REDUCTIONS OF 3-(*N*-ARYLAMINOMETHYLENE)-SUCCINIMIDES‡

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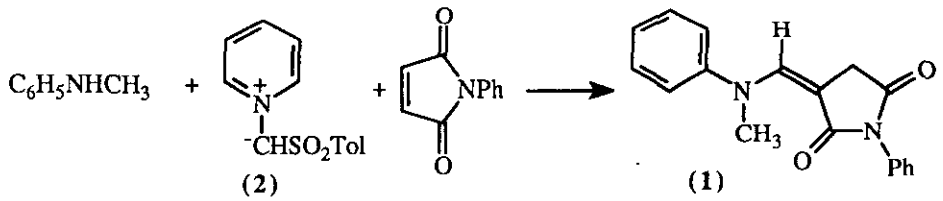
Abstract - The reduction Z-N-methylanilinomethylene-N'-phenylsuccinimide is reported and, depending on the conditions, a variety of products may be formed in reasonable yield. For example, the regioselectivity of the $NaBH_4$/EtOH reduction is different from that predicted in the literature, and LAH reduction under mild conditions gives N-phenylpyrrole-3-carboxaldehyde.

Some time ago, we described the use of pyridinium p-toluenesulfonylmethylide (**1**) as a formylamino equivalent,[1] and its use as an oxy-,[1] amino- and thiomethylenating agent[2] for maleimides. We now report the reduction of arylaminomethylene derivatives which gives rise to an interesting variety of products.

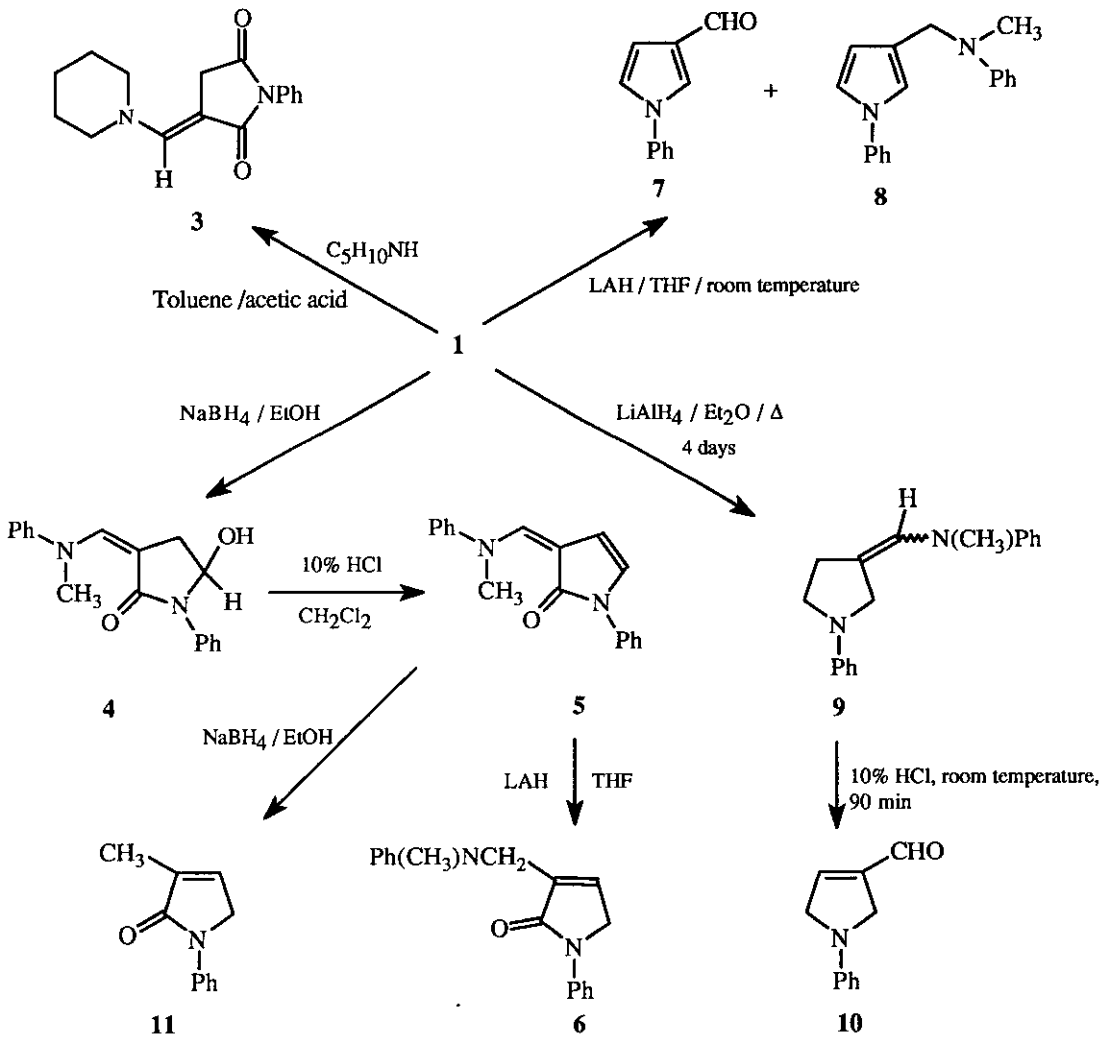
Z-N-Methylanilinomethylene-N'-phenylsuccinimide (**1**) was prepared from N-methylaniline, pyridinium p-toluenesulfonylmethylide (**2**) and N-phenylsuccinimide as described before,[2] but in improved yield (stirring the reaction mixture at room temperature for 18 h) (57%, compared with 28%[2]) (see ref. 2 for assignment of geometry). Heating **1** with dry piperidine in toluene containing a small amount of acetic acid for 27 h gave a low



yield (<10%) of E-**3**, identical with the material prepared before.[2] The corresponding N'-p-nitrophenylsuccinimide, mp 220-221°C,[3] gave the E-piperidino derivative (**3**; p-NO_2Ph instead of phenyl), mp156-157°C, in 68% yield (analytically pure). Reduction of **1** with $NaBH_4$/EtOH surprisingly gave **4** (83%), mp 98.5-99.5°C,[3] and not the expected[4] product of reduction of the other carbonylgroup (the same product, but

‡ Submitted in honor of Professor R. Huisgen's 75th birthday. May you cycloadd for many more years!

in lower yield, was obtained when a trace of HCl was added to the



Scheme 1

reagents[4]). It has been reported that 3-substituted succinimides are reduced regioselectively on the more substituted side to give 5-hydroxy-4-substituted 2-pyrrolidinones with sodium borohydride (EtOH, trace H^+).[4] On the other hand, diborane reduction occurs on the least hindered side.[5] Lithium aluminum hydride reduction of N-substituted succinimides,[6] including the 3-diphenylmethylene derivative,[7] usually gives the pyrrolidines mainly. Speckamp and coworkers[4] had used their hydroxypyrrolidinones to generate the acyliminium ions which underwent intramolecular cyclization, and it had been our hope to apply this to cyclizations onto the

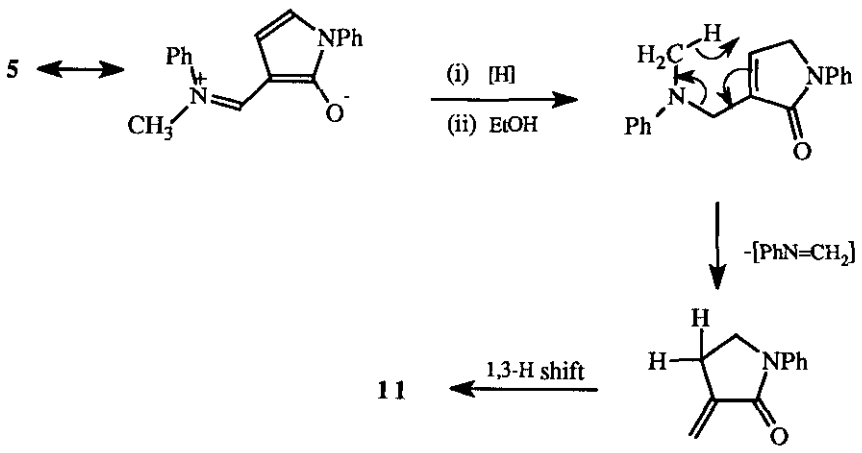
arylamine ring. That the other carbonyl group had been reduced was evident from the nmr spectrum of the product: the 4-methylene group exhibited a 1H doublet at δ 2.6 (J_{gem} = 10 Hz) and a 1H d of d centered at δ 3.1 ($J_{4,5}$ = 6.5 Hz, J_{gem} = 10 Hz; simplifies to a doublet, J = 10 Hz, on irradiation at δ 5.6), while the C_5-H resonated at δ 5.6 (t, 1H, J = 6.5 Hz, collapsing to a doublet upon addition of D_2O). Dehydration under mild conditions (10% HCl, CH_2Cl_2) gave **5** (84%).[3] The latter underwent reduction to **6** in poor yield (18%) with LAH in THF.

To explain their observed regioselective reduction, Speckamp and coworkers proposed that steric hindrance by the C-3 substituent caused the borohydride ion to approach (from the rear and above) the 2-carbonyl group over the less hindred C-4.[4] Süess[5] used a combination of the steric approach control hypotheses of Dunitz[8] and Baldwin[9] to account for the regioselectivities observed with $NaBH_4$[4] and with B_2H_6.[5] With **1** and $NaBH_4$ we found the regioselectivity observed by Süess with B_2H_6. One possible explanation is that C_3 in **1** is sp^2 hybridized and may actually present less hindrance than the sp^3 hybridized methylene at the 5-position. Alternatively, the enamine function in **1** may deactivate the 2-carbonyl group towards nucleophilic attack but not the 5-carbonyl group.

Reduction of **1** with LAH in THF at room temperature for 2.5 h took a most interesting course, resulting in the formation of N-phenylpyrrole-3-carboxaldehyde (**7**)[3] in preparatively useful yield (43%), (bp 100-105°C/0.025 mm; 2,4-DNP derivative, mp 221-223°C[3]), together with a small amount of **8**.[3]

If **1** was reduced with LAH in Et_2O for 4.5 days the N-methyl-N-phenylenanime of N-phenylpyrrolidine-3-carboxaldehyde (**9**) was isolated (58% yield), mp 105.5-107.5°C[3] (cf. ref. 6). This was hydrolyzed to N-phenylpyrrolidine-3-carboxaldehyde (**10**) (56%), bp 70-80°C/0.035 mm with 10% aq. HCl at room temperature (90 min).

Reduction of **5** with $NaBH_4$/EtOH gave **11** (47%), mp 95-96.5°C, identical with an authentic sample.[10] A possible pathway which would account for this product is shown in Scheme 2. Other pathways are conceivable.



Scheme 2

The N-methylsuccinimide corresponding to **1** was readily prepared in 33% yield. Its reduction did not proceed as satisfactorily as that of **1**. For example, with LAH/THF/room temperature for 4 h N-methyl-3-pyrrolecarboxaldehyde (identical with an authentic sample) was obtained in only 6% yield, together N-methylaniline (8%), and an even smaller amount of N-methyl-3-(N-methylanilinomethyl)pyrrole.

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