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Short Communication

The Reaction of Salicylamide with Triethyl Orthoformate

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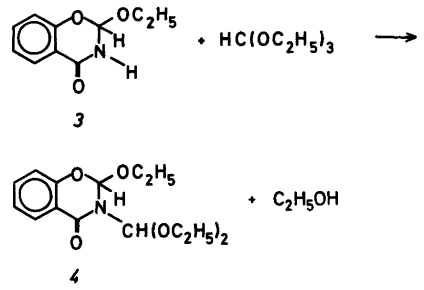
In connection with our work on the formation of *N*-acylformimidates[1] the report of Irie, Kurosawa and Hanada[2] has attracted our interest. Their work is an investigation of the reaction of salicylamide with orthoesters, especially triethyl orthoformate, and an examination of the reaction products.

Salicylamide was reported to react with triethyl orthoformate in the expected way for a carboxamide under formation of a compound with the composition of an imidate *2*. From IR data a cyclic structure *3* was assumed for the reaction product and because of a violet colour reaction with aqueous ferric chloride the cyclic structure was assumed in equilibrium with the open chain form *2* (Scheme 1).

We have repeated these experiments and found that reflux of salicylamide with triethyl orthoformate for 40 h did give the compound *3* beside a liquid compound *4*. Compound *4* could also be prepared by reflux of *3* with more triethyl orthoformate (Scheme 2). The structures of *3* and *4* were established by elemental analysis, MS, IR and NMR.

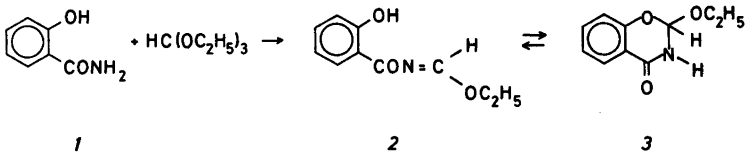
Preparation in accordance with the literature[2] thus gave a mixture of *3* and *4*. When the method for preparation of acylimidates was used, where the reaction is catalyzed with a few drops of conc. sulfuric acid,[1] only *3* was found in almost quantitative yield.



Scheme 2.

The equilibrium between *2* and *3* was investigated by means of ^{1}H NMR. The chemical shift values for CH in *2* must be expected around 8.2 ppm[1] and for *3* it is found at 6.03 ppm. In $CDCl_3$, CCl_4 and DMSO-d_6 only one isomer was observed, namely *3*. If the other isomer *2* is present the amount must be below 1 %. The colour reaction of *3* with $FeCl_3$ could either be explained by the equilibrium between *2* and *3*, by hydrolysis of *3*, or *3* itself could give a colour reaction like *O*-acetylsalicylamide[3] does. The *N*-methyl analog of *3* also gives a slow developing colour reaction although it is unable to form the open chain form.

It seems, however, plausible that an equilibrium between *2* and *3* exists since the normal reactions for acylimidates with nucleophilic reagents is seen.[4] Reaction of *3* (*2*) with *e.g.* amines like benzylamine and diethylamine gave the hitherto unknown *N*-acylformamidines, *N*-benzyl-*N'*-salicyloylformamidine *5a* and N^1,N^1-diethyl-N^2-salicyloylformamidine *5b*. Even methanol reacts with *3* (*2*) under formation of 2-methoxy-2,3-dihydro-1,3-benzoxazin-4-one *6*. It is unlikely that the reactions proceed through the cyclic structure *3* because the *N*-methyl analog of *3*, 2-ethoxy-3-methyl-2,3-di-



Scheme 1.

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hydro-1,3-benzoxazin-4-one did not give reactions with nucleophiles.

In order to prepare the hitherto unknown compound 4-*H*-1,3-benzoxazin-4-one *7* we made several attempts to eliminate ethanol from *3* but none was successful.

We tried with $SOCl_2$, SO_2Cl_2, PCl_3, PCl_5, $POCl_3$, HCl in toluene and xylene and heating *in vacuo*. The method with HCl is reported[5] to give 2-methyl-4-*H*-1,3-benzoxazin-4-one from the 2-ethoxy-2-methyl-2,3-dihydro-1,3-benzoxazin-4-one. In all cases we only obtained *N*-formylsalicylamide.

Conclusively the reaction between salicylamide and triethyl orthoformate proceeds with the formation of *3* and *4* and no imidate *2* could be detected by spectroscopic methods. Very small amounts of *2* may, however, exist in equilibrium with *3* because of the easy reaction of *3* with nucleophiles.

Experimental. The experimental equipment was reported earlier.[1] Melting points are uncorrected.

2-Ethoxy-2,3-dihydro-1,3-benzoxazin-4-one. 3. Salicylamide (10 g) was refluxed for 3 h with triethyl orthoformate (50 ml) and five drops of conc. sulfuric acid. The reaction mixture was cooled and *3* was filtered off. Yield 89 %, m.p. 120 °C. Anal. $C_9H_{11}NO_3$: C, H, N. ^{1}H NMR ($CDCl_3$): δ 1.17 (3 H, t), 3.71 (2 H, q), 6.05 (1 H, s), 6.85–8.16 (4 H, m), 8.56 (1 H, b). IR ($CHCl_3$, cm^{-1}): 3400 (m), 3200 (m), 3000 (m), 1690 (s), 1620 (s), 1480 (s), 1330 (s).

2-Ethoxy-3-diethoxymethyl-2,3-dihydro-1,3-benzoxazin-4-one 4. Salicylamide (0.05 mol) and triethyl orthoformate (0.15 mol) were refluxed so the formed ethanol could distill from the reaction mixture. After the collection of 8.5 ml, the reaction was stopped, excess triethyl orthoformate evaporated and the residue distilled *in vacuo*. Yield 58 %, b.p. 116–120 °C/0.07 mmHg. Anal. $C_{14}H_{21}NO_5$: C, H, N. ^{1}H NMR (CCl_4): δ 0.98–1.40 (9 H, m), 3.38–3.88 (6 H, m), 6.07 (1 H, s), 6.25 (1 H, s), 6.72–7.97 (4 H, m). IR ($CHCl_3$, cm^{-1}): 3000 (m), 1680 (s), 1620 (m), 1480 (s), 1440 (m), 1320 (m).

2-Ethoxy-3-methyl-2,3-dihydro-1,3-benzoxazin-4-one was prepared in accordance with the method previously described.[1] Yield 40 % m.p. 75–78 °C. Anal. $C_{11}H_{13}NO_3$: C, H, N. ^{1}H NMR ($CDCl_3$): δ 1.12 (3 H, t), 3.12 (3 H, s), 3.69 (2 H, q), 5.97 (1 H, s), 6.82–8.20 (4 H, m). IR ($CHCl_3$, cm^{-1}): 3400 (w), 3000 (s), 1670 (s), 1620 (s), 1480 (s).

N-*Benzyl*-N′-*salicyloylformamidine* 5a. *3* (0.01 mol) in anhydrous benzene (30 ml) was stirred with benzylamine (0.01 mol) at room temperature. *5a* was filtered off. Yield 66 %, m.p. 142 °C. Anal. $C_{15}H_{14}N_2O_2$: C, H, N. ^{1}H NMR (DMSO-d_6): δ 4.66 (2 H, s), 6.71–8.20 (10 H, m), 8.34 (0.8 H, s), 8.45 (0.2 H, s), 13.11 (1 H, b). IR ($CHCl_3$, cm^{-1}): 1650 (m), 1610 (s), 1470 (s), 1350 (s).

N^1,N^1-*Diethyl*-N^2-*salicyloylformamidine* 5b. *3* (0.01 mol) in anhydrous toluene (30 ml) was stirred 2 h with diethylamine (0.01 ml) at room temperature. The toluene was evaporated and the residue was recrystallized from ethanol. Yield 60 %, m.p. 81 °C. Anal. $C_{12}H_{16}N_2O_2$: C, H, N. ^{1}H NMR ($CDCl_3$): δ 1.27 (6 H, t), 4.36 (4 H, q), 6.52–8.20 (4 H, m), 8.70 (1 H, s), 13.45 (1 H, b). IR ($CHCl_3$, cm^{-1}). 3000 (m), 1660 (s), 1610 (s), 1470 (s), 1345 (s).

2-Methoxy-2,3-dihydro-1,3-benzoxazin-4-one 6. *3* (0.1 mol) was refluxed 14 h with 60 ml methanol. Cooling and filtering gave 70 % yield of *6*, m.p. 96 °C. Anal. $C_8H_9NO_3$: C, H, N. ^{1}H NMR ($CDCl_3$): δ 3.47 (3 H, s), 6.03 (1 H, s), 6.96–8.20 (4 H, m), 8.86 (1 H, b). IR ($CHCl_3$, cm^{-1}): 3400 (m), 3200 (m), 3000 (m), 1700 (s), 1630 (s), 1480 (s), 1340 (s).

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