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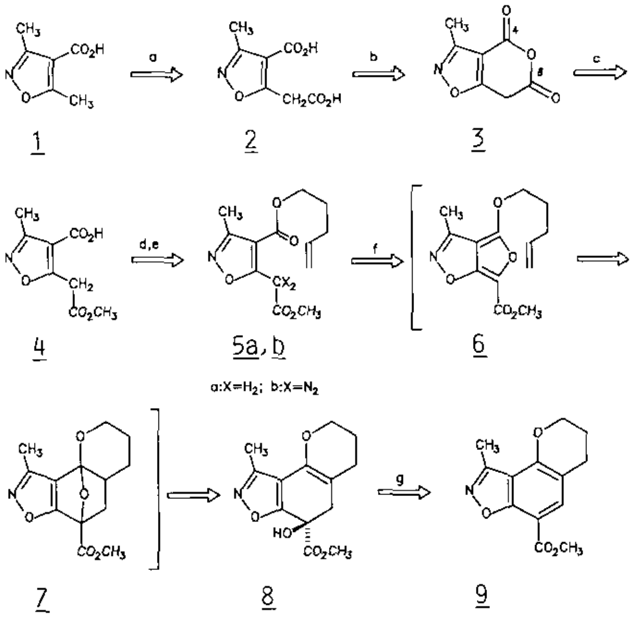
Abstract - Rh$_2$OAc$_4$ catalyzed nitrogen extrusion from 5b yields 8; this novel route to an annelated isoxazole obviously proceeds through a furo[3,4-d]isoxazole of type 6 as an intermediate.

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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REFERENCE

1. V: A.Schöning and W.Friedrichsen, submitted.
2. Review: M.S.Salakhov and S.A.Ismailov,Russ.Chem.Rev., 1986, 55, 2008.
3. 3a. B.Rickborn,'Adv.Theoret.Interest.Molecules' ed. by R.P.Thummel, JAI Press, Conn., 1988. - 3b. R.Rodrigo, Tetrahedron, 1988, 44, 2093. - 3c. W.Friedrichsen, Adv.Heterocycl.Chem., 1980, 26, 135.
4. 4a. K.Hildebrandt, T.Debaerdemaeker, and W.Friedrichsen, Tetrahedron Lett., 1988, 29, 2045.- 4b. A.Schöning and W.Friedrichsen, ibid., 1988, 29, 1137.
5. S.A.Lang and Y.-i Lin, 'Comprehensive Heterocyclic Chemistry', Vol.6, ed. by A.R.Katritzky and C.W.Rees, Pergamon Press, Oxford, 1984,p.1.
6. 6a. N.R.Natale, J.I.McKenna,C.-S.Niou, M.Borth, and H.Hope,J.Org.Chem., 1985, 50, 5660 - 6b. L.Claisen and W.Zedel,Liebigs Ann.Chem., 1893, 277, 162.
7. The course of this reaction seems to be unpredictable by simple MO arguments.
8. A MNDO calculation[9] of both possible lithiated salts reveals that the latter is slightly more stable ($\Delta H \approx 4.5$ kcal/mol).
9. MOPAC package: J.J.P.Stewart, QCPE Bulletin, 1986, 6, 24a.
10. AM1 calculations (M.J.S.Dewar, E.G.Zoebisch, E.F.Healy, and J.J.P.Stewart, J.Am.Chem.Soc., 1985, 107, 3902) show that C(4) is more positive (q_4= 0.3968) than C(6) (q_6=0.3124). The attack of methanol at C(6) however (AM1 reaction path calculations) seems to be less hindered than attack at C(4).
11. B.Neises and W.Steglich, Angew.Chem., 1978, 90, 556; Angew.Chem.Int.Ed. Engl., 1978, 17, 522.
12. M.Regitz and G.Maas, 'Diazo Compounds', Academic Press, New York, 1987.
13. See M.Hamaguchi and T.Ibata, Chem.Lett., 1976, 287 and following papers.

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