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# Reactions of Some Alkynyl Halides with Samarium(II) Iodide

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**Abstract**: Certain alkynyl halides (6-halo-1-ynes) react with samarium(II) iodide ($SmI_2$) to give cyclized products (methylenecyclopentanes) in good yield. We have found some interesting evidence for the presence of radical and unstable organosamarium intermediates in these reductive cyclizations. Methyl 7-halohept-2-ynoates are not, however, good substrates for this cyclization methodology.

## Introduction

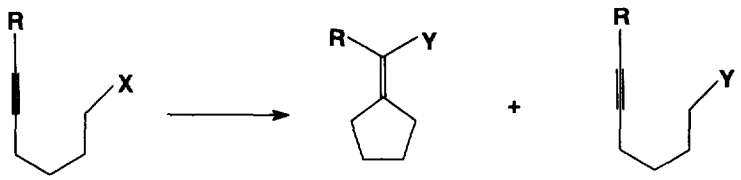
The samarium(II) iodide ($SmI_2$)[1] reduction of alkyl halides to the corresponding alkanes was demonstrated by Kagan[2] more than a decade ago and several years ago we reported that alkynyl halides **1**, **2**, **5** and **10** react with $SmI_2$ in refluxing tetrahydrofuran (THF) to give cyclized products **3**, **6** and **11** in good yield[3] (see figure 1 and table I). Under these conditions, the simple reduction products **4**, **8** and **13** account for only a minor portion of the reaction products. In general, the use of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)pyrimidinone (DMPU), as a cosolvent, improves the efficiency of this process. In theory these cyclizations may involve either radical or anionic reaction intermediates.

We reported that, for substrates **1**, **2**, **5** and **10**, quenching of our reaction mixtures ($SmI_2$/THF or $SmI_2$/THF/DMPU) with $D_2O$ prior to workup, did not result in any detectable amount of deuterium incorporation into our products. On this basis we concluded that reduction to the corresponding carbanion does not occur and that the cyclizations involve radical intermediates. It has since been demonstrated by others[4] that attempts to trap organosamarium species by addition of $D_2O$ at the end of a reaction are not always successful due to the instability of these intermediates; these species can, however, be trapped *in situ* . In this paper we describe some new experiments with compounds **2** and **5** which shed light on the mechanistic aspects of our methodology; we also describe the reactions of four new substrates (**9**, **19**, **23** and **30**) with $SmI_2$ and discuss the significance of the formation of iodine atom transfer cyclization products **7** and **12** from certain reaction mixtures of substrates **5**, **9** and **10**.

## Results and Discussion

The reactions of substrates **1**, **2**, **5** and **10** with commercial solutions of $SmI_2$ under *reflux* conditions in THF or THF/DMPU are summarized in table I and, with the exception of entries f and i, were reported in an earlier communication.[3] The major products of these reductions are the 5-*exo*-cyclization compounds **3**, **6** and **11** with the simple reduction products **4**, **8** and **13** accounting for only a minor portion of the reaction products.

Likewise, compound **9** reacts with $SmI_2$ in THF/DMPU under reflux conditions to give a mixture of compounds **6** (78%) and **8** (13 %) (see table I, entry i).[5]




**1** R = Ph X = Br
**2** R = Ph X = I
**3** R = Ph Y=H
**4** R = Ph Y = H
**5** R = nBu X = Br
**6** R = nBu Y = H
**7** R = nBu Y = I
**8** R = nBu Y = H
**9** R = nBu Y = I
**10** R = TMS X = Br
**11** R = TMS Y = H
**12** R = TMS Y = I
**13** R = TMS Y = H
**14** R = TMS Y = I

**Fig 1: $SmI_2$ induced cyclization of some alkynyl halides**

**TABLE I:** Reactions of alkynyl halides with $SmI_2$ in THF or THF/DMPU under reflux conditions[a]

| Entry | Substrate | Cosolvent | Isolated Compounds[b](%) | | | |
|---|---|---|---|---|---|---|
| a | **1** | DMPU | | **3**(83) | **4**(--[c]) | |
| b | **1** | none | **1**(<1) | **3**(65) | **4**(3) | |
| c | **2** | DMPU | | **3**(80) | **4**(5) | |
| d | **2** | none | | **3**(82) | **4**(1) | |
| e | **5** | DMPU | | **6**(81) | **8**(2) | |
| f | **5** | none | **5**(23) | **6**(47) | **8**(12) | **9**(1) |
| g | **10** | DMPU | | **11**(67) | **13**(8[d]) | |
| h | **10** | none | **10**(<1) | **11**(74) | **13**(1.5[e]) | **14**(<1) |
| i | **9** | DMPU | | **6**(78) | **8**(13) | |

a) Unless otherwise specified, reactions were carried out with 3 equivalents of $SmI_2$ in refluxing THF for 24 h. After workup, the reaction mixtures were purified by flash chromatography (silica, hexanes). b) In those cases where reaction products could not be separated, the ratio of the components were determined by $^1H$ NMR. Compounds **3** and **4** were obtained as an inseparable mixture as were compounds **6** and **8** and compounds **10** and **14**. c) Ratio of **3**:**4** as determined by GC was > 1000: 1; quantity of **4** insufficient to allow detection by NMR. d) GC yield was 8% and the isolated yield was 6%. e) GC yield of compound **13** is reported here as our attempts to isolate it were unsuccessful.

Reaction mixtures tend to be more complex when *room temperature* conditions are used (see figure 1 and table II). Although these results are generally not synthetically useful, they are very interesting from a mechanistic point of view. When the reaction of one of our alkynyl bromides (e.g. **1**, **5** or **10**) with $SmI_2$ is not allowed to go to completion, we recover the unreacted bromide as well as the corresponding iodide (**2**, **9** or **14**). Both halides can of course be transformed into the cyclized products. One possible explanation for the formation of these iodo-compounds **2**, **9** and **14** involves exchange of one of the iodides associated with the samarium ion for a molecule of DMPU, for example, and subsequent nucleophilic attack by the iodide ion on the bromo-compounds (**1**, **5** and **10**).[6] We also observed, for substrates **5**, **9** and **10** (see table II, entries c-f), formation of vinylic iodides **7** and **12**. These compounds presumably arise from the reaction of cyclized vinylic radicals with a molecule of alkynyl iodide (generated *in situ* in the case of substrates **5** and **10**) to give the corresponding iodine atom transfer cyclization products[7] (see figure 2). As one might expect, higher yields of the iodine atom transfer cyclization products are obtained when our starting material is the alkynyl iodide **9**, as opposed to alkynyl bromide **5** (see Table II, entries c and e).

**TABLE II:** Reactions of alkynyl halides with $SmI_2$ in THF or THF/DMPU at room temperature[a]

| Entry | Substrate | Cosolvent | Isolated Compounds[b](%) | | | | |
|---|---|---|---|---|---|---|---|
| a | **1** | DMPU | **1**(14)[c] | **3**(74) | | **4**(1) | **2**(8)[c] |
| b | **2** | DMPU | | **3**(75) | | **4**(3) | |
| c | **5** | DMPU | **5**(47) | **6**(22) | **7**(7) | **8**(17) | **9**(1) |
| d | **10** | DMPU | **10**(41) | **11**(12) | **12**(5) | **13**(<1)[d] | **14**(41) |
| e | **9** | DMPU | | **6**(44) | **7**(41) | **8**(7) | |
| f | **9** | none | **9**(38) | **6**(14) | **7**(22) | **8**(20) | |

a) Unless otherwise specified, reactions were carried out with 3 equivalents of $SmI_2$ (Aldrich) and the reaction time was 24 h. After workup, the crude mixtures were purified by flash chromatography (silica, hexanes). b) In those cases where reaction products could not be separated, the ratio of the components were determined by $^1H$ NMR. Compounds **3** and **4** were obtained as an inseparable mixture as were compounds **6**, **7** and **8** (this mixture was also analyzed by GC-MS). Compounds **10** and **14** as well as compounds **11** and **12** were isolated as inseparable mixtures. c) Isolated as a slightly impure sample. d) GC yield of compound **13** is reported in this table as the product was not isolated.

We felt that the isolation of iodine atom transfer cyclization products, from certain of our reaction mixtures of substrates **5**, **9** and **10**, was good evidence for the presence of vinyl radicals; we did not have any such evidence, however, for substrates **1** and **2**. We therefore decided to carry out some *in situ* trapping experiments with $SmI_2$ (in THF or THF/DMPU), EtOD and compound **2**. Deuterium incorporation at the vinylic position of **3** , under these conditions, would be consistent with an organosamarium reaction intermediate (see figure 3). We also allowed **2** to react with $SmI_2$ in THF-$d_8$.[8] In this case, deuterium incorporation at the vinylic position of **3** is indicative of a radical intermediate (see figure 2).

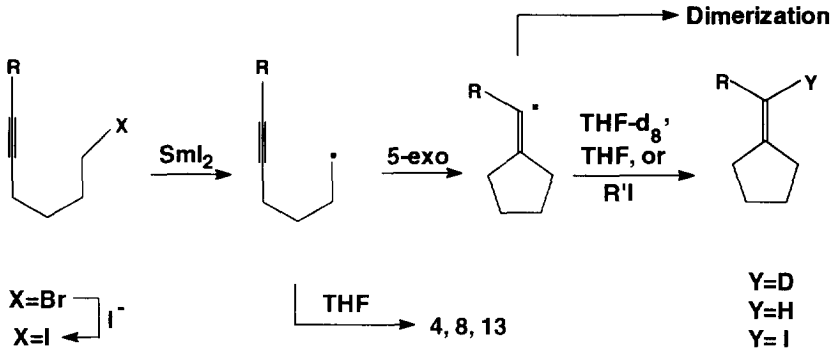



**Fig. 2: Reactions of some alkynyl halides with $SmI_2$ in THF/DMPU via a radical pathway**

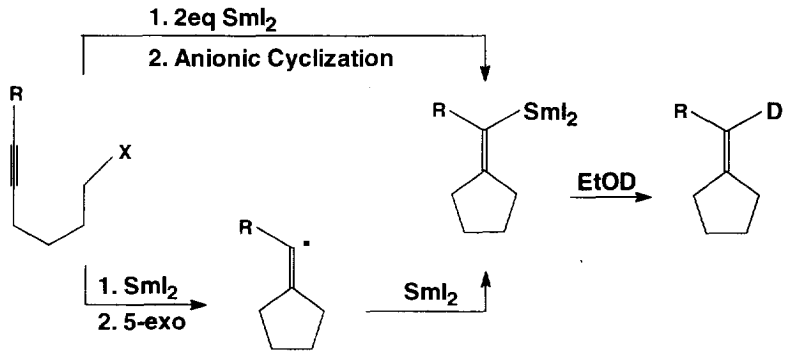
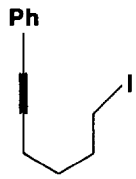


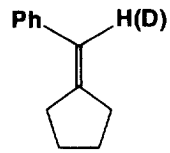

**Fig. 3: Reactions of alkynyl halides with $SmI_2$ via an anionic pathway**

$SmI_2$ was added to a solution of **2** in THF/EtOD or THF/DMPU/EtOD at room temperature; compound **3** was isolated and analyzed by MS and $^1H$ NMR to determine the extent of deuterium incorporation. We observed a 9 % incorporation for the reactions run in THF/EtOD and an 18 % incorporation for the reaction run in THF/DMPU/EtOD. The order of addition is important when DMPU is used as a cosolvent; if EtOD is added to the reaction mixture immediately after the addition of $SmI_2$, we observe only a 2 % incorporation of deuterium. These results suggest that there is at least some formation of organosamarium intermediates under our reaction conditions (see figure 3).

When compound **2** was also allowed to react with an excess of $SmI_2$ in THF-$d_8$ under reflux conditions[9] we isolated four compounds from the reaction mixture: starting material **2** (21%), the expected cyclization product **3** (40% yield; 32 % deuterium incorporation), a small amount of the simple reduction product **4** (5%), and the product of vinyl radical dimerization (**26**, 14 %). The formation of **26** (14%), together with a 32 % level of deuterium incorporation in **3**, is indicative of the presence of cyclized vinyl radicals as reaction intermediates (see figure 2).

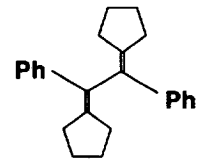



**2**




**3**

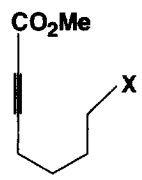

**4**



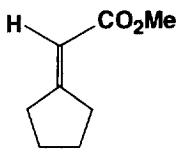

**26**

The results of the deuterium incorporation experiments, together with the experiments described in table II involving the formation of iodine atom transfer cyclization products, are consistent with a radical pathway as the major pathway for the $SmI_2$ induced reductive cyclizations of **1**, **2**, **5**, **9** and **10**. These results do not exclude the possibility of an alternate pathway; we also have evidence, from our EtOD *in situ* quenching experiments with **2**, that organosamarium species are formed to a minor extent. It seems likely that both pathways may be operating under our reaction conditions and we can no longer exclude an *alternate* reaction mechanism involving formation of vinyl organosamarium intermediates (see figure 3). These species may be formed by further reduction of the vinyl radical or may be the intermediate product of an anionic cyclization.

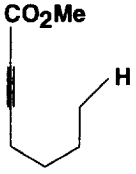
Our study was expanded to include substrates **19**, **23** and **30**; the reactions of these compounds with $SmI_2$ *differ* from the pattern seen with compounds **1**, **2**, **5**, **8** and **9**. The details of these studies are presented in the following paragraphs. Compounds **19** and **23** are known compounds and were prepared from commercially available hex-5-yn-1-ol by a literature procedure.[10]



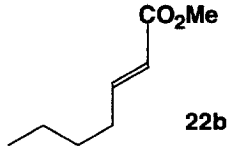

**19 (X = Br)**
**21 (X = H)**
**23 (X = I)**



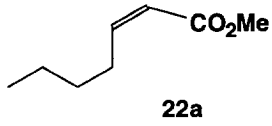

**20**




**21**



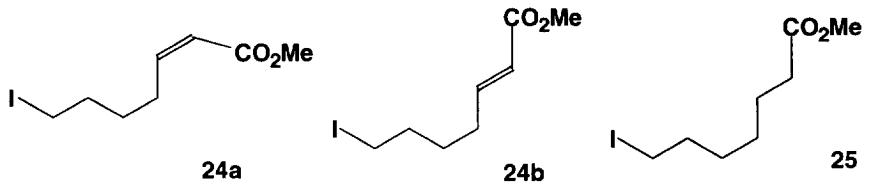

**22b**




**22a**

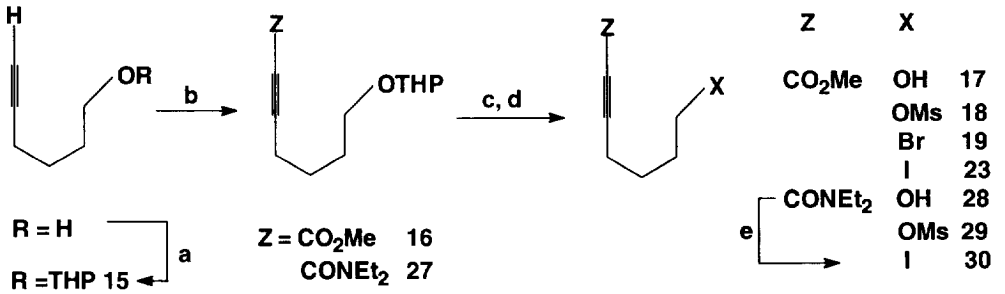
Treatment of bromo-ester **19** with an excess of $SmI_2$ in THF did not result in the formation of either **20** or **21**[11]. We observed degradation of the starting material both under reflux conditions and at 0°C. Analysis of the crude reaction mixtures by GC, TLC and $^1H$ NMR indicated the presence of numerous compounds and attempts to separate the mixture by flash chromatography were unsuccessful. We suspected that, unlike our previously described substrates, reduction of the triple bond was occurring. In fact, treatment of **21** with 3 eq of $SmI_2$ in THF at room temperature for 24 h leads to degradation of our material. This degradation is minimized if milder conditions are used ( i.e. -78 °C, 4 h; 0 °C, 2 h) and if a proton source (MeOH) is added to the mixture. NMR, GC, and GC-MS analysis of the reaction products indicated the presence of three compounds: recovered starting material **21** (66%), and the *Z* and *E* α, β-unsaturated esters **22a** (11%) and **22b** (12%).[11b,12]

We wondered if the use of the *more reactive* iodide substrate **23** would allow formation of the cyclized reduction product but reaction of **23** with $SmI_2$ under our mild reaction conditions did not result in the formation of **20**. We isolated, instead, compounds **24a**, **24b**, and **25**[12] together with some recovered starting material from our reaction mixture. We were unable to find any evidence for carbon-iodine bond reduction products under these conditions.



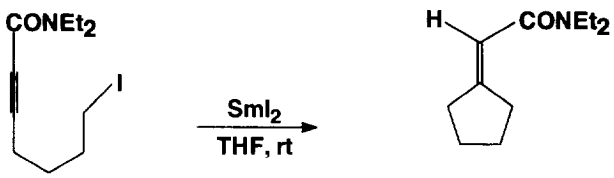

Our attempts to convert iodo-amide **30** to compound **31** led to some interesting results. Reaction mixtures were often complex and separation and purification of the various components was sometimes difficult to achieve. We have, however, been able to define conditions under which **30** can be efficiently and cleanly converted to **31**.

Compound **30** was prepared from commercially available hex-5-yn-1-ol by a route similar to that used to prepare iodo-ester **23**[10] (see figure 4). Compound **30** can be prepared directly from **28** or, alternatively, from the intermediate mesylate **29**.




a) DHP, pTSA·$H_2O$, $CH_2Cl_2$, rt; b) (1) nBuLi,THF and (2) $ClCO_2Me$ to give **16** (83% overall from hex-5-yn-1-ol) or (3) LDA, THF and (4) $ClCONEt_2$ to give **27** (63% overall from hex-5-yn-1-ol); c) MeOH, pTSA·$H_2O$ to give **17** (90%) and **28** (97%); (d) (1) MsCl, $Et_3N$, $CH_2Cl_2$ to give **18** (97%) and **29** [95%] and (2) NaI, acetone to give **23** [69% (89%)] and **30** [95%(97%)] or LiBr, acetone to give **19** (94%); e) $Ph_3P$, imidazole, $I_2$, $CH_2Cl_2$, 94%.[13]

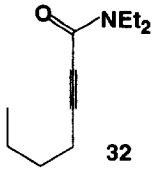
**Fig. 4: Synthesis of Substrates 19, 23 and 30**



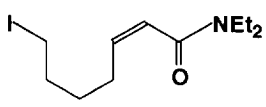

30 31

**Fig. 5: Reductive cyclization of 30 under $SmI_2$/THF/rt conditions**

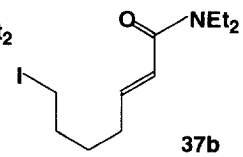
Reduction of **30** with $SmI_2$ (5 eq, THF, 44h; [RI] = 0.015M) at room temperature gave the cyclized product **31** in 41% yield after purification; unreacted starting material was also recovered (44%). We saw no evidence of the simple reduction product **32**[14] (as determined by GC, TLC and $^1H$ NMR) under these conditions. We hoped to improve the yield of **31** and considered a number of possible modifications to our reaction conditions. Some of our early attempts to improve the efficiency of this transformation only served to complicate our reaction mixtures. For example, when $SmI_2$ was added to a THF/MeOH solution of **30** at room temperature minor reaction products **32**, **37a**, **37b** and **38**[12], in addition to compound **31**, were isolated from our reaction mixtures.[15] Before implementing other changes, we first needed to ensure that these modifications did not also result in the undesired reduction of the triple bond or amide functional groups.



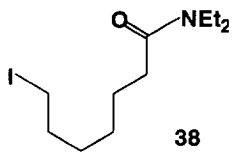

32



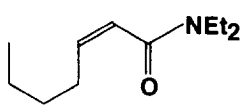

37a



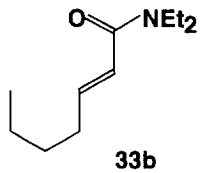

37b



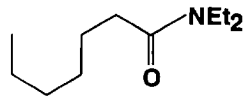

38




33a




33b




34

We investigated the reaction of **32** itself with $SmI_2$ so to define "non-destructive conditions" which could then be applied to our actual substrate **30**. The crude reaction mixtures were analyzed by TLC, GC and / or GC-MS and by $^1H$ NMR so as to determine the extent of any reaction. Compound **32** is less reactive than propargyl ester **21** toward $SmI_2$ reduction but much more reactive than either **4**, **8** or **13**[16]. Propargyl amide **32** is inert to the usual room temperature conditions (3eq $SmI_2$/THF/48h) and is recovered in good yield (87%) from the reaction mixture. It is degraded when larger quantities of $SmI_2$ (8.5 eq, THF, 48h) are used or when HMPA is added as a cosolvent (5%) to the THF solution at either room temperature or 0° C. The material balance under these conditions was poor and we have not been able to isolate analytically pure samples of the reduction products; NMR and GC-MS analysis of the crude and partially purified reaction mixtures indicate the presence of the *Z* and *E* α, β-unsaturated amides **33a** and **33b**, and of alkyl amide **34**.[12] Reduction of the

triple bond of amide **32** under the $SmI_2$-THF-HMPA conditions is minimized or eliminated however if the quantity of $SmI_2$ used is lowered to 1.3 eq and if the reaction mixture is cooled to -78°C.

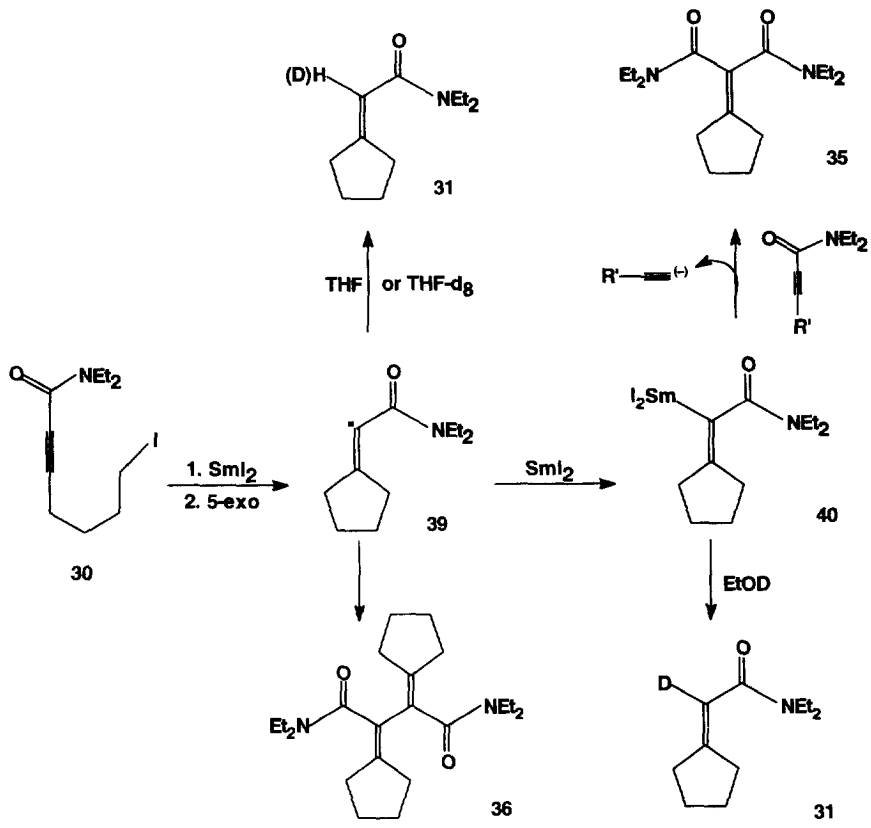



**Fig.6: $SmI_2$ induced reductive cyclization of iodo-alkynyl amide 30**

The addition of either DMPU or HMPA to the reaction mixtures of **30** and $SmI_2$ did not result in an increase in the yield of **31**. The yields of cyclized product were typically less than 30% and purification was complicated by the presence of a number of different side products in the reaction mixture. One of the side products was determined to be the bis amide **35** (see figure 6). GC-MS and high resolution MS analysis of a second side product was consistent with a dimeric species having a molecular formula of $C_{22}H_{36}O_2N_2$. $^1H$ and $^{13}C$ NMR data were consistent with the structure **36** (see figure 6) but our assignment remains tentative due to our failure to obtain an analytically pure sample. In addition, analysis of the $^1H$ and $^{13}C$ spectra is complicated by the possibility of conformational isomers of **36**.

Our attempts to increase the yield of **31** by increasing the reaction temperature led to some interesting results. Under overnight reflux reaction conditions in THF all of our starting material reacts and we obtain a

25% of the cyclized mono-amide **31**. The reaction was quenched by addition of $D_2O$ but we were unable to detect any deuterium incorporation at the vinylic position of **31**. In addition to **31**, we also isolated 19 % of compound **35** from our reaction mixture. If the reaction is carried out in the presence of EtOD (under the same overnight reflux reaction conditions in THF) we are able to increase the yield of **31** to 88 % and avoid formation of **35**. This time we observe a significant amount of deuterium incorporation at the vinylic position i.e. 68% as determined by MS analysis. A complementary experiment was carried out with **30** and $SmI_2$ in THF-$d_8$ under reflux conditions. In this instance the level of deuterium incorporation in **31** is only 7%.

We have rationalized these results as follows (see figure 5): **30** is reduced by $SmI_2$ to give the corresponding alkyl radical which cyclizes in a 5-exo fashion to give the vinylic radical **39**. Radical **39** may then (1) abstract a hydrogen atom from THF to give non-deuterated **31** (or abstract a deuterium atom from THF-$d_8$ to give deuterated **31**); (2) couple with another molecule of **39** to form dimer **36**, or (3) be reduced by a second equivalent of $SmI_2$ to give vinyl organosamarium species **40**[17]. The organosamarium intermediate **40** reacts with EtOD to give deuterated **31** or may (under overnight reflux conditions), in the absence of EtOD, react with a molecule of propargyl amide to give **35** and an acetylide anion.

## Conclusions

Certain alkynyl halides react with $SmI_2$ to give cyclized products in good yields. The reactivity of these 1-substituted-6-halohex-1-ynes is dependent on the nature of the triple bond substituent. We have found some interesting evidence for both vinyl radical and vinyl organosamarium intermediates in these reactions.

Compounds **1**, **2**, **5**, **9** and **10** react with $SmI_2$ in refluxing THF or THF/DMPU to give methylenecyclopentanes in good yield. In general, the simple reduction products account for only a minor portion of the reaction products. The results of our mechanistic studies are consistent with the involvement of alkyl and vinyl radical intermediates in the *major* reaction pathway.

The choice of reaction conditions is essential for the clean and efficient conversion of iodo-amide substrate **30** to the corresponding cyclization product **31**. In contrast to the previously mentioned substrates, transformation of **30** to **31** in refluxing THF appears to involve an unstable organosamarium species as a key intermediate in the *major* reaction pathway; this conclusion is based on the isolation of bis amide **35** from certain reaction mixtures and on *in situ* trapping experiments with EtOD and THF-$d_8$.

Methyl 7-halohept-2-ynoates (**19** and **23**) are not appropriate substrates for this cyclization methodology as they undergo triple bond reduction faster than carbon-iodine bond reduction under our reaction conditions.

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## Experimental

Unless otherwise noted, $^1H$ and $^{13}C$ NMR spectra were recorded in $CDCl_3$ on a Varian Gemini 300 BB instrument. FTIR spectra were recorded on a Perkin Elmer Series 1600 instrument and Mass Spectra were recorded on a Krato 25 RFA instrument. GC spectra were recorded on a Varian 3300 instrument (SPB-5 column, 15 meters length, 0.25μm internal diameter, 2 cm / min flow rate). GC-MS spectra were recorded on a Varian 3500 instrument (DB-5 column, 30 meters length and 0.25μm internal diameter, 2 cm / min flow rate) with a Finnigan 700 Ion Trap Detector.

**Materials**: Compounds **1**, **2**, **5** and **9** were prepared according a literature procedure[18] and our spectral data ($^1H$ NMR, $^{13}C$ NMR, IR and MS) match those previously reported for these compounds[19] Substrate **10**[20] and an authentic sample of **14**[21] were also synthesized according to published procedures. Compounds **8** and **13** were purchased from American Tokyo Kasei inc. and Aldrich respectively. An authentic sample of **4** was made for comparison purposes (see below). Hex-5-yn-1-ol was purchased from Aldrich. Compounds **15**, **16**, **17** and **18** were prepared according to a literature procedure[10a] and our spectral data matched those previously reported for these compounds.[10] THF was always freshly distilled from Na/benzophenone under an argon atmosphere. DMPU was distilled from $CaH_2$ under vacuum and stored over molecular sieves under an argon atmosphere. All manipulations involving $SmI_2$ were done under a carefully controlled argon atmosphere.

**1-Hexynylbenzene (4):** An authentic sample of compound **4** was prepared according to the general procedure described in reference 18. Deprotonation of phenylacetylene (Aldrich) with n-BuLi and alkylation of the corresponding lithium acetylide with 1-bromobutane gave compound **4**. $R_f$ = 0.54 [TLC, silica, hexanes]. **$^1H$ NMR** [$CDCl_3$, 200 MHz] δ 7.40 (m, 2H), 7.28 (m, 3H), 2.41 (t, J = 6.9 Hz, 2H, $CH_2C{\equiv}C$), 1.54 (m, 4H, 2 x $CH_2$), 0.96 (t, J = 7.1 Hz, 3H, $CH_3$). **$^{13}C$ NMR** [$CDCl_3$, 50.3 MHz] δ 131.5, 128.2, 127.4, 124.1, 90.4, 80.6, 30.9, 22.0, 19.1, 13.6. **IR** (film) 2235 - 2240 $cm^{-1}$ (w), 1600 (m). **MS** (low resolution EI, 70 eV) m/z: 158 (53.2 %, $M^{\bullet+}$), 143 (65.8 %, M-$CH_3$), 129 (63.8 %, M-$C_2H_5$), 128 (40.0 %), 115 (100 %, M-$C_3H_7$).

**General Procedure for Reactions with Commercial Solutions of $SmI_2$**: A solution of $SmI_2$ in THF (available from Aldrich; 30 mL of a 0.1 M solution) was transferred via cannula to a solution of the starting material (1 mmol in 20 mL THF) under an argon atmosphere. Where appropriate, DMPU (7.0 mL), HMPA (6.5 mL), EtOD (0.355 mL) or MeOH (0.240 mL) was then added.[22] The reactions were quenched by addition of 0.1 M HCl unless otherwise specified and worked up as follows: the mixture was diluted with $H_2O$ (50 mL) and extracted with ether (3 x 50 mL). The combined extracts were washed with $H_2O$ (50 mL or 3 x 50 mL when DMPU or HMPA was used ), saturated aqueous $Na_2S_2O_3$ (50 mL) and brine (50 mL). The organic layer was dried over $MgSO_4$, and concentrated (where appropriate, GC analysis was carried out at this stage). The crude products were purified by flash chromatography on silica gel using either hexanes, a mixture of EtOAc and hexanes or a mixture of EtOAc and $CH_2Cl_2$ as the eluant. For those reactions involving substrate **10**, a gravity column was run due to the volatility of the reaction products.

**Cyclization products 3, 6 and 11:**

**Benzylidenecyclopentane** (**3**[23], Table I, entry a): $R_f$ = [0.60 (TLC, silica, hexanes). **$^1$H NMR** [$CDCl_3$, 300 MHz] δ 7.35 - 7.12 (m, 5H, aromatic protons), 6.35 (m, 1H, vinylic proton), 2.53 (m, 4H, 2 x $CH_2$ allylic), 1.79 (m, 2H, $CH_2$), 1.67 (m, 2H, $CH_2$). **$^{13}$C** NMR [$CDCl_3$, 50.3 MHz] δ 147.1, 138.9, 128.1, 127.9, 125.6, 120.8, 35.9, 31.1, 27.2, 25.6. **FTIR** (film) 1654 (m), 1600 (m) $cm^{-1}$. **MS** (low resolution , EI, 70 eV) m/z: 158 (100 %, $M^{\bullet+}$), 143 (27.9 %, M - 15), 129 (73.3%, M-$C_2H_5$), 117 (67.2 %), 115 (64.4 %, M - $C_3H_7$), 91 (51.8 %), 67 (78.6 %).

**Pentylidenecyclopentane** (**6**[19] , Table I, entry e): $R_f$ = 0.95 (TLC, silica, hexanes). **$^1$H NMR** [$CDCl_3$, 300 MHz] δ 5.24 (m, 1H, vinylic proton), 2.33 - 2.44 (m, 4H), 2.00 - 1.90 (m, 2H), 1.65 - 1.51 (m, 4H), 1.35 - 1.25 (m, 4H), 0.89 (m, 3H, $CH_3$). **$^{13}$C NMR** [$CDCl_3$, 75 MHz] δ 142.9, 120.3, 33.6, 32.0, 29.3, 28.6, 26.4, 26.3, 22.4, 14.0. **FTIR** (film) 1648 $cm^{-1}$. **MS** (low resolution, EI, 70 eV) m/z: 138 (24 %, $M^{\bullet+}$), 109 (9.3 %, M - $C_2H_5$), 95 (100 %, M - $C_3H_7$).

**Trimethylsilylmethylenecyclopentane** (**11**[24], Table I, entry h): Rf = 0.81 (TLC, silica, hexanes). GC: tr = 2.88 min[Perkin Elmer 3920, 10% OV-17 column; injector = 250 °C; $T_{int}$ = 150 °C (2 min); $T_{fin}$ = 240 °C (rate = 8 °C/min)]. **$^1$H NMR** [$CDCl_3$, 300 MHz] δ 5.37 (m, 1H, vinylic proton), 2.30 (m, 4H, 2 x $CH_2$, allylic protons), 1.78 - 1.54 (m, 4H, 2 x $CH_2$), 0.083 (s, 9H, Si*Me*$_3$). **$^{13}$C NMR** [$CDCl_3$, 75 MHz] δ 163.2, 118.0, 37.5, 32.4, 27.2, 26.0, -0.30. **FTIR** (film) 1621 (s), 1246 (s) $cm^{-1}$. **MS** (low resolution, EI, 70 eV) m/z: 154 (18.7 %, $M^{\bullet+}$), 139 (100 %, M-$CH_3$).

**Iodine atom transfer cyclization products:**

**(1-Iodopentylidene)cyclopentane (7) from substrate 5** (Table II, entry c): A mixture of **5** (0.4347 g, 1.98 mmol), $SmI_2$ (60 mL, 0.1 M, 6.0 mmol), THF (40 mL) and DMPU (14.5 mL) was stirred at room temperature for 24 h. After workup and flash chromatography (silica, hexanes), halides **5** (0.2063 g, 47% recovery) and **9** (7.5 mg, 1%) were separated from an inseparable mixture (0.1575 g) of three known compounds: **6**(22%), **7**(7%) and **8**(17%). Our $^1$H NMR data were compared with those for authentic samples of **6** and **8** and with literature data in the case of **7**.[7b] In addition, this mixture as analyzed by **GC - MS**: [Varian GC 3500 equiped with a 30 m Supelco DB-5 column and a Finnigan ion trap; column conditions: $T_{int}$ = 40 °C, $T_{fin}$ = 180 °C, rate = 10 °C/min] m/z (for **8**, $t_r$ = 6.33 min): 138 (4.3 %, M), 123 (2.8 %, M-$CH_3$), 110 (9.4 %), 96 (43.7 %), 95 (38.2 %), 82 (57.8 %), 81 (100 %, M-$C_4H_9$); m/z (for **6**, $t_r$ = 6.52 min): 138 (74.3 %, M), 123 (2.9 %, M-$CH_3$), 109 (7.3 %, M-$C_2H_5$), 95 (93.6%, M - $C_3H_7$), 81 (66.2 %, M-$C_4H_9$), 67 (100 %); m/z (for **7**, $t_r$ = 12.21 min): 264 (50.3 %, M), 137 (7.1 %, M-I), 95 (82.8%), 81 (100 %), 67 (42 %).

**(1-Iodopentylidene)cyclopentane (7) from substrate 9** (Table II, entry e): A mixture of **9** (0.2636 g, 0.999 mmol), $SmI_2$ (30 mL, 0.1 M, 3.0 mmol), THF (20 mL) and DMPU (7.25 mL) was stirred at room temperature for 24 h. After workup the crude mixture was analyzed by GC and then purified by flash chromatography (silica, hexanes) to give an inseparable mixture (0.1781 g) of known compounds **6** (44%), **7**(41 %) and **8** (7%). The yields of these products were calculated from the $^1$H NMR spectrum.

**Trimethyl[(cyclopentylidene)iodomethyl]silane** (**12**): Compound **12** was one of the products from the reaction mixture of **10** and $SmI_2$ in THF/DMPU under room temperature conditions (Table II, entry d). Compounds **12** was separated from **11** in one instance; due to the difficulty in visualizing these products by TLC, fractions from the column purification were checked by GC; the fractions were combined accordingly and then carefully concentrated to avoid evaporation of the cyclized products. Compound **12** is a known

compound and has the following characteristics[7a]: colourless liquid; $R_f$ = 0.72 [TLC, silica, hexanes]; **GC**: $t_r$ = 8.35 min [Perkin Elmer 3920, 10% OV-17 column; injector = 250 °C; $T_{int}$ = 150 °C (2 min); $T_{fin}$ = 240 °C (rate = 8 °C/min)]. **$^1$H NMR** [$CDCl_3$, 300 MHz] δ 2.47 - 2.30 (m, 4H, 2 x allylic $CH_2$), 1.89 (m, 2H, $CH_2$), 1.68 (m, 2H, $CH_2$), 0.256 (s, 9H, $SiMe_3$). **$^{13}$C NMR** [$CDCl_3$, 75 MHz] δ 164.3, 100.3, 45.7, 34.6, 29.3, 25.5, 0.939. **FTIR** (film) 1595 $cm^{-1}$. **MS** (low resolution , EI) m/z: 280 (60.9%, $M^{\bullet+}$), 265 ( 5.9 %, M-$CH_3$), 185 (78.5%), 153 (100 %, M-I).

**Reaction of compound 2 with $SmI_2$ in THF/DMPU/EtOD**: A solution of $SmI_2$ (17.6 mL, 0.1 M) was transferred via canula to a solution of **2** (0.1664 g, 0.5857 mmol) in a mixture of THF (11.5 mL), EtOD (0.21 mL, Aldrich) and DMPU (4.0 mL). The mixture was stirred at room temperature overnight and then worked up in the usual way. Unreacted starting material **2** (0.0747 g, 44.9 %) was separated from the cyclized product **3** [0.0407, 44 %; 18 % deuterium incorporation as determined by MS (average M/M+1 ratio = 100:35.35)] by use of a Chromatotron (Harrison Research, 2 mm adsorbosil plate, hexanes). $^1$H NMR analysis of **3** is consistent with this level of deuterium incorporation at the vinylic position.

**Reaction of compound 2 with $SmI_2$ in THF-$d_8$**: A solution of $SmI_2$ in THF-$d_8$ (CDN Isotopes) was prepared from Sm metal (Cerac, 40 mesh, flame dried) and freshly distilled $CH_2I_2$ (Aldrich) according to a literature procedure.[4b] i.e.. To a chilled (0°C) suspension of Sm (0.2097g, 1.3947 mmol) in THF-$d_8$ (5.0 mL) was added a solution of freshly distilled $CH_2I_2$ (0.1894 g, 0.7071 mmol) in THF- $d_8$ (2.0 mL in total). The reaction flask was covered in aluminum foil and the mixture stirred at 0°C for 15 min and then at room temperature for 1.5 h. The excess Sm powder was allowed to settle and the resulting dark blue solution (*ca.* 0.1 M solution of $SmI_2$) was transferred via canula to a graduated centrifuge tube (a trace amount of Sm powder settled in the bottom of the tube) and then used as is. This $SmI_2$ solution (3 eq) was transferred, via canula, to a solution of substrate **2** (0.0414 g, 0.1457 mmol, in 1.5 mL THF-$d_8$) and the mixture stirred at reflux overnight until all of the $SmI_2$ was consumed (< 12 h). The reaction was quenched by addition of 0.1 M HCl (10 mL) and worked up as follows: the mixture was diluted with $H_2O$ (10 mL) and extracted with ether (3 x 10 mL). The combined extracts were washed with $H_2O$ (10 mL), saturated aqueous $Na_2S_2O_3$ (10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$, and concentrated. The crude mixture was purified by chromatography using a Chromatotron (Harrison Research, 1 mm adsorbosil plate[25] ) with hexanes as the eluant. Recovered from the reaction mixture was: starting material **2** (0.0088g, 21%), the expected cyclization product **3** (0.0093g, 40.4 % yield; 32 % deuterium incorporation as determined from the MS data (average M/M+1 ratio = 100: 60.4), some simple reduction product (0.0011 g, 4.8 %) and compound **26** (0.0032 g, 14 %) which had the following characteristics: $R_f$ = 0.42 [TLC, silica, hexanes. **$^1$H NMR** [$CDCl_3$, 300 MHz] δ 7.34-7.20 (m, 8H, Ar-H), 7.14 (m, 2H, Ar-H), 2.48 (m, 4H, allylic 2 x $CH_2$), 2.30 (m, 4H, allylic 2 x $CH_2$), 1.67 (m, 8H, homoallylic 4 x $CH_2$). **$^{13}$C NMR** [75 MHz, $CDCl_3$] δ 142.9, 141.7, 133.5, 128.3, 127.7, 125.7, 32.9, 32.5, 27.2, 26.1. **MS** [low resolution EI, 70 eV] m/z: 314 (58%, $M^{\bullet+}$), 245 (100 %). **MS** [low resolution, CI, $NH_3$] m/z: 314 (67.7%, $M^{\bullet+}$), 245 (100 %).

**Methyl 7-bromohept-2-ynoate (19):** Compound **19** was prepared according to a modification of the procedure described in reference 10a. i.e. A mixture of methyl 7-(mesyloxy)hept-2-ynoate (**18**)[10a] (0.7448 g, 3.179 mmol), LiBr (0.8034 g, 9.250 mmol) and acetone (65 mL) was stirred at room temperature under anhydrous conditions for 96 h. The solvent was evaporated and the residue was diluted with $CH_2Cl_2$; the

solution was washed with a saturated aqueous solution of $Na_2S_2O_3$ (50 mL), $H_2O$ (50 mL), and brine (50 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated. Purification by flash chromatography gave **19** [0.6536 g, 94%] as a colourless liquid: $R_f$ = 0.43 [ TLC, silica, 10% EtOAc:hexanes]. **$^1$H NMR** [$CDCl_3$, 300 MHz] δ 3.77 (s, 3H, $OCH_3$), 3.43 (t, J = 6.6 Hz, 2H, $CH_2Br$), 2.40 (t, J = 7.0 Hz, 2H, $CH_2C{\equiv}C$), 2.06 – 1.94 (m, 2H, $CH_2$), 1.82 – 1.70 (m, 2H, $CH_2$). **$^{13}$C NMR** [$CDCl_3$, 75 MHz] δ 154.1, 88.5, 73.4, 52.6, 32.7, 31.4, 25.9, 17.9. **FTIR** (neat) 2236 (m, C≡C), 1713 (s, broad, C=O) $cm^{-1}$. **MS** (low resolution EI, 70 eV) m/z: 220 [$(C_8H_{11}{}^{81}BrO_2)^{+\cdot}$, 4.6%], 218 [$(C_8H_{11}{}^{79}BrO_2)^{+\cdot}$, 4.6%], 111 [100%]. These data were in agreement with those reported for an alternate synthesis of this compound[10b] with the exception of the exact position of the C≡C stretching frequency in the IR spectrum ( i.e. 2220 versus 2236 $cm^{-1}$).

**Methyl 7-iodohept-2-ynoate (23)**: Compound **23** was prepared and purified according to the procedure of reference 10a. **$^1$H NMR** [$CDCl_3$, 300 MHz] δ 3.77 (s, 3H, $OCH_3$), 3.21 (t, J = 6.8 Hz, 2H, $CH_2I$), 2.39 (t, J = 7.0 Hz, 2H, $CH_2C{\equiv}C$), 1.89 - 2.02(m, 2H, $CH_2$), 1.66 - 1.78 (m, 2H, $CH_2$). **$^{13}$C NMR** [$CDCl_3$, 75 MHz] δ 154.1, 88.5, 73.4, 52.6, 32.1, 28.2, 17.6, 5.3. **FTIR** (neat): 2234 (m, C≡C), 1710 (s, broad, C=O) $cm^{-1}$. **MS** (low resolution EI, 70 eV) m/z: 266 [$M^{+\cdot}$, 1.5 %], 235 [M – OMe, 28.2%], 139 [M – I, 14.6 %], 111 [14.8 %], 107 [28.4 %], 79 [ 100%].

**Methyl hept-2-ynoate (21)** is a known compound[11] and was prepared according to the procedure described in reference11b. $R_f$ = 0.33 (TLC, silica, 10% EtOAc : hexanes). **$^1$H NMR** δ: 0.93 (t, J=7.3 Hz, 3H, $CH_3$), 1.43 (m, 2H, $CH_3CH_2$), 1.57 (m, 2H, $C{\equiv}CCH_2CH_2$), 2.34 (t, J = 7.0 Hz, 2H, $C{\equiv}CCH_2$), 3.76 (s, 3H, $OCH_3$). **$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ: 154.3 (C=O); 89.9 (C≡CC=O); 72.9 (C≡CC=O); 52.5 ($OCH_3$); 29.6 ($C{\equiv}CCH_2$); 21.9, 18.3 (2 x $CH_2$); 13.4 ($CH_3$). **FTIR** (neat): 2237 (m, C≡C), 1718 (s, C=O). **MS** (low resolution, EI, 70ev) m/z: 140 (1.1%, $M^{+\cdot}$), 125 (44.6%, M-$CH_3$), 109 (100%, M-$OCH_3$).

**Reaction of ester 21 with $SmI_2$:** A solution of compound **21** (0.1375g, 0.9809 mmol), MeOH (0.12 mL, 3.0 mmol) and $SmI_2$ (14.7 mL, 0.1 M in THF, 1.47 mmol) in THF (30 mL) was stirred at -78 °C for 4 h and then warmed up to 0°C over 2 h 45 min. The reaction was worked up in the usual way and the crude product (0.1230g) was then analyzed. $^1$H NMR, GC and GC-MS indicated the presence of 3 major compounds: **21** (66%), **22a** (11%) and **22b** (12%). The $^1$H NMR of the crude mixture showed the expected signals for each of these compounds. **$^1$H NMR** ($CDCl_3$, 300 MHz) δ: 6.98 (dt, J = 7.0, 15.7 Hz, C*H*=CHCOOMe of **22b**); 6.24 (dt, J = 7.5, 11.5 Hz, C*H*=CHCOOMe of **22a**); 5.80 (m, CH=C*H*COOMe of both **22a** and **22b**); 3.78 (s, $OCH_3$ of **21**); 3.73, 3.71 (2 s, $OCH_3$ of **22a** and **22b**); 2.66 (m, $CH_2CH$=CH of **22a**); 2.34 (t, J = 7.0 Hz, $CH_2C{\equiv}C$ of **21**); 2.21 (m, $CH_2CH$=CH of **22b**); 1.22-1.64 (m, $CH_2$ of **22a**, **22b** and **21**); 0.93 (m, $CH_3$ of **22a**, **22b** and **21**). **$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ: 167.1, 166.8 (C=O of **22a** and **22b**); 154.2 (C=O of **21**), 150.9 (*C*H=CHCOOMe of **22a**); 149.7 (*C*H=CHCOOMe of **22b**); 120.8 (CH=*C*HCOOMe of **22b**); 119.1 (CH=*C*HCOOMe of **22a**); 89.8 (*C*≡CCOOMe of **21**); 72.8 (C≡*C*COOMe of **21**); 52.5 ($OCH_3$ of **21**); 51.3 ($OCH_3$ of **22b**); 50.9 ($OCH_3$ of **22a**); 31.1 ($C_5$ of **22a**); 31.8, 30.1 ($C_5$ and $C_4$ of **22b**); 29.5 (*C*$H_2C{\equiv}CCO$ of **21**); 28.7 ($C_4$ of **22a**); 22.3, 22.1 ($C_6$ of **22a** and **22b**); 21.9, 18.3 (2 x $CH_2$ of **21**); 13.8, 13.7 ($CH_3$ of **22a** and **22b**); 13.4 ($CH_3$ of **21**). The NMR signals attributed to **22a** and **22b** were in agreement with the spectral data reported for an alternate synthesis of these compounds[11b]. **GC – MS** (GC: $T_{int}$ = 50 °C for 1 min followed by gradient of 8 °C / min to a $T_{fin}$ = 100 °C which was held for 4 min; MS: low resolution, EI, 70 eV) m/z for **22a** and **22b**: $t_R$ = 2.43 min [143 (59.84%, $M^{+\cdot}$ + 1), 142 (11.07%, $M^{+\cdot}$), 113 (100%, M-$C_2H_5$), 81 (53.89%), 55 (34.22%)]; $t_R$ = 3.16 min [143 (86.93%, $M^{+\cdot}$ + 1), 142 (10.60%, $M^{+\cdot}$), 113 (38.16%,

M-$C_2H_5$), 81 (42.76%), 55 (99.65%), 39 (100%)]; m/z for **21** ($t_R$ = 3.73 min) [141 (100%, $M^{+\cdot}$+ 1), 140 (5.87%, $M^{+\cdot}$), 125 (30.69%, M-$CH_3$), 109 (64.16%, M-$OCH_3$)].

**Reaction of iodo-ester 23 with $SmI_2$:** A solution of **23** (0.2640 g, 0.992 mmol), MeOH (0.240 mL, 5.93 mmol) and $SmI_2$ (29.70mL, 0.1M, 2.97 mmol) in THF (20 mL) was stirred at -78 °C for 4 h and then warmed up to 0°C over 2 h. The reaction mixture was worked up and the crude residue was purified by flash column chromatography (5% EtOAc: hexanes, 3 x 22 cm silica gel) to allow for the separation of fractions **A, B** and **C** [$R_f$ = 0.31, 0.23, and 0.20 respectively, (TLC, silica, 5% EtOAc: hexanes)]. Further purification of fraction **A** by flash chromatography (3% EtOAc: hexanes, 2x17 cm silica gel) gave the *Z* ester **24a** [0.0390 g, 15% yield, $R_f$ = 0.23 (TLC, silica, 3% EtOAc:Hexanes)] as a colourless liquid. **$^1$H NMR** ($CDCl_3$, 300 MHz) δ: 6.22 (dt, J = 11.4, 7.6 Hz, 1H, *H*C=CHCO$_2$Et), 5.81 (d, J = 11.5 Hz, 1H, HC=C*H*CO$_2$Et), 3.72 (s, 3H, OC*H*$_3$), 3.22 (t, J = 6.9 Hz, 2H, C*H*$_2$I), 2.70 (m, 2H, C*H*$_2$CH=CH), 1.89 (m, 2H, C*H*$_2$), 1.58 (m, 2H, C*H*$_2$). **$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ: 166.7 (C=O); 149.6 (*C*H=CHCO$_2$Et); 119.9 (CH=*C*HCO$_2$Et); 51.1 (OCH$_3$); 33.0, 29.8, 27.8 (3 x CH$_2$); 6.5 (ICH$_2$). **FTIR** (neat): 1719 (s, C=O), 1647 (m, C=C). **MS** (low resolution, EI, 70 eV) m/z: 268 (29.5%, $M^{+\cdot}$) 237 (24.2%, M-$OCH_3$), 141 (100%, M-I), 81 (87.7%). **HRMS** calculated for $C_8H_{13}IO_2$ : 267.9962; found: 267.9965. Further purification of fraction **B** by flash chromatography (5% EtOAc; hexanes, 2 x 16 cm, silica) gave the saturated ester **25** [0.0173g, 7% yield, $R_f$ = 0.24 (TLC, silica, 5% EtOAc: Hexanes)]. **$^1$H NMR** ($CDCl_3$, 300 MHz) δ: 3.70 (s, 3H, $OCH_3$), 3.19 (t, 2H, J=7.0 Hz, $ICH_2$), 2.32 (t, 2H, J=7.5 Hz, C*H*$_2$CO$_2$Me) 1.83 (m, 2H, C*H*$_2$CH$_2$I), 1.65 (m, 2H, C*H*$_2$CH$_2$CO$_2$Et), 1.28-1.45 (m, 4H, C*H*$_2$C*H*$_2$).**$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ: 174.1 (C=O); 51.6 ($OCH_3$); 34.0, 33.3, 30.2, 28.1, 24.8 (5 x $CH_2$); 6.92 ($ICH_2$). **MS** (low resolution EI, 70ev) m/z: 270 (0.8%, $M^{+\cdot}$), 239 (28.8%, M-$OCH_3$), 143 (100%, M-I). Purification of fraction **C** by flash chromatography (10% $CH_2Cl_2$:$CCl_4$, 2.5x22 cm silica gel) allowed the separation of recovered starting material **23** [0.0528g, 20% yield, $R_f$ = 0.26 (TLC, silica, 10% $CH_2Cl_2$: $CCl_4$)] and the *E* ester **24b** [0.0563g, 21% yield, Rf = 0.19 (TLC, silica, 10%, $CH_2Cl_2$:$CCl_4$)]. **$^1$H NMR** ($CDCl_3$, 300 MHz) δ: 6.96 (dt, J=15.7, 6.9 Hz, 1H, C*H*=CHCO$_2$Me), 5.85 (dt, J=15.7, 1.5 Hz, 1H, CH=C*H*CO$_2$Me), 3.74 (s, 3H, OC*H*$_3$), 3.20 ( t, J = 6.9 Hz, 2H, IC*H*$_2$), 2.20 (m, 2H, C*H*$_2$CH=CH), 1.87 (m, 2H, C*H*$_2$CH$_2$I), 1.60 (m, 4H, 2 x $CH_2$). **$^{13}$C NMR** ($CDCl_3$, 75 MHz ) δ: 166.9 (C=O); 148.4 (*C*H=CHCOOMe); 121.5 (CH=*C*HCOOMe); 51.4 ($OCH_3$); 32.7, 31.0, 28.9 (3 x $CH_2$); 6.0 ($CH_2I$). **FTIR** ($CCl_4$): 1728 (s, C=O), 1660 (m, C=C). **MS** (low resolution, 70ev) m/z: 268 (26.4%, $M^{+\cdot}$), 237 (27.2%, M-$OCH_3$), 141 (93.2%, M-I), 81 (100%). **HRMS** calculated for $C_8H_{13}IO_2$ : 267.9962, found: 267.9966.

**N,N-diethyl 7-(tetrahydropyranyloxy)hept-2-ynamide 27:** A freshly prepared solution of LDA (18.5 mL, 1M in THF, 0.0185 mol) was added dropwise over 40 min to a solution of THP ether **15**[10a] (2.7921g, 0.01532 mol) in THF (38.5 mL) at -78°C under an argon atmosphere. The mixture was stirred at -78°C for 60 min before addition of N,N-diethylcarbamyl chloride (2.6 mL, 0.0199 mol). The reaction solution was then stirred at -78°C for another 75 min, warmed to 0°C over 60 min and then warmed up to room temperature overnight. The reaction mixture was quenched with brine (50 mL), diluted with $H_2O$ (40 mL), and the aqueous layer was extracted with $CH_2Cl_2$ (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated. Purification of the residue by flash chromatography (30% EtOAc:hexanes, 22 x 5 cm silica gel) allowed for the separation of recovered starting material **15** [0.7225 g, slightly impure sample by $^1$H NMR, $R_f$ = 0.77 (TLC, silica, 30% EtOAc : hexanes)] from the desired product **27** [3.2275g, yield 75%, $R_f$ = 0.18 (TLC, silica, 30% EtOAc : hexanes)]. **$^1$H NMR** ($CDCl_3$, 300 MHz) δ: 1.13 (t, J=7.2 Hz,

3H, $CH_3$), 1.21 (t, J=7.1 Hz, 3H, $CH_3$), 1.46-1.89 (m, 10H, $CH_2$ x 5), 2.40(m, 2H, C≡C$CH_2$), 3.36-3.92 [m, 8H, $OCH_2$ x 2; $NCH_2$ x 2; includes 2 quartets at 3.41 (J=7.16 Hz), and 3.57(J=7.13 Hz)], 4.58 (m, 1H, OCHO). **$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ: 154.1, 98.9, 91.5, 74.5, 66.8, 62.4, 43.5, 39.1, 30.7, 29.0, 25.5, 24.9, 19.6, 18.8, 14.3, 12.8. **FTIR** (neat): 2247 and 2221 (m, C≡C), 1623 (s, C=O). **MS** (low resolution, 70ev) m/z: 281 (0.9%, $M^{+\cdot}$), 85 (100%, M-$C_{11}H_{18}NO_2$). **HRMS** calculated for $C_{16}H_{27}O_3N$ : 281.1991, found : 281.1995.

**N,N-diethyl 7-hydroxyhept-2-ynamide 28**. To a 50 mL oven dried round bottom flask containing THP ether amide **27** (1.0572g, 3.78 mmol), pTSA·$H_2O$ (0.0715g, 0.376 mmol), was added MeOH (19 mL). The reaction solution was stirred under an argon atmosphere for 22 h. The mixture was quenched with brine (30 mL), diluted with $H_2O$ (20 mL), and the aqueous layer was extracted with EtOAc (3 x 70 mL). The combined organic layers were washed with brine (100 mL), dried over $MgSO_4$, filtered and concentrated. Purification of the residue by flash chromatography (75% EtOAc:hexanes, 3 x 15 cm silica gel) followed by Kugelrohr oven distillation (bp: 188°-193°C (oven), 2.7 mmHg) gave the desired product **28** [0.7176g, 97% yield, $R_f$ = 0.34 (TLC, silica, 75% EtOAc : hexanes)]. **$^1$H NMR** ($CDCl_3$, 300 MHz) δ: 1.13 (t, J=7.2 Hz, 3H, $CH_3$), 1.21 (t, J=7.2 Hz, 3H, $CH_3$), 1.48 (br, 1H, OH, exchanges with $D_2O$), 1.70 (m, 4H, $CH_2CH_2$), 2.41(m, 2H, C≡C$CH_2$), 3.41 (q, J=7.1 Hz, 2H, $NCH_2$), 3.57 (q, J=7.1 Hz, 2H, $NCH_2$), 3.69 ( m, 2H, C$H_2$OH). **$^{13}$C NMR** ($CDCl_3$, 75 MHz ) δ: 154.0, 91.5, 74.7, 62.1, 43.5, 39.1, 31.8, 24.2, 18.7, 14.3, 12.8. **FTIR** (neat): 3417 (s, OH), 2248 and 2223 (m, C≡C), 1610 (s, broad, C=O) $cm^{-1}$. **MS** (low resolution, EI, 70 ev) m/z: 197 (16.6%, $M^{+\cdot}$), 138 (59.6%, M-$C_3H_7O$), 125 (100%, M-$C_4H_{10}N$). **HRMS** calculated for $C_{11}H_{19}O_3N$ : 197.1416; found : 197.1408.

**N,N-diethyl 7-(mesyloxy)hept-2-ynamide 29** To a 50 mL round bottom flask containing hydroxy amide **28** (0.2992g, 1.52 mmol) was added $CH_2Cl_2$ (9.0 mL) and $Et_3N$ (0.375 mL, 2.69 mmol) under an argon atmosphere. The mixture was cooled to 0°C and $CH_3SO_2Cl$ (0.1775 mL, 2.29 mmol) was added dropwise over 3 min; the mixture was then warmed up to room temperature overnight. The reaction was quenched with MeOH (4 mL), and the mixture diluted with $H_2O$ (10 mL). The aqueous layer was extracted with $CH_2Cl_2$ (3 x 50 mL) and the combined organic layers washed with brine (100 mL), dried over $MgSO_4$, filtered and concentrated. Purification of the residue by flash chromatography (EtOAc, 3 x 24 cm silica gel) gave the product **29** [0.3954g, 95%, yield, $R_f$ = 0.66, (TLC, silica, EtOAc)]. **$^1$H NMR** ($CDCl_3$, 300 MHz) δ: 4.28 (t, J = 6.2 Hz, 2H, C$H_2$OMs), 3.57 (q, J = 7.1 Hz, 2H, NC$H_2$$CH_3$), 3.42 (q, J = 7.2 Hz, 2H, NC$H_2$$CH_3$), 3.03 (s, 3H, $OSO_2CH_3$), 2.44 (t, J = 6.9 Hz, 2H, C$H_2$C≡C), 1.91(m, 2H, C$H_2$-$CH_2$OMs), 1.75(m, 2H, C$H_2$$CH_2$C≡C), 1.22 (t, J=7.1 Hz, 3H, $NCH_2CH_3$), 1.14(t, J=7.2 Hz, 3H, $NCH_2CH_3$). **$^{13}$C NMR** ($CDCl_3$, 75 MHz ) δ: 153.8, 90.3, 75.1, 69.1, 43.5, 39.1, 37.4, 28.2, 23.9, 18.4, 14.3, 12.8, **FTIR** (neat): 2248 and 2222 (m, C≡C), 1620 (s, broad, C=O) $cm^{-1}$. **MS** (low resolution, EI, 70 ev) m/z: 275 (1.7%, $M^{+\cdot}$), 196 (70.8%, M-$CH_3SO_2$), 79 (100%, M-$C_{11}H_{18}NO$). **HRMS** calculated for : $C_{12}H_{21}NO_4S$ : 275.1191, found : 275.1201.

**N,N-diethyl 7-iodohept-2-ynamide 30** To a 50 mL round bottom flask containing mesyl amide **29** (0.8248g, 3.0 mmol) was added a solution of NaI (2.0407g, 0.0136 mol) in acetone (21 mL). The reaction soln was allowed to stir at room temperature overnight under anhydrous condition. The solvent was evaporated and the residue was diluted with a saturated aqueous solution of $Na_2S_2O_3$ (50 mL). The mixture was extracted with $CH_2Cl_2$ (3 x 100 mL) and the combined organic layers were washed with brine (100 mL), dried over $MgSO_4$, filtered and concentrated. Purification of the residue by flash chromatography (50% EtOAc : hexanes,

3 x 20 cm silica gel) allowed for the separation of recovered starting material **29** [0.0105g, 1.4 % yield of recovered starting material, $R_f$ = 0.14 (TLC, silica, 50% EtOAc : hexanes)] from the desired product **30** [0.8705g, yield 95%, $R_f$ = 0.57 (TLC, silica, 50% EtOAc : hexanes)] as a pale yellow oil. Attempts to distill this compound led to decomposition of the material . **$^1$H NMR** ($CDCl_3$, 300 MHz) δ: 3.57 (q, J=7.14 Hz, 2H, $NCH_2$), 3.42 (q, J=7.14 Hz, 2H, $NCH_2$), 3.22 (t, J=6.7, 2H, $ICH_2$), 2.42 (t, J=7.0 Hz, 2H, $CH_2C{\equiv}C$), 1.97 (m, 2H, $CH_2CH_2I$), 1.71 (m, 2H, $CH_2CH_2C{\equiv}C$), 1.22 (t, J=7.15 Hz, 3H, $NCH_2CH_3$), 1.14(t, J=7.15 Hz, 3H, $NCH_2CH_3$). **$^{13}$C NMR** ($CDCl_3$, 75 MHz ) δ: 153.9 (C=O); 90.6($C{\equiv}CCONEt_2$); 75.0($C{\equiv}CCONEt_2$); 43.5, 39.0 (2 x $NCH_2$); 32.3, 28.5, 17.9 (3 x $CH_2$); 14.3, 12.8 (2 x $NCH_2CH_3$), 5.6 ($ICH_2$). **FTIR** (neat): 2247, 2220 (m, C≡C), 1622 (s, broad, C=O) $cm^{-1}$. **MS** (low resolution EI, 70ev) m/z: 307 (0.5%, $M^{+\cdot}$), 235 (100%, M-$C_4H_{10}N$). **HRMS** calculated for $C_{11}H_{18}INO$ : 307.0435, found : 307.0434

**Alternate synthesis of 30[13].** To a solution of **28** (0.5693g, 2.886 mmol) in $CH_2Cl_2$ (21.0 mL) at room temperature was added sequentially, and in small portions, $Ph_3P$ (1.1082g, 4.22 mmol), imidazole (0.5744g, 8.437 mmol) and $I_2$ (1.1076g, 4.009 mmol). The reaction mixture was stirred at room temperature for 2 h and filtered over silica gel to remove the white precipitate that had formed during the reaction. The filter cake was washed with EtOAc and the filtrate was concentrated. The residue was dissolved in a minimum of EtOAc. Hexanes were added in order to precipitate the $Ph_3P{=}O$ and the solution was cooled to O°C, filtered and concentrated. Purification of the residue was accomplished by use of a chromatotron (30% EtOAc : hexanes, 4 mm plate, silica gel) to give product **30** [ 0.8347g, 94% yield, $R_f$ = 0.35 (TLC, silica gel, 30% EtOAc : hexanes) ]. This sample was identical to those samples prepared using the mesylation and halogenation sequence.

**N,N-diethyl methylenecyclopentanecarboxamide 31**: A solution of compound **30** (0.2807g, 0.9138 mmol), $SmI_2$ (27.6 mL, 0.1 M solution in THF, 2.76 mmol) and EtOD (0.320 mL, 5.44 mmol) in THF (18.5 mL) was refluxed for 10 h. The reaction mixture was worked up and the crude residue was purified by flash chromatography (5% EtoAc : $CH_2Cl_2$, 2.5 x 23 cm column of silica gel) to give compound **31** [0.1457 g, 88% yield, $R_f$ = 0.35 (TLC, silica, 5% EtoAc:$CH_2Cl_2$)] as a colourless oil (bp: 96.5 °C, Kugelrohr, 4.0 mmHg). **$^1$H NMR** ($CDCl_3$, 300 MHz) δ: 6.06 (m, 0.24 H, $CH{=}C$, deuterium incorporation = 76% as determined by $^1$H NMR), 3.38 [(2 overlapping quartets at δ 3.41 (J = 7.1 Hz) and δ 3.35 (J = 7.1 Hz)), 4H, $NCH_2$ x 2], 2.74 (m, 2H, $CH_2C{=}C$), 2.42 (m, 2H, $CH_2C{=}C$), 1.50 -1.81 (m, 4H, $CH_2CH_2$), 1.16 [(2 overlapping triplets at δ 1.18 (J = 7.1 Hz) and δ 1.14 (J = 7.1 Hz)), 6H, $NCH_2CH_3$ x 2]. **$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ: 167.0 (C=O); 162.6 ($C{=}CHCO$); 111.4 (C=$CHCO$); 42.4, 40.0 (2 x $NCH_2$); 35.7, 32.0 (2 x allylic $CH_2$); 26.6, 25.5 (2 x homoallylic $CH_2$); 14.6 , 13.3 (2 x $CH_3$). **FTIR** (Neat): 1656 (s, C=O), 1621 (s, C=C) $cm^{-1}$. **MS** (low resolution EI, 70ev) m/z: 182 [ 68.3%, $M^{\cdot+}$ for $C_{11}H_{18}DNO$ and (M+1) for $C_{11}H_{19}NO$; deuterium incorporation = 68% ], 181 (30.3%, $M^{+\cdot}$ for $C_{11}H_{19}NO$), 167 (7.3%, $C_{11}H_{18}DNO - CH_3$), 166 (3.1%, $C_{11}H_{19}NO - CH_3$), 153 (19.8%, $C_{11}H_{18}DNO - C_2H_5$), 152 (8.4%, $C_{11}H_{19}NO - C_2H_5$), 110 (100%,

$C_{11}H_{18}DNO$ - $C_4H_{10}N$), 109 (47.7%, $C_{11}H_{19}NO$ - $C_4H_{10}N$). **MS** (for a non-deuterated sample, low resolution EI, 70ev) m/z: 181 (55.7%, $M^{+\cdot}$), 166 (6.4%, M-$CH_3$), 152 (17.9%, M-$C_2H_5$), 109 (100%, M-$C_4H_{10}N$). **HRMS** calculated for $C_{11}H_{19}NO$: 181.1467, found: 181.1465.

**N,N-diethyl hept-2-ynamide 32:** A freshly prepared solution of LDA (16.5 mL, 1M in THF, 0.0165 mol) was added dropwise over 20 min to a cooled (-78°C) solution of hex-1-yne (1.233 g, 0.0150 mol) in THF (37.5 mL) under an argon atmosphere. The mixture was stirred at -78°C for 60 min before addition of N,N-diethylcarbamyl chloride (2.9 mL, 0.0222 mol). The reaction solution was then stirred at -78°C for another 75 min, warmed up to room temperature overnight, and quenched with brine (50 mL). The mixture was diluted with $H_2O$ (40 mL) and the aqueous layer was extracted with $CH_2Cl_2$ (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated. Purification of the residue by flash chromatography (30% EtOAc, hexanes, 22 x 5 cm silica gel) gave the desired product **32** [1.7109g, 63% yield, $R_f$ = 0.33 (TLC, silica, 30% EtOAc : hexanes)]. **$^1$H NMR** δ: 0.93 (t, J=7.2 Hz, 3H, $CH_3$), 1.13 (t, J=7.1 Hz, 3H, $NCH_2CH_3$), 1.21 (t, J=7.1 Hz, 3H, $NCH_2CH_3$), 1.38-1.63 (m, 4H, $CH_2CH_2$), 2.36 (t, J = 7.0 Hz, 2H, $C{\equiv}CCH_2$), 3.42 (q, J = 7.1 Hz, 2H, $NCH_2$), 3.57(q, J=7.1 Hz, 2H, $NCH_2$). **$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ: 154.2 (C=O); 91.8 ($C{\equiv}CC$=O); 74.4 ($C{\equiv}CC$=O); 43.4, 39.1 (2 x $NCH_2$); 29.9 ($C{\equiv}CCH_2$); 22.0, 18.6 (2 x $CH_2$); 14.3, 13.5 (2 x $NCH_2CH_3$); 12.8 ($CH_3$). **FTIR** (neat): 2249 and 2225 (m, C≡C), 1624 (s, broad C=O). **MS** (low resolution, EI, 70ev) m/z: 181 (17.7%, $M^{+\cdot}$), 166 (14.3%, M-$CH_3$), 152 (14.0%, M-$C_2H_5$), 138 (36.3%, M-$C_3H_7$), 109 (100%, M-$C_4H_{10}N$). These data were in agreement with those reported by Fananas and Hoberg for an alternate synthesis of this compound.[14]

**Reaction of amide 32 with $SmI_2$:** A solution of compound **32** (0.0935g, 0.5158 mmol) and $SmI_2$ (43.9 mL, 0.1 M in THF, 4.39 mmol) in THF (10 mL) was stirred for 51 h at room temperature. The crude product was purified by chromatography (47% EtOAc : hexanes) to allow for the partial separation of recovered **32** [0.0025g, 2.7% yield, $R_f$ = 0.64 (TLC, silica, 47% EtOAc : hexanes)] from a mixture of **33a**, **33b** and **34**. Two additional fractions were obtained; the first one was a mixture of **33a**, **34** and recovered **32** [0.0250g, $R_f$ = 0.56 (TLC, silica, 47% EtOAc : hexanes) which contained 0.0052g of **33a** (5.5% yield), 0.0185g of **34** (19.6% yield) and 0.0013g of recovered **32** (1.4% yield) as determined by $^1$H NMR and confirmed by GC-MS]. We were not able to obtain pure samples of compounds **33a** and **34** due to separation problems. The NMR spectra of the mixture was analyzed and the NMR signals which correspond to compounds **33a** and **34** are as follows: **$^1$H NMR** ($CDCl_3$, 300 MHz) δ: 5.98 (dt, J = 1.3, 11.6 Hz, $CH$=CHCONEt$_2$ of **33a**); 5.87 (dt, J = 7.1, 11.6 Hz, CH=$CH$CONEt$_2$ of **33a**); 3.34 (m, $NCH_2$ of both **33a** and **34**); 2.36 (m, $CH_2$CH=CH of **33a**); 2.27 (t, J = 7.7 Hz, $CH_2$CONEt$_2$ of **34**); 1.63 and 1.30 (2m, $CH_2$ of both **33a** and **34**), 1.14 (m, $NCH_2CH_3$ of both **33a** and **34**); 0.88 (m, $CH_3$ of both **33a** and **34**). **$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ: 172.3 (C=O of **34**); 167.1 (C=O of **33a**); 141.4 ($CH$=CHCONEt$_2$ of **33a**); 122.1 (CH=$CH$CONEt$_2$ of **33a**); 42.4 ($NCH_2$ of **33a**); 42.0, 40.0 (2 x

$NCH_2$ of **34**); 39.4 ($NCH_2$ of **33a**); 33.2 ($CH_2CONEt_2$ of **34**); 31.7 ($CH_2CH_2CONEt_2$ of **34**); 31.3 ($CH_2CH$=CH of **33a**); 28.9 (homoallylic $CH_2$ of **33a**); 29.2, 25.5, 22.5 (3 x $CH_2$ of **34**); 22.4 ($CH_2$ of **33a**); 14.4 ($NCH_2CH_3$ of **34**); 14.3 ($NCH_2CH_3$ of **33a**); 14.0 ($NCH_2CH_3$ of **34**); 13.9 ($NCH_2CH_3$ of **33a**); 13.1 ($CH_3$ of both **33a** and **34**). **GC – MS** (GC: $T_{int}$ = 100 °C for 1 min followed by gradient of 4 °C / min to a $T_{fin}$ = 125 °C which was held for 2 min; MS: low resolution, EI, 70 eV) m/z (for **33a** $t_R$ = 4.4 min): 184 (55.53%, $M^{+\cdot}$ + 1), 183 (21.05%, $M^{+\cdot}$), 154 (57.25%, M-$C_2H_5$), 126 (25.80%, M-$C_4H_9$), 55 (100%); m/z (for **34**, $t_R$ = 5.07 min): 186 (66.85%, $M^{+\cdot}$ + 1), 185 (8.04%, $M^{+\cdot}$ ), 115 (38.67%), 100 (68.38%, M-$C_6H_{13}$), 72 (31.78%, M-$C_6H_{13}CO$), 58 (100%). The other fraction was a mixture of 4 compounds: **33a**, **33b**, **34** and recovered **32** [0.0152g, $R_f$ = 0.50 (TLC, silica, 47% EtOAc : hexanes), which contained 0.0023g of **33a** (2.4% yield), 0.0018g of **33b** (1.9% yield), 0.0062g of **34** (6.5% yield) and recovered **32** 0.0049g (5.2% yield) as determined by $^1H$ NMR and confirmed by GC-MS]. It is important to mention that the $^1H$ and $^{13}C$ spectra were not obtained for a pure sample of **33b** due to separation problems. The NMR spectra of the mixture was analyzed and the NMR signals which were attributed to compound **33b** are as follows: **$^1H$ NMR** ($CDCl_3$, 300 MHz) δ: 6.91 (dt, J = 7.1, 15.1 Hz, C*H*=CHCONEt$_2$); 6.18 (dt, J = 1.5, 15.0 Hz, CH=C*H*CONEt$_2$); 3.40 (m, 2 x $NCH_2$); 2.21 (m, $CH_2$CH=CH); 1.06-1.50 (m, 2 x $CH_2$ and 2 x $NCH_2CH_3$); 0.90 (m, $CH_3$). **$^{13}C$ NMR** ($CDCl_3$, 75 MHz) δ: 165.9 (C=O); 146.2 (*C*H=CHCONEt$_2$); 120.3 (CH=*C*HCONEt$_2$); 42.1, 40.7 (2 x $NCH_2$); 32.2 ($CH_2$CH=CH); 30.5, 22.2 (2 x $CH_2$); 14.8, 13.8 (2 x $NCH_2CH_3$). **GC – MS** (GC: $T_{int}$ = 100 °C for 1 min followed by gradient of 4 °C / min to a $T_{fin}$ = 125 °C which was held for 2 min; MS: low resolution, EI, 70 eV) m/z ($t_R$ = 6.02 min): 184 (29.43%, $M^{+\cdot}$ + 1), 183 (3.60%, $M^{+\cdot}$), 126 (35.0%, M-$C_4H_9$), 111 (25.44%, M-$C_4H_{10}N$), 55 (100%).

**Reaction of iodo-amide 30 with $SmI_2$ in the presence of MeOH:** A solution of compound **30** (0.1841g, 0.5993 mmol), $SmI_2$ (18.0 mL, 0.1 M THF, 1.8 mmol) and MeOH (0.15 mL, 3.69 mmol) in THF (11.8 mL) was stired for 9.5 h at room temperature. The crude product was purified by chromatography using a Chromatotron (Harrison Research, 2 mm plate, silica, once using 25% EtOAc : hexanes and another time using 10% ether : $CH_2Cl_2$) to allow for the separation of four fractions. The first fraction contained an inseparable mixture of compound **31** [0.0211g, 19.5% yield, $R_f$ = 0.28 (TLC, silica, 25% EtOAc : hexanes)] and **32** (less than 1% yield as determined by $^1H$ NMR and GC). The second fraction contained recovered starting material **30** [0.0404g, 21.9% yield, $R_f$ = 0.43 (TLC, silica, 10% ether : $CH_2Cl_2$)] and the third fraction was compound **37b** [0.0103g, 5.6% yield, $R_f$ = 0.13 (TLC, silica, 25% EtOAc : hexanes); **$^1H$ NMR** ($CDCl_3$, 300 MHz) δ: 6.88 (dt, J = 15.0, 7.0 Hz, 1H, C*H*=CHCONEt$_2$), 6.21 (dt, J = 15.0, 1.5 Hz, 1H, CH=C*H*CONEt$_2$), 3.40 (m, 4H, $NCH_2$ x 2), 3.20 (t, J = 7.0 Hz, $ICH_2$), 2.26 (m, 2H, $CH_2$CH=CH), 1.87 (m, 2H, $CH_2$), 1.59 (m, 2H, $CH_2$), 1.17 (m, 6H, $CH_3$ x 2); **$^{13}C$ NMR** ($CDCl_3$, 75 MHz) δ: 165.7 (C=O); 144.9 (*C*H=CHCONEt$_2$); 121.1

CH=*C*HCONEt$_2$); 42.1, 40.8 (2 x NCH$_2$); 32.8, 31.2, 29.2 (3 x CH$_2$); 14.9, 13.2 (2 x NCH$_2$*C*H$_3$); 6.2 (ICH$_2$). **FTIR** (neat): 1660 (s, C=O), 1614 (s, C=C), 1379 (m). **MS** (low resolution, EI, 70 eV) m/z: 309 (21.5%, $M^{+\cdot}$), 237 (67.0%, M-$C_4H_{10}N$), 182(100%, M − I), 154 (22.7%, M-$C_2H_4I$), 126 (81.55, M-$C_4H_8I$); High resolution : calculated for $C_{11}H_{20}INO$ : 309.0591; found : 309.0589 ]. The fourth fraction contained 15.8 mg of a mixture of **37a** and **38** [$R_f$ = 0.32 (TLC, silica, 10% ether : $CH_2Cl_2$)] as a slightly impure sample. The yield of each compound was determined by $^1$H NMR (**37a:** 0.0131g, 7%; **38:** 0.0043 g , 2.3 %). **$^1$H NMR** ($CDCl_3$) δ: 6.03 (dt, J = 1.4, 11.5 Hz, C*H*=CHCONEt$_2$ of **37a**); 5.87 (dt, J = 7.3, 11.5 Hz, CH=C*H*CONEt$_2$ of **37a**); 3.34 (m, NCH$_2$ of both **37a** and **38**); 3.19 (m, ICH$_2$ of both **37a** and **38**); 2.41 (m, C*H*$_2$CH=CH of **37a**); 2.35 (t, J = 7.5 Hz, C*H*$_2$CONEt$_2$ of **38**); 1.84 (m), 1.65 (m), 1.54 (m), 1.39 (m) (CH$_2$ of both **37a** and **38**); 1.17 (m, NCH$_2$*C*H$_3$ of both **37a** and **38**). **$^{13}$C NMR** ($CDCl_3$, room temperature, 75 MHz) δ: 172.0(C=O of **38**); 166.8 (CH=CH*C*=O of **37a**); 140.7 (*C*H=CHCONEt$_2$ of **37a**); 122.7 (CH=*C*HCONEt$_2$ of **37a**); 42.4, 41.9, 40.0, 39.5 (NCH$_2$ of both **37a** and **38**); 33.3; 33.0; 32.9; 30.3; 29.9; 28.3; 28.0, 25.1 (4 x CH$_2$ for each of compounds **37a** and **38**); 14.4, 14.3, 13.1 (NCH$_2$*C*H$_3$ of both **37a** and **38**, 13.1 is a broad singlet); 6.8, 7.1 ( ICH$_2$ of both **37a** and **38**). **GC − MS** (GC: $T_{int}$ = 100 °C for 1 min followed by gradient of 8 °C / min to a $T_{fin}$ = 180 °C which was held for 4 min; MS: low resolution, EI, 70 eV) m/z (for **37a,** $t_R$ = 9.8 min): 310 (51.15%, $M^{+\cdot}$ + 1), 309 (15.24%, $M^{+\cdot}$), 237 (2.9%, M-$C_4H_{10}N$), 182 (100%, M − I), 154 (53.69%, M-$C_2H_4I$); m/z (for **38**, $t_R$ = 10.4 min): 313 (13.53%, $M^{+\cdot}$ + 2), 312 (4.26%, $M^{+\cdot}$ + 1), 184 (50.31%, M − I), 115 (40.70%, M-$C_5H_9I$), 100 (100%, M-$C_6H_{12}I$); **MS** (low resolution, CI, $NH_3$ carrier gas) m/z (for a mixture of **37a** and **38**): 312 [20.8%, ($M^{+\cdot}$ + 1) of **38** ], 311 (4.6%, $M^{+\cdot}$ of **38**), 310 [30.6%, ($M^{+\cdot}$ + 1) of **37a** ], 309 (21.8%, $M^{+\cdot}$ of **37a**); **MS** (low resolution, EI, 70ev) m/z (for a mixture of **37a** and **38**): 311 (2.5%, $M^{+\cdot}$ of **38**); 310 [2.1%, ($M^{+\cdot}$ + 1) of **37a** ], 309 (12.3%, $M^{+\cdot}$ of **37a**).

**Bis amide 35**: A solution of **30** (0.3070g, 0.9994 mmol) and $SmI_2$ (29.45 mL, 0.1 M solution in THF, 2.945 mmol) in THF (20 mL) was refluxed overnight and then quenched with $D_2O$. The reaction mixture was worked up and the crude residue was purified by flash chromatography (25% EtOAc : hexanes, 2.5 x 20 cm, silica gel) to allow for the separation of product **31** [0.0444g, 25% yield, $R_f$ = 0.26 (TLC, silica 25%, EtOAc: hexanes)] and **35** [0.0260g, 19% yield, slightly impure by $^1$H NMR, $R_f$ = 0.11 (TLC, silica, 25% EtOAc:hexanes )] as a colourless oil . Attempts to further purify **35** by Kugelrohr distillation led to decomposition of the material. **$^1$H NMR** ($CDCl_3$, 300 MHz) δ: 3.60 (q, J=7.1 Hz, 4H, NC*H*$_2$ x 2), 3.41 (q, J=7.1 Hz, 4H, NC*H*$_2$ x 2), 2.30 (m, 4H, allylic CH$_2$ x 2), 1.69 (m, 4H, homoallylic C*H*$_2$ x 2), 1.14 (multiplet, 12H, C*H*$_3$ x 4); **$^{13}$C NMR** ($CDCl_3$, 75 MHz) δ: 167.0(C=O), 148.0 (*C*=CCONEt$_2$), 126.8 (C=CCONEt$_2$), 42.5, 38.7 (2 x NCH$_2$), 30.8 (allylic CH$_2$), 26.0 (homoallylic CH$_2$), 14.1, 12.6 (2 x CH$_3$); **FTIR** ($CCl_4$): 1624

(s, broad, C=O, C=C) $cm^{-1}$. **MS** (low resolution EI, 70ev) m/z: 280 (18.8%, $M^{+\cdot}$), 208 (15.1%, M-$C_4H_{10}N$), 180(10.4%, M-$C_5H_{10}NO$), 100 (25.4%, M-$C_{11}H_{18}NO$, 72 (100%, M-$C_{12}H_{18}NO_2$); **HRMS** calculated for $C_{16}H_{28}N_2O_2$: 280.2151, found: 280.2145.

**Dimer 36:** HMPA (3.25 mL, 18.5 mmol) was added dropwise over 12 min to a solution of **30** (0.1558g, 0.5072 mmol) and $SmI_2$ (15.2 mL, 1.52 mmol) in THF (10 mL) at $0^oC$. Stirring was continued for another 3 min before the reaction was worked up. The crude product was purified by flash chromatography [ once using 60% EtOAc : hexanes and another time using 30% EtOAc : hexanes ] to allow the separation of very slightly impure samples (as determined by $^1H$ NMR) of the desired product **31** [ 0.0257g, 28% yield, $R_f$ = 0.59 (TLC, silica, 60% EtOAc : hexanes) ], the bis amide **35** [ 0.0029g, 4% yield, $R_f$ = 0.48 (TLC, silica, 60% EtOAc : hexanes) ] and the dimer **36** [ 0.0389g, 42.6% yield, $R_f$ = 0.20 (TLC, silica, 60% EtOAc : hexanes). **$^1H$ NMR** ($CDCl_3$) δ: 3.10 – 3.50 (broad poorly defined signal, $W_{1/2}$ = 88.5Hz, 8H, $NCH_2$ x 4), 1.95 – 2.73 (broad poorly defined multiplet containing signals at δ: 2.60, $W_{1/2}$ = 37.5 Hz, 1H; δ: 2.34, $W_{1/2}$ = 38.4 Hz, 2H; δ: 2.15, $W_{1/2}$ = 15.3 Hz, 5H; allylic $CH_2$ x 4) 1.65 (broad signal, $W_{1/2}$ = 24.0 Hz, 8H, homoallylic $CH_2$ x 4), 1.06 – 1.20 (m, 12H, $CH_3$ x 4); **$^1H$ NMR** (DMSO – $d_6$, 300 MHz, T = ambient) δ: 3.10 – 3.30 (broad m, 8H, $NCH_2$ x 4), 1.93 – 2.29 (broad signal, $W_{1/2}$= 27 Hz, 8H, allylic $CH_2$ x 4), 1.45 – 1.62 (broad signal, $W_{1/2}$ = 21.9 Hz, 8H, homoallylic $CH_2$ x 4), 0.91 – 1.12 (m, 12H, $CH_3$ x 4); **$^1H$ NMR** (DMSO – $d_6$, 300 MHz T = $128^oC$) δ: 3.20 – 3.40 (multiplet, sharper than the corresponding sigal at room temperature), 2.06 – 2.35 [broad multiplet containing signals at δ: 2.30 ($W_{1/2}$ = 13.2 Hz, 2H), δ: 2.19 ($W_{1/2}$ = 12.6 Hz, 2H) and δ: 2.15 ($W_{1/2}$ = 13.8 Hz, 4H); 4 x allylic $CH_2$], 1.53 – 1.68 (broad signal, $W_{1/2}$ = 19.8 Hz, 8H, homoallylic 4 x $CH_2$), 0.99 – 1.12 (m, 12H, 4 x $CH_3$); **$^{13}C$ NMR** ($CDCl_3$, room temperature, 75 MHz) δ: 171.8, 169.8 (2 x C=O); 146.7 (*C*=CCONEt$_2$); 132.4 and 132.3 (*C*=CCONEt$_2$ and C=*C*CONEt$_2$); 128.0 ( C=*C*CONEt$_2$); 43.2 ($NCH_2$); 41.9 (a small broad signal, $NCH_2$); 38.6 ($NCH_2$); 37.8 (a small broad signal, $NCH_2$); 31.7, 31.6, 29.3, 28.1 (4 x allylic $CH_2$); 29.7 (low broad signal, impurity); 26.1, 26.0, 22.7, 22.0 (4 x homoallylic $CH_2$); 14.4, 14.0 (a small broad signal), 12.8, 12.7 (a small broad signal) (4 x $CH_3$). **MS** (low resolution, EI, 70 ev) m/z: 360 (14.7%, $M^{+\cdot}$ ), 287 (32.7%), 260 (100%, M-CONEt$_2$); High resolution : calculated for $C_{22}H_{36}N_2O_2$ : 360.2777; found: 360.2763 ].

**Reaction of 30 with $SmI_2$ in THF-$d_8$:** A freshly prepared solution of $SmI_2$ [2.9 mL, ca. 0.1 M ( see reaction of **2** with $SmI_2$ in THF-$d_8$ for details regarding this preparation)] was transferred via canula to a THF-$d_8$ solution of **30** (0.0307 g, 0.100 mmol, in 2.0 mL) and the solution was stirred at reflux until all of the $SmI_2$ was consumed (35 min). The reaction mixture was worked up and the reaction products separated using a Chromatotron (Harrison Research, 1 mm silica plate, 1:3 EtOAc:hexanes). We isolated some starting material

(0.0155g, 37.5 % recovery) along with the expected compound **31** [0.0058 g, 32 % yield, 7% incorporation as determined by MS analysis (average M/M+1 ratio = 50.2/10.2). $^1$H NMR analysis is consistent with this level of deuterium incorporation at the vinylic position of **31**.

## References and Notes


(1) For some recent reviews regarding this reagent see: a) Curran, D. P.; Fevig, T. L.; Jasperse, C. P.; Totleben, M. J. *Synlett* **1992**, 943-961; b) Molander, G.A. *Chem Rev.* **1992**, *92*, 29-68; c) Soderquist, J. A. *Aldrichimica Acta* **1991**, *24* , 15-23; d) Kagan, H. B. *New J. Chem.* **1990**, *14*, 453-460; e) Molander, G. A. In *The Chemistry of the Metal - Carbon Bond* , Volume 5; Hartley, F. R., Ed.; Wiley: New York, 1989; p319.; f) Kagan, H. B. and Namy, J. L. *Tetrahedron* **1986**, *42* , 6573-6614.

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(5) The reactions of compound **9** were not reported in our earlier communication but were described in the M.Sc. thesis of D. Larouche (Université du Québec à Montréal, **1993**).

(6) The $SmI_2$ reduction of alkyl tosylates to alkanes is believed to involve transformation of the tosylate to the corresponding iodide (see reference 2b)

(7) This is consistent with: a) the report that **14** undergoes an atom transfer cyclization reaction, to give **12**, when subjected to photolytic ditin reaction conditions (see Curran, D. P.; Chen, M.-H.; Kim, D. *J. Amer. Chem. Soc.* **1989**, *111*, 6265.) and b) with a report describing a zinc-induced cyclization of **9** to give **7** which involved a cyclized vinylic radical intermediate (see Crandall, J.K. and Ayers, T.A. *Organometallics*, **1992**, *11*, 473-477).

(8) The THF-$d_8$ experiments were done at the suggestion of the referees; unfortunately the high cost of this solvent prohibited us from carrying out these mechanistic experiments on all of our substrates.

(9) We ran one experiment with $SmI_2$ and **2** in THF-$d_8$/DMPU at room temperature. In this instance the reaction was incomplete and the reaction mixture was complex; we were unable to obtain a sufficiently pure sample of **3** for deuterium incorporation analysis.

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(14) Compound **32** is a known compound and was prepared from commercially available hex-1-yne. Our $^1H$ and $^{13}C$ NMR data match those reported by Fananas, F. J. and Hoberg, H. *J. Organomet. Chem.* **1984**, *277*, 135-142.

(15) Similar results were obtained when EtOD was used as a co-solvent at room temperature.

(16) Compounds **4**, **8**, and **13** were subjected to treatment with $SmI_2$ under reflux conditions overnight (see general experimental conditions for reactions run with commercial solutions of $SmI_2$). The reaction mixtures were worked up in the usual way and the crude residue was analyzed by $^1H$ NMR. We observed no significant reaction of these simple alkynes under these conditions.

(17) We cannot exclude the possibility of **40** being formed via an anionic cyclization route, as illustrated in figure 3.

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(25) See instruction manual for Harrison Research model 7924T Chromatotron.

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