30−7.16 (m, 5H), 4.50 (s, 2H), 3.73 (m, 1H), 2.58−2.47 (m, 2H), 2.21−2.13 (m, 2H), 2.09−2.00 (m, 2H), 1.92−1.81 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 211.3, 138.6, 128.5, 127.7, 127.5, 72.3, 70.3, 37.3, 30.6 (NMR spectroscopic data match those previously reported);[74] IR ($CHCl_3$) 3016, 2943, 2867, 1709 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{13}H_{16}NaO_2$ $(M + Na)^+$ 227.1048, found 227.1054. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.16; H, 8.02.

**4-Methoxycyclohexanone Ethylene Ketal (20).** The procedure was adapted from the synthesis performed by Noland and coworkers.[72] Potassium hydride (35% in mineral oil, 5.80 g, 50.6 mmol) was washed with pentane (3 × 200 mL) and suspended in still-dried tetrahydrofuran (60 mL). The suspension was cooled to −16 °C, and

a solution of 4-hydroxycyclohexanone ethylene ketal (**17**; 2.00 g, 12.6 mmol) in tetrahydrofuran (60 mL) was added to the mixture over 1 min. The reaction mixture was warmed to room temperature over 30 min, and then methyl iodide (3.59 g, 25.3 mmol) was added in one portion. After 48 h at room temperature, saturated aqueous ammonium chloride (100 mL) was added and the mixture was extracted with dichloromethane (3 × 200 mL). The organic phases were filtered through a cotton plug, and the solvent was removed in vacuo. The product was purified by flash chromatography (3/7 ethyl acetate/hexanes) to yield the product as a colorless oil (1.78 g, 82%): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.94−3.86 (m, 4H), 3.32−3.22 (m, 1H), 1.85−1.72 (m, 4H), 1.72−1.61 (m, 2H), 1.56−1.46 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 108.6, 76.3, 64.42, 64.40, 55.9, 31.4, 28.3; IR ($CDCl_3$) 2951, 2886 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_9H_{16}NaO_3$ $(M + Na)^+$ 195.0997, found 195.0999. Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.85; H, 9.58.

**4-Methoxycyclohexanone (21).** To a solution of 4-methoxycyclohexanone ethylene ketal (**20**; 1.03 g, 6.00 mmol) in tetrahydrofuran (24 mL) was added 1 N aqueous HCl (24 mL). The solution was heated to reflux, and after 30 min the reaction mixture was cooled and poured into aqueous saturated sodium bicarbonate (100 mL). The mixture was extracted with dichloromethane (3 × 100 mL). The organic phases were dried with anhydrous sodium sulfate and then filtered through a cotton plug, and the solvent was removed in vacuo. Kugelrohr distillation under vacuum (0.1 mmHg) from 80 to 120 °C gave the product as a colorless oil (0.765 g, 100%): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.48 (m, 1H), 3.26 (s, 3H), 2.45−2.34 (m, 2H), 2.15−2.06 (m, 2H), 1.98−1.90 (m, 2H), 1.84−1.75 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 211.1, 74.1, 55.9, 36.9, 30.0 (NMR spectroscopic data match those previously reported);[73] IR ($CHCl_3$) 3015, 2952, 2888, 2930, 1709; HRMS (ESI) $m/z$ calcd for $C_7H_{12}NaO_2$ $(M + Na)^+$ 151.0735, found 151.0727.

**4-Hydroxycyclohexyl Methyl Carbonate (~1/1 Mixture of Cis and Trans) (23).** To a solution of 1,4-cyclohexanediol (1/1 cis/trans) (**22**; 5.00 g, 43.0 mmol), 4-dimethylaminopyridine (263 mg, 2.15 mmol), and pyridine (3.40 g, 43.0 mmol) in dichloromethane (50 mL) was added methyl chloroformate (4.06 g, 43.0 mmol) by syringe pump addition over 6 h. After 24 h from the start of the addition, the mixture was diluted with dichloromethane (50 mL) and washed with saturated aqueous ammonium chloride (100 mL). The organic phases were filtered through a cotton plug, and the solvent was removed in vacuo. Flash chromatography (5/95 methanol/dichloromethane followed by 3/7 ethyl acetate/hexanes) yielded the product as a colorless oil (3.51 g, 47%). Characterization was performed on a ~1/1 mixture of diastereomers: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.68 (m, 0.57 H), 4.58 (m, 0.41 H), 3.77−3.65 (m, 4H), 2.10 (s, 1H), 2.01 (m, 1H), 1.97−1.87 (m, 2H), 1.72−1.58 (m, 3H), 1.52−1.34 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 155.36, 155.35, 75.9, 74.2, 68.7, 67.7, 54.70, 54.66, 32.0, 30.4, 28.5, 27.4; IR ($CHCl_3$) 3483, 3024, 2955, 2868, 1743, 1445 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_8H_{14}NaO_4$ $(M + Na)^+$ 197.0790, found 197.0792.

**4-(Methoxycarbonyloxy)cyclohexanone (24).** To a stirred solution of 4-hydroxycyclohexyl methyl carbonate (**23**; 3.42 g, 19.6 mmol) in still-dried dichloromethane (200 mL) was added Dess−Martin periodinane (10.0 g, 23.6 mmol). After 1.5 h, the mixture was washed with saturated aqueous sodium bicarbonate (50 mL) and poured through a cotton plug, and the solvent was removed in vacuo. The product was purified by flash chromatography (3/7 ethyl acetate/hexanes) to yield the product as a colorless oil that crystallized upon standing (3.30 g, 98%): mp 34.5−35.5 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.99 (m, 1H), 3.76 (s, 3H), 2.52 (ddd, $J$ = 15.5, 10.0, 6.0 Hz, 2H); 2.30 (dt, $J$ = 15.1, 6.3 Hz, 2H), 2.13 (m, 2H), 2.04 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 209.5, 155.2, 72.5, 54.9, 37.1, 30.4; IR ($CHCl_3$) 3026, 2959, 1744, 1720, 1444 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_8H_{12}NaO_4$ $(M + Na)^+$ 195.0633, found 195.0633. Anal. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 7.02. Found: C, 55.55; H, 7.05.

**4-Hydroxycyclohexyl Methyl Carbamate (26).** To a solution of *trans*-4-aminocyclohexanol (**25**; 5.00 g, 43.4 mmol), and pyridine (3.43 g, 43.4 mmol) in still-dried dichloromethane (50 mL) was added methyl chloroformate (5.33 g, 56.0 mmol) dropwise over 5 min. Heat was evolved, and a white solid precipitated from solution. After 20 min, additional dichloromethane (50 mL) was added. After 1 h, the solids were filtered and the solvent was removed in vacuo. The mixture was placed under high vacuum (0.1 mmHg) for 24 h. The solids were crystallized from toluene to yield the product as an off-white solid (2.51 g, 33%): mp 140−141 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.66 (br s, 1H), 3.78−3.58 (m, 4H), 3.50 (m, 1H) 2.10−1.98 (m, 4H), 1.96 (s, 1H), 1.48−1.37 (m, 2H), 1.30−1.17 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 156.5, 69.8, 52.1, 49.4, 34.0, 31.2; IR ($CHCl_3$) 3442, 3017, 2943, 2861, 1715, 1515 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_8H_{15}NNaO_3$ $(M + Na)^+$ 196.0950, found 196.0943. Anal. Calcd for $C_8H_{15}NO_3$: C, 55.47; H, 8.73. Found: C, 55.61; H, 8.82.

**4-(Methoxycarbonylamino)cyclohexanone (27).** To a solution of 4-hydroxycyclohexyl methyl carbamate (**26**; 1.00 g, 5.77 mmol) in still-dried dichloromethane (60 mL) was added Dess−Martin periodinane (2.94 g, 6.96 mmol). After 2 h, the mixture was washed with saturated aqueous sodium thiosulfate (100 mL) followed by saturated aqueous sodium bicarbonate (100 mL). The organic phases were filtered through a cotton plug, and the solvent was removed in vacuo. Flash chromatography (1/1 ethyl acetate/hexanes) gave the product and Dess−Martin periodinane hydrolysis products. The product was dissolved in dichloromethane, and the remaining solids were removed by filtration. The solvent was removed in vacuo to yield the product as a white solid (0.695 g, 70%): mp 115−116 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.72 (br s, 1H), 3.97 (m, 1H), 3.68 (s, 3H), 2.50−2.36 (m, 4H), 2.29−2.17 (m, 2H), 1.77−1.63 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 209.8, 156.5, 52.4, 48.2, 39.2, 32.4; IR ($CHCl_3$) 3442, 3356, 3022, 2956, 1714, 1514 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_8H_{13}NNaO_3$ $(M + Na)^+$ 194.0793, found 194.0796. Anal. Calcd for $C_8H_{13}NO_3$: C, 56.13; H, 7.65. Found: C, 55.78; H, 7.61.

**4-Hydroxy-4-(trifluoromethyl)cyclohexanone Ethylene Ketal (28).** To a solution of 1,4-dioxaspiro[4.5]decan-8-one (**16**; 5.00 g, 32 mmol) and tetrabutylammonium fluoride (1 M solution in tetrahydrofuran, 1.1 mL, 1.1 mmol) in tetrahydrofuran (100 mL) was added (trifluoromethyl)trimethylsilane (5.01 g, 35 mmol). After it was stirred for 2 days, the reaction mixture was diluted with dichloromethane (300 mL) and washed with saturated aqueous ammonium chloride (300 mL) and saturated aqueous brine (300 mL). The solvent was removed in vacuo, and the solids were dissolved in a solution of tetrabutylammonium fluoride (1 M solution in tetrahydrofuran, 35 mL, 35 mmol). After 1 h, the mixture was diluted with dichloromethane (300 mL) and washed with saturated aqueous brine (2 × 300 mL). The organic phases were filtered through a cotton plug, and the solvent was removed in vacuo. Flash chromatography (3/7 ethyl acetate/hexanes) gave the product as a pale yellow crystalline solid (about 95% pure as determined by $^1$H NMR spectroscopy, 5.57 g, 77%): mp 45−47 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.00−3.90 (m, 4H), 2.18 (s, 1H), 1.98−1.87 (m, 4H), 1.85−1.76 (m, 2H), 1.72−1.63 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 126.5 (q, $J$ = 284.3 Hz), 107.9, 72.0 (q, $J$ = 28.4 Hz), 64.7, 64.5, 29.2, 28.13 (m); IR ($CHCl_3$) 3589, 3434, 3015, 2965, 2889 cm$^{-1}$; HRMS (APCI) $m/z$ calcd for $C_9H_{14}F_3O_3$ $(M + H)^+$ 227.0895, found 227.0899.

**4-Trifluoromethyl-3-cyclohexenone Ethylene Ketal.** To a solution of 4-hydroxy-4-(trifluoromethyl) cyclohexanone ethylene ketal (**28**; 2.98 g, 13.2 mmol), 4-dimethylaminopyridine (0.66 g, 5.38 mmol), and pyridine (36.5 g, 461 mmol) in tetrahydrofuran (120 mL) was added thionyl chloride (15.7 g, 132 mmol). The reaction mixture was heated to reflux. After 24 h, the reaction mixture was cooled to 0 °C in an ice bath, and triethylamine (26.7 g, 263 mmol) was added dropwise over 5 min. Following the triethylamine addition, 60 mL of water was added

dropwise over 5 min. Water (200 mL) was added to the reaction mixture, and the mixture was extracted with pentane (4 × 400 mL). The combined pentane layers were reduced in vacuo to about 400 mL, and the pentane was washed with water (200 mL). The organic phases were dried with anhydrous sodium sulfate, and the solvent was removed in vacuo. The product was further purified by flash chromatography (1/9 diethyl ether/pentane to 1/4 diethyl ether/pentane) followed by Kugelrohr distillation under vacuum (0.1 mmHg) from 70 to 100 °C to yield the product as a clear oil (0.85 mg, 31%). Distillation at higher temperatures led to decomposition: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.22 (m, 1H), 3.98 (m, 4H), 2.42−2.33 (m, 4H), 1.84−1.78 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 128.1 (q, $J$ = 5.8 Hz), 128.0 (q, $J$ = 30.4 Hz), 123.9 (q, $J$ = 271.8 Hz), 107.0, 64.8, 35.2, 30.4, 21.8 (m); IR ($CHCl_3$) 3023, 2962, 2889, 1686 cm$^{-1}$; HRMS (APCI) $m/z$ calcd for $C_9H_{12}F_3O_2$ $(M + H)^+$ 209.0789, found 209.0798. Anal. Calcd for $C_9H_{11}F_3O_2$: C, 51.93; H, 5.33. Found: C, 51.70; H, 5.48.

**4-(Trifluoromethyl)cyclohexanone (29).** To a solution of 4-trifluoromethyl-3-cyclohexenone ethylene ketal (0.66 g, 3.97 mmol) under nitrogen in methanol (20 mL) was added platinum on carbon (5 wt %, 1.2 g, 0.3 mmol). The mixture was sonicated for 15 min and then placed under a hydrogen atmosphere (1 atm) with vigorous stirring. After 16 h, the solids were removed by filtration and washed with methanol (10 mL). The combined organic phases were mixed with 30 mL of 1 N aqueous HCl and stirred. After 1.5 h, the reaction mixture was poured into 100 mL of water and the mixture was extracted with pentane (5 × 150 mL). The combined organic phases were dried with anhydrous sodium sulfate, and the solvent was removed in vacuo. Flash chromatography (1/9 diethyl ether/pentane to 3/7 diethyl ether/pentane) gave the product as a colorless volatile liquid (about 90% pure as determined by $^1$H NMR spectroscopy, 0.32 mg, 60%): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 2.53−2.29 (m, 3H), 2.39−2.27 (m, 2H), 2.27−2.15 (m, 2H), 1.83−1.67 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 208.8, 127.3 (q, $J$ = 278.6 Hz), 40.2 (q, $J$ = 27.4 Hz), 39.2, 24.9 (q, $J$ = 2.5 Hz) ($^1$H NMR and $^{13}$C NMR spectroscopic data match those previously reported);[75] IR ($CHCl_3$) 3022, 2965, 2885, 1719 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_7H_8F_3O$ $(M - H)^-$ 165.0527, found 165.0521.

***cis*-Tetrahydronaphthalene-1,4-dione.** An oven-dried 500 mL three-necked round-bottom flask was equipped with a stir bar, rubber stoppers, a balloon, and a butadiene gas inlet. The flask was flushed with dry nitrogen and charged with benzoquinone freshly recrystallized from petroleum ether (**31**; 10.00 g, 92.5 mmol) and 200 mL of still-dried toluene. The reaction vessel was cooled to −16 °C, and $BF_3 \cdot OEt_2$ (2.28 mL, 18.5 mmol) was added over 1 min with rapid stirring. The flask was charged with butadiene gas, filling the balloon, and the mixture was warmed to room temperature. As the reaction proceeded, the balloon emptied and additional butadiene gas was added until the dark color of the solution faded to red and thin-layer chromatography indicated that no benzoquinone (**31**) was present. After 20 min, the reaction mixture was washed with 200 mL of brine and the solvent was removed in vacuo. The solid was recrystallized with dichloromethane/hexanes to yield the product as a pale yellow solid (12.17 g, 81% yield): mp 47−54 °C (lit.[76] mp 57 °C); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.66 (s, 2H), 5.69 (m, 2H), 3.24 (m, 2H), 2.48 (m, 2H), 2.18, (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 200.2, 139.5, 124.6, 46.5, 24.4 ($^1$H NMR spectroscopic data match those previously reported);[75] IR (PhMe) 1692 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{10}H_9O_2$ $(M - H)^-$ 161.0603, found 161.0598.

**Axial-*cis*-4-hydroxytetrahydronaphthalen-1-one.** To a solution of *cis*-tetrahydronaphthalene-1,4-dione (12.14 g, 74.8 mmol) in methanol (300 mL) was added ammonium chloride (1.60 g, 29.9 mmol). The mixture was cooled to −16 °C, and sodium borohydride (1.13 g, 29.9 mmol) was added with rapid stirring. After 10 min, saturated brine (300 mL) was added. The mixture was extracted with dichloromethane (6 × 300 mL). The combined organic layers were poured through a cotton plug and evaporated. The crude product was recrystallized with dichloromethane/petroleum ether to yield the purified product as a white solid (11.35 g, 92% yield): mp 124−126 °C (lit.[42] mp 131−132 °C); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.70 (m, 1H), 5.99 (m, 1H), 5.66 (m, 2H), 4.91 (m, 1H), 2.89−2.66 (m, 3H), 2.22−1.96 (m, 3H), 1.87 (m, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 199.1, 149.7, 128.9, 125.7, 125.1, 70.7, 44.6, 40.8, 24.0, 21.1 ($^1$H NMR and $^{13}$C NMR spectroscopic data match those previously reported);[42] IR ($CHCl_3$) 3608, 3476, 3026, 2905, 2851, 1679 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{10}H_{12}NaO_2$ $(M + Na)^+$ 187.0735, found 187.0731.

**Axial-*cis*-4-hydroxydecalone.** A three-necked 2 L round-bottom flask was equipped with a stir bar and rubber stopper. The flask was charged with axial-*cis*-4-hydroxytetrahydronaphthalen-1-one (11.32 g, 69.0 mmol) and 1 L of still-dried benzene. The flask was purged with nitrogen, and rhodium on alumina (5 wt %, 0.57 g, 0.3 mmol) was added. The flask was purged with hydrogen gas and placed under three hydrogen balloons with stirring for 36 h. The mixture was filtered through Celite followed by evaporation of the solvent. The solids were purified by precipitation with petroleum ether/dichloromethane at −78 °C. The precipitate was dried under vacuum (0.1 mmHg) to yield the product as a white solid (10.13 g, 87% yield). A small sample was crystallized from petroleum ether/dichloromethane for analysis: mp 108−110 °C (lit.[42] mp 112−114 °C); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.26 (dt, $J$ = 11.5, 4.7 Hz, 1H), 2.57 (m, 1H), 2.40−2.29 (m, 2H), 2.28−2.18 (m, 2H), 2.07−2.00 (m, 1H), 1.94 (qd, $J$ = 12.2, 6.5 Hz, 1H), 1.80 (m, 2H), 1.58 (m, 1H) 1.56−1.50 (m, 1H), 1.45 (qt, $J$ = 13.1, 3.7 Hz, 1H) 1.25−1.11 (m, 2H), 1.00 (m, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 211.0, 71.3, 47.8, 45.3, 38.8, 29.6, 25.9, 25.3, 22.8, 22.3; IR ($CHCl_3$) 3611, 3483, 3015, 2941, 2859, 1707 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{10}H_{15}O_2$ $(M - H)^-$ 167.1072, found 167.1072.

**Axial-*trans*-4-hydroxydecalone (32).** To a solution of axial-*cis*-4-hydroxydecalone (4.07 g, 24.2 mmol) in ethanol (100 mL) was added 1 mL of a potassium hydroxide in ethanol solution (5.0 g/100 mL) dropwise over 1 min. The reaction mixture was heated to 50 °C. After 1.5 h, the reaction mixture was cooled and saturated aqueous ammonium chloride was added, bringing the pH of the solution to 7. The solvent was removed in vacuo. The solids were purified by flash chromatography (3/7 ethyl acetate/hexanes) followed by recrystallization from toluene/pentane to afford the product as a white crystalline solid (3.20 g, 79%): mp 66−67 °C (lit.[42] mp 60−61 °C); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.90 (s, 1H), 2.78 (td, $J$ = 14.1, 6.2 Hz, 1H), 2.48 (m, 1H), 2.22 (ddd, $J$ = 13.8, 4.6, 1.8 Hz, 1H), 2.17 (ddt, $J$ = 13.9, 5.9, 2.6 Hz, 1H), 1.98 (m, 1H), 1.88 (tdd, $J$ = 14.2, 4.6, 2.3 Hz, 1H), 1.82−1.74 (m, 2H), 1.72 (m, 1H), 1.70−1.63 (m, 1H), 1.57−1.47 (m, 2H), 1.27−1.12 (m, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 212.9, 69.1, 48.5, 47.8, 36.3, 33.9, 30.0, 26.0, 25.4, 25.2 ($^1$H NMR spectroscopic data match those previously reported);[42] IR ($CHCl_3$) 3621, 3504, 3015, 2932, 2859, 1704 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{10}H_{15}O_2$ $(M - H)^-$ 167.1072, found 167.1076.

**Axial-4-hydroxydecalone Ethylene Ketal (33).** A 100 mL round-bottom flask was equipped with a stir bar, Dean−Stark apparatus, condenser, and rubber stopper. To the flask was added axial-*trans*-4-hydroxydecalone (**32**; 2.00 g, 11.9 mmol), *p*-toluenesulfonic acid hydrate (0.116 g, 0.61 mmol), ethylene glycol (10 mL, 11 g, 180 mmol), and 50 mL of benzene. The Dean−Stark apparatus was filled with benzene, and the reaction mixture was heated to reflux. After 16 h, the reaction mixture was cooled and 150 mL of diethyl ether was added. The reaction mixture was washed with saturated aqueous sodium bicarbonate (50 mL × 2) and water (50 mL × 2). The organic layers were dried with sodium sulfate, and the solvent was removed in vacuo. Recrystallization from pentane afforded the product as a white solid (2.19 g, 87%): mp 71−72 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.98−3.83 (m, 4H), 3.69 (m, 1H), 1.86−1.66 (m, 7H), 1.63−1.51 (m, 3H), 1.46 (tt, $J$ = 11.7,

2.9 Hz, 1H), 1.32 (qd, $J$ = 12.2, 3.2 Hz, 1H), 1.27−1.02 (m, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 110.3, 69.7, 65.4, 65.3, 43.9, 42.7, 30.7, 29.7, 29.5, 26.4, 26.0, 24.2; IR ($CHCl_3$) 3620, 3497, 3013, 2933, 2886, 2858 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{12}H_{20}NaO_3$ $(M + Na)^+$ 235.1310, found 235.1306. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.82; H, 9.72.

**Axial-4-benzyloxydecalone Ethylene Ketal.** To a suspension of sodium hydride (60% in mineral oil, 1.13 g, 28 mmol) in tetrahydrofuran (200 mL) was added axial-4-hydroxydecalone ethylene ketal (**33**; 2.00 g, 9.4 mmol). The solution was heated to reflux, and benzyl bromide (2.24 mL, 18.8 mmol) was added. After 12 h, the reaction mixture was cooled and poured into water (200 mL). The mixture was extracted with dichloromethane (200 mL × 2). The organic phases were filtered through a cotton plug, and the solvent was removed in vacuo. The product was purified by flash chromatography (benzene followed by 3/7 ethyl acetate/hexanes) to yield a pale yellow oil (2.76 g, 97%): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.38−7.23 (m, 5H), 4.61 (d, $J$ = 12.1 Hz, 1H), 4.37 (d, $J$ = 12.1 Hz, 1H), 4.00−3.85 (m, 4H), 3.37 (m, 1H), 2.01 (dq, $J$ = 14.6, 3.5 Hz, 1H), 1.89 (td, $J$ = 11.5, 3.2 Hz, 1H), 1.86−1.77 (m, 2H), 1.75−1.66 (m, 2H), 1.64−1.42 (m, 5H) 1.26−1.14 (m, 2H), 1.13−1.02 (m, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 139.6, 128.4, 127.5, 127.4, 110.5, 76.7, 70.6, 65.34, 65.25, 44.1, 43.5, 30.0, 29.6, 26.5, 26.1, 26.0, 24.4; IR ($CHCl_3$) 3012, 2934, 2859 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{19}H_{26}NaO_3$ $(M + Na)^+$ 325.1774, found 325.1775.

**Axial-4-methoxydecalone Ethylene Ketal.** To a suspension of sodium hydride (60% in mineral oil, 0.377 g, 9.4 mmol) in tetrahydrofuran (50 mL) under nitrogen was added axial-4-hydroxydecalone ethylene ketal (**33**; 0.500 g, 2.4 mmol). The solution was heated to reflux, and methyl iodide (0.37 mL, 5.9 mmol) was added. After 12 h, the reaction mixture was cooled and poured into water (100 mL). The mixture was extracted with dichloromethane (100 mL × 2). The organic phases were filtered through a cotton plug, and the solvent was removed in vacuo. The product was purified by flash chromatography (3/7 ethyl acetate/hexanes) to yield an oil (0.487 g, 91%): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.95−3.81 (m, 4H), 3.26 (s, 3H), 3.09 (m, 1H), 1.95 (dq, $J$ = 14.4, 3.5 Hz, 1H), 1.78−1.60 (m, 5H), 1.53−1.38 (m, 5H), 1.23−0.97 (m, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 110.4, 78.9, 65.27, 65.22, 56.8, 43.9, 43.4, 29.7, 29.4, 26.4, 25.9, 25.4, 24.4; IR ($CHCl_3$) 3009, 2934, 2886, 2858 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{13}H_{22}NaO_3$ $(M + Na)^+$ 249.1467, found 249.1472.

**Axial-4-benzyloxydecalone (34).** To a solution of axial-4-benzyloxydecalone ethylene ketal (2.68 g, 8.9 mmol) in methanol (160 mL) and water (40 mL) was added 12 N aqueous HCl (4 mL). The reaction mixture was stirred for 12 h and then was poured into methylene chloride (200 mL). The organic phases were extracted with saturated aqueous brine (200 mL × 2). The organic phases were poured through a cotton plug, and the solvent was removed in vacuo. The product was purified by flash chromatography (3/7 ethyl acetate/hexanes) followed by HPLC purification (1/9 ethyl acetate/hexanes, Peeke Scientific Kromasphere 80, 5 $\mu$m silica, 300 × 50 mm i.d. column) to yield a white solid (1.76 g, 77%): mp 47−50 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.42−7.28 (m, 5H), 4.72 (d, $J$ = 11.9 Hz, 1H), 4.50 (d, $J$ = 11.9 Hz, 1H), 3.56 (m, 1H), 2.72 (td, $J$ = 14.0, 6.0 Hz, 1H), 2.55 (td, $J$ = 11.2, 3.0 Hz, 1H), 2.38 (ddt, $J$ = 14.2, 5.8, 2.8 Hz, 1H), 2.22 (ddd, $J$ = 13.7, 4.2, 1.9 Hz, 1H), 1.98 (m, 1H), 1.81−1.65 (m, 4H), 1.61 (m, 1H), 1.54 (tt, $J$ = 11.9, 2.5 Hz, 1H), 1.25−1.11 (m, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 213.0, 139.0, 128.6, 127.8, 127.7, 76.1, 71.3, 48.7, 48.6, 36.6, 29.9, 29.5, 26.0, 25.5, 25.4; IR ($CHCl_3$) 3026, 3013, 2935, 2860, 1703 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{17}H_{22}NaO_2$ $(M + Na)^+$ 281.1518, found 281.1515. Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 79.02; H, 8.76.

**Axial-4-methoxydecalone (35).** To a solution of axial-4-methoxy ketal decalone (0.442 g, 2.0 mmol) in tetrahydrofuran (20 mL) was added 20 mL of 1 N aqueous HCl. The reaction mixture was heated to reflux. After 2 h, the reaction mixture was cooled and saturated aqueous sodium bicarbonate (100 mL) was added. The reaction mixture was extracted with dichloromethane (50 mL × 2). The organic phases were poured through a cotton plug, and the solvent was removed in vacuo. The product was purified by flash chromatography (5/95 to 2/8 diethyl ether/pentane) to yield an oil (0.239 g, 67%): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.39 (s, 3H), 3.28 (m, 1H), 2.59 (td, $J$ = 14.1, 6.1 Hz, 1H), 2.41 (td, $J$ = 11.4, 3.4 Hz, 1H), 2.34 (ddt, $J$ = 14.2, 5.9, 2.7, 1H), 2.16 (ddd, $J$ = 13.7, 4.3, 2.0 Hz, 1H), 1.93 (m, 1H), 1.75−1.66 (m, 2H), 1.66−1.56 (m, 3H), 1.48 (m, 1H), 1.21−1.07 (m, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 213.0, 78.2, 57.2, 48.54, 48.45, 36.4, 29.7, 28.8, 25.9, 25.4, 25.3; IR ($CHCl_3$) 2934, 2859, 1702 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{11}H_{18}NaO_2$ $(M + Na)^+$ 205.1205, found 205.1203.

**Axial-4-(methyoxycarbonyloxy)decalone (36).** To a solution of axial-*trans*-4-hydroxydecalone (**32**; 0.200 g, 1.2 mmol) in dichloromethane (20 mL) was added 4-dimethylaminopyridine (0.011 g, 0.1 mmol) and still-dried pyridine (0.14 mL, 1.8 mmol). Methyl chloroformate (0.56 mL, 7.1 mmol) was added dropwise over 1 min, and the reaction mixture was heated to reflux. After 24 h, the reaction mixture was cooled and poured into diethyl ether (100 mL) and the organic phases were washed with aqueous saturated copper sulfate (100 mL) followed by water (100 mL) and brine (100 mL). The organic phases were dried with anhydrous sodium sulfate, and the solvent was removed in vacuo. The product was purified by flash chromatography (2/8 ethyl acetate/hexanes) to yield a white solid (0.053 g, 13%): mp 106−108 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.89 (m, 1H), 3.82 (s, 3H), 2.65 (td, $J$ = 14.2, 6.2 Hz, 1H), 2.44 (m, 1H), 2.35 (ddt, $J$ = 14.6, 5.7, 2.8 Hz, 1H), 2.28 (ddd, $J$ = 14.1, 4.8, 1.5 Hz, 1H), 2.0 (m, 1H), 1.90 (tdd, $J$ = 14.5, 4.9, 2.4, 1H), 1.79−1.62 (m, 4H), 1.43 (m, 1H), 1.26−1.13 (m, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 211.3, 155.8, 75.8, 55.1, 48.6, 47.0, 36.5, 30.9, 29.6, 25.7, 25.3, 25.1; IR ($CHCl_3$) 3026, 2936, 2860, 1744, 1710 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{12}H_{18}NaO_4$ $(M + Na)^+$ 249.1103, found 249.1098. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.66; H, 8.06.

**4-Oxodecalone Ethylene Ketal.** To a solution of axial-4-hydroxydecalone ethylene ketal (**33**; 1.50 g, 7.1 mmol) in dichloromethane (70 mL) was added Dess−Martin periodinane (3.30 g, 7.8 mmol). After 2 h, saturated aqueous sodium bicarbonate (20 mL) and saturated aqueous $Na_2S_2O_4$ (20 mL) were added and stirring was continued. After 3 h, the aqueous and organic layers were separated. The organic layer was filtered through a cotton plug, and the solvent was removed in vacuo. The product was purified by flash chromatography (3/7 ethyl acetate/hexanes) to yield a white solid (1.37 g, 92%): mp 60−61 °C (lit.[43] mp 61−62.5 °C); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.07−3.93 (m, 4H), 2.65 (td, $J$ = 14.4, 6.3 Hz, 1H), 2.39−2.28 (m, 2H), 2.06 (ddd, $J$ = 13.4, 6.3, 2.2 Hz, 1H), 2.01−1.95 (m, 1H), 1.90−1.70 (m, 5H), 1.31−1.06 (m, 4H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 211.5, 108.5, 65.684, 65.676, 50.2, 49.7, 38.5, 34.9, 25.6, 25.3, 25.2; IR ($CHCl_3$) 3016, 2937, 2887, 2860, 1708 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{12}H_{18}NaO_3$ $(M + Na)^+$ 233.1154, found 233.1157. Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.58; H, 8.67.

**Equatorial-4-hydroxydecalone Ethylene Ketal (37).** To a cooled (0 °C) suspension of lithium aluminum hydride (0.250 mg, 6.6 mmol) in diethyl ether (90 mL) was added a solution of 4-oxodecalone ethylene ketal (2.18 g, 10.3 mmol) dissolved in diethyl ether (45 mL) over 2 min. The reaction mixture was warmed to room temperature. After 2 h, the reaction mixture was cooled to 0 °C and ethyl acetate (1.0 mL) was added followed by water (2.0 mL). The solids were removed from the reaction mixture by vacuum filtration and the organic and aqueous layers were separated. The organic layer was dried with anhydrous sodium sulfate, and the solvent was removed in vacuo. The product was purified by flash chromatography (1/9 to 3/7 ethyl acetate/hexanes) to yield a white solid (1.44 g, 66%): mp 98−99 °C (lit.[43] mp 100−101 °C); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.97−3.85 (m, 4H),

3.24 (ddd, $J$ = 10.9, 9.6, 4.5 Hz, 1H), 2.14 (m, 1H), 1.89 (qt, $J$ = 12.0, 3.9 Hz, 1H), 1.81−1.67 (m, 4H), 1.58 (m, 1H), 1.52−1.42 (m, 2H), 1.39−1.27 (m, 2H), 1.21−1.05 (m, 3H), 0.89 (m, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 109.5, 74.4, 65.4, 65.3, 47.4, 46.5, 33.3, 32.3, 29.9, 25.8, 25.7, 24.2; IR ($CHCl_3$) 3621, 3469, 3013, 2935, 2884, 2858 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{12}H_{20}NaO_3$ $(M + Na)^+$ 235.1310, found 235.1312.

**Equatorial-4-hydroxydecalone (40).** To a solution of equatorial-4-hydroxydecalone ethylene ketal (**37**; 0.283 g, 1.3 mmol) dissolved in tetrahydrofuran (40 mL) and water (10 mL) was added 1 mL of 1 N aqueous HCl. After 12 h, the solution was extracted with dichloromethane (100 mL × 2) and the organic phases were filtered through a cotton plug. The solvent was removed in vacuo and the product recrystallized from pentane to yield a white solid (0.145 g, 65%): mp 99−98 °C (lit.[42] mp 92−93 °C); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.73 (tt, $J$ = 10.3, 4.5 Hz, 1H), 2.48−2.36 (m, 2H), 2.27 (dddd, $J$ = 12.9, 5.9, 4.3, 3.1 Hz, 1H), 2.21 (m, 1H), 2.03−1.92 (m, 2H), 1.84−1.68 (m, 3H), 1.60 (d, $J$ = 4.9 Hz, 1H), 1.38 (m, 1H), 1.26−1.04 (m, 4H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 210.8, 73.1, 50.8, 49.8, 38.8, 34.7, 30.3, 25.1, 25.03, 25.01 ($^1$H NMR spectroscopic data match those previously reported);[42] IR ($CHCl_3$) 3620, 3014, 2936, 2860, 1711 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{10}H_{15}O_2$ $(M - H)^-$ 167.1072, found 167.1077.

**Equatorial-4-benzyloxydecalone Ethylene Ketal.** To a suspension of sodium hydride (60% in mineral oil, 0.283 g, 7.1 mmol) in tetrahydrofuran (50 mL) under nitrogen was added equatorial-4-hydroxydecalone ethylene ketal (**37**; 0.500 g, 2.36 mmol). The solution was heated to reflux, and benzyl bromide (0.56 mL, 4.72 mmol) was added. After 12 h, the reaction mixture was cooled and poured into water (100 mL). The mixture was extracted with dichloromethane (100 mL × 3). The organic phases were filtered through a cotton plug, and the solvent was removed in vacuo. The product was purified by flash chromatography (3/7 ethyl acetate/hexanes) to yield a pale yellow oil (0.691 g, 97%): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.36−7.21 (m, 5H), 4.62 (d, $J$ = 11.7 Hz, 1H), 4.42 (d, $J$ = 11.7 Hz, 1H), 3.96−3.80 (m, 4H), 3.02 (td, $J$ = 10.4, 4.1 Hz, 1H), 2.30 (m, 1H), 2.05 (qd, $J$ = 12.3, 3.6 Hz, 1H), 1.83−1.65 (m, 4H), 1.62−1.45 (m, 2H), 1.45−1.29 (m, 2H), 1.24−1.05 (m, 3H), 0.82 (m, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 139.3, 128.4, 127.8, 127.5, 109.4, 81.5, 70.9, 65.4, 65.2, 47.9, 44.8, 33.2, 30.1, 27.9, 25.9, 25.7, 24.3; IR ($CHCl_3$) 3011, 2935, 2883, 2857 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{19}H_{26}NaO_3$ $(M + Na)^+$ 325.1780, found 325.1782.

**Equatorial-4-methoxydecalone Ethylene Ketal.** To a suspension of sodium hydride (60% in mineral oil, 0.100 g, 2.5 mmol) in tetrahydrofuran (50 mL) under nitrogen was added equatorial-4-hydroxydecalone ethylene ketal (**37**; 0.250 g, 1.2 mmol). The solution was heated to reflux, and methyl iodide (0.15 mL, 2.4 mmol) was added. After 12 h, the reaction mixture was cooled and poured into water (100 mL). The mixture was extracted with dichloromethane (100 mL × 3). The organic phases were filtered through a cotton plug, and the solvent was removed in vacuo. The product was purified by flash chromatography (3/7 ethyl acetate/hexanes) to yield an oil (0.246 g, 91%): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.95−3.83 (m, 4H), 3.31 (s, 3H), 2.77 (td, $J$ = 10.0, 4.3 Hz, 1H), 2.16 (m, 1H), 2.00 (m, 1H), 1.82−1.64 (m, 4H), 1.47−1.29 (m, 4H), 1.22−1.03 (m, 3H), 0.81 (m, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 109.5, 83.2, 65.5, 65.3, 56.7, 47.9, 44.7, 33.2, 30.0, 27.3, 25.9, 25.7, 24.3; IR ($CHCl_3$) 3009, 2935, 2883, 2856 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{13}H_{22}NaO_3$ $(M + Na)^+$ 249.1461, found 249.1468.

**Equatorial-4-benzyloxydecalone (38).** To a solution of equatorial-4-benzyloxydecalone ethylene ketal (0.147 g, 0.5 mmol) in methanol (20 mL) and water (5 mL) was added 12 N aqueous HCl (0.5 mL). The reaction mixture was stirred for 48 h and then poured into methylene chloride (100 mL). The organic phases were extracted with saturated aqueous brine (100 mL × 2). The organic phases were poured through a cotton plug, and the solvent was removed in vacuo. The product was purified by flash chromatography (2/8 ether/pentane) to yield a white solid (0.080 g, 63%): mp 76−78 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.37−7.32 (m, 4H), 7.29 (m, 1H), 4.68 (d, $J$ = 11.6 Hz, 1H), 4.50 (d, $J$ = 11.6 Hz, 1H), 3.46 (td, $J$ = 10.2, 3.8 Hz, 1H), 2.45−2.31 (m, 4H), 2.02−1.91 (m, 2H), 1.80−1.62 (m, 3H), 1.53 (m, 1H), 1.27−1.09 (m, 3H), 1.02 (m, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 211.0, 138.6, 128.6, 127.9, 127.8, 80.0, 71.5, 51.4, 48.7, 38.6, 30.61, 30.60, 25.34, 25.29, 25.2; IR ($CHCl_3$) 3027, 3012, 2936, 2859, 1710 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{17}H_{22}NaO_2$ $(M + Na)^+$ 281.1518, found 281.1517. Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 78.87; H, 8.59.

**Equatorial-4-methoxydecalone (39).** To a solution of equatorial-4-methoxydecalone ethylene ketal (0.195 g, 0.9 mmol) in tetrahydrofuran (20 mL) was added 20 mL of 1 N aqueous HCl. The reaction mixture was then heated to reflux. After 4 h, the reaction mixture was cooled and saturated aqueous $NaHCO_3$ (100 mL) was added. The reaction mixture was extracted with dichloromethane (100 mL × 3). The organic phases were poured through a cotton plug, and the solvent was removed in vacuo. The product was purified by flash chromatography (1/9 to 2/8 diethyl ether/pentane) to yield an oil (0.035 g, 22%): $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 3.40 (s, 3H), 3.22 (m, 1H), 2.43−2.31 (m, 3H), 2.25 (m, 1H), 2.02−1.91 (m, 2H), 1.80−1.69 (m, 2H), 1.62−1.51 (m, 1H), 1.42 (m, 1H), 1.26−1.08 (m, 3H), 1.02 (m, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 211.2, 82.0, 57.3, 51.4, 48.7, 38.6, 30.6, 30.1, 25.36, 25.31, 25.29; IR ($CHCl_3$) 3012, 2934, 2860, 2829, 1710 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{11}H_{18}NaO_2$ $(M + Na)^+$ 205.1205, found 205.1212.

**Equatorial-4-(methyoxycarbonyloxy)decalone (41).** To a solution of equatorial-4-hydroxydecalone (**40**) (0.300 g, 1.8 mmol) under nitrogen in tetrahydrofuran (50 mL) was added 4-dimethylaminopyridine (0.007 mg, 0.06 mmol) and still-dried pyridine (0.095 mL, 1.2 mmol). Methyl chloroformate (4.61 mL, 59.7 mmol) was added dropwise over 1 min, and the reaction mixture was heated to reflux. After 24 h, the reaction mixture was cooled and aqueous saturated sodium bicarbonate (20 mL) was added. The mixture was poured into water (100 mL) and washed with dichloromethane (100 mL × 4). The organic phases were poured through a cotton plug, and the solvent was removed in vacuo. The product was purified by flash chromatography (2/8 ether/pentane) to yield a white solid (0.198 g, 74%): mp 69−70 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.75 (td, $J$ = 10.4, 4.4 Hz, 1H), 3.78 (s, 3H), 2.51−2.34 (m, 3H), 2.09−1.91 (m, 3H), 1.84−1.69 (m, 3H), 1.61 (m, 1H), 1.26−1.04 (m, 4H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 209.7, 155.7, 78.6, 55.1, 51.0, 47.1, 38.4, 30.9, 30.1, 25.2, 25.06, 25.02; IR ($CHCl_3$) 3027, 2941, 2859, 1746, 1714 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{12}H_{18}NaO_4$ $(M + Na)^+$ 249.1097, found 249.1100. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.96; H, 8.18.

**4-Benzyloxycyclohexylbenzylimine (30).** To a solution of 4-benzyloxycyclohexanone (**19**; 0.500 g, 2.5 mmol) in still-dried ether (25 mL) and activated 4 Å molecular sieves (2.0 g) was added benzylamine (1.31 g, 12.2 mmol). After 2 days, the reaction mixture was filtered through a syringe filter under nitrogen and the solvent was removed in vacuo. The excess benzylamine was removed by Kugelrohr distillation (0.1 mmHg) from 80 to 100 °C to yield the crude product as an oil (about 70% pure as determined by $^1$H NMR spectroscopy, 0.724 g, quantitative yield of the impure product). No further purification was possible: $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.42−6.99 (m, 10H, overlap with benzylamine), 4.56−4.35 (m, 4H), 3.62 (tt, $J$ = 6.6, 3.6 Hz, 1H), 2.60−2.45 (m, 2H), 2.28−2.13 (m, 2H), 1.96−1.67 (m, 4H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 172.8, 140.4, 138.9 128.50, 128.46, 127.8, 127.6, 127.5, 126.6, 74.1, 70.2, 54.5, 35.6, 31.6, 31.1, 24.8; IR ($CHCl_3$) 2867, 1656 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{20}H_{24}NO$ $(M + H)^+$ 294.1858, found 294.1855.

**General Procedure for the Formation of the (2,4-Dinitrophenyl)hydrazones from Ketones.** To a solution of the ketone (1.0 equiv) in ethanol (0.1 M) was added 2,4-dinitrophenylhydrazine (0.95 equiv) and 1 drop of acetic acid. The reaction mixture was heated

to reflux and stirred. After 12 h, the reaction mixture was cooled and the product crystallized from the solution. The crude product was washed with cold (−10 °C) ethanol and placed under high vacuum to yield the purified product as a yellow-orange crystalline solid.

**4-Benzyloxycyclohexanone (2,4-Dinitrophenyl)hydrazone (11).** The standard hydrazone formation procedure was followed with 4-benzyloxycyclohexanone (**19**; 0.817 g, 4.0 mmol) followed by an additional recrystallization from ethanol, to yield an orange solid (1.24 g, 80%): mp 125−126 °C (lit.[77] mp 126−128 °C); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 11.19 (s, 1H), 9.12 (d, $J$ = 2.6 Hz, 1H), 8.29 (dd, $J$ = 9.6, 2.4 Hz, 1H), 7.97 (d, $J$ = 9.6 Hz, 1H), 7.40−7.28 (m, 5H), 4.61 (m, 2H), 3.81 (tt, $J$ = 5.9, 3.1 Hz, 1H), 2.80−2.61 (m, 2H), 2.53−2.39 (m, 2H), 2.09−2.00 (m, 2H), 2.00−1.86 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 160.3, 145.5, 138.7, 137.8, 130.2, 129.1, 128.7, 127.9, 127.7, 123.8, 116.5, 73.1, 70.5, 31.2, 31.0, 30.0, 23.0; IR ($CHCl_3$) 3327, 3102, 3022, 2954, 2864, 1619 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{19}H_{19}N_4O_5$ $(M - H)^-$ 383.1356, found 383.1346. Anal. Calcd for $C_{19}H_{20}N_4O_5$: C, 59.37; H, 5.24. Found: C, 59.46; H, 5.43.

**4-Methoxycyclohexanone (2,4-Dinitrophenyl)hydrazone (12).** The standard hydrazone formation procedure was followed with 4-methoxycyclohexanone (**21**; 0.500 g, 3.90 mmol) to yield an orange solid (0.979 g, 82%): mp 139−140 °C (lit.[78] mp 150 °C); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 11.19 (s, 1H), 9.12 (d, $J$ = 2.6 Hz, 1H), 8.29 (dd, $J$ = 9.6, 2.5 Hz, 1H), 7.96 (d, $J$ = 9.6 Hz, 1H), 3.59 (tt, $J$ = 5.8, 3.3 Hz, 1H), 3.40 (s, 3H), 2.71−2.57 (m, 2H), 2.50−2.38 (m, 2H), 2.02−1.85 (m, 4H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 160.2, 145.5, 137.8, 130.2, 129.1, 123.8, 116.5, 75.2, 56.3, 31.0, 30.4, 29.5, 22.9; IR ($CHCl_3$) 3327, 3113, 3018, 2953, 2885, 1619 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{13}H_{16}N_4NaO_5$ $(M + Na)^+$ 331.1018, found 331.1018.

**4-(Methyoxycarbonyloxy)cyclohexanone (2,4-Dinitrophenyl)-hydrazone (13).** The standard hydrazone formation procedure was followed with methyl 4-(methyoxycarbonyloxy)cyclohexanone (**24**; 2.10 g, 12.2 mmol) followed by an additional recrystallization from 1/1 ethanol/ethyl acetate, to yield a yellow solid (3.05 g, 71%): mp 160−162 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 11.15 (s, 1H), 9.07 (d, $J$ = 2.6 Hz, 1H), 8.26 (dd, $J$ = 9.6, 2.5 Hz, 1H), 7.93 (d, $J$ = 9.6 Hz, 1H), 5.00 (m, 1H), 3.80 (s, 3H), 2.74−2.60 (m, 2H), 2.57−2.46 (m, 2H), 2.12−1.98 (m, 4H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 158.3, 155.2, 145.4, 137.9, 130.2, 129.2, 123.7, 116.4, 73.2, 55.1, 31.0, 30.8, 29.6, 22.9; IR ($CHCl_3$) 3327, 3102, 3029, 2959, 1746, 1619 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{14}H_{15}N_4O_7$ $(M - H)^-$ 351.0941, found 351.0947. Anal. Calcd for $C_{14}H_{16}N_4O_7$: C, 47.73; H, 4.58. Found: C, 47.62; H, 4.52.

**4-(Methyoxycarbonylamino)cyclohexanone (2,4-Dinitrophenyl)hydrazone (14).** The standard hydrazone formation procedure was followed with 4-(methyoxycarbonylamino)cyclohexanone (**27**; 0.170 g, 1.0 mmol) to yield a yellow solid (0.292 g, 84%): mp 216−217 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 11.16 (s, 1H), 9.12 (d, $J$ = 2.6 Hz, 1H), 8.30 (dd, $J$ = 9.6, 2.5 Hz, 1H), 7.95 (d, $J$ = 9.6 Hz, 1H), 4.64 (s, 1H), 3.87 (br m, 1H), 3.69 (s, 3H), 2.82 (m, 1H), 2.67 (dtd, $J$ = 14.8, 4.6, 1.8 Hz, 1H), 2.47 (ddd, $J$ = 14.9, 12.0, 5.0 Hz, 1H), 2.34−2.18 (m, 3H), 1.62−1.47 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) $\delta$ 158.3, 156.4, 145.4, 138.0, 130.3, 129.3, 123.8, 116.5, 52.4, 48.8, 33.3, 32.8, 31.7, 24.8; IR ($CH_2Cl_2$) 3436, 3329, 3060, 2970, 2858, 1724 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{14}H_{16}N_5O_6$ $(M - H)^-$ 350.1100, found 350.1108. Anal. Calcd for $C_{14}H_{17}N_5O_6$: C, 47.86; H, 4.88. Found: C, 47.92; H, 4.71.

**4-(Trifluoromethyl)cyclohexanone (2,4-Dinitrophenyl)-hydrazone (15).** The standard hydrazone formation procedure was followed with 4(trifluoromethyl)cyclohexanone (**29**; 0.114 mg, 0.7 mmol). Additional reaction time (3 days) was required. Flash chromatography (5/95 methanol/toluene) gave a yellow solid (0.090 g, 38%): mp 147−148 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 11.18 (s, 1H), 9.12 (d, $J$ = 2.54 Hz, 1H), 8.31 (dd, $J$ = 9.6, 2.5 Hz, 1H), 7.96 (d, $J$ = 9.6 Hz, 1H), 2.97 (m, 1H), 2.77 (m, 1H), 2.48−2.35 (m, 2H), 2.31−2.14 (m, 3H), 1.78−1.60 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 157.5, 145.4, 138.1, 130.3, 129.4, 127.3 (q, $J$ = 278.4 Hz), 123.7, 116.5, 40.8 (q, $J$ = 27.4 Hz), 33.2, 25.1 (m), 25.0, 24.0 (m); IR ($CHCl_3$) 3327, 3103, 3023, 2963, 1619, 1594 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{13}H_{13}F_3N_4NaO_4$ $(M + Na)^+$ 369.0787, found 369.0786. Anal. Calcd for $C_{13}H_{13}F_3N_4O_4$: C, 45.09; H, 3.78. Found: C, 45.14; H, 3.72.

**Axial-4-benzyloxydecalone (2,4-Dinitrophenyl)hydrazone (42).** The standard hydrazone formation procedure was followed with axial-4-benzyloxydecalone (**34**; 0.373 g, 1.4 mmol). Additional purification by flash chromatography (1/9 ethyl acetate/hexanes) yielded a yellow solid (0.252 g, 50%): mp 161−163 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 11.26 (s, 1H), 9.12 (d, $J$ = 2.5 Hz, 1H), 8.28 (dd, $J$ = 9.6, 2.4 Hz, 1H), 7.96 (d, $J$ = 9.6 Hz, 1H), 7.43−7.28 (m, 5H), 4.70 (d, $J$ = 11.8 Hz, 1H), 4.50 (d, $J$ = 11.8 Hz, 1H), 3.58 (m, 1H), 2.70 (m, 1H), 2.55 (td, $J$ = 11.5, 3.1 Hz, 1H), 2.44 (td, $J$ = 14.0 Hz, 5.1 Hz, 1H), 2.37 (m, 1H), 2.20 (m, 1H), 1.89−1.71 (m, 3H), 1.63−1.19 (m, 6H, overlap with $H_2O$); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 162.1, 145.9, 138.9, 137.6, 130.1, 129.0, 128.6, 127.83, 127.75, 123.8, 116.6, 76.3, 71.5, 48.6, 43.1, 29.9, 28.9, 27.5, 26.2, 25.8, 22.1; IR ($CH_2Cl_2$) 3331, 3108, 3061, 2935, 2859, 1619 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{23}H_{26}N_4NaO_5$ $(M + Na)^+$ 461.1801, found 461.1800. Anal. Calcd for $C_{23}H_{26}N_4O_5$: C, 63.00; H, 5.98. Found: C, 63.09; H, 6.09.

**Equatorial-4-benzyloxydecalone (2,4-Dinitrophenyl)-hydrazone (43).** The standard hydrazone formation procedure was followed with equatorial-4-benzyloxydecalone (**38**; 0.050 g, 0.2 mmol). The product was an orange solid (0.077 g, 92%): mp 174−175 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 11.20 (s, 1H), 9.12 (d, $J$ = 2.4 Hz, 1H), 8.29 (dd, $J$ = 9.6, 2.2 Hz, 1H), 7.96 (d, $J$ = 9.6 Hz, 1H), 7.39−7.27 (m, 5H), 4.67 (d, $J$ = 11.6 Hz, 1H), 4.51 (d, $J$ = 11.6 Hz, 1H), 3.35 (td, $J$ = 9.5, 4.4 Hz, 1H), 2.91 (dt, $J$ = 15.0, 4.0 Hz), 2.42−2.32 (m, 2H), 2.21 (m, 1H), 2.14−1.99 (m, 2H), 1.92−1.76 (m, 2H), 1.64−1.53 (m, 1H, overlap with $H_2O$), 1.51−1.39 (m, 2H), 1.32−1.18 (m, 2H), 1.05 (m, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 160.9, 145.8, 138.6, 137.8, 130.2, 129.2, 128.7, 127.99, 127.96, 123.8, 116.7, 80.4, 71.5, 48.9, 46.5, 30.8, 29.5, 27.2, 25.8, 25.7, 24.3; IR ($CH_2Cl_2$) 3330, 3103, 3054, 2932, 2858, 1619 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{23}H_{26}N_4NaO_5$ $(M + Na)^+$ 461.1801, found 461.1798.

**Axial-4-methoxydecalone (2,4-Dinitrophenyl)hydrazone (44).** The standard hydrazone formation procedure was followed with axial-4-methoxydecalone (**35**; 0.202 g, 1.1 mmol). Additional purification by flash chromatography (1/9 ethyl acetate/hexanes) yielded an orange solid (0.340 g, 85%): mp 172−173 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 11.26 (s, 1H), 9.13, (d, $J$ = 2.5 Hz, 1H), 8.28 (dd, $J$ = 9.6, 2.5 Hz, 1H), 7.96 (d, $J$ = 9.6 Hz, 1H), 3.41 (s, 3H), 3.32 (m, 1H), 2.68 (m, 1H), 2.44 (td, $J$ = 11.5, 3.2 Hz, 1H), 2.40−2.30 (m, 2H), 2.19 (m, 1H), 1.88−1.75 (m, 2H), 1.73−1.58 (m, 2H), 1.54−1.34 (m, 3H), 1.34−1.18 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 162.9, 146.0, 137.6, 130.2, 129.0, 123.9, 116.6, 78.4, 57.4, 48.6, 43.1, 29.8, 28.2, 27.5, 26.2, 25.8, 21.9; IR ($CH_2Cl_2$) 3331, 3108, 3056, 2934, 2859, 1619 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{17}H_{22}N_4NaO_5$ $(M + Na)^+$ 385.1488, found 385.1483. Anal. Calcd for $C_{17}H_{22}N_4O_5$: C, 56.34; H, 6.12. Found: C, 56.59; H, 6.16.

**Equatorial-4-methoxydecalone (2,4-Dinitrophenyl)hydrazone (45).** The standard hydrazone formation procedure was followed with equatorial-4-methoxydecalone (**39**; 0.035 g, 0.2 mmol). The reaction time was 3 days. Crystallization from the reaction mixture gave an orange solid (0.046 g, 67%): mp 152−153 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 11.19 (s, 1H), 9.12, (d, $J$ = 2.6 Hz, 1H), 8.29 (dd, $J$ = 9.6, 2.5 Hz, 1H), 7.96 (d, $J$ = 9.6 Hz, 1H), 3.40 (s, 3H), 3.12 (td, $J$ = 9.4, 4.1 Hz, 1H), 2.89 (dt, $J$ = 15.1, 4.5 Hz, 1H), 2.35 (dq, $J$ = 13.3, 4.5 Hz, 1H), 2.30−2.15 (m, 2H), 2.15−1.99 (m, 2H), 1.93−1.75 (m, 2H), 1.55−1.38 (m, 2H), 1.39−1.17 (m, 3H), 1.07 (m, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 161.0, 145.8, 137.8, 130.2, 129.1, 123.8, 116.7, 82.3, 57.2, 48.8, 46.4, 30.8, 28.7, 27.3, 25.8, 25.7, 24.2; IR ($CH_2Cl_2$) 3330, 3107, 3057, 2933, 2858, 1619 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{17}H_{21}N_4O_5$ $(M - H)^-$ 361.1512, found 361.1505. Anal. Calcd for $C_{17}H_{22}N_4O_5$: C, 56.34; H, 6.12. Found: C, 56.51; H, 6.22.

**Axial-4-(methyoxycarbonyloxy)decalone (2,4-Dinitrophenyl)-hydrazone (46).** The standard hydrazone formation procedure was followed with axial-4-(methyoxycarbonyloxy)decalone (**36**; 0.053 g, 0.2 mmol). Additional purification by flash chromatography (100% benzene) yielded a bright yellow solid (0.040 g, 43%): mp 215−217 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 11.25 (s, 1H), 9.13 (d, $J$ = 2.5 Hz, 1H), 8.30 (dd, $J$ = 9.6, 2.4 Hz, 1H), 7.96 (d, $J$ = 9.6 Hz, 1H), 4.92 (m, 1H), 3.84 (s, 3H), 2.77 (m, 1H), 2.47 (td, $J$ = 11.6, 3.1 Hz, 1H), 2.42−2.32 (m, 2H), 2.24 (m, 1H), 1.91−1.68 (m, 4H), 1.64−1.52 (m, 1H, overlap with $H_2O$), 1.51−1.38 (m, 2H), 1.37−1.21 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 160.9, 155.7, 145.9, 137.9, 130.2, 129.2, 123.8, 116.6, 75.9, 55.1, 47.0, 43.1, 30.2, 29.5, 27.4, 25.9, 25.6, 22.1; IR ($CH_2Cl_2$) 3330, 3056, 2936, 2859, 1746, 1620 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{18}H_{21}N_4O_7$ $(M - H)^-$ 405.1410, found 405.1403. Anal. Calcd for $C_{18}H_{22}N_4O_7$: C, 53.20; H, 5.46. Found: C, 53.56; H, 5.48.

**Equatorial-4-(methyoxycarbonyloxy)decalone (2,4-Dinitrophenyl)hydrazone (47).** The standard hydrazone formation procedure was followed with equatorial-4-(methyoxycarbonyloxy)decalone (**41**; 0.072 g, 0.32 mmol). Additional purification by flash chromatography (1/9 ethyl acetate/hexanes) yielded a bright yellow solid (0.090 mg, 69%): mp 195−197 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 11.19 (s, 1H), 9.12 (d, $J$ = 2.5 Hz, 1H), 8.30 (dd, $J$ = 9.6, 2.4 Hz, 1H), 7.95 (d, $J$ = 9.6 Hz, 1H), 4.65 (td, $J$ = 10.1, 4.3 Hz, 1H), 3.81 (s, 3H), 2.93 (dt, $J$ = 15.1, 3.9 Hz, 1H), 2.37 (m, 1H), 2.29−2.04 (m, 4H), 1.95−1.77 (m, 2H), 1.67 (m, 1H), 1.60−1.42 (m, 2H, overlap with $H_2O$), 1.35−1.07 (m, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) $\delta$ 159.2, 155.7, 145.8, 138.0, 130.3, 129.4, 123.7, 116.6, 79.1, 55.1, 47.4, 46.3, 30.1, 30.0, 27.1, 25.6, 25.3, 24.2; IR ($CH_2Cl_2$) 3329, 3063, 2938, 2858, 1747, 1619 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for $C_{18}H_{21}N_4O_7$ $(M - H)^-$ 405.1410, found 405.1413. Anal. Calcd for $C_{18}H_{22}N_4O_7$: C, 53.20; H, 5.46. Found: C, 53.56; H, 5.64.

**General Procedure for the Formation of Tetrafluoroborate Salts of Hydrazones.** To a solution of the hydrazone (1 equiv) in benzene (0.05 M) was added $HBF_4 \cdot OEt_2$ (3 equiv) or triflic acid (3 equiv). Additional toluene or dichloromethane was added as needed to dissolve the substrate. The solution was rapidly stirred and the characteristic dark orange to yellow color of the hydrazone faded rapidly to a pale yellow or colorless solution. The solution was then rapidly cooled in liquid nitrogen, freezing the mixture, which was then placed under high vacuum (0.1 mmHg). The solid was warmed slowly overnight under vacuum. After 24 h, the salt was obtained as either a fine powder or residue in the flask, which was dissolved in deuterated acetonitrile for $^1$H and $^{13}$C NMR spectroscopic analysis. Common impurities present in the NMR spectral analysis include excess $HBF_4 \cdot OEt_2$, decomposed $HBF_4 \cdot OEt_2$, and remaining solvent.

## ■ ASSOCIATED CONTENT

**Supporting Information.** Text, tables, and figures giving spectra for all new compounds and details of the computational studies and CIF files giving crystallographic data for **11**, **42**, and **49**. This material is available free of charge via the Internet at http://pubs.acs.org.

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