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3-NO₂-5,10,15-triarylcorrolato-Cu as a versatile platform for synthesis of novel 3-functionalized corrole derivatives

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Abstract

β -Nitrocorrole derivatives are potentially valuable platforms for the preparation of a wide range of more elaborated corrole derivatives possessing unique chemical functionalities and electronic properties. Here we report our results on the chemical manipulation of a copper 3-NO₂-triarylcorrolate using different organic reactions, all involving the reduction of –NO₂ to –NH₂ at an early stage, followed by further transformations. By way of a β -acylated copper corrolate, a novel corrole derivative bearing an alkyl azide group on the peripheral positions was obtained and exploited in the Huisgen 1,3-dipolar cycloaddition.

Introduction

Corroles are tetrapyrrolic macrocycles belonging to the class of contracted porphyrins, since they lack one methine bridge compared with the parent porphyrin macrocycle. The chemistry of this macrocycle has experienced impressive advancements in the last decade, since its structural features can be nowadays be easily modified by having in hand a rich set of synthetic approaches to address both the *meso*-aryl and β -pyrrolic positions^{1–3}. The possible preparation of a wide range of *meso*-triarylcorroles with tunable properties has allowed a more exhaustive knowledge of the properties of these macrocycles, triggering their promising application in several different fields such as catalysis, medicine and material science⁴. Within this framework, the need to comply with the requirements of a specific application has prompted the development of synthetic procedures leading to corroles functionalized with peripheral substituents, which can be the entry point for subsequent modifications.

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In this regard, the introduction of halogen⁵ and boryl groups⁶ in both the β -pyrrolic and *meso*-phenyl positions was demonstrated to be useful for the further elaboration of the corrole framework using metal-catalyzed coupling reactions; sulfonic and chlorosulfonic groups⁷ also allowed for the preparation of water soluble corroles that can be conjugated with biomolecules³. Starting from formylcorroles⁸, vinyl-⁹ and carboxylic derivatives¹⁰ were also obtained. The former can be used as efficient precursors in cycloaddition reactions, while the latter are potential dyes in solar cells applications³. In this field, we investigated modification of the corrole macrocycle by using the β -nitration reaction of corroles because the nitro group is particularly versatile for introduction of further modifications of the macrocycle¹¹. In the last few years, we have focused our efforts on the definition of several synthetic protocols for the convenient preparation of β -nitrocorrole derivatives bearing from one to four nitro groups, both on corrole free base and metal complexes^{3,12}. Beyond the development of synthetic protocols, these studies also highlighted additional aspects of these nitrated species, such as the electrochemical and spectroscopic features with relation to the number of nitro groups inserted. Furthermore, the per-nitration of the corrole macrocycle also illuminated the unusual reactivity of pyrrole subunit B, which became unexpectedly functionalized although the more reactive pyrroles A and D were still available for substitution^{12g,12h}.

The establishment of these synthetic protocols for the nitration of corroles led us to investigate the exploitation of the nitro group in the preparation of additional novel corrole derivatives. The feasible organic transformations dealing with the nitro functionality can take advantage of its activating effect in nucleophilic substitution reactions, or its easy modification into a different functional group, passing through the amino derivative as a key intermediate. We recently reported the introduction of amino groups onto the β -positions of the corrole framework, describing how copper and germanium 3-nitrocorrole^{12a,12b} and copper 3,17-dinitrocorrole^{12a} derivatives can be used as substrates for direct amination on the C2 and C18 β -carbons in a VNS (Vicarious Nucleophilic Substitution of hydrogen) reaction, where 4-amino-4*H*-1,2,4-triazole constituted the -NH_2 source. To date, the resulting β -amino-nitrocorrole derivatives have represented the first examples of nucleophilic aromatic substitution carried out on a pyrrolic unit of a corrole ring, testifying to the ability of -NO_2 group to switch on the electrophilic character of the adjacent β -carbon even in the electron rich corrole ring.

In the present work, we report the transformation of the nitro group via early catalytic reduction to the amino group, followed by its further modification into other functionality.

The practical synthetic value of nitrocorroles has once again been concretely pointed out, since the preparation of the reactive aminated intermediate (**1**) provides access to several novel β -functionalized corroles with tunable structural as well as electronic properties.

Results and discussion

The straight manipulation of the -NO_2 group for further modifications of corrole ring, where the first step is its reduction to the amino group, is not unprecedented. Indeed aminocorroles substituted on the *orto* and *para meso*-phenyl positions were just reported in literature, being

used as precursors for the preparation of a series of free base hemoprotein corrole analogs¹³ in the former case and for the design of organic-inorganic hybrid materials and photoactive binuclear Ru-Cu species¹⁴ in the latter. Herein, the exploitation of the nitro functionality on a β -pyrrolic unit firstly required the most appropriate synthetic procedure to obtain the key intermediate, copper 3-NH₂-corrolate. In tetrapyrrolic chemistry, the most applied reductive methods for the conversion of –NO₂ into –NH₂ make use of SnCl₂ in concentrated HCl¹⁵ or catalytic hydrogenation systems¹⁶. In our studies, the former approach is *a priori* ruled out, since this method was reported by Maes and co-workers¹⁷ to be an efficient method for the removal of the copper ion from Cu-corrolates. This type of reduction using 3-(NO₂)TtBuCorrCu would have given the corresponding β -aminocorrole free base, which we know to be an unstable species¹⁸ and therefore not useful for further transformations.

Reduction

For the reasons above, to reduce 3-(NO₂)TtBuCorrCu we used palladium, supported on carbon, as catalyst and a 50-fold molar excess of NaBH₄ in a dichloromethane/methanol solution at room temperature under N₂ atmosphere, with good results (Scheme 1, (a)).

In a few minutes, the formation of a new compound having a lower R_f value than the starting copper 3-nitrocorrole was apparent by TLC analysis, and concurrently a blue-shifted Soret band was shown by UV-Vis spectroscopy analysis, as expected for the formation of an electron releasing group on a β position. The chromatographic purification of the reaction mixture was performed on silica gel, eluting with dichloromethane/petroleum ether (2:1 v/v) and this permitted the isolation of the main reaction product in a 35% yield. FAB mass spectroscopy identified the product as the copper 3-aminocorrole (**1**) based on the molecular peak at 770 m/z. On the other hand, its further characterization by ¹H NMR spectroscopy was not decisive, giving both large and unresolved β -pyrrolic proton resonances and an uncertain assignment of the –NH₂ hydrogens in the spectrum. These unfavourable features could be ascribable to aggregation phenomena or to the formation of intramolecular complexes, due to coordination of the amino group by the copper ion, which can also induce paramagnetic character into the analysed sample. On the other hand, the experimental evidence for definitive identification of (**1**) was given by the occurrence of all the organic transformations involving the –NH₂ functionality described below, which unambiguously confirmed our assumption.

The moderate yield obtained for the reduced corrole was due to the progressive decomposition of this Cu complex observed during the chromatographic process. Ultimately, similar limited stability was recently reported for the analogous 2-aminoporphyrins which were shown to be photolabile and easily oxidized¹⁹. As for reactions involving β -aminoporphyrins, we decided to use immediately the crude reaction product containing the 3-aminocorrole (**1**), without further purification for the following transformations, or immediately consume it *in situ*, whenever it was compatible with the reaction conditions.

Acylation

At first we focused our attention on the synthesis of Cu corrolates bearing an amide functionality on the β -pyrrolic position, starting from the corresponding 3-NO₂ derivative. Amide synthesis is a popular reaction for numerous reasons, *e.g.* the relative ease of formation of the amide linkage, its structural rigidity and its biomimetic character, which account for the widespread use of such compounds both in technological and medical applications. Among the many reactants generally used for amide formation from the amino group, we decided to use a series of alkyl anhydrides, which allowed for the ready preparation of copper corroles (**2**), (**3**) and (**4**) in satisfactory yields. The transformation of the -NO₂ group into the -NHC(O)R amide was performed in the case of corroles (**2**) and (**3**) by a “one pot” procedure outlined in Scheme 1(b), first involving the Pd-catalyzed reduction of the substrate 3-(NO₂)TtBuCorrCu at room temperature followed by the *in situ* acylation of the amino derivative with the corresponding anhydride in a dichloromethane/methanol solvent mixture. After the rapid formation of the reduced corrole derivative (**1**), a 12-fold molar excess of acetic or hexanoic anhydride was added, producing in a few minutes a small red-shift of the Soret band. Chromatographic purification on silica gel afforded the desired amides (**2**) and (**3**) as the main reaction products in 56 and 61 % yields, respectively.

The FAB mass spectra showed the new compounds to have a molecular peak at *m/z* 813 and 869, respectively, while the proton NMR spectra showed the amide NH resonance as a sharp singlet at 6.59 and 6.68 ppm, respectively, thus allowing their definitive identification.

In addition, the copper 3-acetylamidocorrole (**2**) gave crystals suitable for an X-ray diffraction study from a CDCl₃/MeOH, solution, which afforded the structural characterization reported in Figure 1.

By least-squares (L.S.) plane analysis, the fitted plane (rms deviation = 0.141 Å) of 3-CH₃C(O)NH-TtBuCorrCu's 23 atom (C₁₉N₄) framework has a conformation best described as “saddled” with the β -pyrrole carbons for the 5-membered rings “A” and “C” residing above (deviations from L.S. plane: min = +0.138 (3) Å/max = +0.236 (4) Å) and “B” and “D” below (deviations from L.S. plane: min = -0.143 (3) Å/max = -0.229 (3) Å) its *intra*-pyrrole nitrogen counterpart (deviations from L.S. plane: N1, -0.141 (3) Å; N3, -0.183 (3) Å; N2, +0.169 (3) Å; N4, +0.206 (3) Å) – see Figure 2 for visual reference.

While the C₁₉N₄ core has nearly spherical anisotropic atomic displacement parameters, the *tert*-butylphenyl group (located at C10) and the *para* substituents (*tert*-butyl groups) on the *meso*-phenyl rings (located at C5 and C15) have positional disorder (not occupational) and were best modelled in 2 or 3 distinct orientations in the average structure. Relative to the corrole, the Cu atomic site is barely above (+0.017 (1) Å) the fitted 23 atom L.S. plane. The *meso*-phenyl rings form dihedral angles from this L.S. plane of 71.5 (1)° at C5, ~65° at C10 (average of 3 refined orientations with dihedral angles of 69.1 (3)°, 68.3 (3)°, and 57.3(4)° in occupancies of 36.2 (2) %, 33.4 (2) %, and 30.4 (2) %, respectively), and 57.3 (4)° at C15.

The occupancies of the 2-component positional disorder of the *tert*-butyl groups attached to the phenyl substituents is practically identical with ratios at C5 of 0.71 (1) : 0.29 (1) and at C15 of 0.705 (5) : 0.295 (5). The 3-acetylamido group (located at C3) deviates significantly

less from the 23 atom framework than the *meso*-substituents with a dihedral angle of 18.4 (2)° relative to the L.S. plane and forms a close contact (intermolecular) to a neighboring 3-acetylamido group as shown in Figure 3.

Considering the efficiency and the facile amide formation by this synthetic pathway, we believed these derivatives to be excellent precursors for the anchoring of further attractive functionalities to the corrole macrocycle. In this context, the possibility to introduce a halogen atom on the R chain of the acyl-amido substituent was particularly appealing, since it should enrich the options in hand to further modify the corrole periphery by nucleophilic substitution reactions.

For this purpose, the use of the chloroacetic anhydride in the above “one pot” procedure was prevented, since collateral dechlorination would occur in the presence of the Pd/C-NaBH₄ reducing system. Hence, for the preparation of copper corrolate (**4**), the catalytic system was removed after the reduction of the nitrocorrole by filtration through a Celite plug and by washing the residue dissolved in CH₂Cl₂ extensively with water.

Then, the amino derivative formed was used as isolated for the acylation, which afforded the title amide in a 64% yield. The ¹H NMR spectrum allowed the identification of this derivative, showing two diagnostic singlets at 8.131 and 3.91 ppm corresponding to the –NHC(O) and –CH₂Cl hydrogens respectively.

Among all the feasible reactions for the chlorine displacement by a nucleophile, the introduction of an azide functionality was particularly attractive in visualizing additional structural enrichment of the corrole framework by applying the click chemistry concept. Therefore, we performed the conversion of the peripheral halogen of amide (**4**) into the –N₃ functionality by reaction with sodium azide in DMF at 60 °C. After five hours, the reaction was complete, as shown by TLC analysis; this pointed to total transformation of the starting material into a new, more polar, compound. Chromatographic purification on silica gel eluting with a CH₂Cl₂/petroleum ether solvent mixture (2:1 v/v) afforded the desired compound (**5**) as the main reaction product in a 56% yield. The molecular peak at 854 m/z obtained by FAB mass spectrometry combined with ¹H NMR spectrum signals at 7.85 and 3.79 ppm of the amide and the azidomethyl groups, respectively, enabled the characterization of this product. The presence of the azido group was further confirmed by IR spectroscopy which afforded an intense band at 2116 cm^{–1} corresponding to the N≡N asymmetric stretching absorption.

Cycloaddition reactions: click chemistry on β-substituted corroles—The preparation of the corrole (**5**), bearing a peripheral azido group, led us to explore its potential application in the copper-catalyzed Huisgen reaction. This reaction is one of the most popular “click” chemistry reactions, transformations characterized by mild conditions, high yields and simple purification procedures²⁰. In the Huisgen cycloaddition, the azido group is reacted with terminal alkynes to give the corresponding triazole derivative and in the porphyrin field this reaction has been successfully applied for the realization of elaborated structures involving different porphyrinoids²¹.

On the other hand, to the best of our knowledge, in the corrole field there is only one recent report on the exploitation of the Huisgen reaction, for the elaboration of the *meso*-phenyl substituent in order to prepare a BODIPY-corrole dyad²².

For this reason we performed the reaction of the obtained β -azidomethylcorrole (**5**) with 4-ethynyltoluene in THF at 70 °C, using sodium ascorbate and CuSO₄·H₂O.

After 48 hours the solvent was evaporated and the residue purified on a silica gel column (CHCl₃ eluant) to afford the cycloaddition product (**6**) (Scheme 3). Although the reaction time is longer than those usually observed for this reaction, the yields, although not optimized, were higher than 90%, so demonstrating the synthetic usefulness of this transformation.

The characterization of the product was straightforward, showing the molecular peak at *m/z* 971 in the FAB mass spectrum. Moreover, the success of the reaction was supported by the ¹H NMR spectrum, showing the two diagnostic resonances at 4.55 and 2.39 ppm, attributable to the proton on –CH₂ linked to the triazole moiety and the tolyl-CH₃ respectively.

N-Formylation

Another valuable organic transformation involving the amino group is *N*-formylation to give formamides, an important class of amine derivative involved in various synthetic procedures leading to drugs, fungicides, formamidines and isocyanides, among others. Although several formylation methods have been developed, in our case the employment of formic acid gave good results, affording the formamide (**7**) in a 71% yield. The condensation reaction of the aminocorrole (**1**) with a large excess of formic acid was carried out in refluxing toluene and was complete in about 20 minutes. The main product was purified on a silica gel column eluted with chloroform; it was structurally identified by the usual spectroscopic techniques. In particular, the two proton resonances in the ¹H NMR spectrum at 7.86 and 6.56 ppm correspond to the formyl and amide hydrogens, respectively.

Experimental

General

¹H NMR spectra were recorded on a Bruker AV300 spectrometer (300 MHz). FAB mass spectra were recorded on a VGQuattro spectrometer in the positive-ion mode using CHCl₃ as solvent and *m*-nitrobenzyl alcohol (Aldrich) as matrix. UV-Vis spectra were measured on a Cary 50 spectrophotometer using CH₂Cl₂ as solvent. IR spectra were recorded in CHCl₃ solutions with a Perkin Elmer 100 FT-IR Spectrometer, using KBr cells.

Chromatographic purification on columns was performed using silica gel 60 (70–230 mesh, Sigma Aldrich). Reagents and solvents (Aldrich, Merck or Fluka) were of the highest grade available and were used without further purification. The compound 3-(NO₂)TtBuCorrCu used as substrate in all the described reactions was prepared using a literature procedure^{12c}. A single crystal X-ray diffraction experiment was conducted at T = 90 K with compound **2** using a Bruker Kappa D8 APEX-II DUO diffractometer equipped with a CCD detector, Cu

K α ($\lambda = 1.54178 \text{ \AA}$) I μ S microfocus tube, and Oxford Cryosystems cryostream cooler. After atomic assignments of fully occupied sites were completed and remaining electron-density deficient atomic sites were identified in the difference map, positionally disordered substituents (two *tert*-butyl groups and one *tert*-butylphenyl group) were refined as segregated components (using PART command) that were restrained/constrained to be structurally similar (using the SAME/EADP command) in SHELXL-2013. All non-hydrogen atoms were refined anisotropically and hydrogen atoms were modelled in riding positions (with the exception on the amide hydrogen).

3-(NH₂)TtBuCorrCu (1)—3-(NO₂)TtBuCorrCu (50 mg, 0.06 mmol) was dissolved in 30 mL of a CH₂Cl₂/MeOH mixture (4:1 v/v) and the solution was purged with nitrogen for 5 min. Then, 10% palladium on carbon catalyst (60 mg) and NaBH₄ (118 mg, 3.12 mmol) were added and the solution was stirred under an inert N₂ atmosphere. The colour of the solution rapidly turned brilliant green and UV-Vis spectroscopy monitoring showed the formation in 10 min of a new compound having a blue-shifted Soret band and a single Q band centred at 419 nm and 640 nm, respectively. After 15 min, the reaction was complete and the solution was filtered through a Celite plug. After solvent evaporation under reduced pressure, the residue was taken up in CH₂Cl₂, washed with H₂O and dried over anhydrous Na₂SO₄. Chromatographic purification on silica gel using a CH₂Cl₂/petroleum ether (2:1 v/v) solvent mixture as eluant, afforded the aminocorrole (**1**) as a brownish fraction, which was collected and obtained in a 35 % yield (17 mg) after crystallization from CH₂Cl₂/MeOH.

Since corrole (**1**) was demonstrated to be unstable during the purification process, all the reactions described hereinafter using this substrate were carried out immediately using this crude product.

General procedure for the “one pot” reduction/acylation of 3-(NO₂)TtBuCorrCu

The reduction of 3-(NO₂)TtBuCorrCu (50 mg, 0.06 mmol) was carried out using the experimental conditions above described. When the substrate was all consumed, a 12-fold molar excess of anhydride was added, causing a rapid colour change of the solution from emerald green to brownish. Monitoring by UV-Vis spectroscopy evidenced a slight red-shifted of *ca.* 2 nm of the Soret band. After 10 min, the reaction was complete; the mixture was evaporated to dryness, taken up in CH₂Cl₂, filtered through a plug of Celite and evaporated under reduced pressure. After the chromatographic purification, the desired amide was obtained as a brown powder after crystallisation from CH₂Cl₂/MeOH.

3-NHC(O)CH₃-TtBuCorrCu (2)—Chromatographic purification on silica gel eluting with CHCl₃ gave 28 mg (56% yield) of the title compound.

Mp > 300 °C. UV-Vis (CH₂Cl₂): λ_{max} , nm (log ϵ) 420 (5.06), 632 (3.91). ¹H NMR (300 MHz, CDCl₃): 8.66 (1H, br s, β -pyrrole), 8.07 (1H, br s, β -pyrrole), 7.77 (1H, br s, β -pyrrole), 7.68 (2H, d, $J = 7.8 \text{ Hz}$ phenyl), 7.51 (12H, m, β -pyrrole+phenyl), 7.33 (1H, d, $J = 3.93 \text{ Hz}$ β -pyrrole), 6.99 (1H, br s, β -pyrrole), 6.59 (1H, s, -NHC(O)CH₃), 1.70 (3H, s, -CH₃), 1.45 (9H, s, -*t*Bu), 1.44 (9H, s, -*t*Bu), 1.42 (9H, s, -*t*Bu). MS (FAB) : m/z 813(M⁺).

Anal. Calcd for $C_{51}H_{51}CuN_5O$: C, 75.29; H, 6.32; N, 8.61%. Found: C, 75.34; H, 6.38; N, 8.63%.

$C_{51}H_{50}CuN_5O$, $M = 812.50$, Triclinic, $a = 8.7172$ (13) Å, $b = 9.5695$ (16) Å, $c = 26.860$ (5) Å, $\alpha = 88.821$ (7)°, $\beta = 89.825$ (9)°, $\gamma = 71.559$ (6)°, $V = 2125.1$ (6) Å³, $T = 90$ (2) K, space group $P-1$, $Z = 2$, μ (Cu K α) = 1.06 mm^{-1} , 20501 reflections measured, 7465 independent reflections ($R_{int} = 0.029$). The final R_1 values were 0.073 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.189 ($I > 2\sigma(I)$). The final R_1 values were 0.076 (all data). The final $wR(F^2)$ values were 0.187 (all data). The goodness of fit on F^2 was 1.06. CCDC number 997609.

3-[NHC(O)(CH₂)₄CH₃]-TtBuCorrCu (3)—Chromatographic purification on a silica gel column using a CH_2Cl_2 /petroleum ether solvent mixture (4:1 v/v) as eluant afforded 33 mg (61% yield) of the title compound.

Mp > 300 °C. UV-vis (CH_2Cl_2): λ_{max} , nm (log ϵ) 420 (5.00), 632 (3.90). ¹H NMR (300 MHz, $CDCl_3$): 8.68 (1H, br s, β -pyrrole), 8.04 (1H, br s, β -pyrrole), 7.78 (1H, d, $J = 3.33$ Hz β -pyrrole), 7.67 (2H, d, $J = 8.1$ Hz phenyl), 7.51 (11H, m, β -pyrrole+phenyl), 7.33 (1H, d, $J = 4.26$ Hz β -pyrrole), 7.24 (1H, br s, β -pyrrole), 6.99 (1H, br s, β -pyrrole), 6.68 (1H, s, -NHC(O)), 1.81 (2H, t, -OCH₂-), 1.46 (9H, s, -tBu), 1.44 (9H, s, -tBu), 1.42 (9H, s, -tBu), 1.24 (6H, m, -OCH₂(CH₂)CH₃), 0.89 (3H, t, -CH₃). MS (FAB) : m/z 869(M⁺). Anal. Calcd for $C_{55}H_{59}CuN_5O$: C, 75.96; H, 6.84; N, 8.05%. Found: C, 75.79; H, 6.81; N, 8.13%.

Preparation of the 3-functionalized corrole derivatives (4),(5) and (6)

3-NHC(O)CH₂Cl-TtBuCorrCu(4)—50 mg (0.06 mmol) of **1** was subjected to reduction as reported above. After work up, the crude product was dissolved in 30 mL of a CH_2Cl_2 /MeOH mixture (4:1 v/v) and acetylated using 123 mg (0.72 mmol) of chloroacetic anhydride. The reaction was complete in 20 min. Chromatographic purification was performed on silica gel eluting with a CH_2Cl_2 /petroleum ether solvent mixture (4:1 v/v). The amide was obtained as a brownish powder (33 mg, 64% yield) by crystallisation from CH_2Cl_2 /MeOH.

Mp > 300 °C. UV-vis (CH_2Cl_2): λ_{max} , nm (log ϵ) 421 (5.03), 632 (3.94). ¹H NMR (300 MHz, $CDCl_3$): 8.75 (br s, 1H, β -pyrrole), 8.11 (s, 1H, -NHC(O)), 8.02 (br s, 1H, β -pyrrole), 7.74 (br s, 1H, β -pyrrole), 7.57 (m, 13H, β -pyrrole+phenyl), 7.32 (br s, 1H, β -pyrrole), 7.08 (br s, 1H, β -pyrrole), 7.05 (br s, 1H, β -pyrrole), 3.91 (s, 2H, -CH₂Cl), 1.44 (br s, 18H, -tBu), 1.42(s, 9H, -tBu). MS (FAB) : m/z 847 (M⁺). Anal. Calcd for $C_{51}H_{50}ClCuN_5O$: C, 72.24; H, 5.94; N, 8.26%. Found: C, 72.31; H, 5.89; N, 8.35%.

3-NHC(O)CH₂N₃-TtBuCorrCu (5)—Amide (**4**) (33 mg, 0.04 mmol) was dissolved in DMF (13 mL) and NaN₃ (51 mg, 0.78 mmol) was added. The solution rapidly turned brilliant green and it was stirred at 60 °C under N₂. After 5 h, distilled water (10 mL) was added and the precipitate formed was filtered. The residue was taken up in CH_2Cl_2 and applied to a silica gel column that was eluted with a CH_2Cl_2 /petroleum ether solvent mixture (2:1 v/v). The main product corresponding to the desired compound was isolated as the first fraction and crystallised from CH_2Cl_2 /MeOH to give 19 mg (56% yield). Mp > 300 °C. UV-Vis (CH_2Cl_2): λ_{max} , nm (log ϵ) 421 (5.03), 630 (3.90). ¹H NMR (300 MHz, $CDCl_3$): 8.64

(1H, br s, β -pyrrole), 7.93 (1H, br s, β -pyrrole), 7.85 (1H, s, 1H, -NHC(O)), 7.74 (1H, br s, β -pyrrole), 7.65 (4H, d, $J = 7.86$ Hz phenyl), 7.51 (8H, m, phenyl), 7.42 (1H, br s, β -pyrrole), 7.32 (1H, d, $J = 3.60$ Hz, β -pyrrole), 7.09 (1H, br s, β -pyrrole), 7.02 (1H, br s, β -pyrrole), 3.79 (2H, s, -CH₂N₃), 1.46 (9H, s, -*t*Bu), 1.44 (9H, s, -*t*Bu), 1.42 (9H, s, -*t*Bu). IR: (CHCl₃): $\nu_{\text{max}}/\text{cm}^{-1}$ 2116. MS (FAB) : m/z 854(M⁺). Anal. Calcd for C₅₁H₅₀CuN₈O: C, 71.68; H, 5.90; N, 13.11%. Found: C, 71.59; H, 5.82; N, 13.23%.

3-NHC(O)CH₂(4-tolyl-triazole)TtBuCorrCu (6)—Amide (**5**) (27 mg, 0.03 mmol) was dissolved in THF (50 mL) and 4-ethynyltoluene (8.4 μ L, 0.066 mmol) was added. Sodium ascorbate (1.2 mg, 0.0066 mmol) and (CuSO₄)·5H₂O (0.9 mg, 0.033 mmol) in aqueous solution were added and the mixture heated at 70 °C, under inert atmosphere. After 20 h 4-ethynyltoluene (0.066 mmol), sodium ascorbate (0.0066 mmol) and (CuSO₄)·5H₂O (0.033 mmol) were added. The course of the reaction was monitored by TLC (silica gel/CHCl₃). After 48 h the starting material was all consumed and the presence of a new, more polar, compound was evident. The solvent was evaporated and the crude of the reaction was taken up with chloroform and purified on a silica plug using CHCl₃ as eluant. The main product was crystallised from CH₂Cl₂/MeOH giving 26.5 mg of the title compound (91% yield). UV-vis (CH₂Cl₂): λ_{max} , nm (log ϵ) 422 (5.10), 630 (3.92). ¹H NMR (300 MHz, CDCl₃): 8.46 (br s, 1H, β -pyrrole), 7.94 (s, 1H, -NHC(O)), 7.86 (br s, 1H, β -pyrrole), 7.74 (d, 4H, $J = 7.7$ Hz, phenyl), 7.69 (br s, 1H, β -pyrrole), 7.55 (m, 9H, phenyl and triazole), 7.44 (br s, 1H, β -pyrrole), 7.29 (br s, 1H, β -pyrrole), 7.23 (m, 4H, phenyl), 7.12 (br s, 1H, β -pyrrole), 6.96 (br s, 1H, β -pyrrole), 4.55 (s, 2H, -CH₂-triazole), 2.39 (s, 3H, -CH₃-tolyl), 1.49 (s, 9H -*t*Bu), 1.44 (s, 9H -*t*Bu), 1.42 (s, 9H -*t*Bu). MS (FAB) : m/z 970(M⁺). Anal. Calcd for C₆₀H₅₇CuN₈O: C, 74.32; H, 5.92; N, 11.56%. Found: C, 74.36; H, 5.89; N, 11.53%.

3-NHC(O)H-TtBuCorrCu (7)—The crude product from the reduction of 3-(NO₂)TtBuCorrCu (50 mg, 0.06 mmol) was dissolved in toluene (13 mL) and the solution was heated to reflux. Then, 1 mL of 85% formic acid was added and the reaction was monitored by UV-Vis spectroscopy. The red-shift of the Soret band was indicative of the effective formylation of the amino group. After 20 min, the solution was cooled and evaporated on a rotary evaporator. The crude material was applied to a silica gel column, using CHCl₃ as eluant. 35 mg of compound **5** were obtained as a brownish powder after crystallization from CHCl₃/MeOH (71% yield). Mp > 300 °C. UV-vis (CH₂Cl₂): λ_{max} , nm (log ϵ) 421 (4.99), 631 (3.92). ¹H NMR (300 MHz, CDCl₃): 8.56 (1H, br s, β -pyrrole), 7.91 (1H, br s, β -pyrrole), 7.86 (1H, s, -NHCHO), 7.72 (1H, br s, β -pyrrole), 7.63 (4H, m, phenyl), 7.53 (8H, m, phenyl), 7.43 (1H, br s, β -pyrrole), 7.31 (1H, d, $J = 3.99$ Hz, β -pyrrole), 7.14 (1H, br s, β -pyrrole), 7.09 (1H, br s, β -pyrrole), 6.56 (1H, s, -NHCHO), 1.45 (9H, s, -*t*Bu), 1.43 (9H, s, -*t*Bu), 1.42 (9H, s, -*t*Bu). MS (FAB) : m/z 799(M⁺). Anal. Calcd for C₅₀H₄₉CuN₅O: C, 75.11; H, 6.18; N, 8.76%. Found: C, 75.21; H, 6.13; N, 8.69%.

Conclusions

Herein we report the first examples of organic manipulation of the nitro group in a β -functionalized copper corrolate. The reduction performed on the Cu 3-NO₂-5,10,15-triarylcorrolato offers the corresponding amino-derivative which was exploited for the

further derivatization of corrole macrocycle, via amide functions. This synthetic tool was demonstrated to be successful, affording easily a number of β -acylated products in good yields. Notably, it is to highlight that the achievement of corrole (**5**) bearing the azidomethyl group has been crucial for further corrole functionalization by Huisgen “click” reaction.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.
The molecular structure of compound 3-CH₃C(O)NH-TtBuCorrCu (**2**)

Figure 2.

For visual reference, deviations of selected atomic sites from a least-squares fitted plane defined by the 23 atom ($C_{19}N_4$) corrole framework are indicated with “+” and “-” symbols (not indicating local atomic charges). This pattern of deviations most closely resembles a “saddled” corrole conformation

Figure 3.

The packing relationship of two neighboring 3-acetylamido groups (with fragment of Cu corrole framework) is shown with a $N5 \cdots C50^i$ intermolecular distance of 3.498 (5) Å along the “interatomic” dashed lines (not indicating bonds). The angles are nearly orthogonal with values of 96.2 (2)° for $N5-C50 \cdots N5^i$ and 83.8 (2)° for $C50-N5 \cdots C50^i$. (Symmetry code: (i) $-x, -y+1, -z$.)

Scheme 1.
Preparation of the copper corrole derivatives **(1)**, **(2)** and **(3)**

Scheme 2.

Preparation of the copper corrole derivatives (4) and (5).

Scheme 3.

Click chemistry on corrole (5) to give corrole (6)

Scheme 4.
Preparation of the copper corrole derivatives (7).