A Novel Route to Arylacetones *via* a Masked α-Acylcarbonium Intermediate

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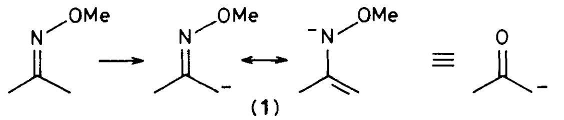
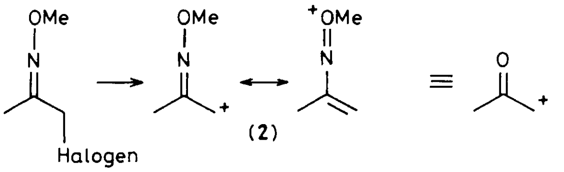
The Ag^+ induced aromatic substitution reaction of bromoacetone *O*-methyloxime is described.

Oxime ethers can be efficiently metallated at the α-carbon atoms and the derived enolate equivalents (**1**) can then participate in a variety of useful carbon–carbon bond-forming reactions.[1] The α-carbon atom might also support a positive charge [*i.e.* (**2**)] stabilized by n-type electron delocalization from the oxime group, and this cation could act as a synthetic equivalent of an λ-acylcarbonium ion($-CO-\underset{+}{C}\langle$).[2] In this communication we describe a method for the conversion of oxime ethers into functionalized ketones using reactive intermediates of type (**1**) or (**2**), employing acetone *O*-methyloxime as a model compound.

Lithiation of acetone *O*-methyloxime (**3**) was achieved with a 1.2 M solution of Bu^nLi in tetrahydrofuran (THF)–hexane in 5 min at −65 °C. Addition of lithiated (**3**) to molecular



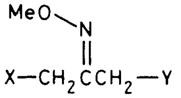
(1)



(2)

bromine in THF at −65 °C over 15 min resulted in the formation of the *Z*-bromo-oxime ether, (**4**). Isomerization of (**4**) in $CHCl_3$–HBr gave the thermodynamically-favoured *E*-isomer, (**5**).† The halogen atom could be exchanged for alkoxy by treatment of (**5**) with 1.1 equiv. of $MeO[CH_2]_2ONa$ in THF for 12 h to give (**6**) in 88% yield.

The bromo-oxime ethers (**4**) and (**5**), were also converted into a reactive intermediate of type (**2**) which reacted in aromatic substitution reactions. Addition of 10 mmol of either (**4**) or (**5**) in 20 ml of dry $Cl[CH_2]_2Cl$ to a solution of 10 mmol of $AgBF_4$ and 10 mmol of the aromatic compound in 20 ml of $Cl[CH_2]_2Cl$ at 25 °C, followed by efficient stirring in the dark for 18 h and then work-up with a 10% KCN–H_2O solution gave good (82—91%) yields of the aromatic substitution products (**7a**—**e**)† as the *E*-isomers. Acid treatment of (**7a**—**e**) (HCl–H_2O–MeOH 1 : 5 : 5) for 10 h at 65 °C and distillation gave the corresponding arylacetones, (**8a**—**e**), in high (90%) yields.



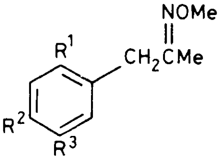
$X{-}CH_2\overset{\overset{\displaystyle MeO\diagdown N}{\|}}{C}CH_2{-}Y$

(**3**) X = Y = H

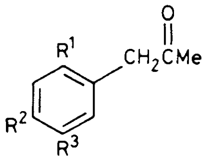
(**4**) X = Br, Y = H

(**5**) X = H, Y = Br

(**6**) X = H, Y = $O[CH_2]_2OMe$



(**7a**—**e**)



(**8a**—**e**)

a ; $R^1 = R^3 = OMe, R^2 = H$

b ; $R^1 = R^3 = H, R^2 = OMe$

c ; $R^1 = R^3 = H, R^2 = OAc$

d ; $R^1 = R^2 = OMe, R^3 = H$

e ; $R^1 = R^3 = Me,\ R^2 = H$

The method described in this paper is related to the silver-induced aromatic substitution reaction studied by Eschenmoser a decade ago using chloroaldonitrones as acylcarbonium ion precursors for the synthesis of aldehydes.[4] Recently we investigated the possibility of extending the nitrone method to the preparation of methyl ketones but our attempts to synthesize suitable halogenated nitrones were unsuccessful.

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† The geometry of the oxime ether moiety was elucidated on the basis of the chemical shift of the ketone Me group in the ^{1}H n.m.r. spectrum (CCl_4), *e.g.*: the methyl hydrogens resonate at δ 2.01 in (**4**) but in (**5**) at δ 1.96. In (**6**), δ_{Me} is at 1.79, (the *E*-isomer has δ_{Me} 1.91), for (**7a**—**e**) the resonances are at δ 1.71, 1.70, 1.70, 1.71, and 1.74, respectively, whereas the corresponding *Z*-isomers have shifts at δ 1.75, 1.73, 1.74, 1.76, and 1.76, respectively. See also ref. 3.