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INTRAMOLECULAR CYCLOADDITIONS WITH ISOBENZOFURANS -VI[1]

A NOVEL ENTRY INTO THE FIELD OF ANNELATED 1,2-BENZISOXAZOLES

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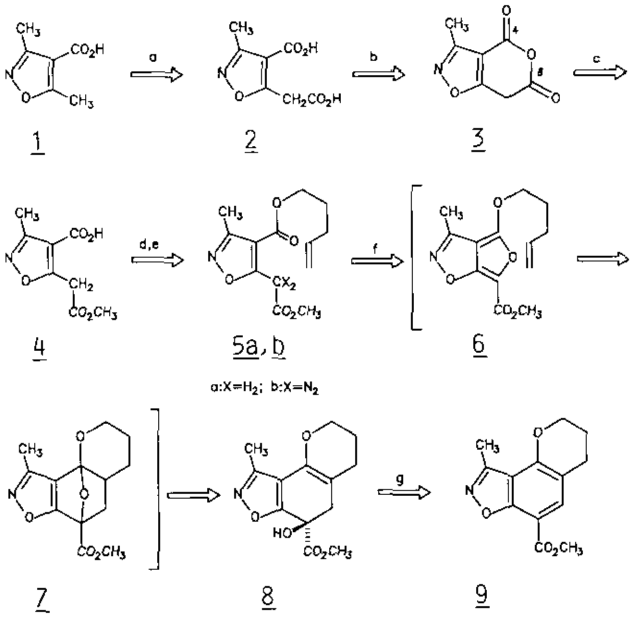
Abstract - Rh$_2$OAc$_4$ catalyzed nitrogen extrusion from 5b yields 8; this novel route to an annelated isoxazole obviously proceeds through a furo[3,4-d]isoxazole of type 6 as an intermediate.

Intramolecular cycloadditions[2] of isobenzofurans[3] offer an attractive route to polycyclic systems. The extension of this strategy to heteroannelated derivatives has also been proven to be possible[1,4]. In this paper the preparation of a 1,2-benzisoxazole 9[5] is described using a furo[3,4-d]isoxazole (6) as a reactive intermediate. Using the methodology developed by Natale and coworkers[6a] *deprotonation of acid* 1[6b] *with n-BuLi and reaction of the* resulting salt[7,8] with carbon dioxide yields 2 (73%, mp 199°C; ir(KBr): 3400-2600 cm^{-1}, 1750, 1710; ^{1}H-nmr(CDCl$_3$/DMSO-d$_6$=1/1): δ=2.42 (s, 3H),4.08 (s, 2 H),9.55 (s, 2H)) which is cyclized with AcCl to give 3 (91%, mp 167°C;



a:n-BuLi,-78°C,CO$_2$; b:AcCl,reflux; c:MeOH,reflux;
d:4-penten-1-ol,DCC,DMAP,RT;e:TsN$_3$,MeCN,Et$_3$N,RT;
f:Rh$_2$OAc$_4$,CH$_2$Cl-CH$_2$Cl,reflux; g:p-TsOH,CH$_2$Cl-CH$_2$Cl

ir(KBr): 1795 cm^{-1}, 1765; ^{1}H-nmr(CDCl$_3$/DMSO-d$_6$=1/1): δ=2.42 (s, 3H),4.07 (s, 2 H)). Treatment of this anhydride with methanol yields 4^{7,10} (92%, mp 107°C; ir(KBr): 3800-2300 cm^{-1}, 1745, 1690, 1680; ^{1}H-nmr(CDCl$_3$/DMSO-d$_6$=1/1): δ=2.50 (s, 3H),3.77 (s, 3 H), 4.17 (s, 2 H),11.53 (s, 1 H)) which is esterified to 5a (68%, oil; ir(film): 1755 cm^{-1}, 1725) using the Steglich procedure^{11}. A diazo transfer reaction^{12} yields 5b (84%, oil; ir(film): 2130 cm^{-1},1760,1720; uv(MeCN):λ$_{max}$:(logε)=246 nm (4.089),280 (4.017),370 (3.718)). The generation of 6^{13} and subsequent ring opening to 8 (mp 121°C; ir (KBr): 3300 cm^{-1}, 1750) was accomplished with Rh$_2$OAc$_4$; 8 can be transformed to 9 (67% [from 5b], mp 213°C; ir(KBr): 1710 cm^{-1}; uv(CH$_2$Cl$_2$): λ$_{max}$(logε)=262 nm (4.206),269 (4.177),307 (4.195),313 (4.189),318 (4.146); ^{1}H-nmr(CDCl$_3$): δ= 1.97-2.20 (m, 2 H),2.60 (s, 3 H),2.83 (t, J=6 Hz, 2 H),3.96 (s, 3 H),4.36 (t, J=6 Hz, 2 H), 7.87 (s, 1 H)). Overall this route seems to be suitable for the preparation of polycyclic systems bearing heterocyclic rings.

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