Reduction of 1,1-Diaryl-Substituted Ethenes with Sodium Metal in Dimethylformamide: A Novel Synthesis of α-Hydroxybutanamides

Carlo Botteghi,* Stefano Gotta,^b Mauro Marchetti,^b and Giovanni Melloni*c

a) Dipartimento di Chimica, Università di Venezia, Calle Larga S. Marta 2137, I-30123 Venezia, Italy
b) Istituto per l'Applicazione delle Tecniche Chimiche Avanzate ai Problemi Agrobiologici, C.N.R., Via Vienna 2, I-07100 Sassari
c) Dipartimento di Chimica, Università di Sassari, Via Vienna 2, I-07100 Sassari, Italy

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Abstract: An unusual reactivity was observed in the reduction of 1,1-diphenylethene and 1-phenyl-1-(2-pyridyl)ethene with Na metal in DMF; the reaction afforded the corresponding N,N-dimethyl-4,4-diaryl-2-hydroxybutanamides in high yields.

As an extension of our research on the electron-transfer reduction of activated carbon-carbon double bonds,¹ the study of the reactivity of aryl-substituted ethenes in the system Na metal/dimethylformamide (DMF) was undertaken. We wish to report herein the results obtained in the reduction of 1,1-diarylethenes, which led to the discovery of a new synthesis of α -hydroxyamides.

In a typical experiment, a solution of 1,1-diphenylethene (1) (1 g, 5.5 mmol) in anhydrous DMF^2 (40 mL), under argon, was treated with an excess of Na metal (1 g) at 80°C under stirring; the metal gradually dissolved in the solvent, and the reaction mixture became dark brown. After 5 h, the reaction mixture was chilled to 0°C and quenched by careful addition of ice-water (CAUTION). Standard work-up afforded N,N-dimethyl-4,4-diphenyl-2-hydroxybutanamide^{3,4} (2) (1.3 g, 93% yield) according to the overall stoicheiometry reported in the equation.

 $\begin{array}{c} \overbrace{Ar}^{+} 2 \xrightarrow{O}_{H} NMe_{2} \xrightarrow{+ 2e^{-}} + 2H^{+} \\ 1 \text{ Ar = Phenyl} \\ 3 \text{ Ar = 2-Pyridyl} \end{array} \qquad \begin{array}{c} + 2e^{-} \\ + 2H^{+} \end{array} \qquad \begin{array}{c} \overbrace{Ar = 2-Phenyl} \\ 4 \text{ Ar = 2-Pyridyl} \end{array}$

In a similar manner, 1-phenyl-1-(2-pyridyl)ethene⁵ (3) gave at room temperature a nearly quantitative yield of *N.N*-dimethyl-4-phenyl-4-(2-pyridyl)-2-hydroxybutanamide^{4,6} (4) as a mixture of diastereomers in the ratio 48:52. Selective oxidation of 4 with chromium(VI) oxide in acetic acid at 100°C afforded *N.N*-dimethyl-4-phenyl-4-(2-pyridyl)-2-oxobutanamide^{4,7} (5) as the only product in 70% yield. No reaction occurred, even at temperatures up to 130°C, with 2-phenylpropene, trans-stilbene, and triphenylethene; under the same conditions, cis-stilbene underwent quantitative isomerization to trans-stilbene in 24 h at 80°C. Surprisingly, no reaction occurred by heating 1 with an excess of Na metal in *N*-pyrrolidinecarboxyaldehyde at 130°C for 12 h.

To the best of our knowledge, this reaction represents the first example of the insertion of two DMF units into a carbon-carbon double bond occurring under electron-transfer reduction conditions. In this context, DMF is known to afford formylation products under a variety of conditions, *e.g.*, at a Pt cathode with styrene and 2-phenylpropene,⁸ or with various alkenyllithium derivatives.⁹ On the other hand, products of amidation of alkenes with DMF were obtained using radical promoters,¹⁰ but in low yields and contaminated by a variety of secondary products, in particular aminoalkylation products.

The synthetic usefulness of the present reaction is noteworthy. In fact, it consists of a one-pot reaction involving the formation of 4,4-diaryl-substituted 2-hydroxyamides having a chain two carbon-atom longer than the starting compound. Furthermore, when followed by oxidation of the 2-hydroxy group, it corresponds to a double carbonylation reaction of an alkene;¹¹ the resulting products are valuable precursors of uncommon α -aminoacids and derivatives.

At the present stage of the research, we are not able to offer a simple rationale for the results obtained; however, taking into account that the reaction proceeds under typical reductive electron-transfer conditions, the intermediacy of the radical anion or dianion of the starting alkene must be taken into consideration.¹² Two hypotheses may then be formulated. (a) An hydroformylation reaction by DMF⁸ followed by nucleophilic attack of the acyl anion ⁻CONMe₂¹³ formed by the action of Na metal on DMF.¹⁴ (b) Reaction of the radical anion or dianion with *N,N*-dimethylglyoxylamide [Me₂NCOCHO], which is known to be formed by dimerization of DMF by treatment with Na metal.¹⁵

REFERENCES and NOTES

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- 2. Anhydrous DMF was obtained by distillation of the commercial product (Aldrich) from anhydrous K2CO3 under vacuum.
- Mp 103°C (from ethanol); ¹H NMR (300 MHz, CDCl₃) δ 2.15 (m, 1H, CH₂), 2.3 (m, 1H, CH₂), 2.63 (s, 3H, N-CH₃), 2.91 (s, 3H, N-CH₃), 3.62 (d, 1H, J=10.25 Hz, CH-OH), 4.09 (pseudo t which on D₂O exchange goes to d, 1H, J=15 Hz, CH-OH), 4.41 (dd, 1H, J=3.41 and 11.35 Hz, Ph₂CH), 7.25 (m, 10H, aromatic); ¹³C NMR (300 MHz, CDCl₃) δ 35.8 (N-CH₃), 35.9 (N-CH₃), 41.1 (CH₂), 46.7 (Ph₂CH), 65.8 (CH-OH), 126-129 (aromatic); IR (KBr): 1637 cm⁻¹; mass spectrum (m/e): 283 (M⁺).
- 4. All new compounds gave satisfactory analytical data (within 1%).
- 5. Prepared following a described procedure: Schubert, R.; Grützmacher, H. F. J. Am. Chem. Soc. 1980, 102, 5323.
- 6. Bp of the mixture: 220°C at 0.5 mm Hg; identified by ¹H and ¹³C NMR (COSY and HETCOR techniques) and oxidation to 5.
- Bp 180°C at 0.5 mm Hg; ¹H NMR (300 MHz, CDCl₃) δ 2.75 (s, 3H, N-CH₃), 2.93 (s, 3H, N-CH₃), 3.22 (dd, 1H, J=4.9 and 21.6 Hz, CH₂), 3.79 (dd, 1H, J=10.8 and 21.6 Hz, CH₂), 4.69 (dd, 1H, J=4.9 and 10.8 Hz, CH), 6.90-8.40 (aromatic).
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