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Iodocarbocyclization of α-iodocycloalkanones bearing an allenyl side chain: synthesis of spirocyclic cycloalkanones

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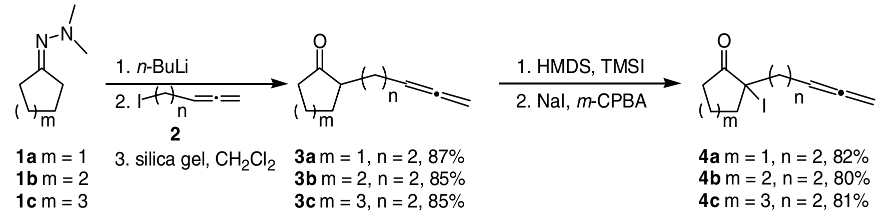
Abstract—$AlCl_3$/ICl-mediated iodocarbocyclizations of α-iodocycloalkanones bearing an allenyl side chain are described. Treatment of iodocycloalkanones **4a**–**i** with $AlCl_3$/ICl gave spirocyclic cycloalkanones **5a**–**i** and **6a**–**i** as a mixture of products.

Ionic iodocarbocyclization reactions involving intramolecular attack of a carbon nucleophile at a double bond activated by an electrophilic iodinating reagent are efficient processes to construct carbocyclic frameworks. Iodocarbocyclization involving 1,3-dicarbonyl compounds, such as 4-alkenyl and 4-alkynyl malonates, was extensively studied by Taguchi and co-workers.[1] The related ionic selenocarbocyclization of α-seleno ketones was investigated by Toru's group.[2] Free-radical atom-transfer cyclization of iodo substrates mediated with hexamethylditin[3] or other reagents[4] has also been reported. We have recently described the $AlCl_3$/ICl-mediated[5] and photo-induced[6] iodocarbocyclization of α-iodocycloalkanones. As an extension, we have investigated $AlCl_3$/ICl-mediated iodocarbocyclization of α-iodocycloalkanones bearing an allenyl side chain. Here, we report our preliminary results.

α-Iodocycloalkanones bearing an allenyl side chain were prepared according to conventional methods (Scheme 1). Deprotonation of hydrazones **1a**–**c** with *n*-BuLi followed by alkylation with allenylalkyl iodides **2** and hydrolysis gave cycloalkanones **3a**–**c**. Treatment of **3a**–**c** with chlorotrimethylsilane and hexamethyldisilazane gave the corresponding trimethylsilylenol ethers. Iodination of these TMS-enol ethers with a mixture of NaI and *m*-CPBA[7] afforded α-iodocycloalkanones **4a**–**c**. Preparation of compounds **4d**–**i** in Scheme 2 and Table 1 according to the same method was reported in our previous paper.[6]

Treatment of iodocycloalkanones **4a**–**f** with $AlCl_3$/ICl in CH_2Cl_2 at 0 °C gave **5a**–**f** as minor products and **6a**–**f** as major products (Scheme 2 and Table 1).[8] When the reactions were performed at −78 °C, compounds **5a**–**f** were obtained predominantly, and compounds **6a**–**f** were formed as minor products. For the formation of the seven-member-ring products, treatment of **4g**–**i** with $AlCl_3$/ICl in CH_2Cl_2 at both −78 °C and 0 °C gave compounds **5g**–**i** as major products and compounds **6g**–**i** as



Scheme 1.

Keywords: Iodocarbocyclization; α-Iodocycloalkanones; Spirocyclic cycloalkanones.

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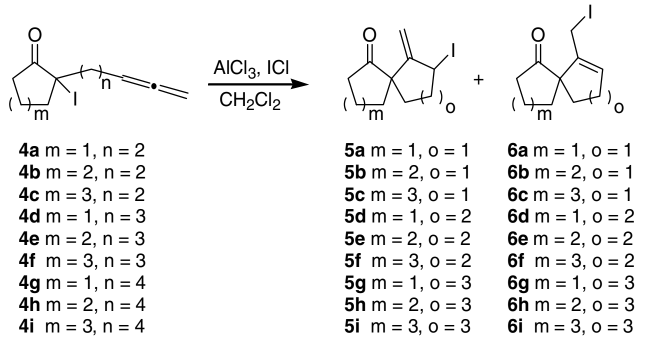
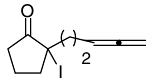
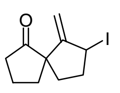
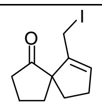
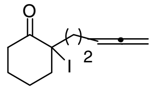
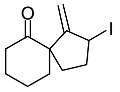
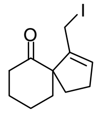
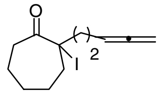
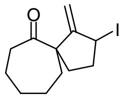
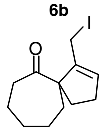
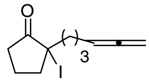
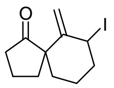
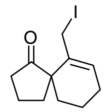
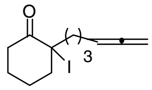
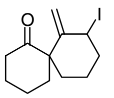
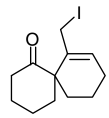
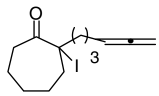
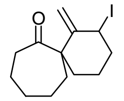
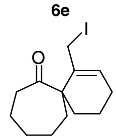
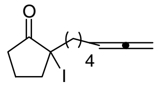
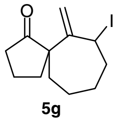
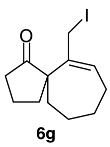
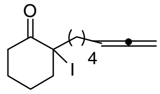
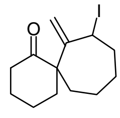
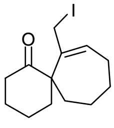
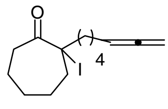
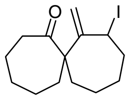
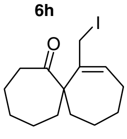


Scheme 2.

minor products. When the reactions were carried out at 30 °C, compounds **5g–i** were formed as minor products and compounds **6g–i** were obtained as major products (Table 2).

To rationalize these results, a plausible reaction mechanism shown in Scheme 3 was proposed. Upon treatment with $AlCl_3$, the iodoketone moiety in **4d** became transformed into dichloroaluminum enolate via intermediate complex **7**. During this reaction, ICl was generated and reacted with the allenyl group. At this point, addition of one extra equivalent of ICl increased the yield of the products. At −78 °C (entries 1–9) and 0 °C (entries

Table 1. Iodocarbocyclizations of α-iodocycloalkanones at 0 and −78 °C

Entry	α-Iodo cycloalkanones	Products	Yields at 0 °C (**5**:**6**)[a,b]	Yields at −78 °C (**5**:**6**)[a,b]
1	 **4a**	 **5a** +  **6a**	83% (1:6)	85% (3:1)
2	 **4b**	 **5b** +  **6b**	81% (1:7)	84% (4:1)
3	 **4c**	 **5c** +  **6c**	85% (1:9)	87% (3:1)
4	 **4d**	 **5d** +  **6d**	91% (1:8)	94% (5:1)
5	 **4e**	 **5e** +  **6e**	91% (1:8)	92% (6:1)
6	 **4f**	 **5f** +  **6f**	96% (1:9)	93% (6:1)
7	 **4g**	 **5g** +  **6g**	72% (2:1)	74% (6:1)
8	 **4h**	 **5h** +  **6h**	71% (3:1)	75% (6:1)
9	 **4i**	 **5i** +  **6i**	75% (2:1)	73% (5:1)

[a] Direct addition of ICl to **4a–i** at the double bonds of the allenyl side chains also occurred to give some trace amount (3–5%) of side products.
[b] Ratio of the products was determined from the ^1H NMR spectra of products.