The trityl group as a removable steric buttress in cycloaddition reactions

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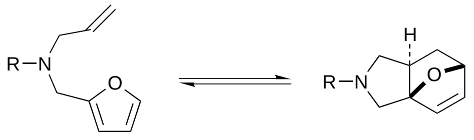
The trityl group is utilised as an effective, temporary, steric buttress in an intramolecular Diels–Alder reaction between an alkene and furan ring.

Steric buttresses have been utilised to accelerate intramolecular cycloaddition reactions but those used hitherto have not been readily removed.[1] Herein we report an example of steric buttressing as an aid to a cycloaddition reaction that is otherwise thermodynamically disfavoured; subsequent to the cycloaddition reaction the steric buttress may be removed.

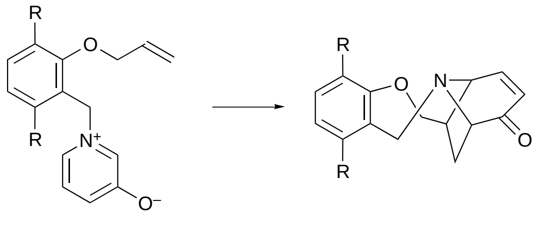
The example involves the attempted cycloaddition of *N*-allylfurfurylamine **1** to the cycloadduct **2**. Heating compound **1** at various temperatures does not show any sign of the cycloadduct product **2**.† This lack of cycloaddition is consistent with several reported attempts at a range of similar intramolecular cycloaddition reactions between isolated alkene bonds and the furan ring.[2] For example, Gshwend *et al.* attempted to prepare the related cycloadduct **3** from the corresponding amide **4** but found that this spontaneously ring opened to form the allyated furfurylamine **5**.[3]

In previous work we have shown that cycloadditions may be encouraged by use of appropriate steric buttressing; an example is with compound **6**, which undergoes cycloaddition to the adduct **8**, whereas the parent compound **7**, in which the methyl buttresses are absent, does not undergo cycloaddition.[4]



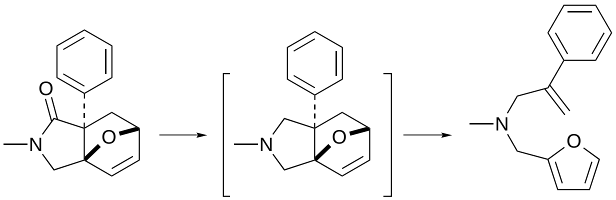
1 R = H
9 R = Ph$_3$C
10 R = Ph$_2$CH
11 R = Bn
12 R = 2,4,6-Me$_3$C$_6$H$_2$CH$_2$

2 R = H
13 R = Ph$_3$C
14 R = Ph$_2$CH
15 R = Bn
16 R = 2,4,6-Me$_3$C$_6$H$_2$CH$_2$



6 R = Me
7 R = H

8 R = Me



4 **3** **5**

We argued that, by restricting the degrees of conformational freedom in the reacting arms of compound **1**, cycloaddition would also be more favourable. The protected amine derivatives **9**–**12** were therefore prepared, using variably sized protecting groups, and their behaviour to cycloaddition examined. Solutions of the protected amines were heated at various temperatures (100–135 °C), monitoring for the appearance of the expected cycloadducts **13**–**16** and thermodynamic equilibration by use of ^{1}H NMR spectroscopy.

Of the derivatives, the *N*-trityl derivative **9** showed the greatest degree of cycloaddition (97.5%) (Table 1). The cycloadduct **13** showed a consistent ^{1}H NMR spectrum—loss of the allyl group and furan protons and replacement by the higher field protons of the tricyclic product. Use of the smaller benzhydryl protecting group, as in **10**, gave an approximately 50 : 50 ratio of cyclised product **14** to the uncyclised material at equilibrium and use of the benzyl derivatives **11** and **12** gave even less of the required cycloadducts.

The trityl group could be easily removed from the cycloadduct, by brief treatment with warm ethanolic hydrochloric acid,[5] to produce the secondary amine **2**. The latter amine was stable for considerable periods at room temperature but, on heating, reverted to the open form **1**. The stereochemistry about the bridgehead proton suggested the depicted stereoisomer was formed (Fig. 1).

Table 1 Thermal equilibration of amines **1**, **9**–**12**

Starting amine	Product[a]	Yield of product (%) isolated	Cyclisation conditions	Open : cyclic[b]
1	**2**	0	110 °C, toluene, several days	100 : 1
9	**13**	85	110 °C, toluene, 40 h	2.5 : 97.5
10	**14**	35	135 °C, xylene, 34 h	50 : 50
11	**15**	—[c]	135 °C, xylene, 60 h	98 : 2
12	**16**	—[c]	135 °C, xylene, 60 h	90 : 10

[a] Isolated by column chromatography. [b] Estimated by 360 MHz ^{1}H NMR spectroscopy after thermal equilibration. [c] Isolation not attempted.

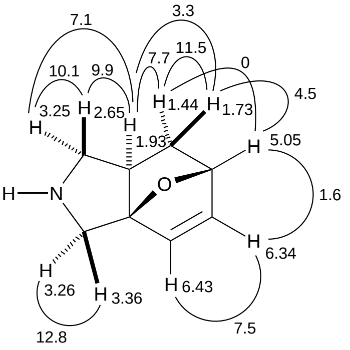


Fig. 1 Chemical shifts and coupling constants for the amine **2**

As a cross-check, the cyclic amine **2** was also converted into the protected forms **14** and **15**; on heating these the thermal equilibrium between the open and closed forms was re-established.

Molecular models show that the trityl group and its derivatives are particularly bulky, thus restricting the conformational freedom of the diene and dienophile groups into ones where they are forced into close proximity. We are currently studying the use of the trityl group as a steric buttress in other modes of cycloaddition.

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Footnote

† All new compounds have been characterised by microanalysis and/or accurate mass measurement.

References

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