Synthesis and Characterization of Copper(II) and Nickel(II) Complexes Derived from α-Substituted Malondialdehydes

V. Salas Reyes\textsuperscript{a}, C. Aguilerab

\textsuperscript{a} Departamento de Química Orgánica
\textsuperscript{b} Departamento de Polímeros Facultad de Ciencias Químicas, Universidad de Concepción, Casilla 3-C, Concepción, Chile

Z. Naturforsch. \textbf{50}b, 205–208 (1995); received September 28, 1994

Malondialdehyde, Acroleins, Formylation, Metallomesogen, Liquid Crystal

The synthesis and characterization of two series of novel bis(4'-alkyloxyphenyl)malondialdehydes of copper(II) and nickel(II), (R=C\textsubscript{n}H\textsubscript{2n+1}, n = 9, 10, 11, 12) from 2-(4'-hydroxyphenyl)-3-dimethylamino acrolein is described.

Introduction

Amongst the different varieties of ligands with coordination properties, we became interested in bidentate ligands structurally related to β-diketones [1], which can give rise to flat bis-ligand complexes with square planar geometries such as α-(4'-alkyloxyphenyl)malondialdehyde metal complexes, to study their potential in the synthesis of metallomesogens. With this purpose we synthesized a series of (4'-O-substituted)-α-aryl-β-dimethylamino acroleins which are known to undergo transformations and condensation reactions with amines [2] and are readily hydrolyzed under strongly alkaline conditions to produce α-arylmalondialdehydes. The first preparation of α-aryl-β-(dimethylamino)acroleins from arylacetic acids of formula RCH\textsubscript{2}CO\textsubscript{2}H (R, aromatic or heterocyclic group) was described by Arnold et al. [3], using the Vilsmeier-Haack condensation. From the preparative point of view this reaction results in the loss of the carboxyl group and the introduction of two formyl residues. An hypothetical ketene intermediate has been proposed for this transformation [3]. Subsequently, alkaline hydrolysis of these compounds to produce 2-aryl malondialdehydes was further discussed by Coppola [4] and coworkers. Only a few α-(4'-O-substituted phenyl)-β-dimethylamino acroleins have been reported, \textit{i.e.} α-(4'-methoxyphenyl)-β-dimethylamino acroleins [4]. To our knowledge, no long chain α-(4'-alkyloxyphenyl)-β-dimethylamino acroleins have been prepared.

Results and Discussion

We have synthesized a series of α-(4'-alkyloxyphenyl)-β-dimethylamino acroleins, which can be hydrolyzed to their corresponding α-(4'-alkyloxyphenyl)-β-malondialdehydes capable of chelation. The preparation of the metal complexes was achieved following the route illustrated in Scheme 1.

The target compounds, the α-(4'-alkyloxyphenyl)malondialdehydes \textbf{6a}–\textbf{d}, were synthesized

\begin{align*}
\text{HO-} & \text{CH_2CH_2COOH} \quad \text{CH_3CO_2} \text{CH_2CH_2COOH} \quad \text{ii} \quad \text{iii} \\
\text{CH_3CO_2} & \text{O} \text{NCH_2Cl} \quad \text{i} \quad \text{iv} \quad \text{HO-} \text{O} \text{NCH_2} \\
\text{R_0} & \text{O} \text{NCH_2} \quad \text{v} \quad \text{vii} \quad \text{RO-} \text{O} \\
\text{RO-} & \text{O} \text{NCH_2} \quad \text{vi} \quad \text{vii} \quad \text{RO-} \text{O} \\
\end{align*}

\textbf{7a}–\textbf{d}, \textbf{8a}–\textbf{d}

\begin{align*}
R & = \text{C}_n\text{H}_{2n+1} \\
M & = \text{Cu, Ni} \\
n & = 9, 10, 11, 12
\end{align*}

Scheme 1. Reagents and conditions: i) Ac\textsubscript{2}O, H\textsuperscript{+}, ii) DMF, OP\textsubscript{Cl}\textsubscript{3}, iii) NaClO\textsubscript{4}, iv) KOH, MeOH, v) DMSO, KOH, RBr, 50 °C, vi) NaOH, EtOH, H\textsubscript{2}O, vii) H\textsuperscript{+}, viii) Cu(OAc)\textsubscript{2}, MeOH reflux, 3 h, Ni(OAc)\textsubscript{2} or NiCl\textsubscript{2}·6 H\textsubscript{2}O, EtOH reflux, 3 h.

\begin{center}
0932–0776/95/0200–0205 $06.00 © 1995 Verlag der Zeitschrift für Naturforschung. All rights reserved.
\end{center}
from 4-hydroxyphenyl acetic acid protected as an acetate. Compound 3 was prepared as a crystalline solid via a Vilsmeier-Haack formylation of 2 with dimethylformamide (DMF) and phosphorus oxychloride (POCl₃) under relatively mild conditions [3], followed by addition of a cold sodium perchlorate solution. Alkaline hydrolysis of 3 yields 4 as a crystalline compound. A more drastic treatment by alkali leads as far as the substituted β-dialdehyde of 4. Usually a Williamson type ether synthesis is used for the alkylation of phenolic hydroxides. A different approach [5] described by Johnstone et al. which is simpler and milder than the conventional ether formation was used for the alkylation of 4 leading to 4′-alkyloxy-acroleins in good yields. This involves the use of finely ground KOH in DMSO at 50 °C with vigourous stirring. Thus α-(4′-alkyloxyphenyl)-β-dimethylamino acroleins 5a-d were obtained in 55–70% yields. These acroleins were directly hydrolyzed to α-(4′-alkyloxyphenyl)-β-malondialdehydes 6a-d by reflux with NaOH in ethanol-water, after HCl addition.

Metal complexes 7a-d and 8a-d were prepared as illustrated above, following a procedure described in the literature [6]. A solution of ligands 6a-d in methanol with a solution of anhydrous Cu(OAc)₂ gave complexes 7a-d. When nickel complexes 8a-d were prepared ethanol was used as solvent either with Ni(OAc)₂ or NiCl₂·6 H₂O. In the last case stoichiometric amount of KOH was added. Spectroscopic data for all compounds are in agreement with the structures proposed. The substituted malondialdehydes 6a-d exhibit enol proton resonances at 13.50 to 14.35 ppm, evidence of complete enolization, as reported for phenylmalondialdehyde [4] and 4-pentylphenylmalondialdehyde [7]. The elemental analysis (Table I) of the metal complexes as well as the IR data agree well with the assumed structures. As supporting evidence, the IR spectra of these compounds show ν(C=O) stretch bands at 1620 cm⁻¹, whereas in the enolized ligands this stretch appears at 1550 cm⁻¹. Moreover, the Fermi resonance of the aldehydic hydrogen of the ligands at 2650 cm⁻¹ disappears on chelation. These observations are all consistent with metal complexation as described in similar systems [8]. The two series of metal complexes synthesized exhibit liquid crystallinity, and are under further investigation.

**Experimental**

All melting points are uncorrected. IR spectra were recorded with a Perkin Elmer 577 infrared spectrophotometer, NMR spectra with a Bruker 300 spectrometer (300 MHz, ¹H NMR). Mass spectra were measured (70 eV) on a Varian Mat CH-7 A mass spectrometer. Elemental analyses were carried out with a Heraeus combustion oven.

**4′-Acetoxyphenylacetic acid (2)**

A mixture of 4′-hydroxyphenylacetic acid (15 g, 0.11 mol), acetic anhydride (50 g, 0.44 mol) and a few drops of concentrated H₂SO₄ was warmed on a water bath at 50–60 °C for 2 h with efficient stirring. The mixture was allowed to cool and stirred occasionally. Water, 200 ml, was added and the solid obtained upon cooling was collected, washed with cold water and dried in a desiccator under vacuum to give white crystals of 2; yield (18 g, 85%).

α-(p-Acetoxyphenyl)-β-dimethylaminacraldehyde dimethylimonium perchlorate (3)

Dimethylformamide (32.4 g, 0.44 mol) was added dropwise to (55.2 g, 0.36 mol) phosphorus oxychloride. During the addition the temperature was maintained at 30 °C by intermittent cooling. After the addition was completed, the mixture was stirred for 10 min, then a solution of (23.3 g, 0.12 mol) of 2 in 80 ml of DMF was added over a period of 10 min. The resulting solution was stirred at 70 °C for 6 h. The excess of DMF was distilled off in vacuo and the residue decomposed by pouring on ice. The solution was treated with sodium perchlorate (14.7 g, 0.12 mol) and dissolved in water. After cooling, the precipitated material was collected and recrystallized from methanol ether. Yield (18 g, 85%).

**Experimental**

All melting points are uncorrected. IR spectra were recorded with a Perkin Elmer 577 infrared spectrophotometer, NMR spectra with a Bruker 300 spectrometer (300 MHz, ¹H NMR). Mass spectra were measured (70 eV) on a Varian Mat CH-7 A mass spectrometer. Elemental analyses were carried out with a Heraeus combustion oven.

**4′-Acetoxyphenylacetic acid (2)**

A mixture of 4′-hydroxyphenylacetic acid (15 g, 0.11 mol), acetic anhydride (50 g, 0.44 mol) and a few drops of concentrated H₂SO₄ was warmed on a water bath at 50–60 °C for 2 h with efficient stirring. The mixture was allowed to cool and stirred occasionally. Water, 200 ml, was added and the solid obtained upon cooling was collected, washed with cold water and dried in a desiccator under vacuum to give white crystals of 2; yield (18 g, 85%).

**α-(p-Acetoxyphenyl)-β-dimethylaminacraldehyde dimethylimonium perchlorate (3)**

Dimethylformamide (32.4 g, 0.44 mol) was added dropwise to (55.2 g, 0.36 mol) phosphorus oxychloride. During the addition the temperature was maintained at 30 °C by intermittent cooling. After the addition was completed, the mixture was stirred for 10 min, then a solution of (23.3 g, 0.12 mol) of 2 in 80 ml of DMF was added over a period of 10 min. The resulting solution was stirred at 70 °C for 6 h. The excess of DMF was distilled off in vacuo and the residue decomposed by pouring on ice. The solution was treated with sodium perchlorate (14.7 g, 0.12 mol) and dissolved in water. After cooling, the precipitated material was collected and recrystallized from methanol ether. Yield (18 g, 85%).
IR (KBr) cm⁻¹: 2930, 1740, 1575, 1395, 1290, 1200, 1080. – ¹H NMR (CDCl₃): 7.81 (s, 2H, CH’s), 7.33 (d, 2H, Ar’s), 7.30 (d, 2H, Ar’s), 3.35 (s, 6H, CH₂N), 2.52 (s, 6H, CH₃N), 2.32 (s, 3H, CH₃CO₂).

α-(p-Hydroxyphenyl)-β-dimethylamino acrolein (4)

A mixture of perchlorate 3, (27.6 g, 0.077 mol) and KOH (8.59 g, 0.153 mol) in methanol (100 ml) was stirred at 50 °C for 5 h. Methanol was removed and the residue dissolved in water. The solution was carefully neutralized with 2N HCl, and the solid obtained on cooling was filtered, washed with water and recrystallized from methanol ether. Yield (14.3 g, 95%), m.p. = 196–198 °C.

IR (KBr) cm⁻¹: 3140, 3000, 2720, 1570, 1380, 1260, 1200, 1090, 840, 785. – ¹H NMR (60 MHz, DMSO-d₆): 9.16 (s, 1H); 8.83 (s, 1H); 7.27 (d, 2H); 7.07 (d, 2H); 3.06 (s, 6H). – EI-MS: m/z. M⁺.

General procedure

Alkylation of 4 was performed essentially by the method of Johnstone et al. [5] slightly modified. The mixture was stirred for 3 h at 50 °C, after which it was poured into water (20 ml) and extracted with dichloromethane (3×20 ml). The combined organic extracts were washed with water (5×20 ml) and dried (Na₂SO₄). Flash column chromatography of the product (ethylacetate) gave 5a–d. Yields (43–50%).

5a. IR (film) cm⁻¹: 3040, 2920, 2850, 2720, 1580, 1380, 1240, 1170, 1090, 835, 780, 720. – ¹H NMR (CDCl₃): 9.0 (s, 1H, CHO’s), 7.06 (d, 2H, Ar’s), 6.75 (broad 3H, Ar’s, CHN), 3.9 (b, 2H, CH₂O), 2.75 (b, 6H, N(CH₃)₂), 1.75 (m, 2H, CH₂), 1.1–1.5 (m, 12H, CH₂’s), 0.88 (b, 3H, CH₃).

5b. IR (film) cm⁻¹: 3040, 2920, 2850, 2720, 1580, 1380, 1240, 1170, 1090, 835, 780, 720. – ¹H NMR (CDCl₃): 9.0 (s, 1H, CHO’s), 7.1 (d, 2H, Ar’s), 6.8 (d, 2H, Ar’s), 6.75 (b, 1H, CHN), 3.9 (t, 2H, CH₂O), 2.7 (b, 6H, N(CH₃)₂), 1.75 (m, 2H, CH₂), 1.2–1.5 (m, 14H, CH₂’s), 0.9 (t, 3H, CH₃).

5c. IR (film) cm⁻¹: 3030, 2920, 2860, 2700, 1570, 1370, 1240, 1090, 840, 780, 720. – ¹H NMR (CDCl₃): 9.1 (s, 1H, CHO’s), 7.1 (d, 2H, Ar’s), 6.85 (d, 2H, Ar’s), 6.75 (b, 1H, CHN), 3.95 (t, 2H, –CH₂O), 2.85 (b, 6H, N(CH₃)₂), 1.75 (m, 2H, CH₂), 1.1–1.5 (m, 16H, CH₂’s), 0.9 (t, 3H, CH₃).

5d. IR (film) cm⁻¹: 3030, 2920, 2860, 2700, 1570, 1370, 1240, 1200, 1090, 840, 780, 720. – ¹H NMR (CDCl₃): 9.1 (s, 1H, CHO’s), 7.1 (d, 2H, Ar’s), 6.87 (d, 2H, Ar’s), 6.80 (b, 1H, CHN), 3.95 (t, 2H, –CH₂O), 2.82 (b, 6H, N(CH₃)₂), 1.76 (m, 2H, CH₂), 1.1–1.5 (m, 18H, CH₂’s), 0.88 (t, 3H, CH₃).

Preparation of α-(p-alkoxyphenyl)-β-malonodialdehydes (6a–d)

General procedure

To a stirred solution of 0.1 mol of the appropriate acroleins 5a–d in 15 ml of ethanol was added 20 ml of 25% aqueous NaOH. The resulting two phase mixture was refluxed for 3 h after which ethanol was removed from the reaction. The mixture was cooled and the sodium salt of the product was filtered and washed with CH₂Cl₂. The product was dissolved in water, acidified with 2N HCl, and the resulting solid washed with water, dried and recrystallized from ether. Yields (75–80%).

6a. IR (KBr) cm⁻¹: 3800–2200 broad, 3040, 2950, 2920, 2840, 2660, 1550, 1390, 1355, 1290, 1245, 1100, 1010, 835, 820, 760, 712. – ¹H NMR (CDCl₃): 14.1 (broad, 1H, OH, enolic), exchangeable with D₂O, 8.55 (s, 2H, CHO’s), 7.18 (d, 2H, Ar’s), 6.93 (d, 2H, Ar’s), 3.95 (t, 2H, CH₂O), 1.78 (m, 2H, CH₂), 1.50–1.20 (m, 12H, CH₂’s), 0.88 (t, 3H, CH₃).

6b. IR (KBr) cm⁻¹: 3300–2100 broad, 3040, 2910, 2840, 2660, 1660, 1595, 1500, 1460, 1420, 1300, 1250, 1165, 980, 930, 845, 718. – ¹H NMR (CDCl₃): 13.5 (b, 1H, OH, enolic), exchangeable with D₂O, 8.53 (2H, CHO’s), 7.25 (d, 2H, Ar’s), 6.92 (d, 2H, Ar’s), 3.95 (t, 2H, CH₂O), 1.78 (m, 2H, CH₂), 1.50–1.20 (m, 16H, CH₂’s), 0.88 (t, 3H, CH₃).

6c. IR (KBr) cm⁻¹: 3300–2200 broad, 3040, 2960, 2920, 2850, 2660, 1550, 1510, 1360, 1290, 1250, 1010, 840, 760, 715. – ¹H NMR (CDCl₃): 14.35 (b, 1H, OH, enolic), exchangeable with D₂O, 8.56 (s, 2H, CHO’s), 7.18 (d, 2H, Ar’s), 6.93 (d, 2H, Ar’s), 3.95 (t, 2H, CH₂O), 1.80 (m, 2H, CH₂), 1.50–1.20 (m, 16H, CH₂’s), 0.88 (t, 3H, CH₃).

6d. IR (KBr) cm⁻¹: 3300–2200 broad, 3040, 2950, 2930, 2910, 2840, 2650, 1550, 1510, 1390, 1355, 1290, 1245, 1180, 835, 820, 760, 715. – ¹H NMR (CDCl₃): 14.20 (b, 1H, OH, enolic), exchangeable with D₂O, 8.57 (s, 2H, CHO’s), 7.20
Preparation of bis-α-(p-alkyloxyphenyl)-β-malonodialdehydes of Cu(II) (7a–d)

To a solution of each of the compounds 6a–d (0.728 g, 2.46 mmol) in warm absolute methanol (20 ml), anhydrous copper(II) acetate (0.223 g, 1.23 mmol) was added. The copper complexes precipitated immediately, and the mixtures were refluxed for 3 h. The complexes were collected, washed with methanol, dried, and recrystallized from tetrahydrofuran to give complexes 7a–d.

Preparation of bis-α-(p-alkyloxyphenyl)-β-malonodialdehydes of Ni(II) (8a–d)

These complexes were prepared exactly as described for 7a–d, using ethanol as solvent. When NiCl₂·6H₂O was used, KOH was added to procedure light green complexes.

Acknowledgement

The authors gratefully acknowledge to the Dirección de Investigación, Universidad de Concepción for financial support (project DI 20.13.74) and partial support from Stiftung Volkswagenwerk.