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Intramolecular (3 + 2) Cycloadditions

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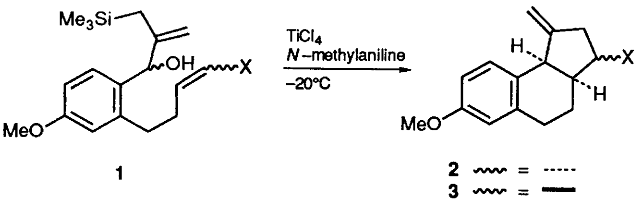
1-(1-Hydroxy-2-trimethylsilylmethylprop-2-enyl)-2-(4-methoxybut-3-enyl)-4-methoxybenzene, prepared by a short synthesis, underwent (3 + 2) cycloaddition to form predominantly the *cis*-fused tricycle 3,7-dimethoxy-1-methylene-2,3,3a,4,5,9b-hexhydro-1*H*-benz[*e*]indene upon treatment with $TiCl_4$ or triflic anhydride.

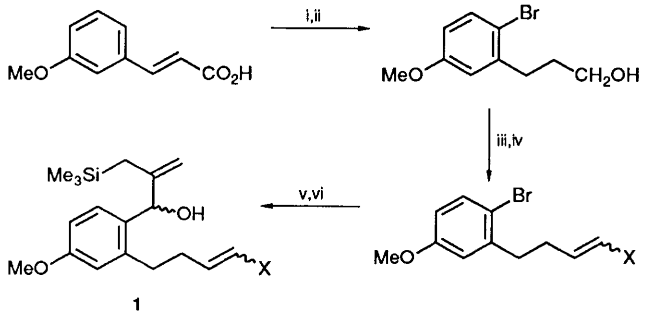
There are numerous reported intermolecular (3 + 2) cycloadditions involving allyl cations,[1] but only a small number of examples that involve the corresponding intramolecular process.[2] We have investigated the transformation shown in Scheme 1, and can report that it is both reasonably efficient and stereoselective.



Group X	Ratio Z:*E* in **1**	Yield (%)	Ratio **2**:**3**
OMe	1:3	45–85	3–5:1
OCH_2Ph	3:7	30	5:1
SMe	2:3	40–50	only **2**

Scheme 1

The various substrates **1** for the cycloadditions were prepared by the route shown in Scheme 2, and these were then treated with $TiCl_4$ in the presence of *N*-methylaniline in dichloromethane at −20 °C, or with triflic anhydride in dichloromethane at −78 °C.† Careful examination of the ^1H NMR spectra (coupling and NOE data), revealed that in each instance the major product was the *cis*-fused cycloadduct with a *syn*-alkoxy or thioalkoxy group **2**. Small amounts of the alternative *anti*-product **3** were also obtained. Extensive investigation of the cycloaddition with **1a** (up to a 1 g scale), showed that the ratio of **2a**:**3a** was apparently independent of the stereochemical composition of the enol ethers **1a** (*trans*:*cis* was varied from 1:0 to 1:1). This is probably a reflection of the relative stabilities of the final products arising from a common intermediate **4**. Confirmation of the all-*syn* stereochemistry of **2a** was obtained through an X-ray crystallographic study on the ketone **5** (*vide infra*). The ORTEP representation is shown in Fig. 1.[3]



Scheme 2 *Reagents and conditions:* i, $LiAlH_4$ (65–75%); ii, bromine (70%); iii, pyridinium chlorochromate (80–90%); iv, $Ph_3P{=}CHX$ (30–75%) (X = OMe, SMe, OCH_2Ph); v, BuLi then DMF (75%); vi, 3-trimethylsilyl-2-bromomagnesiopropene (70–95%)

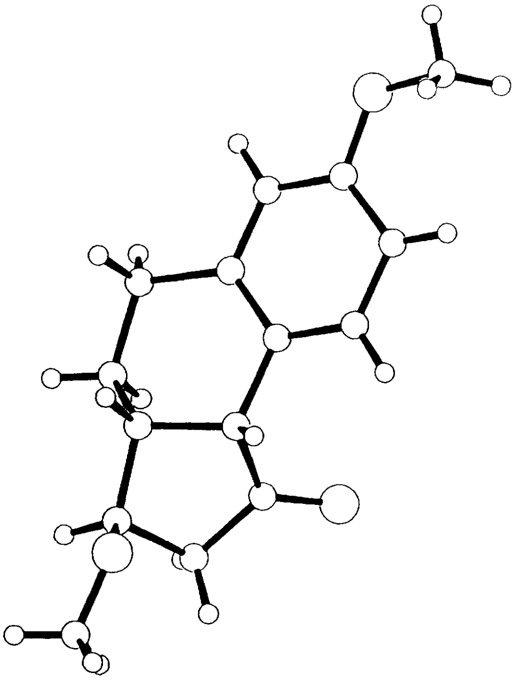


Fig. 1

The tricycles **2** are potentially useful intermediates for the construction of estrogens and benzophenanthridine alkaloids, and some preliminary transformations of **2a** have been investigated. Ozonolysis yielded the ketone **5** (55%), which was converted into the oxime **6** (70%). Attempted Beckmann rearrangement using a range of reagents[4] resulted in fragmentation and obtention of the nitrile **7** (75%). Finally, reaction of **5** with BBr_3 in dichloromethane at −10 °C, followed by

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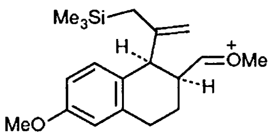
† *Typical experimental procedure. N*-Methylaniline (2 equiv.) was added to titanium tetrachloride (1.8 equiv. of a 1 M solution in dichloromethane) in dry dichloromethane at 0 °C. After 0.5 h the solution was cooled to −20 °C, and the enol ether (or thioether) **1** (1 equiv.) in dichloromethane was added, and the reaction mixture stirred at the same temperature for 1 h. Ether was added, followed by 1M HCl, the organic layer was collected and the products purified by flash chromatography.



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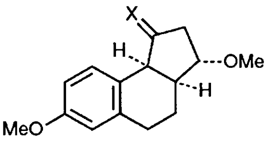
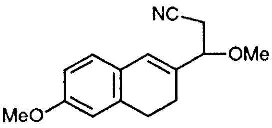


2a X = CH_2
5 X = O
6 X = NOH



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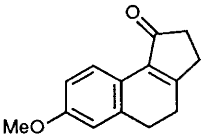

8

treatment with an ethanolic solution of silver nitrate,[5] yielded the enone **8**. This should allow access to the *trans*-fused tricycle. Further experiments to establish the synthetic utility of the tricycles **2** are underway.

Acknowledgements

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3 W. thank Dr. M. G. B. Drew for these X-ray studies which will be reported in detail in our full paper.

4 These reagents included: i, PCl_5, $CHCl_3$ (−20 °C); ii, $SOCl_2$, CCl_4 (0 °C); iii, trimethylsilyl polyphosphate, CH_2Cl_2 (RT); iv, tosyl chloride, pyridine (−20 °C); and v, *hν* (254 nm, 12 W low-pressure lamp), MeOH.

5 J. Kueh, M. Meller, and G. Pattenden, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1052.

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