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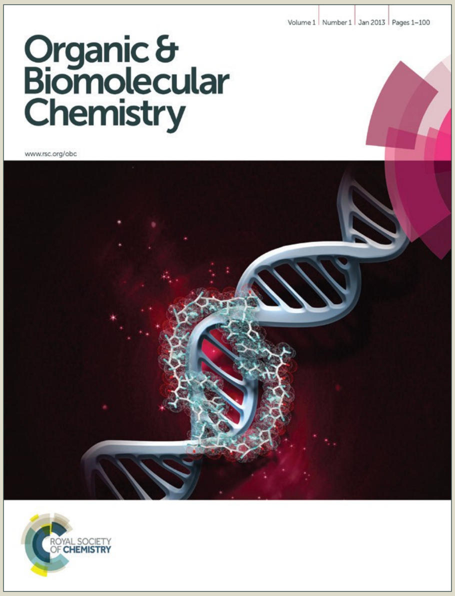

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Corrole and nucleophilic aromatic substitution are not incompatible: a novel route to 2,3-difunctionalized copper corrolates

M. Stefanelli,[*a] F. Mandoj,[a] S. Nardis,[a] M. Raggio,[a] F.R. Fronczek,[b] G.T. McCandless,[c] K. M. Smith,[b] and R. Paolesse[a]

The insertion of a –NO_2 group onto the corrole framework represents a key step for subsequent synthetic manipulation of the macrocycle based on the chemical versatility of such a functionality. Here we report results on the investigation of a copper 3-NO_2-triarylcorrolate in nucleophilic aromatic substitution reactions with "active" methylene carbanions, namely diethyl malonate and diethyl 2-chloromalonate. Although similar reactions on nitroporphyrins afford chlorin derivatives, nucleophilic attack on carbon-2 of corrole produces 2,3-difunctionalized Cu corrolates in acceptable yields (*ca.* 30%), evidencing once again the erratic chemistry of this contracted porphyrinoid.

Introduction

Among all the porphyrin-related compounds, corroles have experienced particular attention in recent decades, thanks to their peculiar chemistry and photophysical properties. The presence of a direct pyrrole-pyrrole link contracts the aromatic ring, which, together with its trianionic ligand character, results in a unique reactivity profile for the macrocycle in various transformations.

A significant contribution to this corrole interest was offered from the synthetic methodologies developed at the end of the 1990s by the Gross[1] and Paolesse[2] groups for the experditious preparation of meso-triarylcorroles using commercial pyrroles and aldehydes, which reduced the synthetic difficulties for the preparation of this macrocycle. The route to β-alkylcorroles in fact involves multistep and time-consuming synthetic procedures that prevented in depth investigations on such the macrocycle for a long time.

Taking advantage of further optimized synthetic methodologies,[3] the scientific interest on corroles has continously increased, as witnessed by the abundance in the literature of accounts dealing with the theoretical[4] as well as more application-related aspects[5-8] and moving through chemical reactivity[9] and coordination ability of the corrole porphyrinoid.[10]

In addition to the definition of convenient synthetic routes to corroles and their metal complexes, our corrole-centered research activity has been extensively focused on the chemical modification of the macrocycle skeleton, with the dual purpose of investigating its chemical behaviour and designing new molecules with tunable properties for specific applications. Our attempts in most cases led to the target transformations, such as the peripheral insertion of varied functionalities[11] (halogens, formyl, nitro and sulphonic groups) or β-fused aromatic rings,[12] but they also serendipitously led to corrole metamorphosis into new intriguing macrocycles such as isocorroles,[13] hemiporphycenes[14] and aza-hemiporphycenes,[15] evidencing the unique reactivity of this contracted porphyrinoid. In particular the nitration reaction on β-pyrrolic positions was thoroughly studied by our group and to date several mono-, bis- and tris-functionalized[16] corrole derivatives have been achieved by using different reaction protocols. The reasons for our interest in such functionalizations have to be clearly found in the intrinsic synthetic value of the nitro group, which makes nitrocorroles excellent starting platforms for further elaboration. Indeed both the activating effect towards nucleophiles and the well-known chemical versatility of the -NO_2 group in many organic transformations can be exploited to generate novel β-substituted corrole derivatives with additional stimulating properties. Regarding this, we have recently reported the chemical manipulation of a copper 3-NO_2-triarylcorrolate, in which the initial reduction of –NO_2 to –NH_2 group was followed by further transformations.[17] The amidation proceeded efficiently and different β-acylated

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[a] *Dipartimento di Scienze e Tecnologie Chimiche, Università di Roma Tor Vergata, 00133 Roma, Italy. E-mail: manuela.stefanelli@uniroma2.it; Fax: +39 0672594328; Tel: +39 0672594752.*

[b] *Department of Chemistry, Louisiana State University, Baton Rouge, LA 70803, USA.*

[c] *Department of Chemistry, The University of Texas at Dallas, Richardson, TX 75080, USA.*

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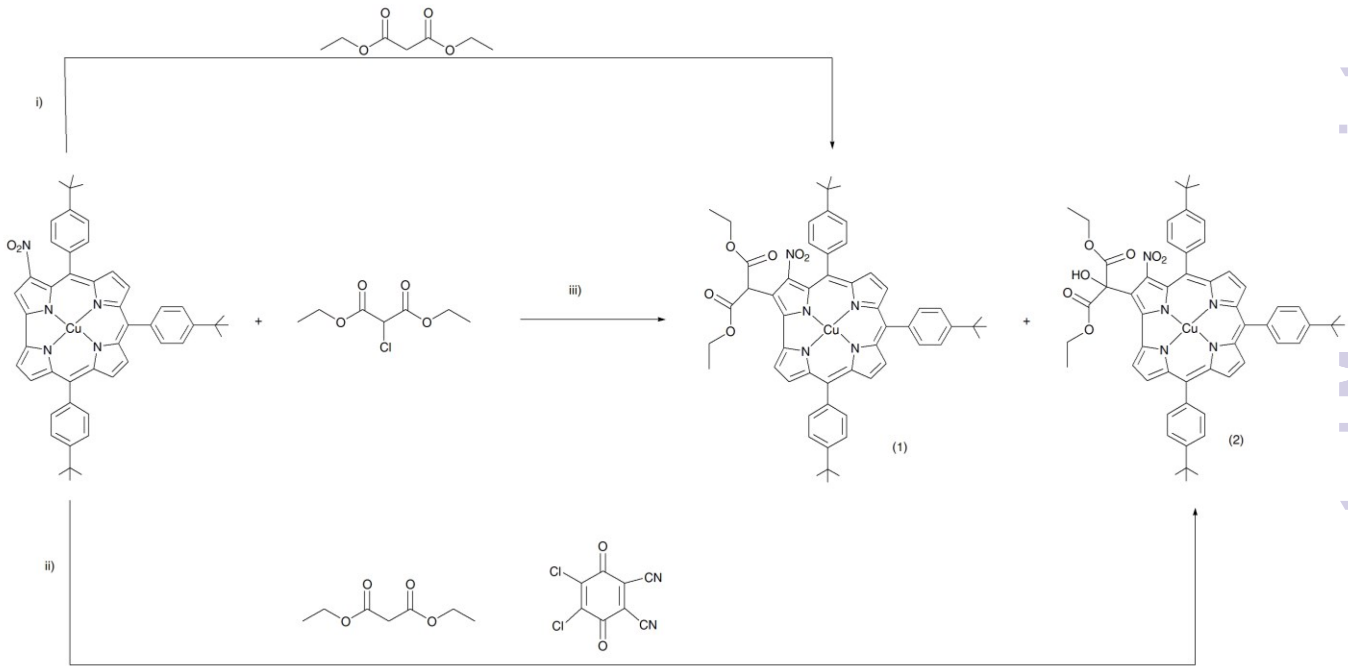

Scheme 1: Preparation of nitrocorrole derivatives **(1)** and **(2)** reported in this work. i) corrole/diethyl malonate/NaOH (1:10:10), toluene/EtOH (20:1), 80°C, 30 min; ii) corrole/diethyl malonate/NaOH (1:10:10), toluene/EtOH (20:1), 80°C, 15 min, then DDQ, 20 min; iii) corrole/diethyl 2-chloromalonate/NaOH (1:10:10), toluene/EtOH (20:1) 80°C, 30 min.

copper corrolates were obtained, the more interesting being the derivative bearing an alkyl azide group on the peripheral positions. The use of such a compound in the Huisgen 1,3-dipolar ("click") cycloaddition was also reported and represents to date one of the few examples of the application of this approach in the corrole field. The results reported in the present work arise from the investigation of the other possibility to exploit the nitro group for modification of the corrole skeleton, which is the switch of the reactivity of the position adjacent to the NO_2 group towards nucleophilic reagents. This aspect has been extensively investigated in porphyrin chemistry, where the insertion of $-NO_2$ group on β-pyrrolic positions allowed for preparation of a range of 2-substituted or 2-nitro-3-substituted porphyrins or chlorins by reaction with different nucleophiles.[18] In the case of corrole it should be noted, however, that the use of nucleophilic reactions for ring functionalization is particularly challenging, since this macrocycle is more electron rich than porphyrins. To the best of our knowledge, the β-amination reaction on nitrocorrolates is to date the only example in the literature dealing with this kind of research in corrole chemistry.[16b] With the aim to expand these investigations in corrole macrocycle, we used the Cu corrole complex 3-(NO_2)TtBuCorrCu in reactions at the C2 pyrrolic position with carbon-centered nucleophiles, as outlined in Scheme 1. The 2,3-difunctionalized corrolates (**1**) and (**2**) were obtained in acceptable yields, introducing nucleophilic aromatic substitution reactions as a synthetic tool for peripheral functionalization of the electron-rich corrole ring.

Results and discussion

Being inspired by the numerous examples of organic reactions involving the NO_2 group on nitroporphyrins, we engaged in the investigation of a copper β-nitrocorrole in analogous tranformations. Our interest was initially focused on the application of one of the most interesting reactions of NO_2-porphyrins reported, which led to the [3,4-b]pyrroloporphyrins by means of the Barton Zard cycloaddition with an alkyl isocyanoacetate.[19] This reaction opened the way to π-extended porphyrin oligomeric species, endowed with high-intensity luminescence in the near IR-region.[20] We were interested in applying the same reaction in the case of corrole, since to date only few examples of corrole-based arrays directly linked both by the β- and the meso-positions are reported in the literature,[21] with β-fused oligomers being absent.

Therefore we reacted 3-(NO_2)TtBuCorrCu and ethyl isocyanoacetate using the procedure reported in the literature,[19b] in which different metallo-2-nitroporphyrins were reacted with isocyanoacetates using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as base and a THF/alcohol solvent mixture, to give the fused pyrrole-ring formation. Unfortunately the application of this methodology on copper nitrocorrole was not productive, since most of the starting material was left unreacted and no β-fused system was detected. Similarly, the use of potassium carbonate in dry THF proved to be unsuccessful. In both cases we observed a quick change of the solution colour, from brownish to emerald-green, upon addition of the base to the copper complex. The monitoring of such a variation by UV-vis spectroscopy evidenced the rapid formation, upon base addition, of the singly reduced form of copper 3-nitrocorrolate (Figure 1, dashed line), whose facile generation in the presence of DBU has been recently observed by us during the electrochemical characterization of the $(NO_2)_x$-TtBuPCorrCu compounds (x= 0,1,2).[16b]

The failure of the reaction with ethyl isocyanoacetate could be reasonably explained, considering that the reduced form of the substrate quickly produced in those basic environments is negatively charged, so deactivated toward to the carbanion nucleophilic attack. This unexpected susceptibility of copper nitrocorrole to basic conditions prompted new reaction conditions, in which the starting complex had to remain in the neutral form suitable for the nucleophilic addition on the pyrrole bearing the nitro group. Polar solvents as THF, DMF or DMSO typically used for nucleophilic substitution reactions associated with strong bases as tBuOK, DBU, NaOH and NaH rapidly transformed the copper complex into the singly reduced product. On the contrary, the combined use of a (20:1)(v/v) toluene/EtOH solvent mixture and NaOH was found to be a good system to leave the substrate intact. The reaction with ethyl isocyanoacetate was then attempted under these new experimental conditions, but once again it was not successful, since neither pyrrole β-fused nor 2- and 2,3-functionalized products were isolated.

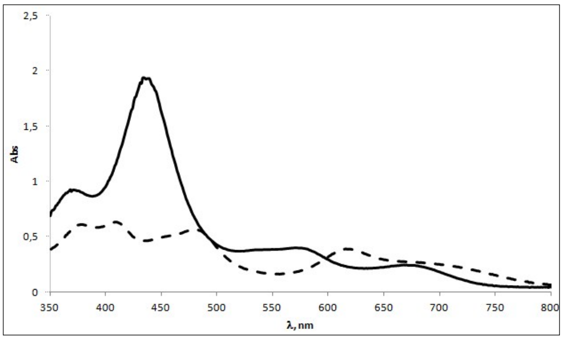

Figure 1. Solid line: UV-vis spectrum of a micromolar solution in THF of 3-(NO_2)TtBuCorrCu(A); Dashed line: UV-vis spectral features changing of (A) upon DBU addition.

Since the construction of the β-fused pyrrolic unit on the tetrapyrrolic macrocycle involves a conjugate addition of a carbon-centered nucleophile to a nitroalkene-like species, we decided to test the effective reactivity of the C2 position of copper 3-nitrocorrolate using diethyl malonate as nucleophile; this diester shares chemical features with α-isocyanoacetic esters. It is worth mentioning that the employment of this reagent and similar "active" methylene carbanions, such as malonates or alkylcyanoacetates, in reactions with different 2-nitro-5,10,15,20-tetraphenylporphyrins enabled the achievement of stable chlorin derivatives in good yields, as reported in the literature.[22] Making slight variations to the experimental conditions reported in these studies on nitroporphyrins, we reacted 3-(NO_2)TtBuCorrCu with diethyl malonate in a toluene/EtOH solvent mixture, using NaOH as a base. The monitoring of the reaction by TLC analysis showed the rapid formation of a brown chromatographic band having a lower R_f value than the starting complex. Column chromatographic purification allowed for the recovery of the unreacted substrate as the first fraction (4% yield) and the isolation of a more polar compound in a 34% yield. The polarity of such a fraction evidenced by TLC led us to suppose the hypothetical functionalization of the corrole ring with the $(EtCO_2)_2CH$- moiety, but concurrently the UV-vis spectral features being almost identical to the starting material ruled out a probable reduction of the C2-C3 pyrrolic double bond occurring in similar conditions on nitroporphyrins, suggestive of a corrolin-type product (dihydrocorrole).[23] The FAB mass spectrum of this isolated compound showed a molecular peak at m/z 959 indicating the insertion of one nucleophilic moiety, whose position on C2 of the corrole periphery was confirmed by the proton NMR spectrum, which showed the disappearance of the corresponding pyrrolic hydrogen. All the diagnostic resonances of an inserted diethyl malonate were also detected, both the singlet at 5.48 ppm and the quartet at 4.25 ppm being evident and corresponding to the α-CH and the CH_2 of the two ethoxy groups, respectively. The unambiguous identification of the compound as the 2-[bis(ethoxycarbonyl)methyl]-3-nitro derivative of copper corrolate (**1**) (Figure 2) resulted by the X-ray crystallographic analysis carried out on a single crystal of a chloroform solvate obtained by slow diffusion of methanol into a diluted chloroform solution.

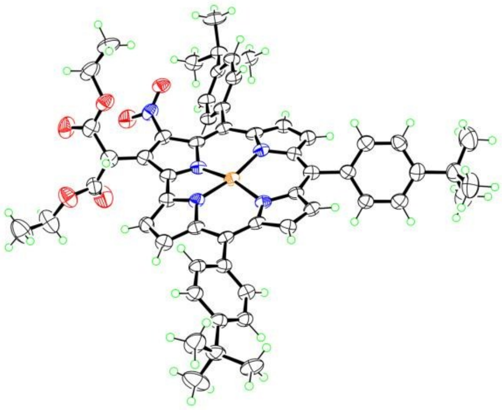

Figure 2. The molecular structure of (**1**) with 50% ellipsoids. The solvent is not shown.

The coordination of the Cu atom is square planar with a slight tetrahedral distortion, N atoms alternating above and below the CuN_4 plane by a mean value of 0.178 Å. Cu-N distances are within the range 1.888(5) to 1.913(5) Å. The corrole core has a saddle conformation, with the beta carbon atoms lying out of the 23-atom corrole plane by up to 0.34 Å (mean of eight, 0.291 Å).

This reaction is an example of a nucleophilic aromatic substitution of hydrogen (S_NAr), in which the addition of the nucleophilic species to the ring to form the anionic σ-adduct is followed by the elimination of hydride, to give the desired substituted product. In similar reactions the departure of H^- rarely occurs spontaneously, so an additional oxidant species is generally required. Since the reaction is formally an oxidation, the overall process is usually reported as an Oxidative Nucleophilic Substitution of Hydrogen (ONSH), a term coined by Mąkosza at the end of the 1980s during studies on novel reactions between electron-deficient arenes and nucleophiles.[24] Despite the many oxidants generally employed in organic chemistry, only a limited number have been successfully used for the oxidation of these nitronate σ-adducts, namely DDQ, Br_2, $KMnO_4$ or O_2, [24b,24c] even though electrochemical methods were also exploited.[25] In particular there are several examples in the literature of ONSH processes occurring in nitroarenes with stabilized primary and secondary carbanions dues to O_2 being dissolved in the reaction medium,[26] as likely happens in our reaction with diethylmalonate in which no oxidant species was voluntarily introduced into the system. The outcome of an ONSH process depends on several elements, such as the nucleophile resistance to oxidation and its nucleophilicity, the electrophilicity of the arenes and the nature of the oxidant used, the latter having to faster oxidize the nitronate adduct than the nucleophilic reactant.

In order to evaluate the influence of the oxidant on the reaction of Cu 3-nitrocorrolate with diethyl malonate, we decided to add DDQ during the reaction. In particular the oxidant was introduced after 15 minutes and the mixture was left for an additional 20 minutes. The monitoring of the crude reaction by TLC analysis evidenced some decomposition products and the formation of one main compound, more polar compared with the starting complex. Chromatographic purification on a column enabled the isolation of a little unreacted substrate (*ca* 4% recovery) and the isolation of a single fraction (32 % yield), having UV–vis spectral features similar to corrole 2-DEM-3NO_2-TtBuPCorrCu **1**. However the molecular mass obtained by FAB mass spectroscopy for this compound was higher than that expected for (**1**), since a molecular peak at m/z 975 was evident. Although ^{1}H NMR spectroscopy again revealed a substitution occurring at C2 of the corrole ring, a different pattern for the proton resonances for diethyl malonate was indeed observed. In more detail, the spectrum showed a singlet at 4.77 ppm and two multiplets centered at 4.33 and 4.20 ppm, respectively, each one corresponding to 2H. Based on the difference in mass units in the mass FAB spectra of the two compounds, their relative polarity, and information gathered from the proton NMR spectrum, we identified the main product obtained from the oxidation with DDQ as the α-hydroxyderivative of the copper corrole (**1**). This assignment was further supported by an example reported in the literature in which Mąkosza and co-workers[27] described different ONSH products for the nucleophilic hydrogen substitution in nitroarenes with the carbanion of phenylacetic acid derivatives depending on the oxidant used. As in that case, we can surmise that the initially formed ONSH product (**1**) was further deprotonated by the excess of NaOH and oxidized by the added DDQ to give the α-hydroxy ester, 2-DEM(OH)-3NO_2-TtBuPCorrCu **2**. Therefore, in this case, we did not observe any influence of the oxidant used on the extent of nucleophilic substitution, which afforded the 2,3-difunctionalized compound in similar yield; at the same time, we have noted a different action of DDQ with respect to molecular oxygen, resulting in a different final ONSH product.

Another approach to obtain products of the nucleophilic substitution of hydrogen developed by Mąkosza and co-workers, is known as the "vicarious" nucleophilic substitution (VNS) of hydrogen, which makes use of carbanions containing leaving groups "X" at the carbanion center.[28] In these reactions, the compounds are able to lose the X^- with a simultaneous 1,2-hydride shift, to give products of hydrogen substitution with the nucleophile moiety after the elimination of HX from the intermediate σ-adduct. In fact, the introduction of one or two amino groups on Cu and Ge nitrocorrolates by using 4-amino-4H-1,2,4-triazole as nucleophile[16b] is just such an example of VNS reaction on the corrole macrocycle.

Regarding this class of reactions, we selected diethyl 2-chloromalonate as a nucleophilic agent to react with the substrate 3-(NO_2)TtBuCorrCu, with the aim to still obtain the Cu 2-diethylmalonate-3-nitrocorrolate **1**, but with increased yields. Thus, we reacted the copper nitrocorrolate with this nucleophile using the same reaction conditions described before for the reaction with diethyl malonate. The TLC analysis of the reaction showed complete consumption of the starting material in about 30 minutes. Although some decomposition of the starting material was observed, three brownish bands were apparent and were identified after chromatographic purification. The first eluted band was isolated in 3% yield, and its amount was sufficient for its complete spectroscopic characterization. The ^{1}H NMR spectrum was characteristic of a 2,3-difunctionalized product since the proton resonance on C2 was missing. In addition, the quartet at 4.52 ppm corresponding to two protons was indicative of an ethoxy group insertion close to the nitro group, further corroborated by the mass FAB spectrum which afforded the corresponding molecular peak at m/z 844. Finally, the identification of this product as the 2-EtO-3-(NO_2)TtBuCorrCu **3** was unambiguously corroborated by the molecular structure obtained by X-ray crystallographic characterization (Figure 3).

The crystal is the chloroform solvate, grown from chloroform/methanol. The structure is very similar to that of copper corrole (**1**). The coordination of the Cu atom is square planar with a slight tetrahedral distortion, N atoms alternating above and below the CuN_4 plane by a mean value of 0.151 Å. Cu-N distances are within the range 1.890(3) to 1.911(4) Å. The corrole core has a saddle conformation, with the beta carbon atoms lying out of the 23-atom corrole plane by up to 0.42 Å (mean of eight 0.380 Å). The other two chromatographic bands were worked up and the products were characterized (in 28% and 13% yields) as the copper complexes (**1**) and (**2**), respectively. Other than the expected product (**1**), in this case we observed also the formation of the additional products (**2**) and (**3**). While the formation in small yields of the 2-EtO derivative **3** can be reasonably attributed to the competition of the ethoxy group derived from the ethanol used as solvent for the nuclophilic attack, the formation of the hydroxy ester **2** is more surprising and, to the best of our knowledge, has no precedent in the literature. In this case the initial β-elimination of HCl is not followed by the protonation of the carbanion to give the 2-DEM-3NO_2-TtBuPCorrCu **1**, but this intermediate is oxidized by molecular oxygen to give the corresponding α-hydroxy derivative **2**.

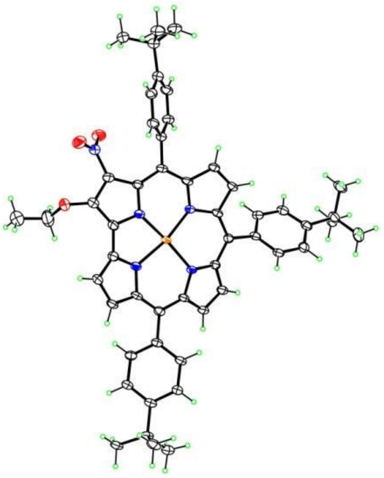

Figure 3. The molecular structure of (**3**) with 50% ellipsoids. The solvent is not shown.

It is worth mentioning that in all the described reactions the exclusive formation of 2,3-difunctionalized metallocorroles has been observed, with derivatives reduced at the pyrrolic double bond and denitrated species being absent; such compounds are typically obtained in the analogous reactions of nitroporphyrins. This finding represents a further confirmation of the peculiar chemical reactivity distinguishing the corrole macrocycle from its parent porphyrin system.

Experimental

General

^{1}H NMR spectra were recorded on a Bruker AV300 spectrometer (300 MHz). FAB mass spectra were obtained on a VGQuattro spectrometer in the positive-ion mode using $CHCl_3$ as solvent and m-nitrobenzyl alcohol (Aldrich) as matrix. UV-vis spectra were measured on a Cary 50 spectrophotometer using dichloromethane as solvent.

Purification by column chromatography was performed using silica gel 60 (70-230 mesh, Sigma Aldrich) as the stationary phase. Reagents and solvents (Aldrich, Merck or Fluka) were of the highest grade available and were used without further purification.

Crystallography

Single crystal X-ray diffraction data was collected for Cu corroles (**1**) and (**3**) using a Bruker Kappa APEXII Duo diffractometer with IµS microfocus radiation source (Cu Kα, λ = 1.54184 Å), Oxford Cryosystems cryostream (T = 90 K), and CCD detector. Both data sets were integrated with Bruker SAINT and scaled with Bruker SADABS (multi-scan absorption correction). Space group determination was conducted using Bruker XPREP and preliminary models were created using SIR97.[29] After refinement was completed in SHELXL2014,[30] missing symmetry (ADDSYM)[31] and structural voids (SQUEEZE)[32] were evaluated with PLATON single-crystal structure validation program. All non-hydrogen atomic sites were refined anisotropically with H atoms in “riding” positions. Both chloroform molecules in 2 were positionally disordered, and one was occupationally disordered.

Crystal data for **2-DEM-3NO$_2$-TtBuPCorrCu(1)**: $C_{56}H_{56}CuN_5O_6\cdot1.647(CHCl_3)$, M_r = 1155.20, monoclinic, a = 19.775(6) Å, b = 18.874(8) Å, c = 16.723(4) Å, β = 114.545(15)°, V = 5678(3) Å^3, T = 90(2) K, space group $P2_{1/c}$, Z = 4, μ(CuKα) = 3.11 mm^{-1}, 60751 reflections measured, ϑ_{max} = 59.1°, 8061 independent reflections (R_{int} = 0.150). The final R_1 values were 0.074 ($I > 2\sigma(I)$) and 0.125 (all data)). The final $wR(F^2)$ values were 0.192 ($I > 2\sigma(I)$) and 0.221 (all data). CCDC 1056807.

For **2-EtO-3-(NO$_2$)TtBuCorrCu (3)**: $C_{51}H_{50}CuN_5O_3\cdot CHCl_3$, M_r = 963.87, triclinic, a = 10.989(3) Å, b = 12.2170(18) Å, c = 18.019(3) Å, α = 95.030(10)°, β = 107.036(15)°, γ = 91.*279*(7)° V = 2301.1(8) Å^3, T = 90(2) K, space group P-1, Z = 2, μ(CuKα) = 2.67 mm^{-1}, 27375 reflections measured, 7993 independent reflections (R_{int} = 0.064). The final R_1 values were 0.0676 ($I > 2\sigma(I)$) and 0.0936 (all data). The final $wR(F^2)$ values were 0.1876 ($I > 2\sigma(I)$) and 0.2054 (all data). CCDC 1056808.

Synthesis

The preparation of 3-(NO$_2$)TtBuCorrCu was accomplished using the procedure reported in the literature.[16b]

Reactions of 3-(NO$_2$)TtBuCorrCu with diethyl malonate

2-DEM-3NO$_2$-TtBuPCorrCu(1): 3NO$_2$-TtBuPCorrCu (50 mg, 0.062 mmol) and diethyl malonate (95 µL, 0.62 mmol) were mixed in toluene/ethanol (20:1) (32 mL) and the solution was stirred at room temperature until the complete dissolution of all reagents. The temperature was then raised to 80 °C and NaOH (25 mg, 0.62 mmol) added. After 30 min, TLC monitoring showed the almost quantitative consumption of the starting complex; hence, the reaction mixture was cooled and the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2, washed with H_2O and dried over anhydrous Na_2SO_4. The crude residue was purified on a silica gel column, first eluting with CH_2Cl_2 to recover the unreacted starting material (2 mg, 4%) and then with $CHCl_3$ to separate the desired compound. The corresponding fraction was crystallized from CH_2Cl_2/MeOH, affording the title compound as a brown-reddish powder (20 mg, 34% yield).

Mp >300°C. UV-vis (CH_2Cl_2): λ_{max}, nm (log ε) nm 370 (4.57), 433 (4.88), 575 (4.16), 671 (3.93).

^{1}HNMR δ_H($CDCl_3$, J [Hz]): 7.95 (d, 1H, J=4.0 Hz, β-pyrrole), 7.69 (m, 7H, β-pyrroles+phenyls), 7.47 (m, 10H, β-pyrroles+phenyls), 5.48 (s, 1H, -$CH(CO_2CH_2CH_3)_2$), 4.25 (q, 4H, -$CO_2CH_2CH_3$), 1.45 (s, 18H, p-tBu), 1.42 (s, 9H, p-tBu), 1.22 (br t, 6H, -$CO_2CH_2CH_3$).

MS (FAB) : m/z 959 (M^+). Anal. Calcd for $C_{56}H_{57}CuN_5O_6$: C, 70.09; H, 5.99; N, 7.30 %. Found C, 70.14; H, 6.08; N, 7.37 %.

2-DEM(OH)-3NO$_2$-TtBuPCorrCu(2): The reaction between 50 mg of Cu 3-NO_2TtBuTPC and a 10-molar fold excess of diethyl malonate was carried out as described above. After 15 min DDQ (17 mg, 0.075 mol) was added and the reaction was heated for further 20 min. The solvent was then evaporated, the residue taken up with CH_2Cl_2, washed with H_2O, and then dried over anhydrous Na_2SO_4. Purification of the residue on a silica gel column eluting with CH_2Cl_2 afforded the unreacted starting material as the first fraction (1.8 mg, 3.6%), while the use of a CH_2Cl_2/MeOH (98:2 v:v) solvent mixture allowed the isolation of the fraction corresponding to compound (**2**). Crystallization from CH_2Cl_2/MeOH gave the title compound as a brownish powder (19 mg, 32 % yield).
Mp >300°C. UV-vis (CH_2Cl_2): λ_{max}, nm (log ε) nm 370 (4.57), 430 (4.81), 570 (4.12), 669 (3.92).
^{1}H NMR δ_H ($CDCl_3$, J [Hz]): 8.04 (d, 1H, J=4.2 Hz, β-pyrrole), 7.69 (m, 7H, β-pyrroles+phenyls), 7.49 (m,10H, β-pyrroles+phenyls), 4.77 (s, 1H, -OH), 4.34 (m, 2H,-$CO_2CH_2CH_3$), 4.20 (m, 2H,-$CO_2CH_2CH_3$), 1. 45 (s, 18H, p-tBu), 1.42 (s, 9H, p-tBu), 1.19 (br t, 6H, -$CO_2CH_2CH_3$).
MS (FAB) : m/z 975 (M^+). Anal. Calcd for $C_{56}H_{57}CuN_5O_7$: C, 68.94; H, 5.89; N, 7.18. Found C, 69.03; H, 5.91; N, 7.27%.

Reaction of 3-(NO_2)TtBuCorrCu with diethyl 2-chloromalonate

The application of the same protocol reported above ([copper corrolate]/[nucelophile]/[base]= 1 :10 :10) for the reaction of 50 mg of 3NO_2-TtBuPCorrCu and an excess of diethyl 2-chloromalonate (100 µL, 0.62 mmol) afforded, after a short chromatographic column (silica gel ; $CHCl_3$ as eluent), traces of compound (**3**) (1.6 mg, 3 %) as the first fraction, followed by compounds (**1**) and (**2**) in 28% and 13% yields, respectively.
(**3**): Mp >300°C. UV-vis (CH_2Cl_2): λ_{max}, nm (log ε) nm 370 (4.57), 432 (4.85), 567 (4.08), 640 (3.90).^{1}H NMR δ_H($CDCl_3$, J [Hz]): 7.74 (d, 1H, J=4.2 Hz, β-pyrrole), 7.66 (m, 7H, β-pyrroles+phenyls), 7.47 (m,6H, β-pyrroles+phenyls), 7.33 (m,3H, β-pyrroles+phenyls), 7.21 (d, 1H, J=4.6 Hz, β-pyrrole), 4.52 (q, 2H, -OCH_2CH_3), 1.44 (s, 9H, p-tBu), 1.43 (s, 9H, p-tBu), 1.41 (s, 9H, p-tBu), 1.48 (brm, 3H, -OCH_2CH_3).
MS (FAB): m/z 844 (M^+) Anal. Calcd for $C_{51}H_{50}CuN_5O_3$: C, 72.53; H, 5.97; N, 8.29. Found C, 72.41; H, 5.89; N, 8.26%.

Conclusions

The possibility to functionalize the periphery of the corrole ring with carbanions has been here investigated. Exploiting the ability of the nitro group of activating the nearest β-pyrrole carbon towards nucleophilic reagents, it was possible to obtain new 2,3-difunctionalized corrole derivatives by reacting the Cu 3-(NO_2)corrolate with alkyl malonates. The functionalization of the macrocycle proceeds following different reaction mechanisms (either ONSH or VNS), depending on the nucleophile used. The products were obtained in lower yields if compared with similar nucleophilic aromatic substitution of hydrogen reactions reported for nitroporphyrins.[33] We can account for this by pointing out that the choice of toluene/ethanol mixture as reaction medium was undoubtedly unfavourable for the nucleophilic attack, but it was compelled to the need of mantaining the copper nitrocorrolate in the neutral form. Moreover, the not entirely negligible decomposition observed in all the tested reactions was due to the dramatic sensitivity in basic environments usually displayed by copper corrolates. The search for different conditions that are able to further promote the nucleophile insertion on the corrole ring is surely needed and, regarding this, additional studies are currently ongoing in our laboratories.

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