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STEREOSPECIFIC SYN-ACYLAMIDATION OF OLEFINS

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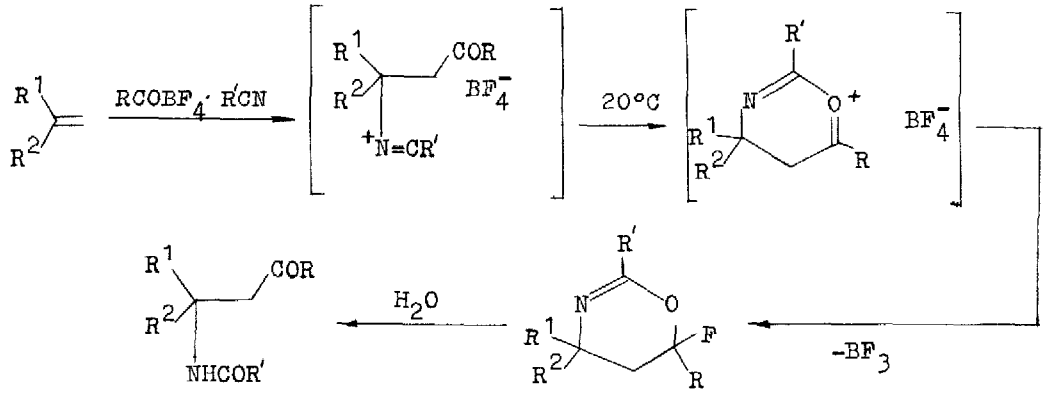
Abstract; Acylamidation of 1-methylcyclopentene by acetyl boronfluoride - acetonitrile complex proceeds stereospecifically with syn-addition.

Stereochemistry of the addition of carbenium ions to carbon-carbon double bonds has been scarcely studied.[1] High anti-stereospecifity is known in intramolecular biomimetic cyclisations.[2] Electrophilic alkylation of olefines by diarylchloromethanes in the presence of $ZnCl_2$ leads to mixtures of stereoisomers,although anti-addition proceeds in most cases.[1]

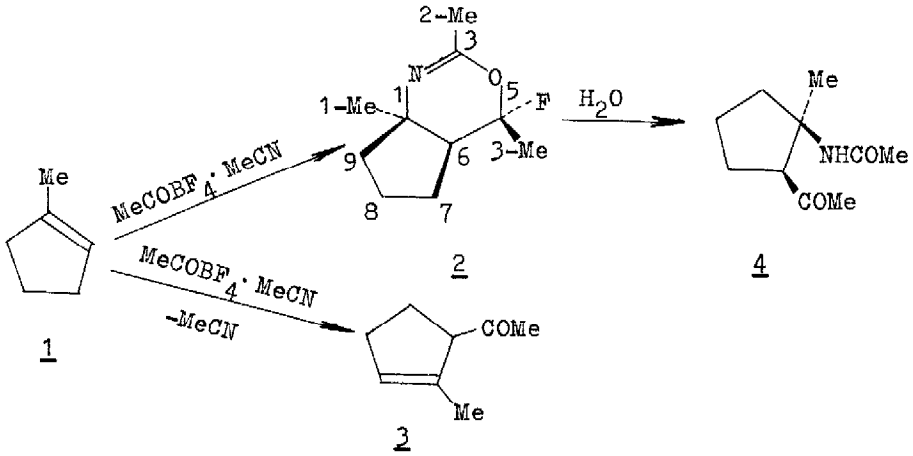
The reaction of acylamidation of olefins by acylium salt-nitrile complexes is a new example of electrophylic additions of C-electrophiles to carbon-carbon double bonds. This reaction leads to products of conjugated addition - corresponding 6-fluoro-5,6-dihydro-1,3-oxazines and N-acyl-β-aminoketones.[3,4]



$R^1 = R^2 = CH_3$; R^1 = Ph , R^2 = H ; R^1 = cyclo-$(CH_2)_3$, R^2 = H ; $R^1 + R^2 = (CH_2)_3$.
R = Alk ; R' = Alk , Ph , CH_2Cl .

We now report on the stereospecifity of acylamidation, illustrated by syn-acylamidation of 1-methylcyclopentene 1.

Interaction between the acetyl boronfluoride-acetonitrile complex and 1-methylcyclopentene 1 yielded cis-5-fluoro-1,3,5-trimethyl-2-aza-4-oxa-cis-bicyclo[4.3.0]non-2-ene 2 (66%). A small amount of 2-methyl-3-acetyl-cyclopentene 3 (17%) was separated from the reaction mixture. Hydrolysis of fluorooxazine 2 yields quantitatively Z-1-methyl-1-N-acetylamino-2-acetyl-cyclopentane 4:



Configurations of the compounds 2 and 4 were determined by NMR spectroscopy. Analysis of ^1H NMR spectra at 360 MHz of protons 1-H and 7-H of compound 4 was performed by using the total line shape approach and the NMRCON program.[5] The reduced spin systems 1-H,2-H,3-H and 7-H,6-H,5-H,4-H were applied for the analysis of subspectra of 1-H and 7-H protons, respectively. The analysis allowed us to obtain the following proton-proton coupling constants: 8.46 (0.05), 8.94 (0.05) Hz (vicinal) for 1-H wiyh R-factor of 5.4%, and 4.68 (0.04), 8.26 (0.04) Hz (vicinal), -12.71 (0.04) Hz (geminal) for 7-H with R-factor of 5.5%. Unfortunately, the data on vicinal couplings for 1-H and 7-H protons were not sufficient to obtain any strict conclusion about the cinfiguration of 4. For the determination of structure of 4 NOE experiments[6] were used (Fig. 1). The values of NOE $\eta_{2\text{-H}}(1\text{-H})$ are comparable with $\eta_{6\text{-H}}(1\text{-H})$ and $\eta_{1\text{-Me}}(1\text{-H})$ which corresponds to the cis, cis-configuration of 1-H,6-H and 1-Me. The presence of NOE $\eta_{NH}(7\text{-H})$ (1.6%) and the absence of $\eta_{1\text{-Me}}(7\text{-H})$ confirms the suggested cis-structure of 4.

Hydrolysis of 2 to 4 does not affect 5-C,6-C and 1-C,N bonds formed in the addition. Thus, the compound 2 is also cis-isomer. Analysis of spectrum of proton 1-H of 2 using the four-spin system approximation 1-H,2-H, 3-H,F with R-factor equal to 9.3% led to two vicinal ^1H, ^1H coupling con-

stants 9.71 (0.03) and 9.10 (0.03) Hz and one vicinal ^{1}H, ^{19}F coupling constant 5.68 (0.03) Hz. The latter value allows us to exlude the aa-conformation of 6-C,1-H and 5-C,F bonds,as the corresponding $^{3}J(H,F)$ values are about 40 Hz.[7] The NOE values of $\eta_{1\text{-Me}}(1\text{-H})$ (1.6%) and $\eta_{3\text{-Me}}(1\text{-H})$ (0.0%) are indicative of a cis-configuration of 6-C,1-H and 1-C,1-Me bonds and a trans-configuration of 6-C,1-H and 5-C,3-Me bonds. The cis-structure of 2 proves syn-acylamidation of 1-methylcyclopentene 1.

The $^{13}C,^{19}F$ coupling constants were also measured in ^{13}C NMR spectrum of 2. The $^{4}J(1\text{-Me},F)$ coupling constant was found to be 7.2 Hz while the $^{3}J(1\text{-C},F)$ coupling constant was near zero. This data does not agree with the data on ^{13}C, ^{19}F couplings in fluorinated cyclohexanes.[8] However,it is unlikely that there is a stereochemical analogy between cyclohexane and oxazine rings. Similar unexpected $^{13}C,^{19}F$ coupling constants through three and four bonds were previously observed in oxazine derivatives.[4] It should be noted also that a long-range $^{5}J(H,F)$ coupling constant exists between fluorine and protons in 1-Me group in 2.

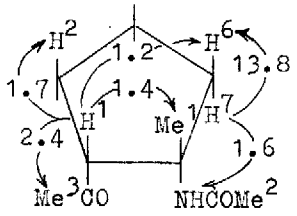


Fig.1.NOE data for compound 4.

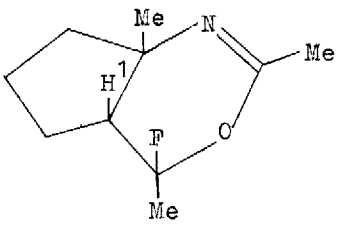


Fig.2. Stereochemistry of compound 2.

Thus,the formation of fluorooxazine 2 is a stereospecific process with syn-addition to the double bond. No other isomers were observed in the NMR of the crude reaction product.

Stereospecific syn-acylamidation of 1-methylcyclopentene can be used in the stereocontroled synthesis of cyclopentane derivatives.

Acylamidation of 1-methylcyclopentene and hydrolysis of compound 2 were performed in accordance with general procedures as described.[4] Compounds 2 and 3 were separated by vacuum distillation.

The ^{1}H NMR spectra of 2 and 4 were measured on a Bruker AM-360 spectrometer at 360.13 MHz resonance frequency. The NOE values were measured using the NOE difference mode. Spectral parameters used are as follows: 7.5 s presaturation time, 4.5 s aquisition time, 30 s pulse delay, 128 (4 x 32) number of transients.

Structures of the compounds obtained are in accordance with the data

of IR- and mass-spectroscopy and have satisfactory elemental analysis.

cis-5-fluoro-1,3,5-trimethyl-2-aza-4-oxa-cis-bicyclo[4.3.0] non-2-ene 2: b.p. 78°C (7 mm), n_D^{20} 1.4550.
^{1}H NMR data (360 MHz in $CDCl_3$, δ ppm): 1.39 (1-Me, d, $^5J(H,F)$ = 1.5 Hz), 1.55 (3-Me, d, $^3J(H,F)$ = 19.0 Hz), 1.39-1.88 ($3CH_2$, m), 2.02 (2-Me, s), 2.17 (1-H, dt, $^3J(1\text{-}H,F)$ = 5.68 Hz; $^3J(1\text{-}H,H)$ = 9.71, 9.10 Hz).
^{13}C NMR data (90 MHz in $CDCl_3$, δ ppm): 151.82 (3-C), 111.26 (5-C, d, $^1J(5\text{-}C,F)$ = 218.2 Hz), 60.75 (1-C), 46.31 (6-C, d, $^2J(6\text{-}C,F)$ = 23.9 Hz), 42.29 (9-C), 28.04 (7-C, d, $^3J(7\text{-}C,F)$ = 8.3 Hz), 27.05 (1-Me, d, $^4J(1\text{-}Me,F)$ = 7.2 Hz), 24.56 (3-Me, d, $^2J(3\text{-}Me,F)$ = 28.8 Hz), 21.24 (8-C), 20.49 (2-Me).

Z-1-methyl-1-N-acetylamino-2-acetylcyclopentane 4.
^{1}H NMR data (360 MHz in $CDCl_3$, δ ppm): 1.40 (1-Me, s), 1.45 (6-H, m), 1.60-1.82 (3-H,4-H,5-H, m), 1.82 (2-Me, s), 1.90 (2-H, m), 2.16 (3-Me,s), 2.50 (7-H, ddd, $^2J(7\text{-}H,6\text{-}H)$ = -12.91 Hz, ^3J = 8.26, 4.68 Hz), 2.89 (1-H, t, $^3J(1\text{-}H,H)$ = 8.46, 8.94 Hz), 6.65 (NH, br.s).

2-methyl-3-acetylcyclopentene 3: b.p. 42°C (7 mm), n_D^{20} 1.4732.
^{1}H NMR data (360 MHz in $CDCl_3$, δ ppm): 1.69 (Me, br.s), 2.11 (MeCO, s), 2.30-2.50 ($2CH_2$, m), 3.39 (CH, br.t), 5.58 (CH=, m).

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