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PUMMERER REACTION INTERMEDIATE AS AN INITIATING FUNCTION FOR CATIONIC OLEFIN CYCLIZATION

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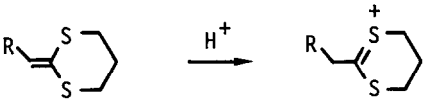
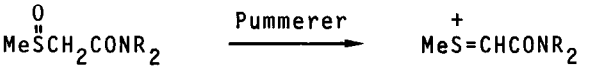
Summary: Treatment of N-(2-methyl-2-propenyl)-N-methyl-α-(methylsulfinyl)acetamide (6a) with trifluoroacetic anhydride caused the cationic olefin cyclization through a Pummerer reaction intermediate to give the six-membered lactams 7 and 8. Similar reaction converted N-2-butenyl-N-methyl-α-(methylsulfinyl)acetamide (6b) to the five-membered lactam 9, and N-2-propenyl-N-methyl-α-(methylsulfinyl)-acetamide (6c) to the five-membered lactams 11 and 12.

In recent years, growing attention has been devoted to discovering the cationic species acting as an initiating center for cationic olefin cyclization.[1] As such cationic species containing hetero-atom, α-acyliminium ion (1a)[2] and oxonium ion (1b)[3] have been extensively investigated. However, little is known about the sulfur-containing species (1c); the only reported example is the 1,3-dithienium ion 3 generated by protonation of the ylidene dithian 2.[4] We have now found that the Pummerer reaction intermediate (5) of α-(methylsulfinyl)acetamides (4) behaves as a highly reactive initiating center for cationic olefin cyclization, i.e., N-2-alkenyl-N-methyl-α-(methylsulfinyl)acetamides (6a-c) cyclize to the six- and five-membered lactams 7-12 under the Pummerer reaction conditions (Scheme 1).

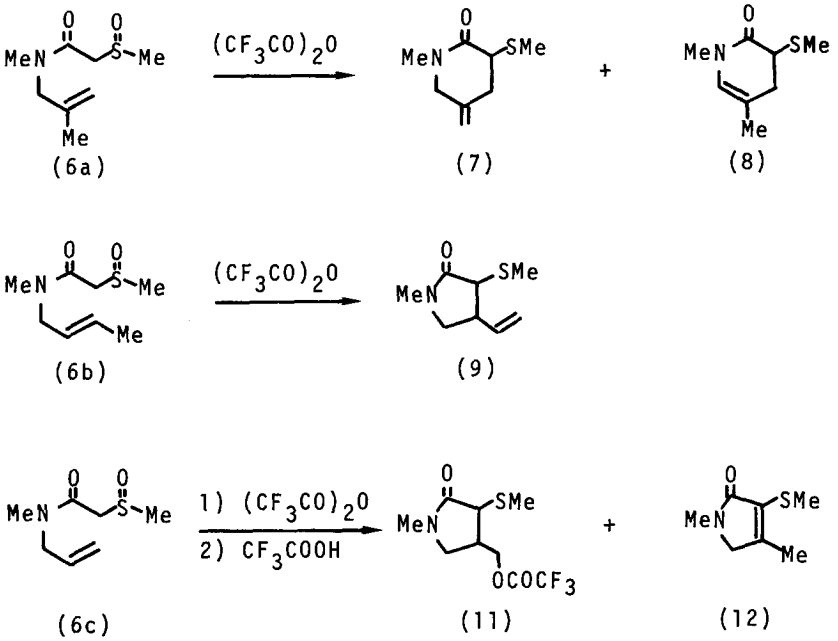
(1a) X=NCOR
(1b) X=O
(1c) X=S



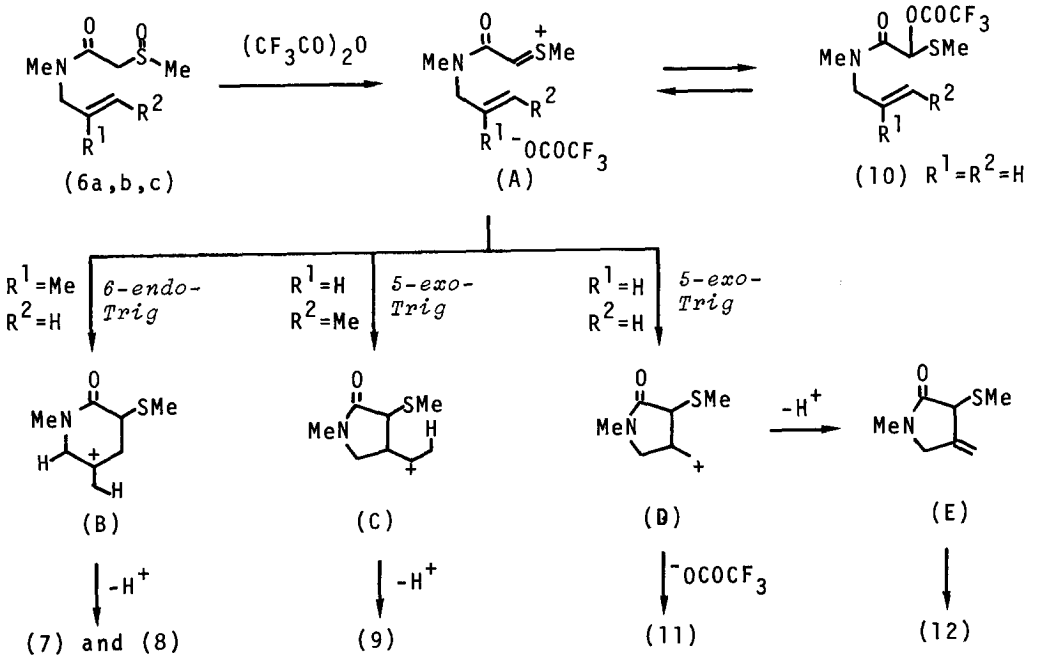
(2) (3)



(4) (5)



Scheme 1

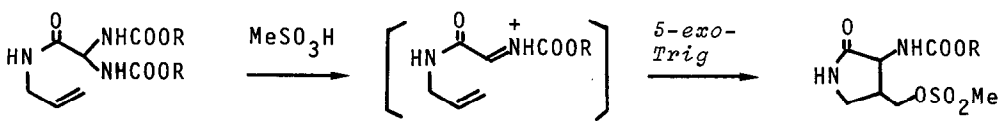


Scheme 2

The starting materials 6a-c were prepared by N-acylation of N-(2-alkenyl)-methylamines with α-(methylthio)acetyl chloride[5] followed by oxidation of the resulting N-2-alkenyl-N-methyl-α-(methylthio)acetamides with sodium metaperiodate in aqueous methanol.

Cyclizations of N-(2-methyl-2-propenyl)-(6a) and N-2-butenyl-N-methyl-α-(methylsulfinyl)acetamide (6b) were effected by treatment with an equimolar amount of trifluoroacetic anhydride in methylene chloride at room temperature; 6a gave the 5-methylene-2-piperidinone 7 and the 3,4-dihydro-2(1H)-pyridone 8 in 43 and 35% yields, respectively [7: oil, δ 1630 cm^{-1} (six-membered lactam), δ 2.27 (s, 3H, SMe), 2.58 (dd, 1H, H-4, J=14, 4 Hz), 2.8-3.1 (m, 1H, H-4), 2.95 (s, 3H, NMe), 3.37 (t, 1H, H-3, J=4 Hz), 3.96 (bs, 2H, H-6), 4.98 (bs, 2H, $C=CH_2$); 8: oil, ν 1640 cm^{-1} (six-membered lactam), δ 1.73 (bs, 3H, C=CMe), 2.18 (dd, 1H, H-4, J=17 3 Hz), 2.19 (s, 3H, SMe), 2.6-3.0 (m, 1H, H-4), 3.01 (s, 3H, NMe), 3.29 (dd, 1H, H-3, J=6, 3 Hz), 5.65-5.8 (m, 1H, H-6); the compounds 7 and 8 do not interconvert under the reaction conditions], and 6b gave the 4-vinyl-2-pyrrolidinone 9 [oil, ν 1680 cm^{-1} (five-membered lactam), δ 2.25 (s, 3H, SMe), 2.5-3.7 (m, 4H, H-3, 4 and 5), 2.89 (s, 3H, NMe), 4.9-6.2 (m, 3H, $CH=CH_2$)] in 92% yield as a mixture of stereoisomers (ca. 2:1).[6] Treatment of N-2-propenyl-N-methyl-α-(methylsulfinyl)-acetamide (6c) by a similar method to that employed for the cyclizations of 6a,b did not afford a cyclized product but a Pummerer rearrangement product 10.[7] However, further treatment of 10 with trifluoroacetic acid (in the absence of methylene chloride) caused cyclization to give the 2-pyrrolidinone 11 and the 3-pyrroline-2-one 12 in 9 and 39% yields, respectively [11: oil, ν 1785 (ester), 1685 cm^{-1} (five-membered lactam), δ 2.25 (s, 3H, SMe), 2.89 (s, 3H, NMe), 2.6-3.9 (m, 4H), 4.47 (d, 2H, J=6 Hz, OCH_2); 12: oil, ν 1665 (five-membered lactam), δ 2.10 (s, 3H, C=CMe), 2.42 (s, 3H, SMe), 3.02 (s, 3H, NMe), 3.82 (s, 2H, NCH_2); the compound 11 is not converted into 12 under the reaction conditions].

Cyclizations of 6a-c are considered to proceed via the discrete steps shown in Scheme 2 which involve the ring closure of the reactive species A leading to the new cations B-D. The modes of these cyclizations are, except the case of 6a, in accord with those of the cyclizations of the allylamides of bisalkoxycarbonylaminoacetic acid 13[8], in which the reactive intermediate F cyclizes in a 5-*exo-Trig* fashion[9] giving the five-membered product 14 but no six-membered product. The 6-*endo-Trig* cyclization of 6a to the six-membered lactams 7 and 8 is probably due to the high stability of the intermediary cation B.



(13) (F) (14)

The present result clearly demonstrates the usefulness of the α-acyl-α-thiocarbocation 5 in cationic olefin cyclization. Coupled with the ease of performance and the ability to gain a variety types of cyclic compounds its synthetic applicability seems highly promising.

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3 See Ref. 1c.

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6 The ratio was determined by ^{1}H-NMR spectrum using shift reagent, Eu(fod)$_3$.

7 δ 2.27 (s, 3H, SMe), 3.04, 3.14 (2s, 3H, NMe), 3.9-4.3 (m, 2H, NCH_2), 5.0-6.2 (m, 3H, $CH=CH_2$), and 6.34 (s, 1H, SCH).

8 See Ref. 2i.

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