Radical allylations by reaction of azides with allylindium dichloride†‡

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Allylindium dichloride is an effective reagent for carrying out photolytically initiated radical allylation reactions, as also proved by EPR experiments. In the presence of suitable azides that can give rise to electrophilic radicals, a homolytic chain reaction occurs with formation of allylated compounds. With δ-azido esters and chlorides generation of primary indiumaminyl radicals is followed by a very efficient 1,5-H shift process that gives rise to electrophilic carbon-centred radicals, whose subsequent allylation by the starting indium reagent, followed by aqueous workup, eventually affords allylated nitrogen heterocycles in good yields. Some comparative theoretical calculations accounted for the observation that analogous reactions with an organoallyltin reagent did not work at all. The results show that the reaction with allylindium dichloride seems strongly favoured by both a lower BDE of the allyl-metal bond and a considerably faster, exothermic 1,5-H migration step.

Introduction

Radical reactions are now recognised as very powerful tools for synthetic organic chemists[1] and, rather than further establishing their synthetic value, many of the current efforts to exploit radical reactions are devoted to discovering novel, efficient procedures that avoid using toxic metal reagents or, especially, the organotin compounds that still play a dominant role in radical chemistry.[2]

In recent years, indium metal, indium halides, and organoindium reagents have been employed as benign, *green* alternatives to other metal-based catalysts.[3] In the field of radical reactions, indium hydrides and allylindium derivatives have been successfully used as valid alternatives to organostannanes in many radical processes.[4] Allylindium compounds, in particular, although rarely employed, have given excellent results in allylations of electrophilic radicals,[4o] as suitable allylstannane substitutes, and in cyclisations of the corresponding allyl radicals.[4p,r] The reactions can be triggered by either standard radical initiators, *e.g.* BEt_3/O_2,[4o] or photolysis.[4p,r,5]

Following our interest in the synthetic utility of azides and their radical reactions,[6] we have recently shown that organic azides are easily converted by dichloroindium hydride to the corresponding amines under very mild conditions and in a highly chemoselective fashion.[7] Furthermore, in the presence of side chains bearing cyano groups, they give rise to outstanding 5-membered cyclisations affording pyrrolidin-2-imines. Both processes probably entail the intermediacy of indium-aminyl radicals arising from addition of indium radicals to the azide moiety. Indium radicals would then behave in a similar way to the tin congeners similarly affording stannylaminyl radicals,[8] which are key intermediates in numerous worthwhile azide processes including, *inter alia*, reductions as well as cyclisations onto suitable radicophilic groups.[6a,c,8d–g,m]

These encouraging results prompted us to study different conditions for carrying out radical decompositions of azides, mainly by avoiding the use of rather unstable indium hydrides and, at the same time, by accessing final reaction products that could be even more synthetically interesting. From this point of view, allylindium reagents were in principle very good candidates, since, compared to the corresponding hydrides, they are more readily accessible and also much less sensitive to both water and oxygen. Furthermore, like allylstannanes, they allow introduction of the allyl moiety into the final products. Here we report the preliminary results obtained by reacting some organic azides with allylindium dichloride under photolytic initiation.

Results and discussion

Synthesis and mechanistic discussion

Allylindium dichloride was prepared by treatment of indium trichloride with allylmagnesium chloride in THF, as previously described.[4o] After replacement of THF with benzene and addition of a suitable substrate, photolysis was performed at r.t. with a 150 W medium pressure Hg vapour lamp with a pyrex filter. At the outset of the present work there was just one example of allyl radical generation by photolysis of organoindium compounds, in particular allylindium sesquihalides produced from allylic (cinnamyl) derivatives and indium metal.[4p] Therefore, before reacting the azides, we decided to try our photolytic conditions on the radical allylation reaction reported by Oshima under triethylborane initiation.[4o] We actually found that photolysis at r.t. of allylindium dichloride in the presence of ethyl α-bromoacetate brought to ethyl α-allylacetate in virtually quantitative yield, hence proving that our initiation method can be a very good substitute for chemical initiators.

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† Electronic supplementary information (ESI) available: Calculation details, calculated values for the BDEs of tetraalkylstannanes, plot of calculated BDEs *vs.* experimental values, calculated BDEs of allyltrimethylstannane and allylindium dichloride, reaction pathway and calculated energies for the species involved in 1,5-H transfer of indium- or tin-substituted aminyl radicals, cartesian coordinates of all compounds, intermediates, and transition states. See DOI: 10.1039/c001848a

‡ This paper is heartily dedicated to Prof. Rino Leardini on the occasion of his retirement.

Since no direct evidence for homolytic cleavage of the carbon-indium bonds had been obtained to date, with the exception of alkylindium(III) tetraphenylporphyrin,[9] we also tried to demonstrate the possible generation of allyl and indyl radicals upon photolysis of allylindium dichloride by means of EPR spectroscopic experiments. When a degassed solution of allylindium dichloride in *tert*-butylbenzene was photolysed at −13 °C with a 500 W super pressure Hg arc lamp inside the EPR resonant cavity, the unambiguous spectrum of the allyl radical was recorded.[10] Fig. 1 shows the spectrum obtained after 30 scans (upper panel) and the corresponding simulation (lower panel): the latter was obtained with hyperfine splitting constants [$a(1\text{H}) = 4.0$ G, $a(2\text{H}) = 13.9$ G, $a(2\text{H}) = 14.8$ G] and g-factor (2.00254) *i.e.* virtually identical to those reported in the literature.[11]

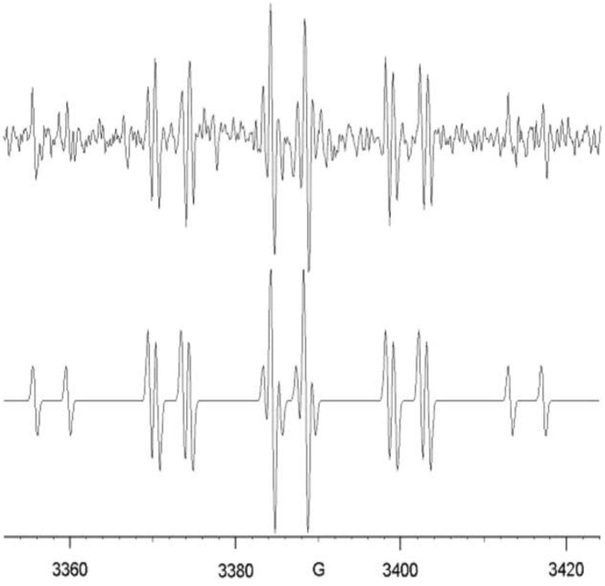


Fig. 1 Upper panel: EPR spectrum of the allyl radical (MW frequency: 9.5 GHz; 260 K; power: 2.0 mW; modulation amplitude 0.6 G_{pp}, 1st derivative; 30 scans). Lower panel: simulation obtained with $a(1\text{H}) = 4.0$ G, $a(2\text{H}) = 13.9$ G, and $a(2\text{H}) = 14.8$ G.

This experiment provided the first evidence of generation of allyl radicals, and thence, indirectly, of dichloroindium radicals, from photolysis of an allylindium compound.

It is worth noting that the quite weak signal observed (30 scans were needed in order to record a reasonable quality spectrum) could be due to a somewhat inefficient photolysis process or, more likely, to reversible scission of the In–CH_2 bond that, without any trapping of dichloroindyl radicals, could keep the concentration of free allyl radicals low, due to the recombination process. However, this photochemical outcome should not spoil the possible efficiency of synthetic applications, since any trap of the indium-centred radicals would shift the reagent dissociation equilibrium and, moreover, photolysis would be just needed for bringing about initiation of the chain reaction.

Photolysis of allylindium dichloride in the presence of various azides (*i.e.* azides **1–4**, Fig. 2) showed evident evolution of small gas bubbles inside the reaction mixtures and concomitant, although not complete, disappearance of the starting azide. This strongly suggested that the experimental conditions triggered decomposition of those azides to the corresponding indium-aminyl radicals.

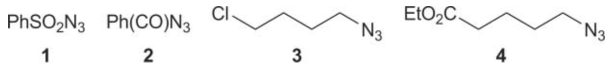
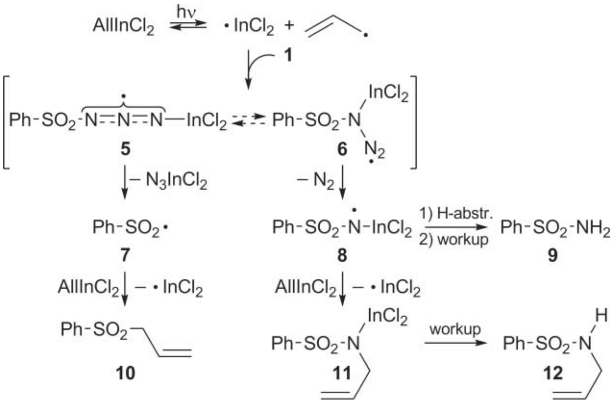


Fig. 2 Azides reacted with allylindium dichloride under photolysis.

However, all attempts to detect ensuing aminyl radicals were unsuccessful, the allyl radical being the only identifiable species. Presumably, decomposition of indium-aminyl radicals was fast enough to lower their concentration below the limit for detection. Indeed, as it will be shown below, sulfonyl/acyl azides **1**,**2** can form electrophilic aminyl (and sulfonyl) radicals capable of initiating an effective chain reaction with the allylindium reagent, whereas alkyl azides **3**,**4** could form nucleophilic aminyl radicals highly able to rearrange to electrophilic carbon radicals, which were again prone to promote a fair chain reaction with allylindium dichloride.

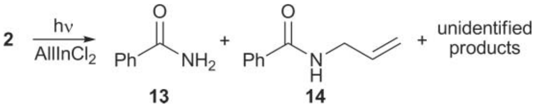
When azide **1** was reacted for 3 h with allylindium dichloride in benzene solution at r.t. with photolytic initiation[12] it gave, besides small amounts of unreacted starting material (*ca.* 10%), benzenesulfonamide **9**, allylsulfonylbenzene **10**, and *N*-allyl benzenesulfonamide **12**. ^{1}H-NMR spectroscopic analysis revealed that **9** and **10** were the major products in a *ca.* 1 : 1 ratio, whereas the *N*-allyl derivative **12** was a minor product (**12**/**10** ≈ 1/2). These results are clearly consistent with the radical mechanism shown in Scheme 1, which is analogous to that previously invoked for similar reactions of arenesulfonyl azides with allylstannanes under thermal conditions.[13]



Scheme 1 Reaction mechanism of sulfonyl azide **1** with allylindium dichloride.

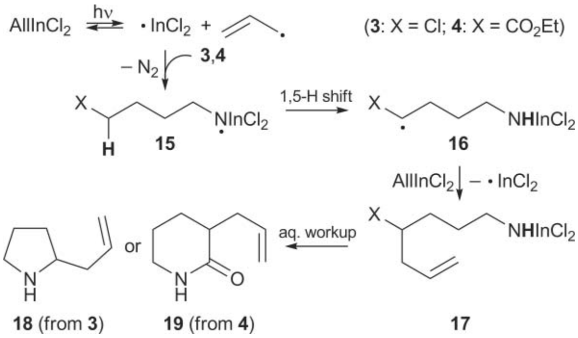
Indeed, after initial generation of 1,3-(**5**) and/or 3,3-substituted-(**6**) triazenyl radicals, allylsulfonylbenzene **10** can be easily accounted for through a radical deazidation pathway followed by allylation of the resulting sulfonyl radical **7** by the starting allylindium dichloride (AllInCl_2). Competing formation of indium-sulfonamidyl radical **8** by nitrogen extrusion, followed by reaction with the starting allylindium reagent and final hydrolysis, explains the formation of allylsulfonamide **12**. The additional formation of **9**, entailing hydrogen abstraction by radical **8** followed by hydrolysis, was not unexpected, since it was also observed to a certain extent in related radical reactions of azide **1** with allylstannanes.[13] However, preferential production of compound **9** at the expense of **12** was rather surprising. For unclear reasons radical **8** would prefer to undergo allylic hydrogen atom abstraction from the starting allylindium reagent rather than alternative allylation.[13,14] Also, product **10** occurred to a greater extent than in the allylstannane-mediated reactions: this suggests that indyl radicals are more prone to perform attack at the terminal azide nitrogen, resulting in deazidation, than the stannyl congeners.[15]

By way of contrast, deazidation was not observed at all for azide **2**, which furnished again the reduced benzamide **13** as the major reaction product together with minor amounts of *N*-allyl benzamide **14** (**13**/**14** ratio *ca.* 3 : 1) (Scheme 2). Unfortunately, this reaction was not very significant, since it also yielded considerable amounts of unidentified by-products. In such case the resultant electrophilic benzamidyl radical would be even less selective than sulfonamidyl **8** in bringing about the radical chain.



Scheme 2 Reaction products of acyl azide **2** with allylindium dichloride.

More interesting results were obtained with azides **3** and **4**.[16] These azides were chosen on the assumption that, in general, indiumaminyl radicals would give very fast hydrogen abstraction reactions. Even faster reactions are expected to occur whenever intramolecular H-shifts are feasible, especially if polar effects can operate in the transition state,[17] as when nucleophilic aminyls abstract a hydrogen atom vicinal to an electron-withdrawing group. The resulting electrophilic carbon radicals should in turn add quickly to allylindium dichloride, hence bringing about the radical chain. Our overall results obtained with azides **3** and **4** are depicted in Scheme 3.



Scheme 3 Reaction mechanism of alkyl azides **3** and **4** with allylindium dichloride.

Addition of dichloroindium radicals to the azides gives rise to (nucleophilic) indium-aminyl radicals **15** able to undergo 1,5-H shifts affording (electrophilic) α-halo- (from **3**) and α-carbonyl- (from **4**) substituted alkyl radicals **16**. Allylation of the latter by the starting allylindium dichloride yields allylated *N*-indylamines **17**, which, upon aqueous basic workup, are finally converted into mixtures of the respective amines and their (ionic) cyclisation products **18** (from **3**) and **19** (from **4**). When the aqueous workup mixtures were stirred overnight at r.t., 2-allylpyrrolidine **18** and 3-allylpiperidin-2-one **19** were obtained as the exclusive reaction products in 60% and 65% yield, respectively. Side products derived from other possible reactions of radicals **15**, such as *N*-allylation and/or intermolecular H-abstraction, were not observed at all.

This radical protocol therefore provides a novel, appealing one-pot synthesis of allylated nitrogen heterocycles such as **18** and **19** using easily available azido precursors.[18]

Theoretical calculations

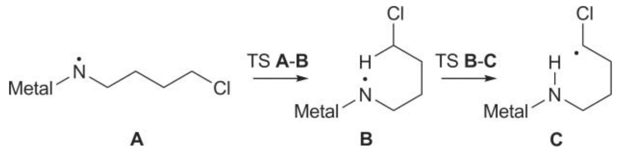
It is worth noting that the reactions of azides **3** and **4** described in the above section could not be carried out by replacing allylindium dichloride with allyltributylstannane: prolonged photolysis of the reaction mixtures in the presence of the latter reagent gave mostly unreacted starting material. These findings were quite unexpected, since allylstannanes are well-known photolytical initiators of radical allylation chain reactions.[19,20] We then became interested in ascertaining the reasons why the allylindium and allyltin compounds could behave so differently with azides **3** and **4**.

A preliminary approach could be to turn our attention to the All-In and All-Sn BDEs (bond dissociation energies). Unfortunately, no experimental data are available for either metallorganic compounds, and hence we evaluated the respective energies by performing some theoretical calculations. These were carried out with the Gaussian03 package;[21] Density Functional Theory (DFT) was employed at the B3LYP level[22] using the LanL2DZ basis set with Effective Core Potentials (ECP) on all atoms[23] (see ESI†). These options have already been exploited for calculations involving group XIII and XIV organometallic compounds (including organoindium derivatives) and seemed therefore both the best level and basis set for our study.[24] Nonetheless, before attempting calculations of the BDEs of allylindium dichloride and allyltrimethyltin (the simplest model for allyltributyltin), we initially derived the BDEs of a series of simple tetraalkylstannanes for which experimental BDE values are available.[25] Actually, DFT calculations allowed a quite careful estimation of the tin-alkyl BDEs of methyl-, ethyl-, *iso*-propyl-, and *tert*-butyl-trimethylstannane, with deviations from the experimental values ranging from 1.8% (*iso*-propyl) to 6.7% maximum (methyl). It is worth pointing out that the same calculations carried out by an analogous HF method, while well reproducing the relative bond weakening by passing from methyl to *tert*-butyl, totally failed to estimate the absolute values, with deviations ranging from 25.3% (methyl) to so much as 31.3% (*tert*-butyl) (see ESI for details†).

Persuaded we had a dependable tool in our hands, we turned back to the allyl derivatives and calculated the BDEs of the All-In and All-Sn bonds in allylindium dichloride and allyltrimethyltin as 42.3 and 49.8 kcal mol^{-1}, respectively, with a quite noteworthy difference of 7.5 kcal mol^{-1} in favor of the indium compound. Once again, HF calculations properly predicted the trend (ΔBDE = 7.7 kcal mol^{-1}) but were completely unreliable as to the absolute values, estimating energies (19.0 and 26.7 kcal mol^{-1} for All-In and All-Sn bonds, respectively) that are evidently far away from reality.

Theoretical data clearly suggest that the indium-allyl bond in allylindium dichloride is significantly weaker than the tin-allyl bond of an allyltrialkylstannane, and hence the radical allylation performed with the former reagent seems to be appreciably favoured, at least as far as the initiation step is concerned. These results, though, do not seem sufficient to explain thoroughly the dramatically different behaviours of tin and indium allyls. Indeed, if an efficient radical chain reaction were to start by scission of the metal-allyl bond, in principle even very few radicals would be capable of bringing about the whole process, and at least some products would be observed. Consequently, either all of the (few) tin radicals arising from the allylstannane are scavenged by pathways competitive with addition to the azide moiety (but it seems unlikely),[20,26] or a different step is responsible for the profoundly altered reaction outcome.

Therefore, we were prompted to turn our attention to the 1,5-H migration transforming metal-aminyls **15** into carbon-centred radicals **16**, which are the crucial intermediates for the effectiveness of the chain reaction.[12] Theoretical calculations were carried out on radical intermediates **A**, **B**, and **C** (Metal = Me_3Sn or Cl_2In) and the transition states connecting them (Scheme 4, see ESI for details†).[27] On the basis of the previous results, calculations were performed with the DFT method at the spin-unrestricted UB3LYP level (LanL2DZ ECP basis set), but a HF method was again employed as well to test as before the consistency of *relative* data. Fig. 3 shows the reaction profiles obtained by DFT with the two different metal moieties.



Scheme 4 Intermediates and transition states (TS) involved in calculations on 1,5-H migration of tin- and indium-aminyl radicals (Metal = Me_3Sn, Cl_2In).

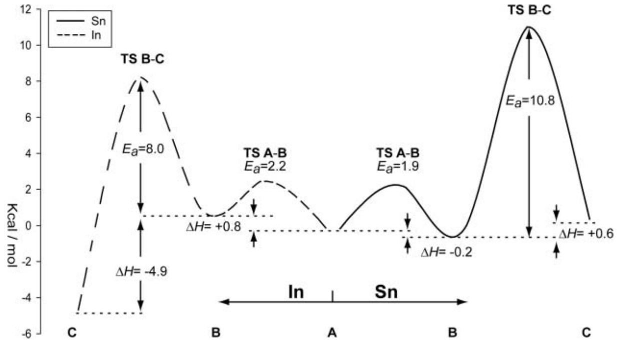


Fig. 3 Reaction profiles for 1,5-H shift of tin- and indium-aminyls (UB3LYP, LanL2DZ ECP).

When metal = Me_3Sn, conversion of **A** into **B** is a nearly isoenthalpic process, with an activation barrier of about 2 kcal mol^{-1} ($\Delta H = -0.2$ kcal mol^{-1}, $E_a = 1.9$ kcal mol^{-1} [DFT], $\Delta H = 0.2$ kcal mol^{-1}, $E_a = 2.5$ kcal mol^{-1} [HF]). When metal = Cl_2In the conformational transformation becomes slightly endothermic by about 1 kcal mol^{-1}, with an activation energy comparable to that estimated for tin ($\Delta H = 0.8$ kcal mol^{-1}, $E_a = 2.2$ kcal mol^{-1} [DFT], $\Delta H = 1.5$ kcal mol^{-1}, $E_a = 2.7$ kcal mol^{-1} [HF]). Hence, calculations suggest that this process does not seem to justify any difference between tin and indium in this crucial step.

More significant divergencies were observed instead for the subsequent step, *i.e.* the key hydrogen shift. Indeed, with tin the rearrangement is somewhat *endo*thermic ($\Delta H = 0.6$ kcal mol^{-1} [DFT] or = 2.6 kcal mol^{-1} [HF]), whereas with indium it becomes notably *exo*thermic ($\Delta H = -4.9$ kcal mol^{-1} [DFT] or = −2.6 kcal mol^{-1} [HF]). An even more significant difference was also found in the corresponding activation barriers, which differ by about 3 kcal mol^{-1} (tin: $E_a = 10.8$ kcal mol^{-1} [DFT] or 29.6 kcal mol^{-1} [HF]; indium: $E_a = 8.0$ kcal mol^{-1} [DFT] or 26.0 kcal mol^{-1} [HF]).[28]

Such a significant difference in activation energies suggests that, under our conditions, 1,5-H shift of aminyls, besides being enthalpically favoured, is much faster in indium-substituted radicals with respect to the tin-congeners. Even taking into account a possible reversibility of this step, the equilibrium converting stannylaminyls into the corresponding carbon-centred radicals would be expected to be strongly shifted towards the former species, thus preventing a useful concentration of the latter to be formed. On the contrary, with indiumaminyls the rearrangement equilibrium would unquestionably be shifted towards the carbon-centred radicals, hence strongly favouring the formation of the species that are crucial for the effectiveness of the whole radical chain reaction.

The reason why so remarkable a difference between tin- and indium-substituted aminyls is observed (and theoretically predicted) remains so far rather obscure. Since intramolecular radical hydrogen migrations are supposed to occur through transition states entailing significant charge separation developing on both the involved atoms, we thought that tin or indium moieties could bring significant differences on the nucleophilicity of the corresponding aminyl, and hence on the extent of charge separation in the 1,5-H shift transition state. Unfortunately, calculations predicted for TS **B**-**C** charge density maps strictly independent of the presence of tin or indium moieties,[29] hence making this hypothesis unlikely for explaining experimental and theoretical evidences. Currently, the only noticeable distinction between tin- and indium-aminyls can be found in hybridation of the corresponding nitrogen atom, which, while being nearly planar in TS **B**-**C** (Metal = Cl_2In), appears slightly pyramidal in TS **B**-**C** (metal = Me_3Sn): this could appreciably affect orbital overlapping in the transition state and hence the reaction rate. This is, though, just a preliminary account and further studies are definitely needed to develop a more consistent explanation.

Conclusions

Allylindium dichloride was shown to be an effective reagent for photolytically initiated radical allylation of azido compounds. Photolysis in the presence of azido chloride **3** and azido ester **4** led to eventual occurrence of allylated pyrrolidine/pyperidinone products **18** and **19**, respectively, primarily due to a tandem radical process entailing 1,5-H transfer reaction of initial (nucleophilic) indium-aminyl radicals, followed by allylation of the (electrophilic) translocated carbon radicals by the allylindium reagent. These findings provide the first example of valuable synthetic use of an allylindium compound triggered by photochemical homolytic fragmentation of the carbon-indium bond.

Some comparative theoretical calculations allowed us to account for the observation that analogous azide reactions are totally prevented when using an organoallyltin reagent in place of allylindium dichloride. The results show that the reaction with allylindium dichloride seems strongly favoured with respect to the one carried out with an allylstannane by both a lower BDE of the allyl-metal bond and a considerably faster, exothermic 1,5-H migration step. When the latter process is hindered, as calculations suggest is the case of the allylstannane, the formation of the crucial carbon-centred radical is seriously hampered and the radical chain cannot be sustained.

Studies are underway to fully exploit the synthetic potential of our radical allylation reactions of azides with allylindium dichloride.

Experimental

General procedures

^{1}H and ^{13}C NMR spectra were recorded in deuteriochloroform on a Varian Mercury Plus 400 instrument (^{1}H: 400 MHz, ^{13}C: 100 MHz) using the residual solvent signal (^{1}H NMR spectra, δ 7.26 ppm; ^{13}C NMR spectra, δ 77.0) as the internal standard. In reporting spectral data, the following abbreviations were used: m = multiplet, br s = broad singlet. IR spectra were recorded in $CHCl_3$ on a FT-IR Perkin Elmer Spectrum RXI instrument. Mass spectra were recorded either by the electron spray ionization (ESI) method or under electron impact (EI, 70 eV) conditions with Waters–Micromass ZQ4000 and Thermo–Finnigan MAT95 XP instruments, respectively. GC-MS analyses were carried out using a ThermoFisher–Focus DSQ system. Column chromatography was performed on ICN silica gel (70–230 or 230–400 mesh) by gradual elution with mixtures of light petroleum (bp 40–70 °C) and diethyl ether or dichloromethane or methanol and final elution with methanol. Photolyses were performed with a 150 W medium pressure Hg arc UV lamp or with a 500 W super high pressure Hg arc UV lamp (ESR). ESR spectra were obtained with a Bruker EMX 10/12 spectrometer operating at 9.5 GHz with 100 kHz modulation (power 2.0 mW, modulation amplitude 0.6 G_{pp}). Samples were contained in quartz capillary tubes (*ca.* 1 mm i.d.), deaerated by bubbling nitrogen for *ca.* 15 min. Simulations were carried out with the Bruker Simfonia software package. Anhydrous indium trichloride was commercially available (Aldrich) and was dried prior to each reaction by heating at 130 °C under argon for 1 h. Allylindium dichloride was prepared by treatment of dry indium trichloride with allylmagnesium chloride (1 eq) in THF, according to a reported procedure.[30] Azides **1**,[13] **2**,[31] **3**,[32] and **4**[33] were prepared according to previous literature procedures.

Photolysis of allylindium dichloride: ESR analyses

A 1.0 M THF solution of allylmagnesium chloride (1 mmol) was added dropwise under argon at r.t. to a stirred solution of dry indium trichloride (1 mmol) in dry THF (2 mL). After 20 min the solvent was removed *in vacuo* and replaced by *tert*-butylbenzene (2 mL); the resulting solution was degassed with nitrogen and transferred into a quartz tube, which was then sealed, inserted into the ESR cavity, and photolysed with the 500 W super high pressure Hg arc UV lamp. The optimised spectrum reported in Fig. 1 was obtained at −13 °C. In some experiments carried out in the presence of various azides no species other than the allyl radical could be detected.

Photolytic reactions of azides with allylindium dichloride: general procedure

A 1.0 M THF solution of allylmagnesium chloride (2 mmol) was added dropwise under argon at r.t. to a stirred solution of dry indium trichloride (2 mmol) in dry THF (3 mL). After 20 min the solvent was removed *in vacuo* and replaced by benzene (3 mL);[34] the azide (1 mmol) was then added and the resulting solution was photolysed for 3 h with the 150 W medium pressure Hg arc UV lamp. The reaction crude was treated with an alkaline (NaOH) aqueous solution, extracted with diethyl ether and purified by column chromatography.

Photolytic reactions of azides with allylindium dichloride: results

Azide **1** afforded unreacted starting material (10%), *N*-allylbenzenesulfonamide **12** (15%), benzenesulfonamide **9** (30%), and allyl phenyl sulfone **10** (33%). All products were identified by spectral comparison with authentic samples.[13]

Azide **2** yielded *N*-allylbenzamide **14** (19%), identified by spectral comparison with an authentic sample,[35] and benzamide **13** (60%).[36]

Azide **3** gave a reaction crude that, after usual workup, contained (GC-MS analysis) a mixture of pyrrolidine **18** and its presumable precursor **17** ($X = Cl$, $NHInCl_2 = NH_2$). The latter compound [m/z 108 ($M^+ + 2 - 41$, 30%), 106 ($M^+ - 41$, 100%)] could not be isolated and the whole reaction mixture was stirred overnight with an aqueous NaOH solution to transform **17** into the allylated heterocycle **18**. After extraction with diethyl ether and chromatography, 2-allylpyrrolidine **18** was isolated in 60% yield and identified by spectral comparison with an authentic sample; ^{1}H NMR δ 1.70–1.83 (m, 1H), 2.02–2.19 (m, 2H), 2.24–2.30 (m, 1H), 2.46–2.53 (m, 1H), 2.61–2.67 (m, 1H), 3.33–3.45 (m, 2H), 3.70–3.76 (m, 1H), 3.80–3.94 (br s, 1H, N*H*), 5.26–5.37 (m, 2H), 5.88–6.00 (m, 1H);[37] ^{13}C NMR δ 26.0 (CH_2), 32.4 (CH_2), 39.2 (CH_2), 48.3 (CH_2), 63.2 (CH), 122.1 (CH_2), 138.5 (CH) [lit.[37] ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 24.0, 30.4, 36.9, 45.2, 59.7, 119.4, 133.0];[38] m/z (EI, rel. abund.) 70 ($M^+ - 41$, 100), 68 (15), 43 (10), 41 (10).

Azide **4** analogously afforded a reaction crude containing a mixture of piperidinone **19** and its probable precursor **17** ($X = CO_2Et$, $NHInCl_2 = NH_2$), which could not be isolated. The whole reaction mixture was stirred overnight with an aqueous NaOH solution to completely transform **17** into the allylated heterocycle **19**. After extraction with diethyl ether and chromatography, 3-allylpiperidin-2-one **19** was isolated in 65% yield and identified by spectral comparison with an authentic sample; ^{1}H NMR δ 1.45–2.35 (m, 7H), 3.21–3.51 (m, 2H), 4.88–5.21 (m, 2H), 5.52–6.15 (m, 1H), 6.65 (br s, 1H, N*H*);[39] ^{13}C NMR δ 22.3 (CH_2), 27.0 (CH_2), 37.2 (CH_2), 42.0 (CH_2), 43.8 (CH), 118.0 (CH_2), 137.8 (CH), 175.3 (CO).[39]

Acknowledgements

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Notes and references

1 For a comprehensive review on synthetic radical chemistry, see: *Radicals in Organic Synthesis*, vol. 1 and 2, ed. P. Renaud and M. P. Sibi, Wiley-VCH, Weinheim, 2001.

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28 The E_a values obtained by HF calculations are unmistakably far away from reality but, like in the case of the BDEs reported above, it is worth pointing out that they confirm the *relative* trend, giving *differences* in enthalpies and activation barriers strictly comparable with those obtained by DFT, hence providing further support to the mechanistic discussion.

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