

Studies on Electrolytic Substitution Reactions. XIX.* Anodic Oxidation of *N,N*-Di-*tert*-butylformamide and *N*-Formyl-2,2,6,6-tetramethylpiperidine

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Formation of *N*- α methoxylated *N,N*-disubstituted carboxamides by anodic oxidation is a well-established synthetic procedure, as demonstrated by a multitude of reports from this and other laboratories.¹⁻⁵ The mechanism, as yet not fully confirmed, is believed to be of the ECE type. Thus, the radical cation formed after the removal of one electron is rapidly quenched by loss of a proton, followed by the removal of the second electron. In the presence of a nucleophile, such as methanol, the resulting cation is immediately captured thus forming the *N*- α methoxylated amide [eqn. (1)].

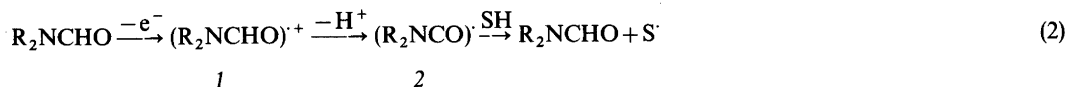
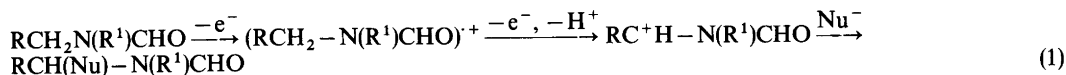
Although our previous work in this field deals almost exclusively with the synthetic applications of amide methoxylations, we now report the oxidation of two compounds which lack the *N*- α protons necessary to form methoxylation products, in order to illuminate a mechanistic problem: Can the formyl hydrogen be substituted at all?

Results and discussion. During our investigations of anodic methoxylations we occasionally encountered cases seemingly suitable for substitution but where product formation was inexplicably slow or negligible.⁶ Among the possible interpretations was loss of the formyl hydrogen in the radical cation, causing the formation of an intermediate radical^{7,8}

* Part XVIII, see Blum, Z., Malmberg, M. and Nyberg, K. *Acta Chem. Scand. B* 35 (1981) 739.

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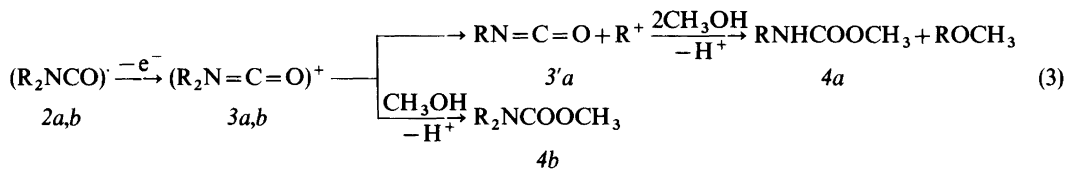
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with the ability of regenerating the starting material by abstracting a hydrogen atom from a solvent molecule [eqn. (2)].

As the fate of the solvent radical, *i.e.* $\cdot\text{CH}_2\text{OH}$, would ultimately be the formation of formaldehyde, indistinguishable from the formaldehyde produced by direct oxidation at the anode, its detection could not be used as an indication that the mechanism proposed was at work. Learning that the hitherto elusive *N,N*-di-*tert*-butylformamide was now available⁹ we recognized its aptitude to contribute to the elucidation of the mechanism of eqn. (2). Being fully substituted at the α -*N* carbon atom the radical cation 1, deprived of the opportunity to participate in the ordinary methoxylation process, would be forced to form the deprotonated intermediate 2. Competitive reactions might then interfere with hydrogen abstraction, thus forming unique and detectable products. As C-N cleavage was anticipated the inclusion of *N*-formyl-2,2,6,6-tetramethylpiperidine in the study was imperative. The ring structure would prohibit any small fragment to cleave off, facilitating the detection and analysis of products formed *via* C-N cleavage.

The title compounds were oxidized in methanol solution at a platinum anode. As expected both compounds were almost but not completely inert toward these reaction conditions. GLC analysis revealed the slow formation of a single product in both cases. After passage of 12-14 F/mol the electrolysis was discontinued since the formation of detectable products reached its maximum. MS analysis of the product formed from *N,N*-di-*tert*-butylformamide suggested it to be methyl *N-tert*-butylcarbamate and this was demonstrated by comparison with an authentic sample. MS analysis of the product from the oxidation of *N*-formyl-2,2,6,6-tetramethylpiperidine indicated the formation of *N*-methoxycarbonyl-2,2,6,6-tetramethylpiperidine. The product was isolated by preparative GLC, providing enough material to allow for NMR and IR examination, the results of which confirmed the structure indicated by MS. Evidently the abstraction of the formyl hydrogen is a feasible process under conditions usually employed in anodic oxidation of amides [eqns. (2) and (3)].

As to the difference in product structure, this may be attributed to features within the parent molecules. Di-*tert*-butylformamide, being a highly



a: R = *t*-C₄H₉ -

b: R₂ = -C(CH₃)₂CH₂CH₂CH₂C(CH₃)₂ -

crowded molecule,⁹ could find an opportunity to relieve steric strain by expelling the *tert*-butyl cation from 3a. The resulting *tert*-butyl isocyanate 3'a would then be captured by methanol to form the observed carbamate 4a. *N*-Formyl-2,2,6,6-tetramethylpiperidine apparently finds sufficient strain relief by forming the linear cation 3b which is then rapidly consumed by solvent leading to carbamate 4b.

Experimental. ¹H NMR spectra were recorded in CDCl₃ on a Jeol MH-100 instrument. GLC/MS analyses were obtained on a Finnegan 4021 spectrometer operating at 70 eV. GLC analyses were performed on an HP-5830 A gas chromatograph fitted with an HP-18850 A recorder/integrator. Columns used were 3 m × 3 mm 5% OV 17 on Chromosorb W or 0.5 m × 3 mm 3% Dexil 300 on Chromosorb W AW. IR spectra were recorded on a Perkin-Elmer 298 spectrophotometer. Methanol was of highest available commercial quality and was used as received. Tetrabutylammonium tetrafluoroborate was prepared according to a published method.¹⁰

Di-tert-Butylformamide was prepared from di-*tert*-butylamine according to the method of Smith *et al.*⁹

*N-Formyl-2,2,6,6-tetramethylpiperidine.*¹¹ The method of Smith *et al.* was adopted. A mixture of 2,2,6,6-tetramethylpiperidine (1.41 g, 10 mmol), ethanol-free chloroform (11.0 g, 92 mmol), dichloromethane (32.3 ml), benzyltriethylammonium chloride (1.03 g, 4.5 mmol) and 24.5 ml of 12.5 M sodium hydroxide was refluxed overnight. On cooling, the mixture was diluted with water and extracted with dichloromethane. After washing with brine and dilute hydrochloric acid the dichloromethane solution was dried over MgSO₄ and the solvent was removed. The crude crystalline mass was purified by vacuum sublimation (0.1 mm Hg, 50°C bath temperature), yielding 1.35 g of pure material (80%), m.p.: 47.5–48.5°C. MS: *m/e* (% rel int): 169(10, M), 154 (52), 109 (67), 86 (97), 69 (100), 58 (58), 46 (28). ¹H NMR: 1.43 (12 H, br s), 1.61 (6 H, s), 8.53 (1 H, s).

Electrolyses were carried out in a 10 ml water-jacketed cell with a magnetic stirrer. Electrolytes

were 1.0 M in substrate and 0.1 M in supporting electrolyte. Platinum foil was used as both anode and cathode material. Current was passed by means of a PAR 373 potentiostat/galvanostat in the galvanostatic mode, and was monitored by an electronic integrator. The current density was maintained at 25 mA/cm². When GLC analysis indicated the maximum achievable amount of product, equalling the passage of 12–14 F/mol, electrolysis was interrupted and the electrolyte was further analyzed.

N-Methoxycarbonyl-2,2,6,6-tetramethylpiperidine. A solution of *N*-formyl-2,2,6,6-tetramethylpiperidine (507 mg, 0.003 mol) in 3 ml of methanol, 0.1 M in Bu₄NBF₄, was oxidized until GLC showed no further increase of the product concentration (at 14.3 F/mol). The solvent was evaporated and the remaining oil was redissolved in 0.5 ml of methanol. The product was isolated by preparative GLC using a Perkin-Elmer F 21 preparative gas chromatograph fitted with a 3 m × 8 mm 20% OV 17 on Chromosorb W column. Yield 43 mg, 7%, 29% on consumed starting material. MS: *m/e* (% rel int): 199 (1, M), 184 (39), 116 (43), 109 (74), 69 (100), 56 (42). ¹H NMR: 1.42 (12 H, s), 1.67 (6 H, m), 3.64 (3 H, s). IR: 1690 cm⁻¹ (C=O).

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