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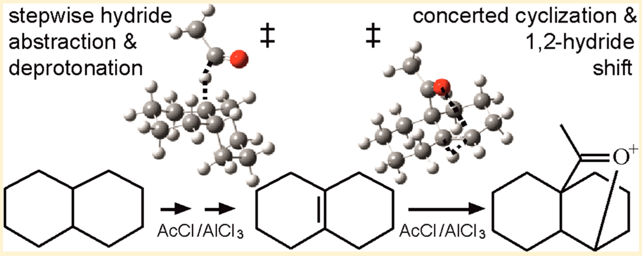
C–H Functionalization of sp^3 Centers with Aluminum: A Computational and Mechanistic Study of the Baddeley Reaction of Decalin

Catherine L. Lyall,[†] Makoto Sato,[‡] Mario Uosis-Martin,[†] Syeda Farina Asghar,[†,§] Matthew D. Jones,[†] Ian H. Williams,*[,†] and Simon E. Lewis*[,†]

[†]Department of Chemistry, University of Bath, Bath, U.K. BA2 7AY
[‡]Department of Chemistry, Rikkyo University, Toshima-ku, Tokyo 171-8501, Japan
[§]Department of Chemistry, University of Azad Jammu & Kashmir, Muzaffarabad, 13100 Azad Jammu & Kashmir, Pakistan

S *Supporting Information*

ABSTRACT: Decalin undergoes reaction with aluminum trichloride and acetyl chloride to form a tricyclic enol ether in good yield, as first reported by Baddeley. This eye-catching transformation, which may be considered to be an aliphatic Friedel–Crafts reaction, has not previously been studied mechanistically. Here we report experimental and computational studies to elucidate the mechanism of this reaction. We give supporting evidence for the proposition that, in the absence of unsaturation, an acylium ion acts as a hydride acceptor, forming a tertiary carbocation. Loss of a proton introduces an alkene, which reacts with a further acylium ion. A concerted 1,2-hydride shift/oxonium formation, followed by elimination, leads to formation of the observed product.



INTRODUCTION

The Friedel–Crafts reaction[1] is one of the first aromatic transformations students encounter, often in their preuniversity education. It can be considered the archetypal C–H functionalization reaction and is ubiquitous in organic synthesis.[2] It remains a focus of much current research, with particular activity devoted to the development of asymmetric variants.[3]

C–H functionalization more broadly is a rapidly expanding field[4] because, unlike traditional functional group interconversions, C–H activation is a conceptually distinct approach wherein functionality is introduced at locations where none was present beforehand. Such methodology permits the use of entirely new strategies to effect complex molecule synthesis.[5]

Uses of C–H functionalization in synthesis can be subcategorized as either reactions performed on substrates with extensive existing functionality or reactions carried out on substrates having little or no functionality whatsoever. In the first category, the presence of pre-existing functionality necessitates that the C–H functionalization methodology used displays wide functional group tolerance; regio- and chemoselectivity are also prerequisites. Thus, not all reported methodologies are applicable.[6] "Late stage" C–H functionalizations of this type most typically employ expensive or hard-to-access transition metal-based catalysts,[7] although the value of the final products so accessed justifies this approach.[5c] On the other hand, in the second category, the lack of functionality allows for a wider range of methodologies to be used successfully. However, use of expensive catalysts/reagents is not practicable in this case, as the C–H functionalization of a saturated hydrocarbon will most likely be the first step of a synthetic sequence, and therefore will likely be carried out on a large scale. As such, the cost of the reagents for C–H functionalization and also of the substrate itself are paramount if the transformation is to be synthetically useful.

A standout example of a transformation in this second category is the work of Baddeley et al. on the reaction of decalin with aluminum trichloride and acetyl chloride.[8] Using an excess of $AlCl_3$, multiple products are observed[8a,c] (Scheme 1a), but using an excess of AcCl (at a lower temperature) leads cleanly to formation of tricyclic enol ether **6**[8b–f] (Scheme 1b).

This transformation can be considered to be an aliphatic Friedel–Crafts acylation, which is not without precedent: such reactions have been reported for other simple, unfunctionalized alkanes.[9] (It should be noted that Friedel–Crafts acylations of several alkenes are also known.[10]) The products arising from these transformations have been deployed for synthesis, and the area has been reviewed.[11] Most recently, we have demonstrated the applicability of the Baddeley reaction to a range of bicycloalkyls and bicyclo[*x*.*y*.0]alkanes (Scheme 2).[12]

Of these various examples, the transformation of decalin is particularly appealing in the context of C–H functionalization for several reasons. The product is formed in acceptable yield

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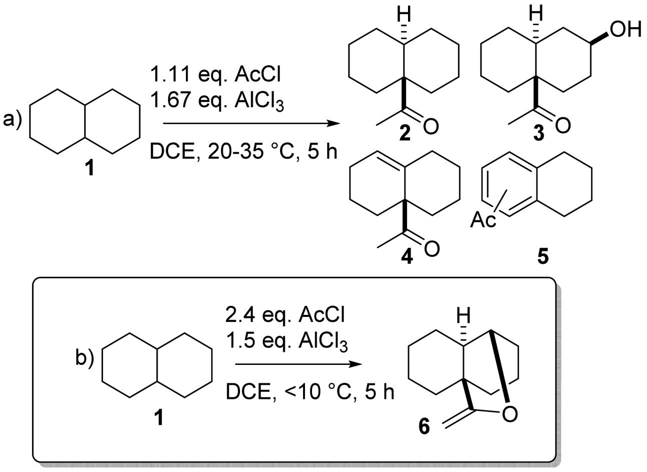
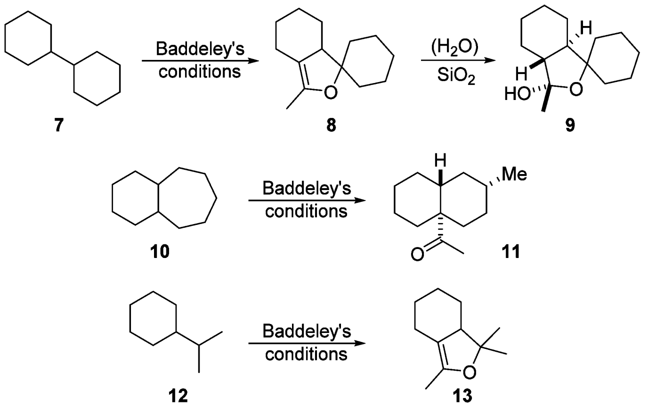
Scheme 1. C−H Functionalization of Decalin with Aluminum Trichloride and Acetyl Chloride



Scheme 2. Selected Applications of the Baddeley Reaction

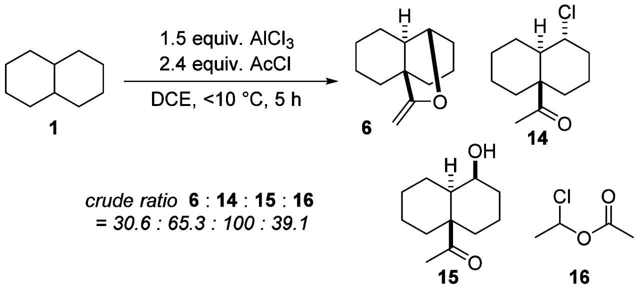


(30−46%),[8c] and the substrate and reagents are of very low cost. In addition, enol ether **6** boils at a temperature significantly different from those of unreacted decalin (which comprises most of the mass balance) and any byproducts. Therefore, large-scale purification of **6** by distillation is possible; we have prepared it on a ~100 g scale. The enol ether is especially valuable as a building block for synthesis by virtue of the fact that it has been selectively functionalized at C1 and C10—there is a dearth of other methods in the literature for accessing this substitution pattern of decalin in a concise fashion. Indeed, **6** has seen diverse uses, from synthesis of potential antiviral agents to natural products.[13] More generally, functionalized decalins are crucial building blocks for terpenoid[14] and steroid[15] natural products and are also of key importance in the fragrance industry.[16] Other examples of the functionalization of decalin with AlCl$_3$ include the use of benzenesulfonyl chloride to form several monosubstituted chlorodecalins.[17]

■ RESULTS AND DISCUSSION

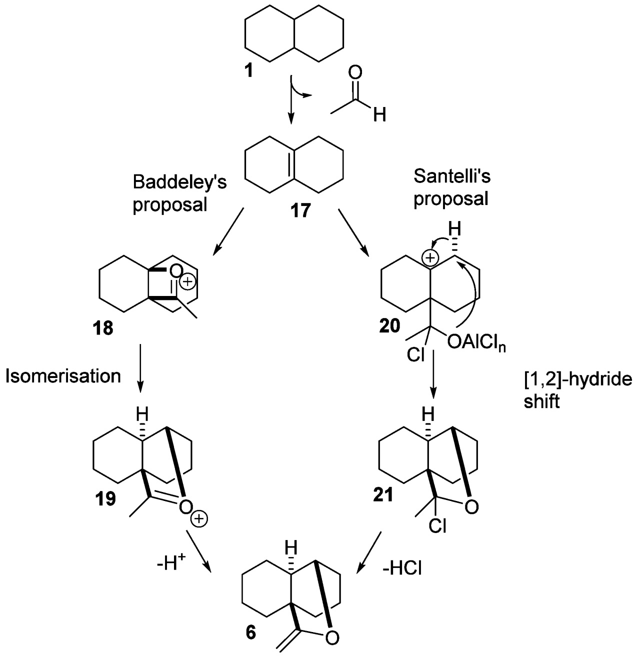
Experimental Aspects. Upon replication of the Baddeley reaction, in addition to the originally reported products (enol ether **6** and *trans*-decalin), we were also able to isolate and identify additional products (Scheme 3). The chloroketone **14** is known to be formed from **6** upon treatment with hydrochloric acid, and we have found that it is in fact also formed as a minor product in the Baddeley reaction itself.[8b] Additionally, hydroxyketone **15**, previously reported to be formed from **6** upon treatment with sulfuric acid, was identified as another product of the reaction.[8b,13e] However, as seen by Baddeley,[5b] **15** is observed to equilibrate with **6** upon heating. Another side-product was identified as 1-chloroethyl acetate **16**, which is formed from acetaldehyde (vide infra).

Scheme 3. Additional Byproducts Identified from the Baddeley Reaction



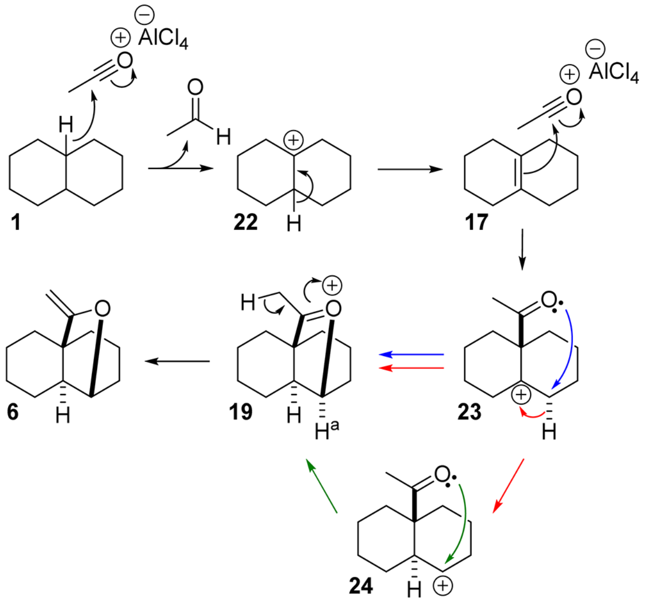
Mechanistic Proposals. The original proposal by Baddeley and co-workers[8b] involved the dehydrogenation of decalin to $\Delta^{9,10}$-octalin **17**, followed by formation of a tricyclic oxonium intermediate (**18**, Scheme 4). This intermediate, possessing two sp^2 hybridized atoms in a four-membered ring, would be rather strained. Over 30 years later, Santelli and co-workers[9m] were the first to posit a mechanism that did not include such a strained intermediate, instead invoking a carbocation intermediate **20**, which cyclizes by means of a [1,2]-hydride shift (Scheme 4).

Scheme 4. Mechanisms Proposed in the Literature for the Baddeley Reaction



Our mechanistic proposal (Scheme 5), which we have disclosed previously,[12] is a variant of the proposals in Scheme 4. The acylating agent initially acts as a hydride sink (such reactivity is precedented[11]), because, at the outset of the reaction, there is no unsaturation present. Thus, hydride abstraction leads to the formation of a tertiary cation at the ring

Scheme 5. Our Mechanistic Proposal for the Baddeley Reaction



junction, **22**. Deprotonation gives $\Delta^{9,10}$-octalin **17**. Another equivalent of acylium ion is then able to react with the newly formed unsaturation, affording acyl cation **23**. Discounting formation of a 4-membered ring, we propose instead the [1,2]-hydride shift and attack of the oxygen at the position α- to the ring junction, as per Santelli's proposal. Crucially, these two events may be concerted or stepwise. The concerted process is represented by the direct transformation of **23** into **19** (red and blue arrows). Alternatively, a stepwise process can also be envisaged whereby a [1,2]-hydride shift of **23** gives isomeric cation **24** (red arrow only), followed by nucleophilic attack of the carbonyl oxygen as a separate step (green arrow) to give **19**. The stepwise process may seem less likely, given that it involves the transformation of a tertiary cation (**23**) into a secondary one (**24**). However, it should be noted that in **24** the positive charge is further from the electron-withdrawing carbonyl and the ring junction carbon is no longer planar, thus allowing for alteration of the conformation of the bicyclic system. Thus, this mechanism was not dismissed out of hand, and a key aspect of this current work was to determine whether this process is indeed concerted (vide infra). Finally only on workup does the final deprotonation of **19** occur to give enol ether **6**. Overall, our proposal varies from Santelli's in that **23** and **19** comprise an sp^2 carbon (Santelli proposes the same carbon to be sp^3 with a bond to a chlorine, cf. **20** and **21**).

We justify the variance from Santelli's proposal as follows. Various studies have confirmed the formation of free acylium ion from AcCl/$AlCl_3$ under various conditions.[18] For this reason, we have invoked a free acylium ion as the reactive species that reacts with $\Delta^{9,10}$-octalin **17**. The product of this reaction would be **23** (i.e., with an sp^2 carbonyl carbon and no chlorine incorporated), not **20**. It is conceivable that **20** could then be formed from **23**, but this would necessitate intermolecular transfer of a chloride anion from the highly stable $[AlCl_4]^-$ anion, as opposed to intramolecular direct cyclization of **23** to **19**. More conclusively, in situ reaction monitoring by NMR spectroscopy unambiguously shows the presence of cyclized oxonium **19** prior to workup: the diagnostic proton H^a (Scheme 5) resonates at 6.08 ppm in the ^{1}H NMR spectrum (Figure 1, shown in red), a comparable shift to similar compounds in the literature.[19] Such deshielding of H^a can only be accounted for by its proximity to the positively charged oxygen in **19**. In contrast, in neutral species **21**, H^a would not be so far downfield, and no other proton environment would be so deshielded. Thus, we have excluded Santelli's proposal. Additionally, we have excluded Baddeley's proposal on the basis of computational data (vide infra).

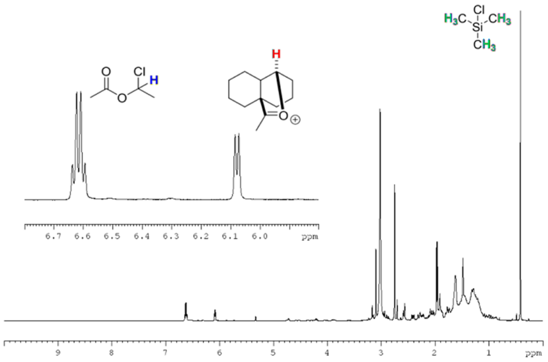


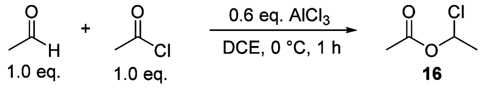
Figure 1. ^{1}H NMR spectrum of the Baddeley reaction prior to workup, with chlorotrimethylsilane standard (400 MHz, 273 K, CD_2Cl_2).

Hydride Abstraction. In the original report, Baddeley made no comment on the isomeric composition of the decalin starting material, save that it was of technical grade. Such a grade would be expected to consist of a mixture of the *cis* and *trans* isomers. It has previously been reported that *cis*-decalin was the only reactive isomer, as *trans*-decalin was recovered unreacted.[9m] (Also of note, functionalization of decalin with $AlCl_3$ and benzenesulfonyl chloride proceeded only with *cis*-decalin.[17]) However, in our hands the Baddeley reaction of pure *trans*-decalin did in fact yield some enol ether, **6**, albeit in a poorer yield, 0.9%, as well as the chloroketone **14** in 3.6% yield. The *trans*-decalin recovered from this reaction, depleted of any trace of *cis*-decalin that may have been present, was resubmitted to the reaction conditions, and the same result was obtained. Pure *cis*-decalin gave the enol ether, **6**, in 27% yield and recovered starting material in 31% yield (10% of **14** was also isolated). Crucially, *the recovered decalin was entirely the trans isomer*. Thus, it can be concluded that, when performing the Baddeley reaction on a mixture of decalin isomers, although *cis*-decalin is undisputedly more reactive, the recovered *trans*-decalin is both unreacted *trans*-decalin and isomerized *cis*-decalin. Indeed, under other reaction conditions it has been shown that $AlCl_3$ alone can isomerize *cis*-decalin into *trans*-decalin.[20]

Experimental investigations to determine the mechanism of the reaction initially focused on the hydride abstraction from the tertiary position of decalin. Reacting $AlCl_3$with a mixture of *cis*- and *trans*-decalin in 1,2-dichloroethane yielded pure *trans*-decalin, indicating $AlCl_3$ is capable of acting as a hydride abstractor toward *cis*-decalin under our reaction conditions. However, it should be considered that, in the Baddeley reaction, the optimized conditions employ 1.5 and 2.4 equiv of $AlCl_3$ and AcCl, respectively, premixed. In reacting these reagents together prior to addition of the decalin, the formation of the "ate" complex inhibits the ability of $AlCl_3$ to act as a hydride abstractor, as $[AlCl_3]$ is very low.

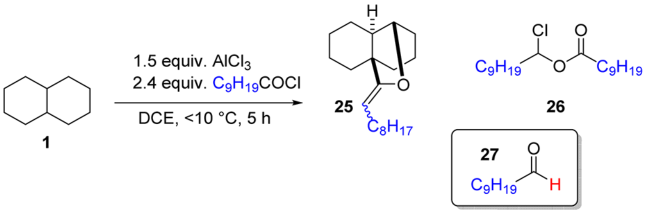
Reaction of AcCl with $AlCl_3$ also generates the acylium cation (Ac^+), which could plausibly be considered as the hydride abstractor; such a reaction would yield acetaldehyde (cf. Scheme 5). However, in fact no acetaldehyde is observed (in ^1H and ^{13}C NMR spectra of the unpurified products). This could be attributed to its volatility, but we also entertained the possibility that the acetaldehyde formed in the reaction undergoes further transformation. To probe this, we subjected acetaldehyde to reaction conditions comparable to those present in the original reaction mixture after acetaldehyde had been formed (i.e., 1 equiv of $AlCl_3$ and AcCl have already been consumed), but omitting the decalin. As shown in Scheme 6, this led to formation of 1-chloroethyl acetate **16**, which we had previously observed in the crude reaction mixture (cf. Scheme 3). Thus, the ultimate fate of at least some of the abstracted hydrides is to be incorporated into **16**. This pathway also accounts for the consumption to up to 1 equiv of AcCl in a nonproductive fashion and somewhat rationalizes the fact that the yield for the reaction never approaches quantitative. (Because 2 equiv of AcCl are needed for formation of **6**, and because only 2.4 equiv of AcCl are in fact used, it is the case that formation of >0.4 equiv of **16** would leave insufficient AcCl for quantitative formation of **6**.) It follows that an increase in the equivalents of AcCl could lead to an increase in conversion to product; we have observed this indeed to be the case (Figure S10, Supporting Information). It should be noted that the reaction of acetaldehyde and AcCl to form 1-chloroethyl acetate has been reported before, mediated by zinc chloride in substoichiometric quantities.[21]

Scheme 6. Control Reaction: Formation of 1-Chloroethyl Acetate 16



Performing the Baddeley reaction with decanoyl chloride instead of AcCl led to the observation of the nonvolatile aldehyde decanal **27** in the ^1H NMR spectrum of the distillate, as well as peaks indicative of enol ether **25** and chloroester **26** (Scheme 7). From these investigations it is inferred that Ac^+ is both abstracting and retaining the hydride originating from the decalin ring junction.

Scheme 7. Use of a Long-Chain Acyl Chloride Allows Direct Observation of the Aldehyde By-product 27



Kinetic Experiments. With the intention of establishing the order of reaction in both *cis*-decalin and the acylating complex, a set of reactions were undertaken by varying the starting concentrations of *cis*-decalin and subsequently the starting concentrations of the $AlCl_3{\cdot}AcCl$ complex. These reactions were performed in an NMR tube at 273 K with a trimethylsilyl chloride standard. Unfortunately, due to the overlapping peaks in the aliphatic region of the proton NMR spectra, it was not possible to observe directly the consumption of *cis*-decalin. In lieu of this, it was possible to follow the growth of resonances representing both the cyclized oxonium, **19** (an effective surrogate for the final product **6**), and also the 1-chloroethyl acetate byproduct, **16**. A representative ^1H NMR spectrum recorded is reproduced in Figure 1, with the species of interest and their relevant protons highlighted next to their key diagnostic resonances.

The initial rates of reaction could be determined for various concentrations of *cis*-decalin and of the preformed $AlCl_3{\cdot}AcCl$ complex. In all reactions the ratio of AcCl to $AlCl_3$ was maintained at 1.6:1.0 (as per Baddeley's original procedure) because alteration of this ratio has been shown to result in product variation (vide supra, Scheme 1a). Figure 2 shows plots of concentration of cyclized oxonium **19** against time for the initial period of the reaction. The observed rate law may be expressed as eq 1, which, upon taking logarithms of both sides, yields eq 2. According to the method of initial rates, the kinetic order x with respect to decalin is obtained as the slope of a plot (see Supporting information) of $\ln(\text{rate}_0)$ against the natural logarithm of the initial decalin concentration for a constant value of the initial $AlCl_3{\cdot}AcCl$ complex concentration; the initial rates, rate_0, are the slopes of the plots shown in Figure 2A. Similarly, the kinetic order y with respect to the $AlCl_3{\cdot}AcCl$ complex is obtained as the slope of a plot of $\ln(\text{rate}_0)$ against the natural logarithm of the initial $AlCl_3{\cdot}AcCl$ complex concentration for a constant value of the initial decalin concentration; the initial rates are the slopes of the plots shown in Figure 2B.

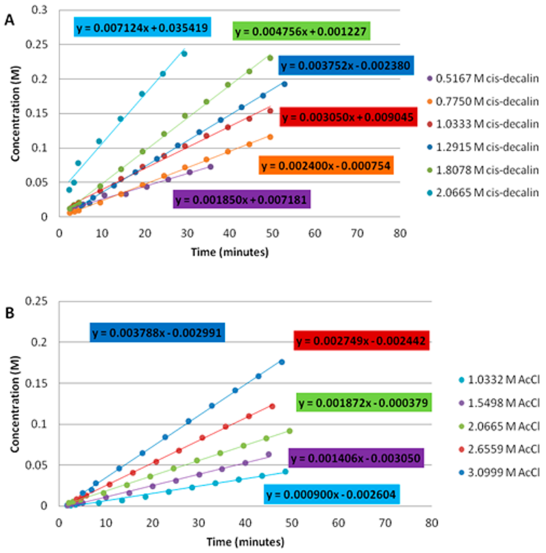


Figure 2. (A) Concentration of cyclized oxonium, **19**, vs time with varying initial concentrations of *cis*-decalin. (B) Concentration of cyclized oxonium, **19**, vs time with varying initial concentrations of $1.6AcCl{\cdot}1.0AlCl_3$.

$$\text{rate}_0 \propto [\text{decalin}]_0{}^x[1.6\text{AcCl}\cdot 1.0\text{AlCl}_3]_0{}^y \qquad (1)$$

$$\ln(\text{rate}_0) = x\ln([\text{decalin}]_0) + y\ln([1.6\text{AcCl}\cdot 1.0\text{AlCl}_3]_0) + c \qquad (2)$$

The experimentally determined order of reaction in *cis*-decalin was 0.9 ± 0.1, indicative of the reaction being first order in *cis*-

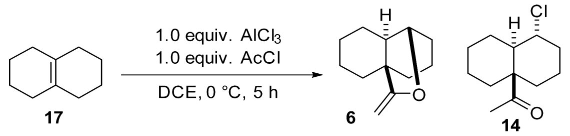
decalin. The experimentally determined order of reaction in the $AlCl_3$•AcCl mixture was 1.3 ± 0.1. This result is indicative of the reaction being greater than first order in the ionic complex generated from AcCl and $AlCl_3$, which can be explained by the possibility of more than one rate-limiting step.

The experimentally observed difference in reactivity between *cis*-decalin and *trans*-decalin implies that the initial hydride abstraction is at least partly rate-limiting. If it were wholly rate-limiting, the reaction would obey first-order kinetics with respect to the $AlCl_3$•AcCl mixture. However, a noninteger order >1 suggests another step in the reaction mechanism is also partially determining the reaction rate, and this step involves another molecule of acylating reagent. The other step involving an additional molecule of acylating reagent is nucleophilic attack on an acylium ion by the $\Delta^{9,10}$ -octalin, **17**, affording **23**. Computational results discussed later show that this is likely to be the case.

Intermediacy of Octalin. The focus of our experimental investigations then turned toward the proposed alkene intermediate, $\Delta^{9,10}$-octalin **17**. Subsequent to abstraction of a hydride from the tertiary position of **1**, two pathways for deprotonation can be envisaged: loss of a proton from the other tertiary position, giving **17**, or from an adjacent secondary position, giving the isomeric $\Delta^{1,9}$-octalin. Our previous studies have determined that formation of **17** is favored.[12]

It follows from our proposed mechanism that subjecting **17** to the Baddeley reaction conditions would furnish the same products as seen in the reaction of decalin itself. As the hydride abstraction step would not occur, fewer equivalents of AcCl and $AlCl_3$ would be required. We found that reaction of **17** (readily prepared by literature procedures[22,23]) with 1 equiv of $AlCl_3$ and AcCl formed **6** in 32% yield as well as **14** in 5% yield (Scheme 8). This finding is strongly supportive of the intermediacy of **17** in the formation of **6** from decalin **1**.

Scheme 8. Experimental Evidence Supporting the Intermediacy of 17



Computational. *Gibbs Energy Profile.*

Figure 3 shows the overall Gibbs energy profile for the Baddeley reaction of *cis*-decalin. Relative energies (kJ mol^{-1}, sums of single-point MP2/cc-PVTZ electronic and optimized MP2/6-31+G* thermal free energies with solvation treated by the polarized continuum model (PCM); see Supporting Information for details) are shown with respect to (separated) $\Delta^{9,10}$-octalin **17** and protonated acetaldehyde (AcH_2^+), which are the common products of reaction of both isomers of decalin. With this method of calculation (at 298.15 K, 1 atm), formation of Ac^+ and $AlCl_4^-$ from AcCl and $AlCl_3$ is favorable by 89 kJ mol^{-1} and 2 equiv of Ac^+ are required to complete the full reaction. The starting point (left-hand end) of the profile therefore involves *cis*-decalin + $2Ac^+$ + $2AlCl_4^-$, and the finishing point (right-hand end) involves **PC-CYC** (≡**19**) + AcH_2^+ + $2AlCl_4^-$. Note that the acid−base neutralization $AcH_2^+ + AlCl_4^- \rightarrow AcH + AlCl_3 + HCl$ is unfavorable by 74 kJ mol^{-1} with the MP2/cc-pVTZ//MP2/6-31+G* method. For the purposes of this discussion, it is only necessary to consider relative energies within the encounter complexes in solution.

The first phase of the reaction (hydride transfer and proton transfer), which consumes the first equivalent of Ac^+, is shown in black on the left-hand side of Figure 3. The second phase (addition and cyclization), which consumes the second equivalent of Ac^+, is shown in blue on the right-hand side of Figure 3. Note that, relative to octalin (D_2 conformation; see Supporting Information) + Ac^+ + AcH_2^+ + $2AlCl_4^-$, the transition structures (TS) **TS-HT** (+ Ac^+ + $2AlCl_4^-$) and **TS-CYC** (+ AcH_2^+ + $2AlCl_4^-$) have essentially the same Gibbs energy, suggesting that at 298.15 K and 1 atm both would be kinetically significant.

Hydride Abstraction and Alkene Formation. The MP2/6-31+G* Gibbs energy profiles for hydride abstraction in CH_2Cl_2 by Ac^+ from *cis*-decalin (black) and *trans*-decalin (red) are shown in Figure 4. Although, of course, the lowest energy chair/chair conformer of *trans*-decalin is ~14 kJ mol^{-1} lower than that of *cis*-decalin, the transition structure ***cis*-TS-HT** for hydride transfer from the latter is ~5 kJ mol^{-1} lower than that from *trans*-decalin, ***trans*-TS-HT**, and the resulting difference of 19 kJ mol^{-1} between the Gibbs energy barriers (54 and 73 kJ mol^{-1}, respectively) corresponds to a factor of about 5000 in relative reactivity at 0 °C.

The imaginary frequency corresponding to the transition vector ("reaction-coordinate vibrational mode") is $i472$ and $i414$ cm^{-1}, respectively, in the *cis*- and *trans*-TSs, and the atomic displacements in this normal coordinate are dominated by hydride transfer and the angle bending associated with rehybridization of the donor and acceptor carbons, C_d and C_a. The angle $C_dH'C_a$ is much less bent (176°) in the *trans*-TS than in the *cis*-TS (155°), probably owing to greater steric interactions, and the Pauling bond order[24] for the breaking C_dH' bond in the *trans*-TS is slightly lower (0.45 vs 0.50) than that in the *cis*-TS. The sum of the breaking C_dH' and making $H'C_a$ bond lengths in each TS is entirely typical of hydride-transfer reactions.[25]

The complex between AcH and decalinyl cation **22** is a stable intermediate that has several readily interconvertible conformers. Relative rotation of these components is a prerequisite for proton transfer via transition structure **TS-PT** for formation of $\Delta^{9,10}$-octalin **17** and AcH_2^+. The potential energy surface for proton transfer is very flat: the Gibbs energy of the transition structure for deprotonation of the lower-energy C_2-symmetric decalinyl cation is apparently also lower than that of either the reactant or product complex that precede and follow it, respectively, along the proton transfer reaction path,[26] and it is ~10 kJ mol^{-1} lower than the TS for deprotonation of the C_s-symmetric conformer.

We have also investigated proton transfer from the decalinyl cation to $AlCl_4^-$ as base and have located the corresponding reaction paths and TSs (see Supporting Information). However, with the method of calculation employed, the relative basicity of AcH is found to be ~18 kJ mol^{-1} greater than that of $AlCl_4^-$, meaning that formation of octalin + $AlCl_4H$ is endoergic. Whichever species serves as the base, deprotonation is in no way rate-limiting.

Addition, Cyclization, and Enol Ether Formation. There are two low-energy conformers of $\Delta^{9,10}$-octalin **17**: the C_{2h}-symmetric conformer is 3 kJ mol^{-1} higher than the D_2 conformer, and there is a Gibbs energy barrier of 23 kJ mol^{-1} for conversion of the former to the latter. Similarly, the complex of Ac^+ with the D_2 octalin conformer is ~4 kJ mol^{-1}

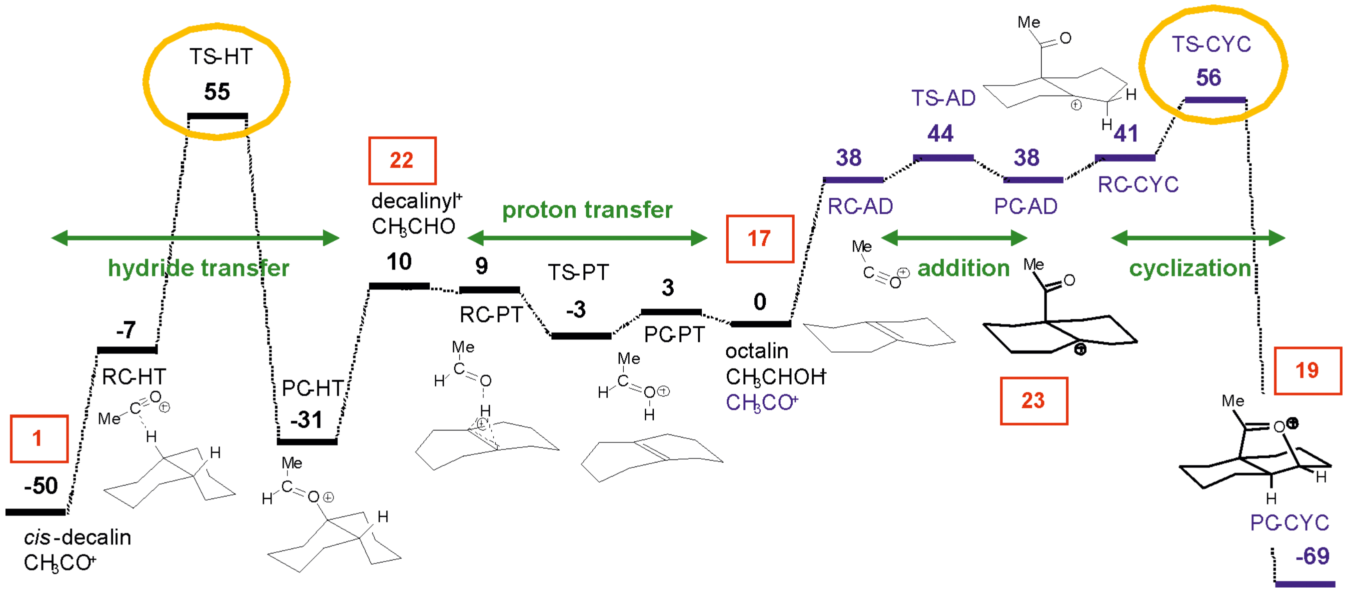


Figure 3. MP2/cc-pVTZ//MP2/6-31+G* Gibbs energy profiles in PCM CH_2Cl_2 for overall reaction from *cis*-decalin. Relative energies are in kJ mol^{-1}. Boxed red numbers correspond to species in Scheme 5.

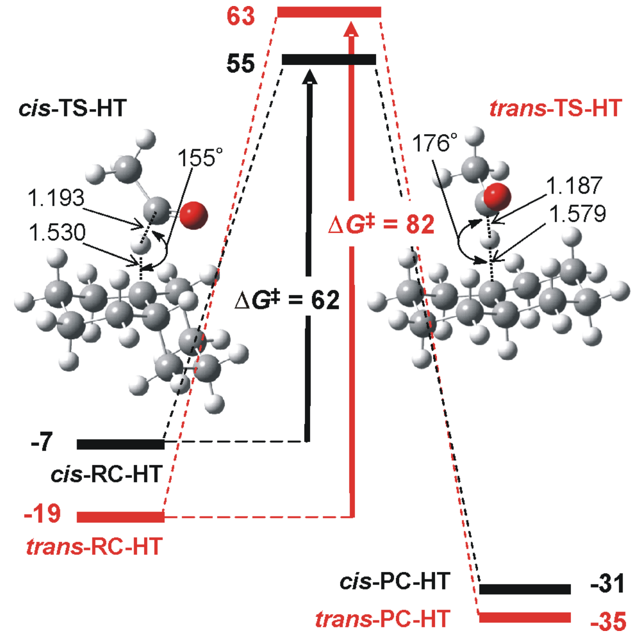


Figure 4. MP2/cc-pVTZ//MP2/6-31+G* Gibbs energy profiles in PCM CH_2Cl_2 for hydride abstraction from *cis*- and *trans*-decalin. Bond lengths are in Å, and angles in degrees. Energies are relative to separated CH_3CHOH^+ and octalin **17**.

lower than that with the C_{2h} conformer, but each complex lies at least 30 kJ mol^{-1} above the separated reactants. The reactivity of the octalin intermediate should not depend on whether it was formed under the experimental conditions from either *cis*- or *trans*-decalin.

Addition of Ac^+ to octalin **17** gives a covalent adduct **23** ($\equiv$ **PC-CYC**) that then undergoes cyclization accompanied by a [1,2]-hydride shift. The adduct derived from the C_{2h} octalin conformer has a slightly longer CC bond (1.57 vs 1.54 Å) between the two species than the D_2 conformer, but it also has a lower Gibbs energy (23 vs 28 kJ mol^{-1}) relative to the separated components; more significantly, the TS for its formation is lower: 39 vs 44 kJ mol^{-1}.

The acyl moiety in the C_{2h} octalin-derived adduct **PC-AD** (**23**) adopts an orientation that is essentially symmetrical with respect to both fused chair-cyclohexyl rings, but the lowest-energy pathway for cyclization begins with a conformational change of one of these rings (right-hand side as shown in Figure 5) from chair to twist-boat in the reactant complex **RC-CYC**, which is another local minimum. Figure 5 shows both the relative Gibbs energies (black) for **RC-CYC**, **TS-CYC**, and the protonated enol ether product **PC-CYC** (**19**) and the potential energy profiles (blue) along the forward and reverse segments of the intrinsic reaction coordinate (IRC) path in each direction from the TS. The structural changes occurring along the entire IRC path show that the transformation, although concerted, is highly asynchronous. The initial phase from **RC-CYC** toward **TC-CYC** (bottom-left of Figure 5; note the expanded energy scale) continues the conformational change in the right-hand ring (as drawn) toward a half-chair conformation in which carbon atoms 1, 9, 10, and 4 are almost coplanar. Then the hydride shift from C4 (donor) to C10 (acceptor) occurs, *trans* to the acyl group, which does not participate in the motion. At the start of this intramolecular hydride transfer, both the bond angle C10C4H′ and the dihedral angle between these atoms and C9 are essentially 90°. In **TS-CYC** the C4H′ and H′C10 bond lengths (respectively, 1.54 and 1.20 Å) are again entirely typical of an asymmetric hydride transfer, and the angle C4H′C10 is only 59°; the distance between the oxygen atom and C1 diminishes very little from its value in **RC-CYC** and corresponds to a Pauling bond order of only ~0.1 in the TS. The imaginary frequency corresponding to the transition vector is *i*388 cm^{-1}, and the atomic displacements in this normal coordinate are dominated by hydride transfer and the angle bending associated with rehybridization of the donor and acceptor carbons. Once the TS is passed, then the final phase of the transformation takes place: the O···C4 distance becomes shorter and the ring conformation changes toward the slightly distorted chair found in the cyclized product **PC-CYC**.

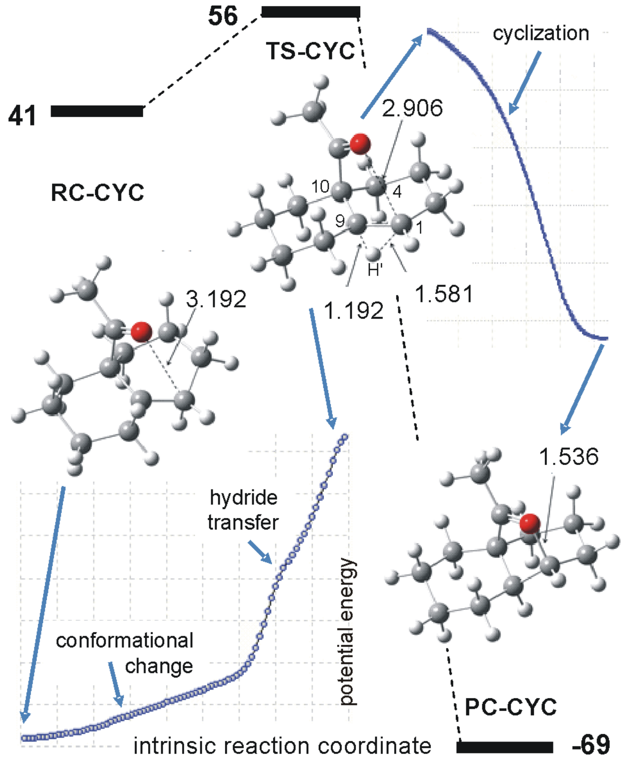


Figure 5. MP2/cc-pVTZ//MP2/6-31+G* Gibbs energy profile (black) in PCM CH_2Cl_2 for cyclization of acylium−octalin adduct with concerted hydride shift, together with MP2/6-31+G* intrinsic reaction coordinate energy profiles (blue; note the different energy scales for the forward and reverse segments). Bond lengths are in Å, and angles in degrees. Energies are relative to separated CH_3CHOH^+ and octalin **17**.

The Gibbs energy for the transition structure **TS-CYC** shown in Figure 5 is 56 kJ mol^{-1} relative to octalin + Ac^+; this species is derived from the C_{2h} octalin conformer. Other TSs derived from the D_2 conformer are all much higher in energy ($\Delta G^{\ddagger}$ = 68, 75, and 85 kJ mol^{-1}) and involve *trans*-hydride shifts from either of two nonequivalent hydrogens (at C4 or C5) or a frontside *cis*-hydride shift. Clearly these are not kinetically competitive. Finally, deprotonation of the cyclized adduct **19** (≡ **PC-CYC**) yields the product enol ether **6**.

The preceding discussion concerns the cyclization and [1,2]-hydride shift from **23** to **19** occurring by a concerted mechanism (blue and red arrows in Scheme 5). The question remains whether a stepwise mechanism involving the intermediacy of **24** is also possible. Despite our best efforts, no local minimum species corresponding to this secondary carbocation on the MP2/6-31+G* potential energy surface has been found. Another question concerns the possible involvement of Baddeley's postulated oxonium intermediate (**18**, Scheme 4). The Gibbs energy of transition structure **4MR-TS** (Supporting Information) is lower than that of **TS-CYC** by 4 kJ mol^{-1}, but the four-membered ring **18** (**PC-4MR**) lies 78 kJ mol^{-1} above the less-strained five-membered ring oxonium **19** (**PC-CYC**). The isomerization of **18** to **19** is formally a dyotropic rearrangement involving concerted intramolecular nucleophilic substitution at vicinal carbon atoms: the leaving group of one component is the nucleophile for the other, and vice versa.[27] However, all attempts to locate a transition structure for this direct isomerization have been unsuccessful, finding only **TS-CYC**, which interconnects **RC-CYC** with **PC-CYC**; it seems that **18** is a cul de sac in the mechanistic scheme.

With respect to the octalin intermediate **17**, the lowest Gibbs energy barriers for the forward reaction (56 kJ mol^{-1} to enol ether **6**) and the reverse reaction (55 kJ mol^{-1} to decalin **1**) involve similar Gibbs energy barriers. Although each of these calculated energy barriers may be subject to an uncertainty of perhaps several kJ mol^{-1}, nonetheless this computational observation implies that under experimental conditions the initial hydride abstraction from decalin may not be entirely rate-limiting. Cyclization of the octalin−acylium adduct is at least partially rate-limiting and offers a potential branching point in the mechanism in competition with formation of the 1-chloroethyl acetate byproduct. This computational result is in agreement with the kinetic data presented above.

■ CONCLUSIONS

We have presented a mechanism for the Baddeley reaction that is supported by both experimental and computational data. Key characteristics of this mechanism are (a) the rate difference for *cis*- and *trans*-decalin, (b) the hydride-abstracting ability of the acylium ion, (c) the intermediacy of unsaturated species **17**, and (d) the concerted nature of the cyclization/[1,2]-hydride shift. Mechanistic elucidation of this so-called aliphatic Friedel−Crafts reaction allows for rational selection of other saturated hydrocarbon substrates and prediction of the products that would be formed. Such transformations would serve to add significant value by providing rapid access to complex polycyclic oxygenated architectures, and we have already reported several such transformations.[12] Additional studies focusing on employing the Baddeley reaction in natural product target synthesis are ongoing and will be disclosed in due course.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Full computational details and further kinetic data, NMR spectra, and experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

I.H.Williams@bath.ac.uk.
S.E.Lewis@bath.ac.uk.

Notes

The authors declare no competing financial interest.

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(26) This may be an artifact of the harmonic oscillator approximation used for zero-point energies, thermal corrections, and vibrational entropies, or it may indicate a vibrationally bound complex. **TS-PT** is a true first-order saddle point on the PCM/MP2/6-31+G* potential energy surface, lying 7.3 kJ mol^{-1} above **RC-PT** derived from the C_2-symmetrical decalinyl cation but 0.9 kJ mol^{-1} below it on the Gibbs energy surface. An alternative structure for **TS-PT** (3.5 kJ mol^{-1} higher in energy) is derived from the C_s-symmetrical decalinyl cation: this is also a true first-order saddle point on the PCM/MP2/6-31+G* potential energy surface, lying 6.4 kJ mol^{-1} above the corresponding **RC-PT** structure but also 3.5 kJ mol^{-1} above it on the Gibbs energy surface. Combining the single-point MP2/cc-pVTZ//MP2/6-31+G* potential energies with the MP2/6-31+G* thermal corrections to the

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