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Intermolecular Heck-Diels-Alder Cascade Processes of Alkylallenes

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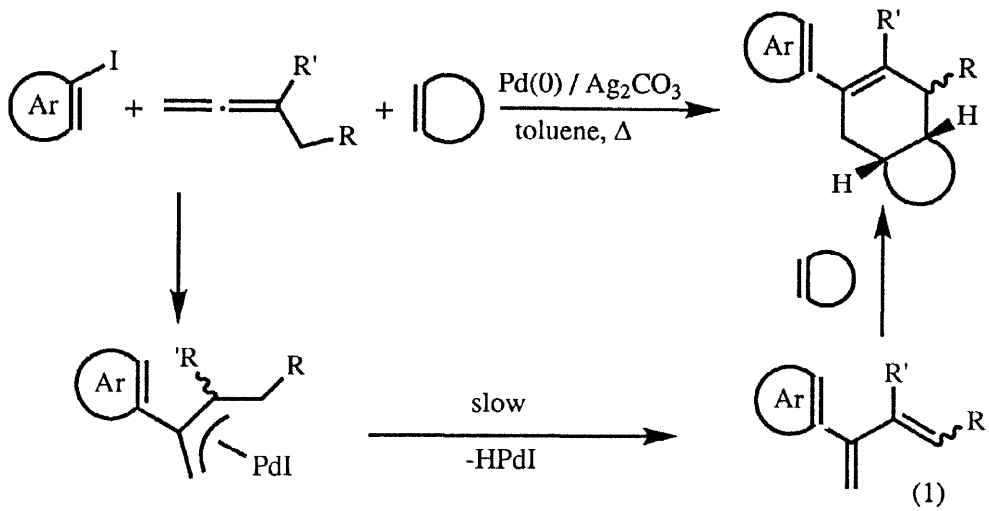
Abstract: Intermolecular Heck reaction of a wide variety of aryl/heteroaryl iodides with alkylallenes furnishes 1,3-dienes which undergo *in situ* Diels-Alder cycloaddition to N-methylmaleimide. This cascade can be further extended by interfacing with a prior Pd catalysed cyclisation.

The versatility of allenes as substrates in palladium catalysed processes is amply demonstrated by the recent surge of publications covering both intermolecular and cyclisation/cycloaddition processes.[1,2] We have previously demonstrated the extension of palladium catalysed cyclisations onto proximate allenes to extended cascades involving subsequent Diels-Alder or 1,3-dipolar cycloaddition reactions.[3,4] As part of our continuing interest in cascade methodology we now report intermolecular Heck-Diels-Alder cascade processes involving alkylallenes. The general process is summarised in Scheme 1.



Scheme 1.

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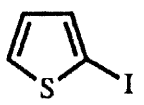
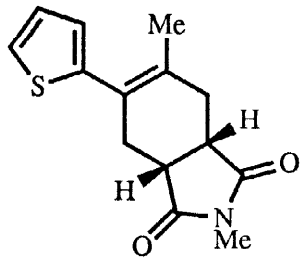
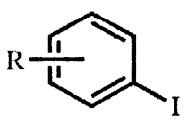
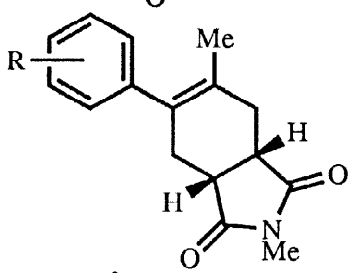
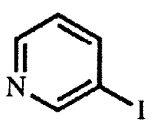
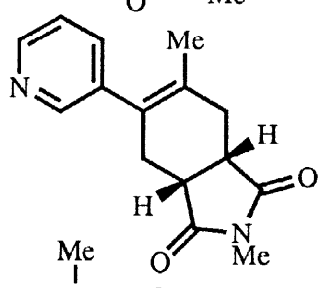
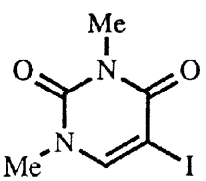
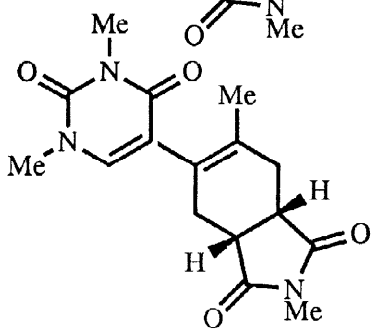
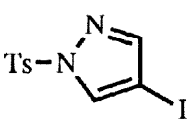
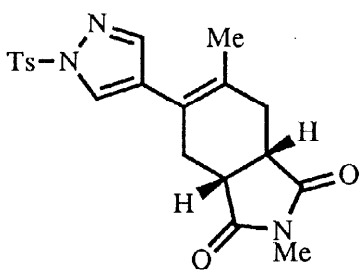
Table 1. Products of Intermolecular Heck-Diels-Alder Cascades of 1,1-Dimethylallene.[a]

Aryl Iodide	Product	Yield(%)[b]
		84
		R H 76 *p*-Me 71 *p*-SMe 56 *m*-OMe 71 *o*-OMe 40
		78
		65
		50

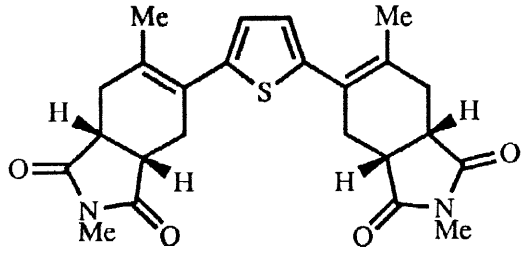
a. All reactions carried out in toluene [120°C(bath temp.) 48h] in a Schlenk tube, with 1,1-dimethylallene (5mmol), aryl / heteroaryl iodide (1mmol) and N-methyl-maleimide (1.1mmol). The catalyst system comprised $Pd(OAc)_2$ (0.1mmol), PPh_3 (0.2mmol) and Ag_2CO_3 (2mmol).

b. Isolated yields.

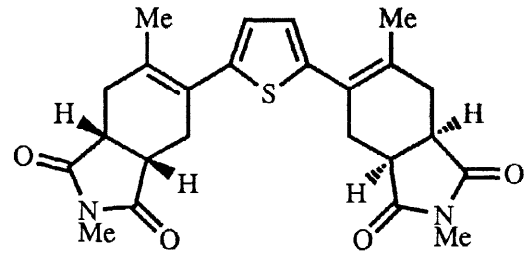
A wide range of aryl and heteroaryl iodides undergo oxidative addition of Pd(0) followed by addition of the resulting RPdI species to the centre carbon atom of the allene moiety generating a π-allylpalladium (II) species. In the absence of a suitable nucleophile the latter species undergoes a slow β-hydride elimination generating a substituted 1,3-diene (1) (Scheme 1). If this intermolecular Heck reaction is carried out in the presence of a suitable dienophile the 1,3-diene is trapped in a subsequent Diels-Alder reaction.

For our initial survey we selected 1,1-dimethyl allene as the allene component. Reaction of aryl or heteroaryl iodides, 1,1-dimethylallene and *N*-methylmaleimide with a catalyst system comprising 10 mol% $Pd(OAc)_2$, 20 mol% PPh_3 and Ag_2CO_3 (2 mol eq) in toluene [120°C (bath temperature), 48h] afforded the expected products (Table 1) derived from the Diels-Alder reaction of 1,3 diene (1, R=H, R^1=Me) in moderate to good yield. These cascades involve formation of three new bonds and one ring.

When an analogous cascade was carried out on 2,5-diiodothiophene employing double the amount of all the other reagents except $Pd(OAc)_2$ and PPh_3, which remained at 10 and 20 mol% respectively, the expected product (2) was obtained in 50% yield via formation of 6 new bonds and two rings. Two diastereoisomers (2a) and (2b) are possible, one of which, (2a), has a plane of symmetry and the other, (2b), a C_2-axis of symmetry. The ^{1}H and ^{13}C n.m.r. spectra ($CDCl_3$) of isolated (2) indicate a single diastereomer.

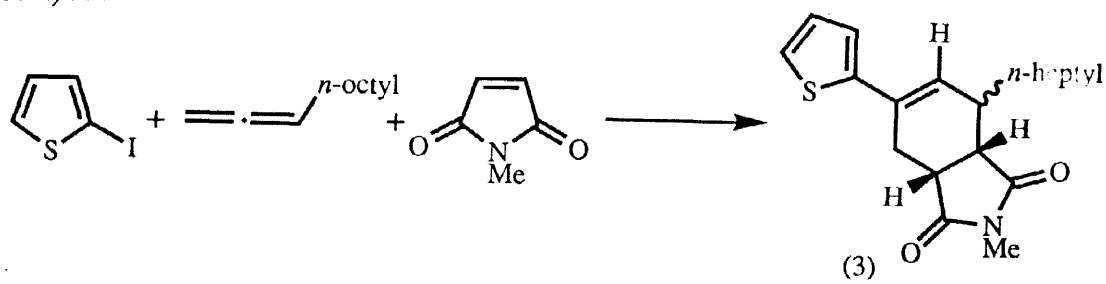


(2a)



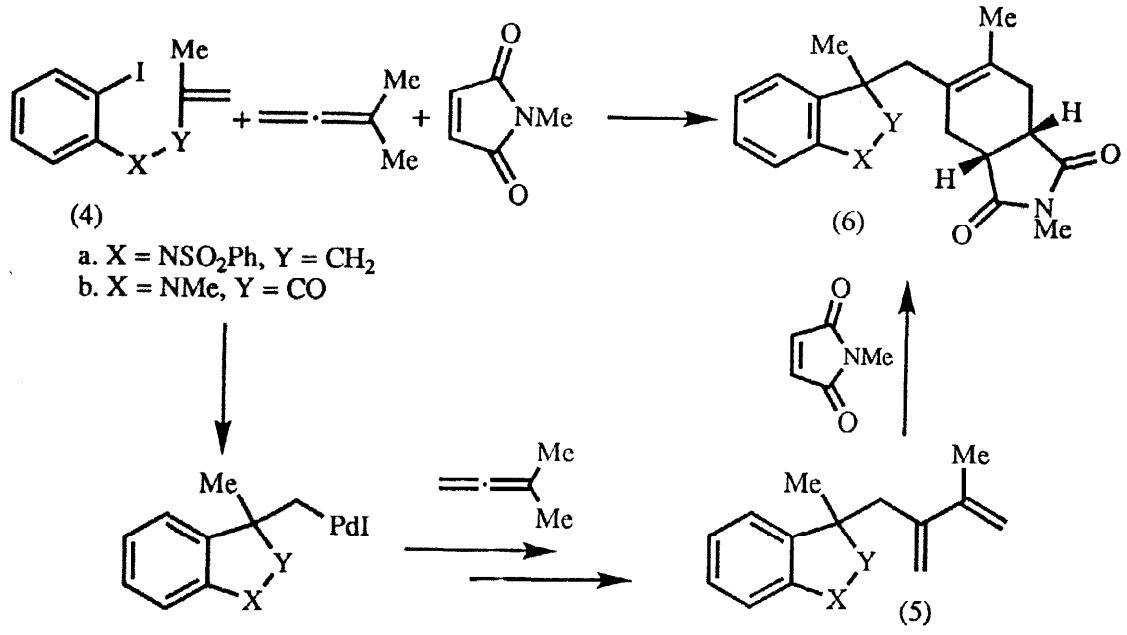
(2b)

Varying the allene substitution allows a wide variety of dienes to be generated *in situ*. Thus the reaction of *n*-octylallene, 2-iodothiophene and *N*-methylmaleimide under the conditions noted previously gave (3) (80%) as a 4:1 mixture of diastereoisomers.



(3)

The intermolecular Heck-Diels-Alder cascade can be further extended by interfacing it with our cyclisation-anion capture methodology.[1,4] Thus (4a,b) react (Scheme 2) with 1,1-dimethylallene and *N*-methylmaleimide under the same conditions and with the same catalyst system described above to give (6a,b) (69 and 72%) *via* dienes (5a,b). These cascades generate four new C-C bonds and two new rings.



Scheme 2.

Inspection of the ^{1}H n.m.r. spectrum (6a) ($CDCl_3$) shows it to comprise a 1.7:1 mixture of diastereomers whilst the ^{1}H n.m.r. spectrum of (6b) indicates a 1.5:1 mixture of diastereomers.

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