Ag^+ Induced Cycloaddition of α-Bromoacetone *O*-Methyloxime to Olefinic Double Bonds

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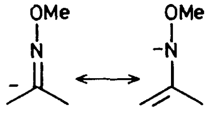
The title reaction, which proceeds *via* the intermediacy of an *N*-alkoxyaza-allyl cation (**2**), was investigated.

Although a variety of synthetic reactions using the *N*-alkoxyaza-allyl anion (**1**) have been reported in the literature,[1] the properties of its cationic analogue (**2**) have not been described. Recently we presented the first example of an Ag^+ induced aromatic substitution reaction with α-bromoacetone *O*-methyloxime (**4**), assuming that the masked α-acyl cation (**2**) was the electrophilic intermediate in the C–C bond formation to give (**5**) starting from activated systems like (**3**).[2]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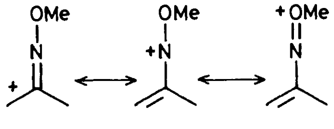
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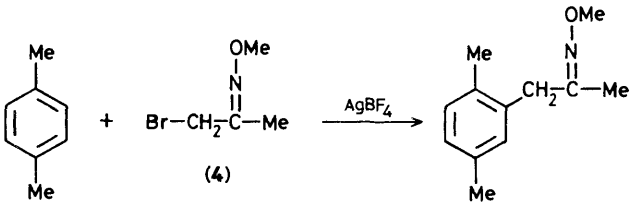
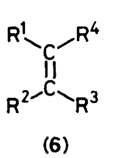

(3) **(4)** **(5)**

We now report on the synthetic utility of the positively charged species (**2**) as a reaction partner in the synthesis of heterocycles. We have examined the reaction of (**2**) with several representative alkenes, (**6a**—**g**), in the Ag^+ induced cycloaddition of (**4**) to the olefinic double bonds. This resulted in the formation of pyrrolidine derivatives (**7a**—**g**), isolated as their CN^- addition products (**8a**—**g**).

The procedure was as follows. Addition of (**4**) (10 mmol) in dry $ClCH_2CH_2Cl$ (20 ml) to a solution of $AgBF_4$ (10 mmol) and the alkene, (**6a**—**g**), (4 mmol) in $ClCH_2CH_2Cl$ (20 ml) at 25 °C was followed by efficient stirring in the dark for 18 h and then workup with 10% $KCN–H_2O$ solution. The products were isolated by chromatography on SiO_2 and characterized by n.m.r. and i.r. spectroscopy.

In the case of symmetric simple alkenes such as cyclohexene (**6a**) and 1,2-dimethylcyclohexene (**6b**) only cycloaddition products were formed. As expected, a 1 : 1 (h.p.l.c.) mixture of the corresponding nitriles was isolated after workup in 76 and 68% yield respectively. These were shown to be C-2 stereoisomers by transforming each of the corresponding nitriles to the *N*-methoxyiminium salts (**7a**) and (**7b**) respectively. Stereoselective cycloaddition was also observed with *cis* and *trans* stilbene, yielding the corresponding 3,4-*cis* and 3,4-*trans* pyrrolidine derivatives (**8c**) (57%) and (**8d**) (68%) as reaction products.†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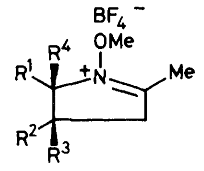
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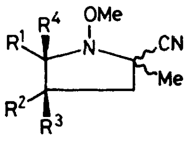
(8)

	R^1	R^2	R^3	R^4
a;	$-[CH_2]_4-$		H	H
b;	$-[CH_2]_4-$		Me	Me
c;	Ph	Ph	H	H
d;	Ph	H	Ph	H
e;	Ph	H	H	H
f;	$-[CH_2]_4-$		H	Me
g;	$-[CH_2]_4-$		$-[CH_2]_3-O-$	

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† The *cis* and *trans* relation of the phenyl groups in nitriles (**8c**) and (**8d**) was elucidated on the basis of the coupling constants of the C-5 proton in the ^1H n.m.r. spectrum ($CDCl_3$), *e.g.*: in (**8c**) this proton resonates in one isomer at δ 4.71 (*J* 1.2 Hz) and in the other at 4.60 (*J* 1.5 Hz) while in (**8d**) it was found that in one isomer it resonates at 4.17 (*J* 10.2 Hz) and in the other at 3.91 (*J* 8.5 Hz).

Asymmetrically substituted alkenes were also found to react with **(4)** under the same conditions: reaction of styrene **(6e)** afforded, after workup, the nitrile mixture **(8e)** (73%), 1-methylcyclohexene **(6f)** afforded **(8f)**, and the bicyclic enol ether **(6g)** gave the propellane **(8g)** in 72% yield. However, attempts to react methyl acrylate or cyclohexen-3-one with **(4)** under these conditions were abortive and the alkenes were recovered unchanged. We established in competition experiments that the relative Ag^+ induced cycloaddition rates of the substituted alkenes **(6g)**, **(6b)**, **(6f)**, and **(6a)** with **(4)** were 14 : 7 : 3 : 1 respectively.

Although the cycloaddition reaction was highly regio- and stereo-selective, byproduct analyses showed that competing aromatic and double bond substitution reactions occur as well. Fortunately, aromatic substitution products from *cis* and *trans* stilbene were isolated only in 12 and 14% yields and the double bond substitution product was formed in the reaction with 1-methylcyclohexene in only 8% yield.

An explanation for the stereo- and regio-selectivity observed in this reaction is that the C–C and C–N bonds are formed successively in different stages of the cycloaddition reaction pathway, each preferring a situation where the more substituted $>C^{\delta+}-$ is involved. However, the C–N bond is formed faster than rotation around the C-1–C-2 bond occurs.[3]

Received, 2nd July 1984; Com. 938

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