

Is phenyl a good migrating group in the rearrangement of organoborates generated from sulfur ylides?†

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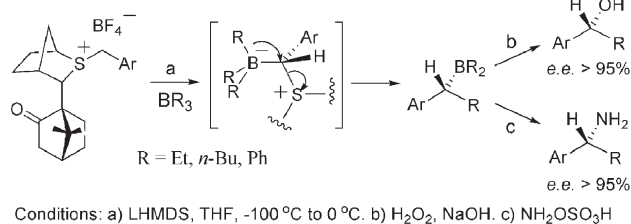
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Calculations show that the unexpected low phenyl migratory aptitude observed in reactions of mixed alkyl–aryl boranes with benzylic sulfur ylides can be attributed to (1) a conformational issue, (2) the reduction of the usual neighbouring effect of the phenyl in the transition state by the benzylic nature of the migrating terminus, (3) steric hindrance suffered by the larger phenyl group migrating to the hindered migrating terminus and this despite (4) the increase in the barrier to alkyl migration by the presence of a ‘non-migrating’ phenyl on the boron atom.

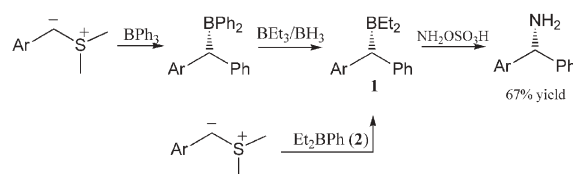
Organoboranes are versatile synthetic intermediates in organic chemistry.¹ Recently, we described the highly enantioselective synthesis of functionalized boranes through the reaction of chiral sulfur ylides with organoboranes (Scheme 1).² This process involves formation of a tetrasubstituted borane (ate complex), which after 1,2-migration of one of the groups bound to the boron atom with concomitant expulsion of the sulfide, yields homologated organoboranes with high enantioselectivity.



Scheme 1 Asymmetric synthesis of chiral borane.

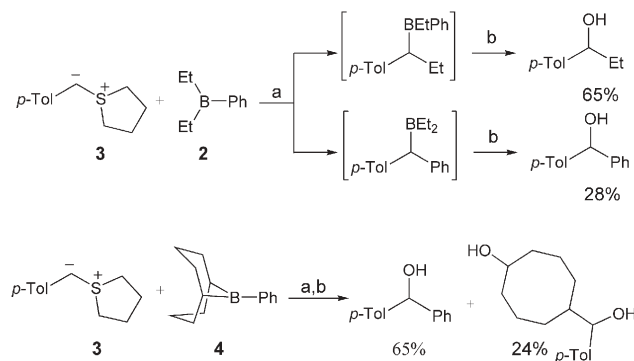
However, in the conversion of the homologated organoborane to the amine, we encountered low yields (17%) in the case of R = Ph. Since only two of the three groups attached to boron can be efficiently aminated,³ the low yield can be accounted for, given the higher propensity towards migration of phenyl groups over alkyl groups. Although we were able to overcome the problem by effecting a borane redistribution reaction (Scheme 2),⁴ we thought that we could access the mixed borane **1** directly and more efficiently through reaction with the mixed borane **2**.

In the event, reaction of ylide **3** with borane **2** gave predominantly the product resulting from *alkyl migration*



Scheme 2 Access to the amination product.

(Scheme 3): a 2.3 : 1 ratio in favour of ethyl migration over phenyl migration was observed. The result was mirrored with dihexylphenylborane as well (see Supporting Information†). Even using the 9-BBN derivative **4**, which has been effectively used as a non-migrating group in several cases,^{5,6} a substantial amount of alkyl (side-chain) migration was observed.



Scheme 3 Reactions of phenyl substituted boranes **2** and **4**.

We were very surprised at these results given that phenyl is well known to be an excellent migrating group in pinacol⁷ and Wagner–Meerwein⁸ rearrangements; in both systems the relative migratory aptitudes are H > aryl > alkyl. This large migratory aptitude of aryl groups is usually explained by participation of π -orbitals enabling the charge to delocalize from the carbonium ion center into the aromatic ring.^{7a-e,8a-b} Although the relative migratory aptitude of phenyl *versus* alkyl substituents has not been previously evaluated in rearrangements of organoborate complexes,⁹ we nevertheless expected the same migratory order since the current and above rearrangements are mechanistically related.

This unexpected and dramatic difference in relative migratory aptitude compared to those reported for the pinacol⁷ and Wagner–Meerwein⁸ rearrangements prompted us to examine, by computational means, the relative migratory aptitude of alkyl *versus* phenyl groups in organoborate rearrangements.¹⁰ We have studied the

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reaction of the dimethylphenylborane¹¹ with CH₂SMe₂ and PhCHSM₂ at the MP2/6-311+G**//B3LYP/6-31G* level of theory (Fig. 1).[‡]

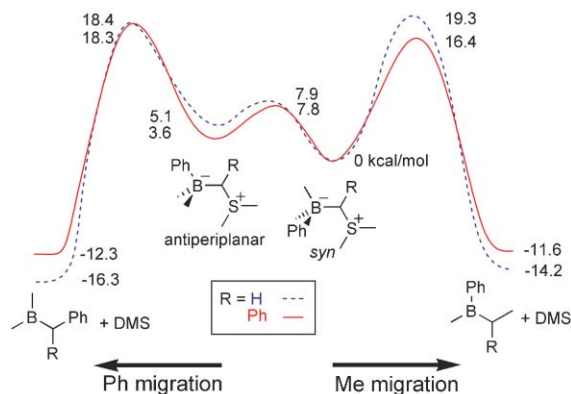


Fig. 1 Computational potential energy surface[‡] (relative energies in kcal mol⁻¹) for the reaction of BMe₂Ph with CH₂SMe₂ (dotted blue line; R = H) and PhCHSM₂ (plain red line; R = Ph).

The high exothermicity of ate complex formation (≈ 40 kcal mol⁻¹) suggests that this step will not be reversible.¹² A careful investigation of the potential energy surface around the ate complex revealed that the conformer presenting the phenyl *syn* to the sulfonium group is more stable than the corresponding antiperiplanar conformer by 3.6 and 5.1 kcal mol⁻¹, respectively for R = H and Ph. The barrier to rotation between the two conformers is low, indicating a rapid equilibrium. This conformational preference can be understood by the stabilising electrostatic interaction (CH $\cdots\pi$ hydrogen bonding) between the phenyl ring and the C–H bond of the positively charged sulfonium group allowed in the *syn* conformer (Fig. 2). Such aromatic \cdots CH(onium ion) interactions are well documented¹³ and have been observed in X-ray structures of sulfonium salts bearing aromatic rings.¹⁴ The lower discrimination between the two conformers when R = Ph can be rationalised by the fact that the sulfonium group in the latter case is already partially stabilised by the ylidic phenyl group.

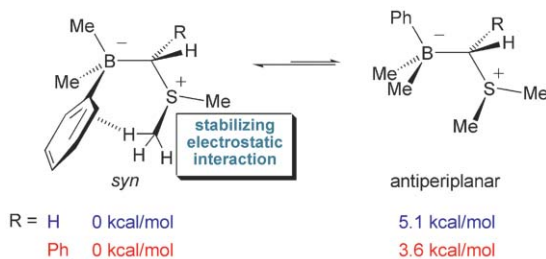


Fig. 2 Conformational equilibrium of the ate complex.

In the case of the benzylic ylide PhCHSM₂, the barrier for methyl migration was found to be lower than for phenyl migration, in agreement with experiment. In contrast and rather surprisingly, in the absence of phenyl substitution on the ylide (model ylide CH₂SMe₂), computations predict a small preference for phenyl migration.

There is a stereoelectronic requirement for the migrating group to orient itself antiperiplanar to the leaving group.¹⁵ The

experimental results (Scheme 3) can thus be readily understood without challenging the prevailing dogma regarding migratory aptitude. As can be seen in Fig. 1 (plain red line) phenyl is intrinsically a better migrating group than methyl (14.7 vs. 16.4 kcal mol⁻¹ with respect to starting conformation) but there is a significant price to pay in orienting the phenyl group antiperiplanar to the leaving group (loss of stabilising electrostatic interactions). However, other subtle factors are clearly operative since in the case of the CH₂SMe₂ ylide (Fig. 1, dotted blue line) orienting the phenyl group antiperiplanar to the sulfonium group is even more disfavoured and yet phenyl is calculated to migrate preferentially.

In order to identify the other important factors and excluding conformation, we have examined the energy difference between the transition state and the conformer presenting the migrating group antiperiplanar to the sulfonium group (Fig. 3). Comparison of eqn (1a)/eqn (2a) and eqn (1b)/eqn (2b) in Fig. 3 shows that phenyl is a better migrating group than methyl since in both cases the barrier to methyl migration is higher. However, comparison of eqn (2a)/eqn (3a) and eqn (2b)/eqn (3b) reveals that the presence of a phenyl group on boron impedes methyl group migration by about 4 kcal mol⁻¹. Such dependence of migratory aptitude on the nature of the other substituents linked to the boron atom has also been noted in related systems.¹⁰

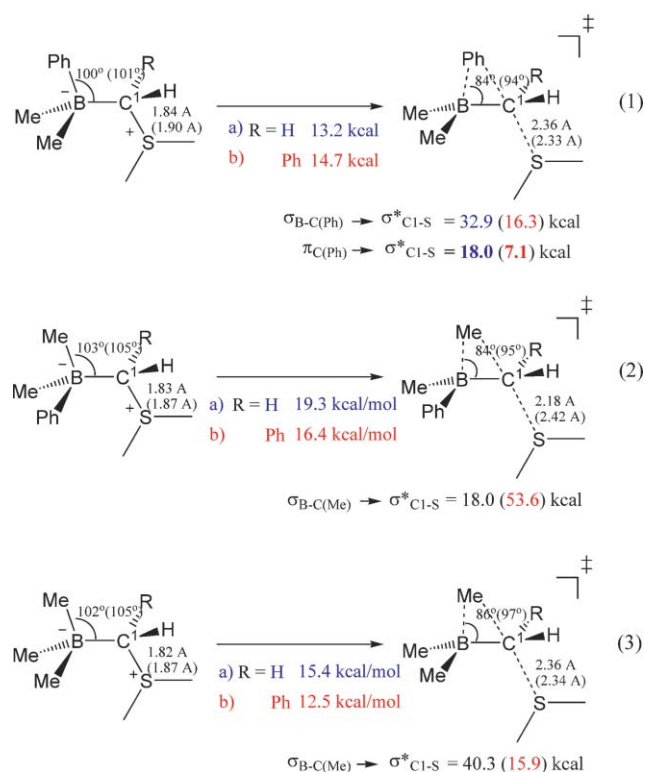


Fig. 3 Comparison of phenyl and methyl migratory aptitudes (energies in kcal mol⁻¹).[‡] Values in brackets are for R = Ph.

In order to compare intrinsic migratory aptitudes of phenyl *versus* methyl it is more instructive to compare eqn (1) with eqn (3) where any impediment to methyl group migration is removed. This comparison reveals that whilst phenyl is a better migrating group when R = H, it is actually a poorer one when R = Ph!

To understand this lower phenyl migratory aptitude when R = Ph, we analysed the electronic structure of the transition states for the phenyl migration using NBO second order perturbation theory analysis,¹⁶ at the B3LYP/6-31G* level of theory.† Using the bonding pattern of the reactant as a reference, the transition state is stabilised by two key orbital interactions: donation of an electron pair from the $\sigma_{\text{B-C(Ph)}}$ orbital and the $\pi_{\text{C(Ph)}}$ orbital, respectively, into the $\sigma^*_{\text{C1-S}}$ orbital. The stabilization arising from the second interaction is analogous to the neighbouring group effect found in phenonium ions,¹⁷ and varies with the electrophilic character of the C1 carbon. It is larger for the R = H transition state ($E(2) = 18.0 \text{ kcal mol}^{-1}$) than for the R = Ph transition state ($7.1 \text{ kcal mol}^{-1}$), where benzylic positive charge delocalization at C1 makes this position less electrophilic. For Wagner–Meerwein rearrangement of $\text{Me}_2\text{PhCCH}_2(\text{OH}_2)^+$, in which exclusive phenyl migration is known to occur,^{8b} $E(2)$ is even larger ($22.9 \text{ kcal mol}^{-1}$, details in Supplementary Material†). We can thus now understand why phenyl is a better migrating group than methyl when R = H but a poorer one when R = Ph. In the case of R = Ph, the developing positive charge on the migrating terminus is delocalized and so the benefit gained from the aromatic ring using its π system to aid migration is strongly attenuated. Furthermore, migration of the larger phenyl group (compared to methyl) towards the hindered migration terminus will result in increased steric interactions which may now be responsible for the increased barrier to phenyl migration.

In summary, we have shown that the following factors impact on which group migrates in mixed aryl–dialkylborates:

(1) Conformation of the ate complex. There is a preference for the phenyl group to be *syn* to the sulfonium group because of stabilising electrostatic interactions.²⁰ This favours alkyl group migration.

(2) The presence of a phenyl group on boron inherently impedes the migration of the other (alkyl) groups.

(3) The phenyl group is usually a better migrating group than methyl because it can stabilise the transition state by donation of an electron pair from its π system into the $\sigma^*_{\text{C1-S}}$ orbital (neighbouring effect). This effect however is highly attenuated when the migrating terminus (C1) is less electrophilic (*e.g.* when R = Ph).

(4) Steric effects also play a role. Larger groups will suffer increased barrier to migration when the migrating terminus is hindered.

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Notes and references

† The MP2/6-311+G**/B3LYP/6-31G* method has been selected to be the more adequate for the studied system after investigation of the model reaction of BMe_3 with CH_2SMe_2 at a variety of different levels of theory (see Supporting Information for details†). DFT calculations were carried out using the Jaguar 4.0 pseudospectral program package¹⁸ and MP2 single-point calculations using the Gaussian 03 program package.¹⁹

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