

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

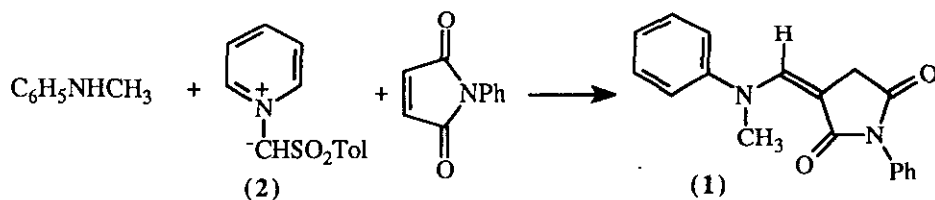
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**Abstract** - The reduction *Z*-*N*-methylanilinomethylene-*N*'-phenylsuccinimide is reported and, depending on the conditions, a variety of products may be formed in reasonable yield. For example, the regioselectivity of the NaBH<sub>4</sub>/EtOH 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,<sup>1</sup> and its use as an oxy-,<sup>1</sup> amino- and thiomethylenating agent<sup>2</sup> for maleimides. We now report the reduction of arylaminomethylene derivatives which gives rise to an interesting variety of products.

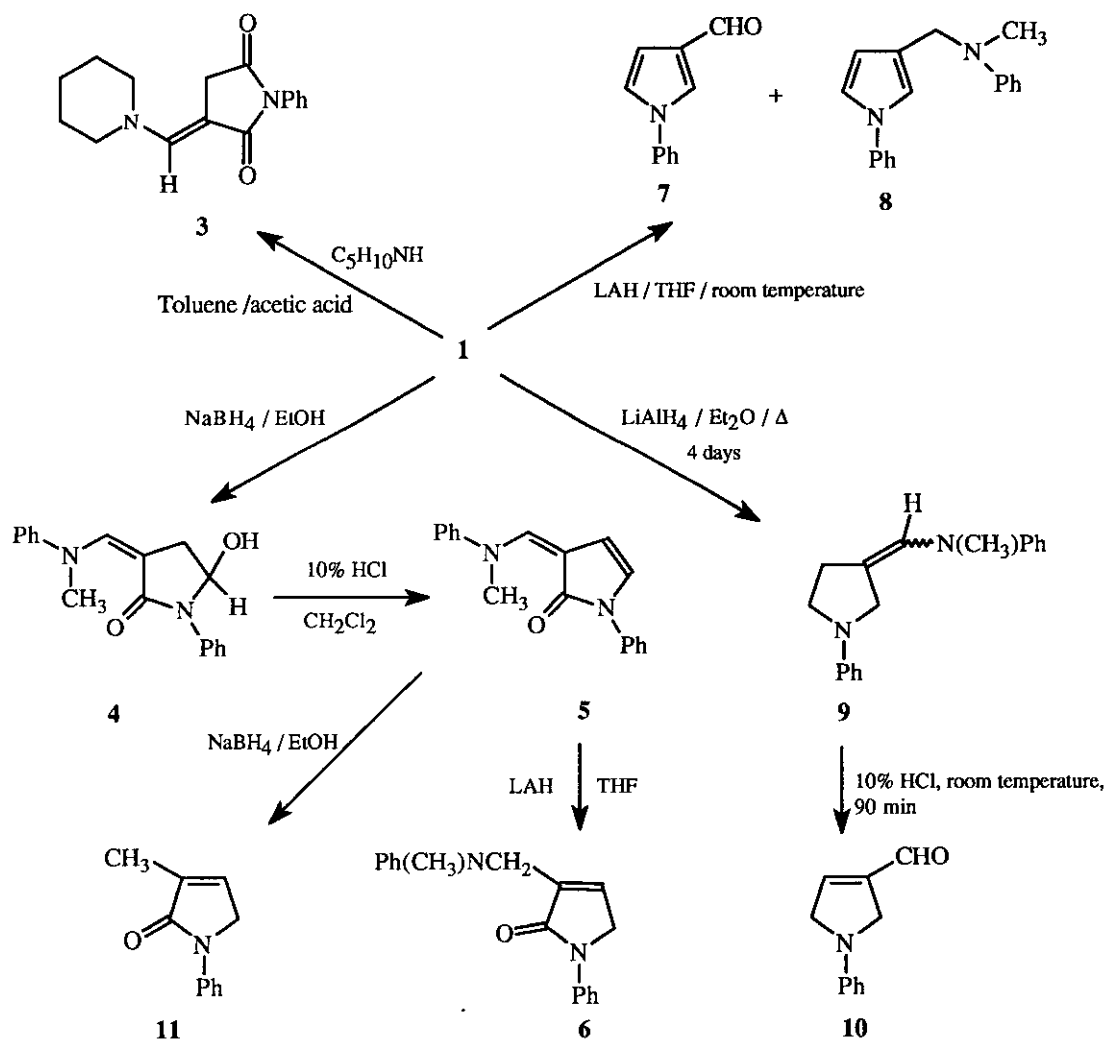
*Z*-*N*-Methylanilinomethylene-*N*'-phenylsuccinimide (1) was prepared from *N*-methylaniline, pyridinium *p*-toluenesulfonylmethylide (2) and *N*-phenylsuccinimide as described before,<sup>2</sup> but in improved yield (stirring the reaction mixture at room temperature for 18 h) (57%, compared with 28%<sup>2</sup>) (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.<sup>2</sup> The corresponding *N*'-*p*-nitrophenylsuccinimide, mp 220-221°C,<sup>3</sup> gave the *E*-piperidino derivative (3; *p*-NO<sub>2</sub>Ph instead of phenyl), mp 156-157°C, in 68% yield (analytically pure). Reduction of 1 with NaBH<sub>4</sub>/EtOH surprisingly gave 4 (83%), mp 98.5-99.5°C,<sup>3</sup> and not the expected<sup>4</sup> product of reduction of the other carbonyl group (the same product, but

‡ Submitted in honor of Professor R. Huisgen's 75<sup>th</sup> 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<sup>4</sup>). 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<sup>+</sup>).<sup>4</sup> On the other hand, diborane reduction occurs on the least hindered side.<sup>5</sup> Lithium aluminum hydride reduction of *N*-substituted succinimides,<sup>6</sup> including the 3-diphenylmethylene derivative,<sup>7</sup> usually gives the pyrrolidines mainly. Speckamp and coworkers<sup>4</sup> 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

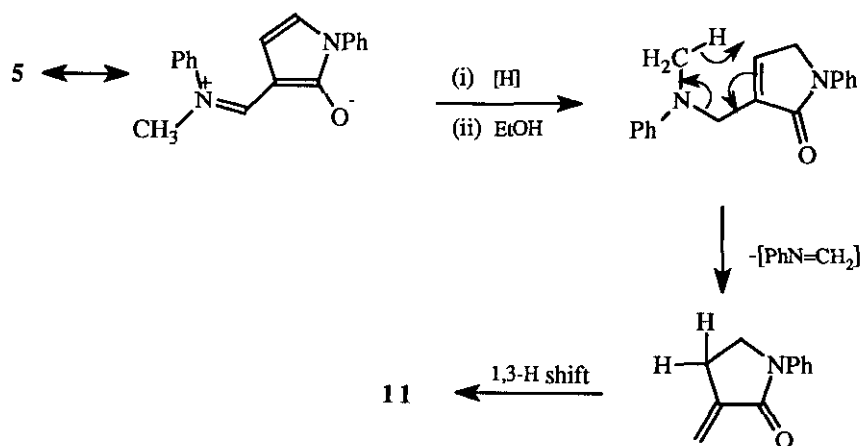
arylamine ring. That the other carbonyl group had been reduced was evident from the nmr spectrum of the product: the 4-methylene group exhibited a 1H doublet at  $\delta$  2.6 ( $J_{gem} = 10$  Hz) and a 1H d of d centered at  $\delta$  3.1 ( $J_{4,5} = 6.5$  Hz,  $J_{gem} = 10$  Hz; simplifies to a doublet,  $J = 10$  Hz, on irradiation at  $\delta$  5.6), while the C<sub>5</sub>-H resonated at  $\delta$  5.6 (t, 1H,  $J = 6.5$  Hz, collapsing to a doublet upon addition of D<sub>2</sub>O). Dehydration under mild conditions (10% HCl, CH<sub>2</sub>Cl<sub>2</sub>) gave **5** (84%).<sup>3</sup> 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 hindered C-4.<sup>4</sup> Süess<sup>5</sup> used a combination of the steric approach control hypotheses of Dunitz<sup>8</sup> and Baldwin<sup>9</sup> to account for the regioselectivities observed with NaBH<sub>4</sub><sup>4</sup> and with B<sub>2</sub>H<sub>6</sub>.<sup>5</sup> With **1** and NaBH<sub>4</sub> we found the regioselectivity observed by Süess with B<sub>2</sub>H<sub>6</sub>. One possible explanation is that C<sub>3</sub> in **1** is *sp*<sup>2</sup> hybridized and may actually present less hindrance than the *sp*<sup>3</sup> 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**)<sup>3</sup> in preparatively useful yield (43%), (bp 100-105°C/0.025 mm; 2,4-DNP derivative, mp 221-223°C<sup>3</sup>), together with a small amount of **8**.<sup>3</sup>

If **1** was reduced with LAH in Et<sub>2</sub>O for 4.5 days the *N*-methyl-*N*-phenylenamine of *N*-phenylpyrrolidine-3-carboxaldehyde (**9**) was isolated (58% yield), mp 105.5-107.5°C<sup>3</sup> (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<sub>4</sub>/EtOH gave **11** (47%), mp 95-96.5°C, identical with an authentic sample.<sup>10</sup> 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-pyrrolicarboxaldehyde (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.

## ACKNOWLEDGMENTS

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## REFERENCES

1. R.A. Abramovitch, S.S. Mathur, D.W. Saunders, and D.P. Vanderpool, *Tetrahedron Lett.*, **1980**, 21, 705.
2. R.A. Abramovitch and L. Floch, *Heterocycles*, **1981**, 15, 391.
3. All new compounds were completely characterized by ir, nmr and mass spectroscopy, and had acceptable microanalytical data. Stereochemical assignments have been discussed in ref. 2.
4. (a) J.C. Hubert, J.B.P.A. Wijnberg, and W.M. Speckamp, *Tetrahedron*, **1975**, 31, 1437. (b) J.B.P.A. Wijnberg, N.E. Schoemaker, and W.N. Speckamp, *Tetrahedron*, **1978**, 34, 179.
5. R. Süess, *Helv. Chim. Acta*, **1977**, 60, 1650.
6. K.C. Schreiber and V.P. Fernandez, *J. Org. Chem.*, **1961**, 26, 1744.
7. S. Okhi, N. Ozawa, Y. Yabe, and H. Matsuda, *Chem. Pharm. Bull.*, **1976**, 24, 1362.
8. H.B. Bürgi, J.D. Dunitz, J.M. Lehn, and G. Wipff, *Tetrahedron*, **1974**, 30, 1563. H.B. Bürgi, J.D. Dunitz, and E. Shefter, *J. Am. Chem. Soc.*, **1973**, 95, 5065.
9. J.E. Balwin, *J. Chem. Soc., Chem Commun.*, **1976**, 738.
10. Authentic **10** was prepared from 3-methyl-*N*-phenylsuccinimide by a Speckamp reduction<sup>4</sup> followed by dehydration to give a mixture of **10** (19%) (identical with our product -- vinyl proton at  $\delta$  6.73) and the isomeric 4-methyl-*N*-phenyl- $\Delta^3$ -pyrroline-2-one (8.7%) (vinyl proton at  $\delta$  5.9).
11. B.E. Maryanoff, *J. Org. Chem.*, **1979**, 44, 4410.

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