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A NEW METHOD FOR GENERATION AND INTRAMOLECULAR DIELS-ALDER REACTION OF *N*-ACYL AND *N*-ALKOXYCARBONYL-1-AZA-1,3-BUTADIENES. A ONE-POT SYNTHESIS OF 1,7,8,8a-TETRAHYDRO-3(2*H*)-INDOLIZINONES AND 1,2,3,8,9,9a-HEXAHYDRO-4(4*H*)-QUINOLIZINONES FROM α,β-UNSATURATED ALDEHYDES

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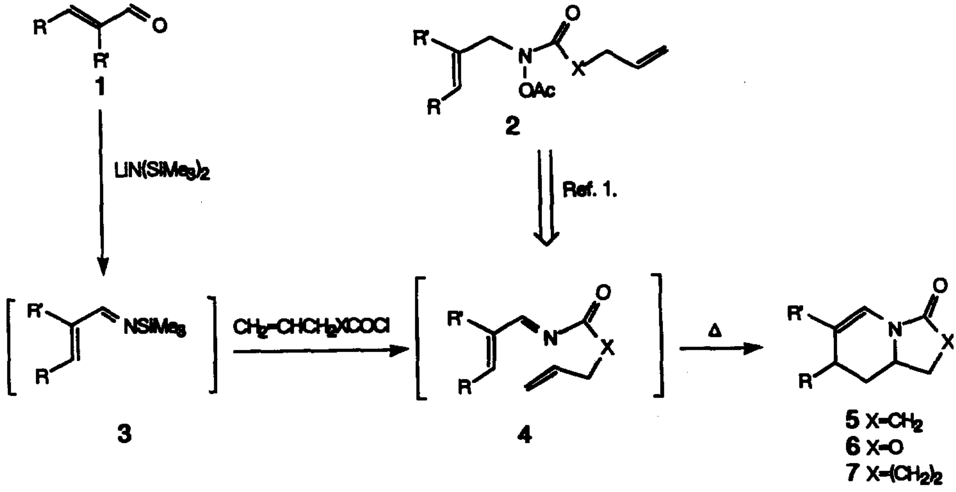
A one-pot transformation, made up of i) generation of *N*-trimethylsilylaldimines from α,β-unsaturated aldehyde, ii) exchange of the silyl group by acyl and oxycarbonyl groups, and iii) intramolecular Diels-Alder reaction of the resulting ψ',ω'-unsaturated *N*-acyl- and a related *N*-oxycarbonyl-1-aza-1,3-butadienes in boiling xylene, gave 1,7,8,8a-tetrahydro-3(2*H*)-indolizinones (5), the 2-oxa derivatives of 5, and 1,2,3,8,9,9a-hexahydro-4(4*H*)-quinolizinones in practical yields.

Intramolecular Diels-Alder reaction of *N*-acyl derivatives of 1-aza-1,3-butadiene (4) is a quite useful method to prepare nitrogen containing heterocyclic compounds, such as 1,7,8,8a-tetrahydro-3(2*H*)-indolizinones (5), the 2-oxa derivatives of 5 (6), and 1,2,3,8,9,9a-hexahydro-4(4*H*)-quinolizinones (7), and also indolizidine and quinolizidine alkaloids.[1] The only general method for preparation of 4 was the flash vacuum pyrolysis (FVP) of *N*-acyl-*O*-acetyl derivatives of *N*-allylhydroxylamines (2).[1,2] We now report a one-pot method for generation



and cycloaddition of *N*-acyl-1-aza-1,3-butadienes **4** starting from commercially available α,β-unsaturated aldehydes (**1**) via the corresponding *N*-trimethylsilyl-1-aza-1,3-butadienes (**3**).

The FVP for generation and cycloaddition of **4** have been carried out at approximately 650°C.[1] If we can generate **4** under more mild conditions, the synthetic utility of the intramolecular Diels-Alder reaction should be increased.[2] On the other hand, acylation and alkoxycarbonylation of *N*-trimethylsilylbenzaldimine proceed by treatment with acyl chlorides and alkyl chlorocarbonates, respectively, with removal of chlorotrimethylsilane.[3] If the silyl group of **3** can be replaced by a suitable acyl group, we can attempt intramolecular Diels-Alder reaction of the resulting **4** under mild conditions. Nonenolizable *N*-trimethylsilylaldimines are generated in excellent yields from nonenolizable aldehydes and lithium hexamethyldisilazide at low temperature.[4,5] This method seemed to be useful to prepare **3** from nonenolizable α,β-unsaturated aldehydes. Since synthetic intermediates **3** and **4** were unstable, we designed a one-pot synthesis of the nitrogen containing heterocyclic compounds (**5**, **6**, and **7**) from α,β-unsaturated aldehydes (**1**). The results are summarized in Table 1.[6] The following is the general procedure.

To a solution of lithium hexamethyldisilazide (1.2 mmol) in THF (2 ml) at 0°C under an argon atmosphere was added acrolein (**1a**, 1.0 mmol). The mixture was allowed to warm to room temperature and stirred for 1 h. Chlorotrimethylsilane (1.2 mmol) was added and the mixture was stirred for an additional hour to generate the *N*-trimethylsilylaldimine completely. To the resulting solution was added at 0°C allyl chlorocarbonate (**9**, 1.2 mmol). The solution was allowed to warm to room temperature, stirred for 1 h, and then diluted with xylene (20 ml). The xylene solution was heated under reflux for 20 h. Chromatography of the solution on silica gel (20 g) eluted with hexane-triethylamine (99 : 1) to remove xylene and then with hexane-ethyl acetate-triethylamine (99 : 20 : 1) gave the heterocyclic compound (**6a**)[1b] as a colorless oil in 53% yield.

Table 1 shows that i) *N*-trimethylsilyl-1-aza-1,3-butadiene itself[1a] and its 2-methyl derivative can be generated in reasonable yields from α,β-unsaturated aldehydes **1a** and **1c**, respectively, by treatment with lithium hexamethyldisilazide, ii) acylation and allyloxycarbonylation of *N*-trimethylsilyl-1-aza-1,3-butadienes proceed smoothly by treatment with acyl chlorides **8** and **10** and allyl chlorocarbonate (**9**), and iii) intramolecular Diels-Alder reactions of *N*-acyl- and *N*-alkoxycarbonyl-1-aza-1,3-butadienes with inverse electron demand can be carried out by simply heating under reflux in xylene.

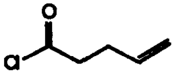
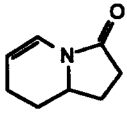
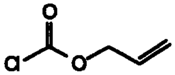
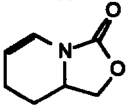
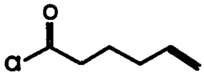
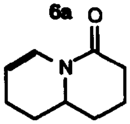
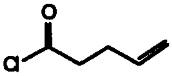
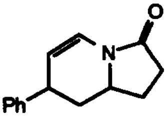
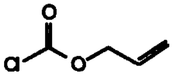
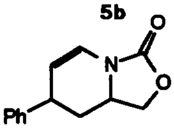
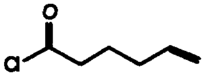
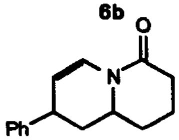
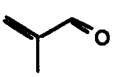
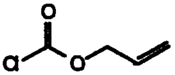
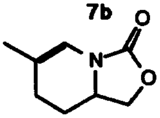
The stereostructures of the heterocyclic compounds were determined on the basis of their ^{1}H-NMR spectra. The large $J_{7,8\text{-endo}}$ value (12.0 Hz) of **6b-endo** indicates that the conformation of 7-H, 7-C, 8-C, 8-endo-H is almost antiperiplaner. The large value of the allylic coupling ($J_{5,7}$=2.5 Hz) of **6b-endo** also suggests the presence of the pseudoaxial 7-H.[6] The structures of **5b-exo** and **-endo** and **7b-exo** were confirmed similarly.

Preferential formation of the exo addition products is consistent with that observed in the FVP to give 7-methyl derivative of **5a**.[1b]

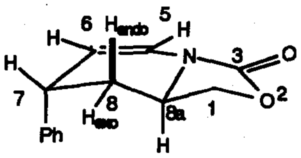
Attempts to isolate *N*-acyl- and *N*-allyloxycarbonyl-1-aza-1,3-butadienes under nonaqueous conditions were all unsuccessful. The intramolecular Diels-Alder reaction leading to **6b** did not proceed in boiling THF and benzene. In boiling toluene, the cycloaddition proceeded to give **6b** in 57-60% yields.

In conclusion, we have developed a practical method to prepare 1,7,8,8a-tetrahydro-3(2*H*)-indolizinones **5**, the 2-oxa derivatives of **5** (**6**), and 1,2,3,8,9,9a-hexahydro-4*H*-quinolizin-4-ones **7**, in one pot from commercially available reagents, α,β-unsaturated aldehydes, lithium hexamethyldisilazide, ψ,ω-unsaturated carboxylic acid chlorides, and allyl chlorocarbonate.

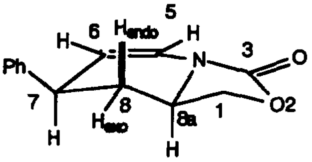
Table 1 One-pot synthesis of nitrogen containing heterocyclic compounds starting from α,β-unsaturated aldehydes via *N*-acyl- and *N*-oxycarbonyl-1-aza-1,3-butadienes [a]

aldehyde	acyl chloride/ chlorocarbonate	product	yield /% (endo/exo)
 1a	 8	 5a	38
 1a	 9	 6a	53
 1a	 10	 7a	57
 1b	 8	 5b	45 (12:1)
 1b	 9	 6b	65 (7.7:1)
 1b	 10	 7b	46 (exo)
 1c	 9	 6c	44

[a] The exo/endo ratios were determined on the basis of the ^{1}H-NMR spectra. Compound **5b-exo** was isolated by silica-gel chromatography. Compounds **6b-exo** and **-endo** were isolated by HPLC using a LiChrosorb® Si 60 column.



6b-exo



6b-endo

References and Notes

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(2) Preparation and cycloaddition of N-acyl-α-cyano-1-aza-1,3-butadiene, see: M. Teng and F. W. Fowler, *Tetrahedron Lett.*, 1989, **30**, 2481.

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(6) All new compounds, except **5b-endo**, gave satisfactory spectral and high-resolution mass data.

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