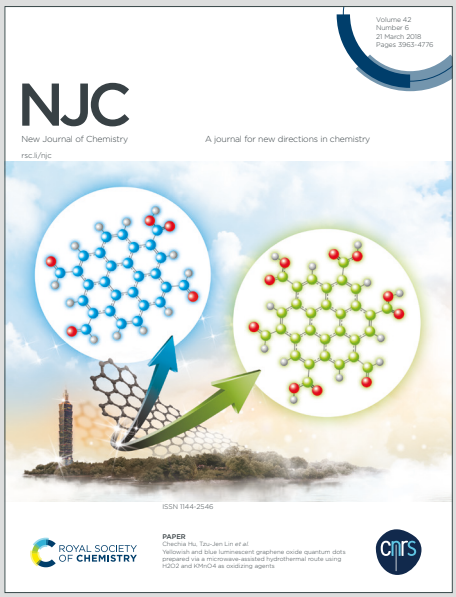
NJC

New Journal of Chemistry

A journal for new directions in chemistry

Accepted Manuscript



ROYAL SOCIETY OF CHEMISTRY

rsc.li/njc

NJC

View Article Online
DOI: 10.1039/C9NJ02026H

PAPER

Copper complexes and carbon nanotube-copper ferrite-catalyzed benzenoid A-ring selenation of quinones: An efficient method for the synthesis of trypanocidal agents†

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

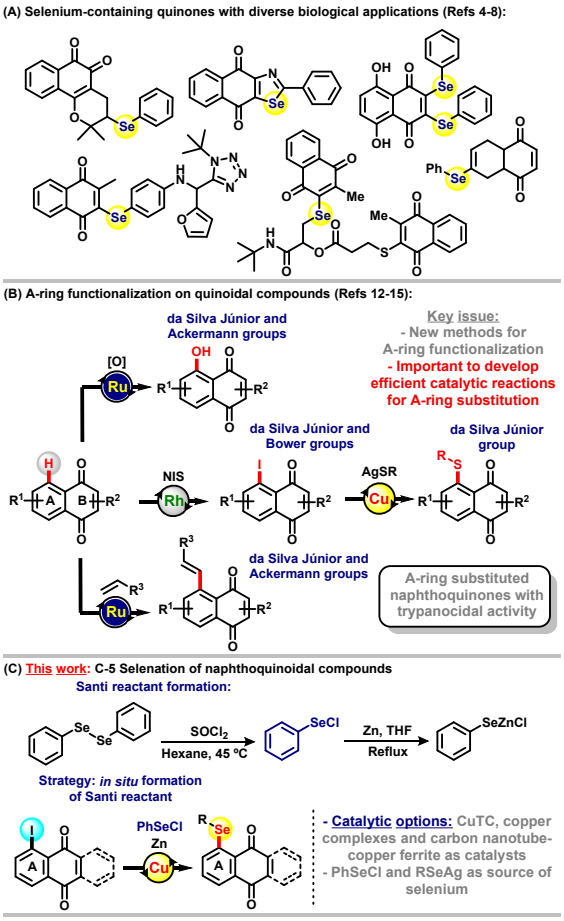
Guilherme A. M. Jardim,[a,b] Icaro A. O. Bozzi,[a] Willian X. C. Oliveira,[a] Camila Mesquita-Rodrigues,[c] Rubem F. S. Menna-Barreto,[c] Ramar A. Kumar,[d,e] Edmond Gravel,[d] Eric Doris,[d]* Antonio L. Braga[b] and Eufrânio N. da Silva Júnior[a,f]*

We report a new method for A-ring selenation of naphthoquinones and anthraquinones and discuss the relevant trypanocidal activity of the synthesized compounds. We have demonstrated three efficient strategies for the preparation of the target selenium derivatives, *i.e.* a) copper(I) thiophene-2-carboxylate and *in situ* generated Santi reagent were used to prepare selenium-substituted benzenoid quinones, b) copper complexes and c) carbon nanotube-supported copper ferrite as catalysts in the presence of AgSeR-salts were also used for the synthesis of selenium-containing quinoidal derivatives. These new methods provide efficient and practical strategies for the preparation of selenium-based quinones. In addition, we have discovered nine compounds with potent trypanocidal activity. The derivatives **2a**-**2e** showed potent trypanocidal activity with IC_{50} values in the range of 13.3 to 37.0 µM.

1. Introduction

Selenium-containing compounds have attracted increasing interest in the scientific community due to their implication in various redox processes, which has led to the discovery of biologically-active molecules with, for example, antitumor properties.[1] In general, Se-based compounds exert their cytotoxic effects by acting as pro-oxidants that alter cellular redox homeostasis. Yet, the precise intracellular targets and mechanisms of cell death are intrinsically related to the chemical properties of the respective seleno-compounds, as recently discussed by Fernandes and co-authors.[2]

There are several well-known compounds based on chalcogens,[3] for instance, hybrid redox substances have been prepared by combining the quinoidal system and the selenium atom (Scheme 1A).[4-8] In this context, different research groups, including Bates,[4] Ruan and Fan,[5] Batteux, Herling and Jacob,[6] Wessjohann,[7] as well as Braga and da Silva Júnior,[8] have developed several synthetic methods to introduce selenium into the quinoidal backbone and evaluated their biological potential. It has been found that selenoquinones are involved in the downregulation of the Bcl-2 and Ki-67 expression levels and also activate the expression of caspase-8 in hepatocellular carcinoma cells (HepG2). These results have led researchers to postulate that selenoquinones possess anti-HepG2 activity.[7]



Scheme 1 Overview.

[a] Institute of Exact Sciences, Department of Chemistry, Federal University of Minas Gerais, Belo Horizonte, MG, 31270-901, Brazil. E-mail: eufranio@ufmg.br.
[b] Department of Chemistry, Federal University of Santa Catarina, 88040-900 Florianópolis, Brazil
[c] Oswaldo Cruz Institute, FIOCRUZ, Rio de Janeiro, RJ, 21045-900, Brazil
[d] Service de Chimie Bioorganique et de Marquage (SCBM) CEA, Université Paris-Saclay 91191 Gif-sur-Yvette (France), E-mail: eric.doris@cea.fr
[e] SRM Research Institute, Department of Chemistry, SRM Institute of Science and Technology, Kattankulathur, 603203 Chennai, India
[f] Institut für Organische und Biomolekulare Chemie, Georg-August-Universität Göttingen, Tammannstraße 2, 37077, Göttingen, Germany
† Electronic Supplementary Information (ESI) available with spectra for all selenated compounds. See DOI: 10.1039/x0xx00000x

In addition, chalcogen-containing β-lapachone derivatives have shown cytotoxic activity against various cancer cell lines (leukemia, human colon carcinoma, prostate, human metastatic prostate, ovarian, central nervous system and breast), demonstrating, in some cases, IC_{50} values below 1 μM.[8b,8c] These two cases exemplify the biological potential of selenium-containing quinones as antitumor agents.

Methods for the insertion of chalcogens at the C-2 or C-3 positions of quinonoid systems with the use of nucleophilic selenium sources are well developed.[9] Simple modifications to the B-ring of the naphthoquinoidal moiety *via* Michael addition reactions[10] or the formation of radicals[11] have been exhaustively explored in the literature on the chemistry of quinones.

To address the lack of methods for benzenoid A-ring functionalization of naphthoquinones, the research groups of Bower and da Silva Júnior described the first and robust method for C-5 selective C–H iodination of deactivated naphthoquinones *via* catalysis with rhodium complexes.[12] Later, the groups of da Silva Júnior and Ackermann reported ruthenium-catalyzed reactions for C-5 selective C–H oxygenation of naphthoquinones and anthraquinones.[13] This method allowed the A-ring oxygenation of quinones, providing access to an important class of bioactive hydroxylated compounds. Following the same strategy, the same authors also described C–H alkenylation of unactivated naphthoquinones.[14a] These methods were versatile for the direct preparation of trypanocidal compounds. In general terms, all of the methods encompass C–H bond reactions through weak *O*-coordination by means of rhodium or ruthenium species.[14b] Recently, our group also developed a direct sequential C–H iodination/organoylthiolation method for the benzenoid A-ring modification of quinonoid deactivated systems.[15] In this work, the insertion of sulfur into the quinone was shown to be an important factor for increasing the trypanocidal activity of the compounds, reflecting the importance of preparing hybrid substances containing redox quinoidal and chalcogen systems (Scheme 1B).

Given our recent success in the preparation of naphthoquinones A-ring functionalized *via* reactions in only one or two steps (Scheme 1B), we report herein an efficient and reliable strategy for the installation of selenium atoms in a broad range of 1,4-naphthoquinones (1,4-NQs) and 9,10-anthraquinones. For the first time, a strategy for the A-ring selenation of 1,4-NQs was established by employing different sources of copper as catalysts. In addition, we evaluated the action of the compounds against *Trypanosoma cruzi*, the etiological agent of Chagas disease.

2. Results and discussion

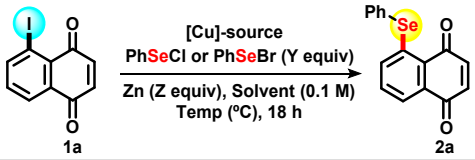
Santi and co-workers demonstrated the efficient use of bench-stable phenyl selenolate as a nucleophilic reagent in various organic transformations.[16] Based on these findings, we planned the selenation of iodinated 1,4-NQs with the use of PhSeCl or PhSeBr in the presence of zinc powder to generate the Santi reagent *in situ,* and with a copper source as the catalyst (Scheme 1C). Preliminary studies involved the reaction of 5-iodo-1,4-naphthoquinone **1a** with PhSeCl and zinc (1.0 equiv. of both reactants), 5.0 mol% of copper and dimethylacetamide (DMAc) as the solvent at room temperature but, under these conditions, only traces (≤5%) of the product **2a** were observed (Table 1, entry 1). As the formation of the desired product was detected in very low quantities, we applied higher temperature (100 °C) and increased the amount of zinc to 3.0 equiv. Under these conditions, **2a** was isolated in 64% yield (entry 2). Subsequently, we used 1.5 equiv. of PhSeCl and 3.0 equiv. of zinc powder to improve the reaction conditions (entry 3). These conditions allowed the preparation of **2a** with a slight improvement of the yield (68%) in comparison with entry 2 (64%). Further refinement aimed at maximizing the yield of **2a** was accomplished as shown in entry 4. When 10 mol% of copper, 2.0 equiv. of PhSeCl and 5.0 equiv. of zinc were used, the selenated derivative **2a** was obtained in 81% yield.

In a previous study on the preparation of thiolated benzenoid A-ring-modified quinonoid compounds, we demonstrated the effectiveness of copper(I) thiophene-2-carboxylate (CuTC) for the insertion of the chalcogenium into iodinated naphthoquinones.[15] Thus, CuTC was our first choice for the study reported herein. Despite the effectiveness of the system (entry 4), we also evaluated CuI as an alternative source of copper but it was much less active for the introduction of selenium at the C-5 position of 1,4-NQs, as the product **2a** was obtained in only 22% yield (entry 5).

The use of different solvents, for instance, DMF and DCE did not promote any further improvement (entries 6 and 7), nor did different temperatures (entries 8-10). In all cases, **2a** was obtained in yields not higher than 81% (entry 4).

Using PhSeBr instead of PhSeCl led to a decrease in the yield of **2a**, which was isolated in 33% yield (entry 11). Finally, two control experiments confirmed the essential role played by copper (entry 12) and zinc (entry 13) in the obtention of **2a**.

Table 1 Selected optimization results.



Entry	[Cu]-source (mol %)	Y	Z	Solvent	Temp (°C)	Yield (%)
1	CuTC (5)	1.0	1.0	DMAc	rt	Traces
2	CuTC (5)	1.0	3.0	DMAc	100	64
3	CuTC (5)	1.5	3.0	DMAc	100	68
4	**CuTC (10)**	**2.0**	**5.0**	**DMAc**	**100**	**81**
5	CuI (10)	2.0	5.0	DMAc	100	22
6	CuTC (10)	2.0	5.0	DMF	100	40
7	CuTC (10)	2.0	5.0	DCE	100	NR
8	CuTC (10)	2.0	5.0	DMAc	60	36
9	CuTC (10)	2.0	5.0	DMAc	80	78
10	CuTC (10)	2.0	5.0	DMAc	130	26
11[a]	CuTC (10)	2.0	5.0	DMAc	100	33
12	-	2.0	5.0	DMAc	100	Traces
13	CuTC (10)	2.0	-	DMAc	100	NR

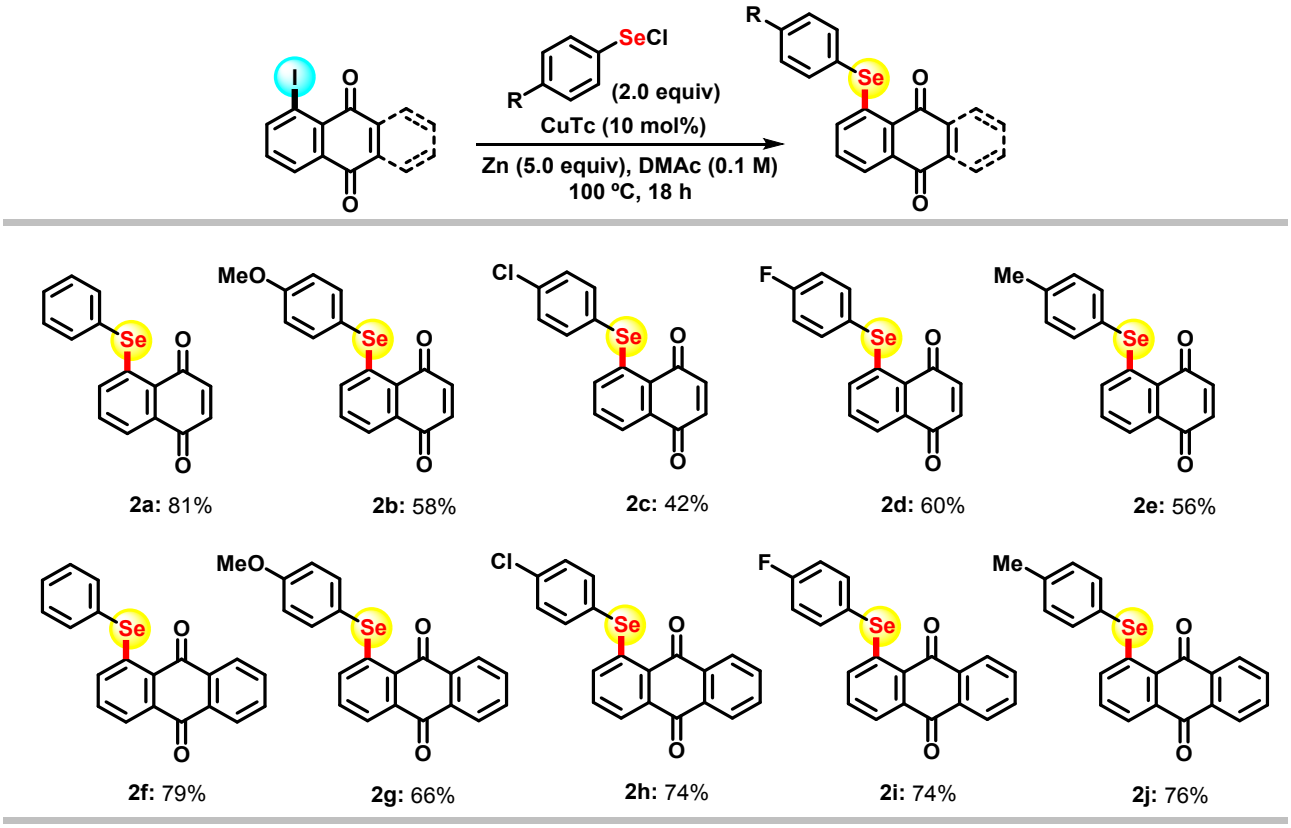
General reaction conditions: (**1a**) (0.1 mmol), PhSeCl (0.2 mmol), CuTc or CuI (5.0 or 10.0 mol %), Zn (1.0, 3.0 or 5.0 mmol); Solvent (1 mL). NR = For all cases starting material was recovered. Yields of isolated products. [a]PhSeBr was used.

Exemplification of the process

To evaluate the scope and limitations of this novel method, we prepared a set of RSeCl that were used to synthesize selenated

View Article Online
DOI: 10.1039/C9NJ03036H

quinones from 5-iodo-1,4-naphthoquinone **1a**. Nakanishi and collaborators have previously described the synthesis of selenated anthraquinones using diselenide as a reactant.[17] In this report, we also outline the preparation of selenium-containing anthraquinones via the protocol described herein. These new naphthoquinone derivatives and anthraquinones are shown in Scheme 2.



Scheme 2 Scope of the selective selenation protocol involving 1,4-naphthoquinones and 9,10-anthraquinones using CuTC as catalyst.

In order to confirm the structure of the selenated products, we prepared crystals of the naphthoquinones **2a**, **2c**, **2d** and **2e** and anthraquinones **2h** and **2i** for subsequent crystallographic analysis. The structures were solved by X-ray analysis and desired products were confirmed. ORTEP-3 representations of the asymmetric unit of the compounds are shown in Figure 1.

Based on the methodology previously described by our group,[15] we postulated that the use of AgSeR-salts[18] could be beneficial for preparing the chalcogen-containing quinones. This method would allow the synthesis of the desired molecules in the absence of Zn powder. Our initial attempts involved the reaction of **1a** with the CuTC catalyst at room temperature (Table 2, entry 1). Here, the C-5 selenation was achieved but only traces of the product **2a** (≤5%) were obtained. The use of 10 mol% of CuTC and a high temperature (100 °C) was adequate for the formation of **2a** in 85% yield (entry 2). Next, we accomplished further refinements aimed at minimizing the amount of CuTC. With the use of 5 mol% of the catalyst, compound **2a** was achieved in 86% yield (entry 3). Even with this valuable result in hand, we decided to continue our efforts toward obtaining alternative copper-based catalysts. Consequently, $Cu(DMPHEN)_2Cl$ and $Cu(PPh_3)_3Br$ were also evaluated as copper sources. To our delight, the use of 5 mol% of these catalysts allowed the isolation of **2a** in 96 and 95% yield, respectively. On decreasing the catalyst loading to 2.5 mol%, **2a** was produced in 56% yield when $Cu(DMPHEN)_2Cl$ was used as the catalyst (entry 6) and 96% yield with the use of $Cu(PPh_3)_3Br$ as the copper source (entry 7). Experiments aimed at reducing the catalyst loading to 1.0 mol% (entry 8) and decreasing the temperature (entry 9) were also carried out, however with unsatisfactory outcomes. Finally, the reaction in the absence of copper was also investigated but resulted in no formation of **2a** (entry 10).

The optimized method described in Table 2 was used for the synthesis of selenium-based quinones from iodinated derivatives of naphthoquinones and anthraquinones. The scope of this methodology is outlined in Scheme 3. Initially, the quinonoid compounds described in Scheme 2 were also prepared using this alternative method. Compounds were synthesized in moderate to high yields (Scheme 3). In general, the method involving the use of AgSeR-salts and $Cu(PPh_3)_3Br$ as the catalyst was the most effective, as molecules were obtained in better yields when compared to the Santi reagent-based method.

View Article Online
DOI: 10.1039/C9NJ02026H

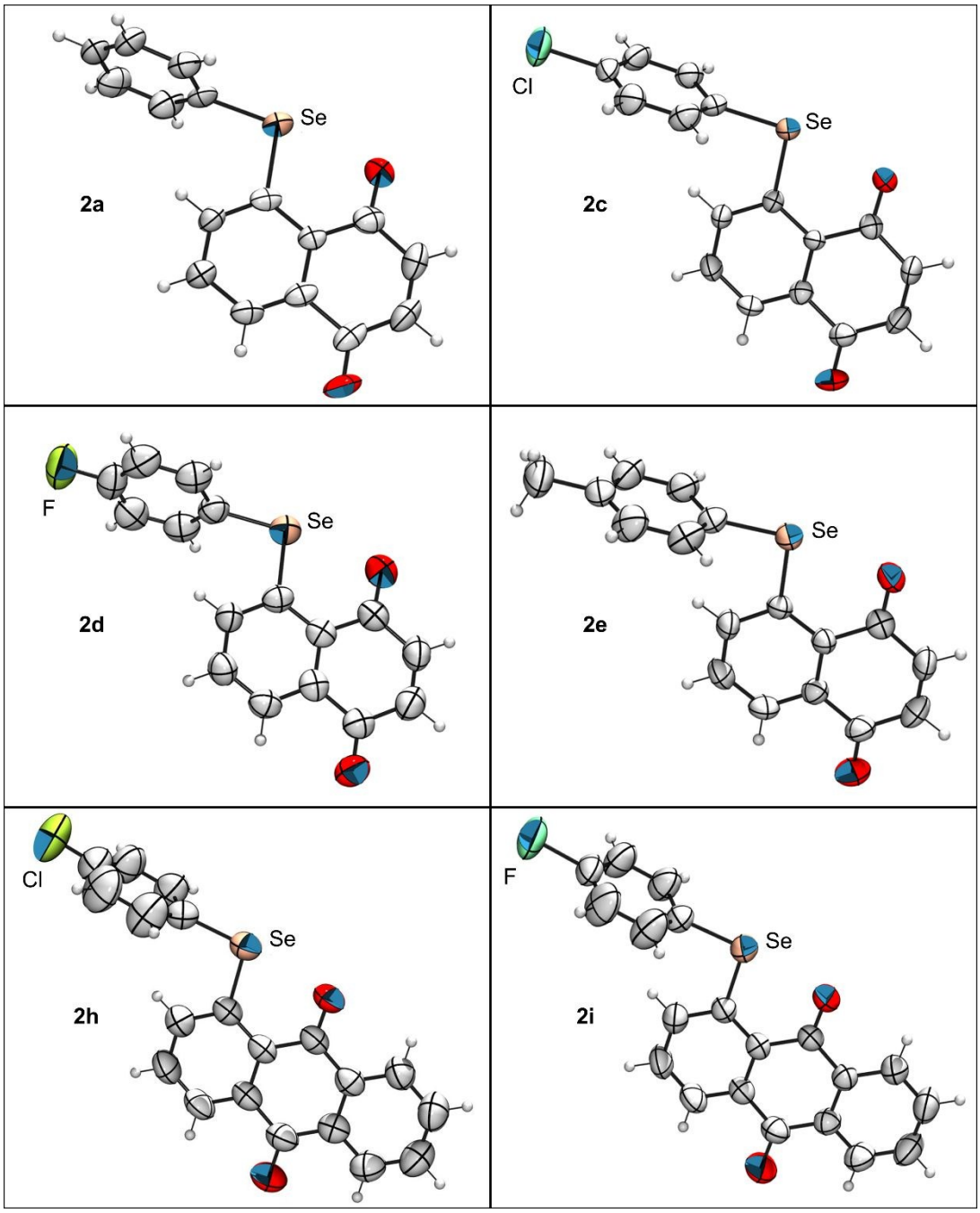
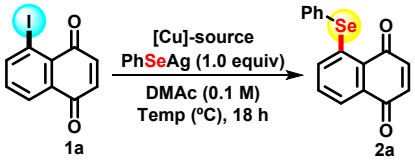


Fig. 1 ORTEP-3 projections of naphthoquinones **2a**, **2c**, **2d** and **2e** and anthraquinones **2h** and **2i** with displacement ellipsoids at the 70% probability level.

View Article Online
DOI: 10.1039/C9NJ02026H

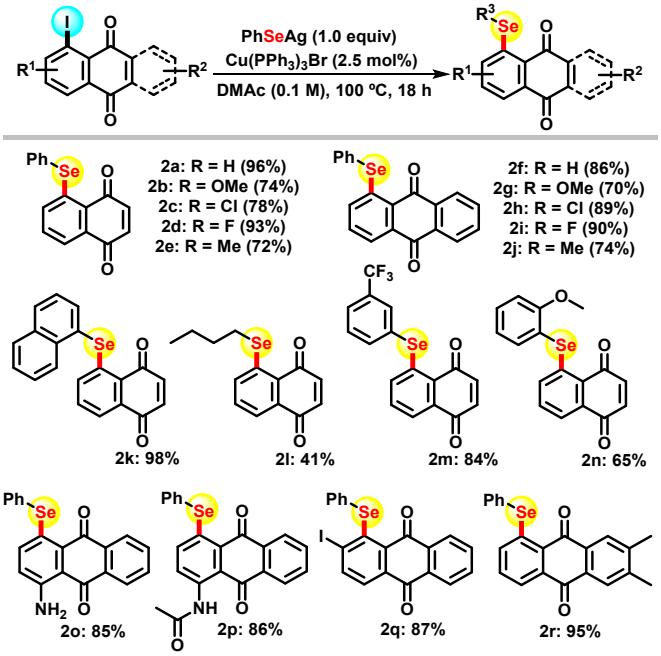
Table 2 Selected optimization results for the selenation reaction in the absence of Zn.



Entry	[Cu]-source (mol %)	Temp (°C)	Yield (%)
1	CuTc (10)	rt	Traces
2	CuTc (10)	100	85
3	CuTc (5)	100	86
4	$Cu(DMPHEN)_2Cl$ (5)	100	96
5	$Cu(PPh_3)_3Br$ (5)	100	95
6	$Cu(DMPHEN)_2Cl$ (2.5)	100	56
7	**$Cu(PPh_3)_3Br$ (2.5)**	**100**	**96**
8	$Cu(PPh_3)_3Br$ (1)	100	71
9	$Cu(PPh_3)_3Br$ (2.5)	80	82
10	-	100	NR

General reaction conditions: (**1a**) (0.1 mmol), PhSeAg (0.1 mmol), Solvent (1.0 mL). NR = Starting material was recovered. Yields of isolated products.

After the preparation of compounds **2a**-**2j**, we considered the synthesis of novel molecules using different selenium salts and 1,4-NQs. We also used anthraquinones with different substitution patterns. Compounds **2k**-**2r** were prepared in good to excellent yields, with the exceptions of compounds **2l** and **2n** which were obtained in 41 and 65% yield, respectively (Scheme 3). Suitable crystals of **2q** for X-ray crystallographic studies were obtained aiming at the unequivocal determination of the position that the selenation reaction has occurred. ORTEP-3 representation of product **2q** is shown in Figure 3, clearly indicating that the reaction occurred on the iodine *ortho* to the carbonyl group.



Scheme 3 Scope of the selenation protocol involving 1,4-naphthoquinones and 9,10-anthraquinones using $Cu(PPh_3)_3Br$ as the catalyst.

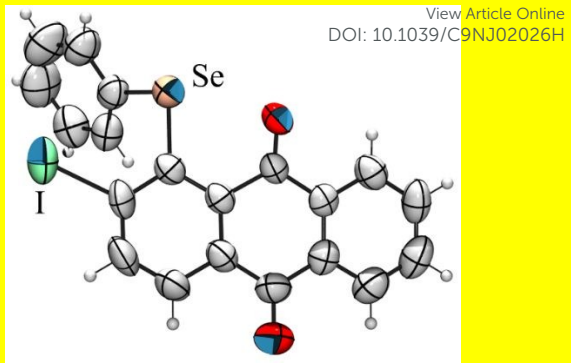


Fig. 2 ORTEP-3 projection of anthraquinone **2q** with displacement ellipsoids at the 70% probability level.

Use of copper supported on carbon nanotubes as catalyst

In the past decade, some of us have been involved in the development of novel multi-walled carbon nanotubes (MWCNTs)-based heterogeneous catalysts.[19] These hybrids are prepared according to a layer-by-layer strategy, taking advantage of the self-assembly properties of a nano-ring-forming amphiphile (DANTA) and using a cationic polymer (PDADMAC) as a stabilizing layer for metal particles (Figure 3).[19] The method allows the dense and robust anchoring of metal species at the surface of the nanotubes and the catalyst produced can be used for the promotion of organic transformations. The approach has been applied to the immobilization of various noble metals such as gold,[20] rhodium,[21] ruthenium[22] and palladium[23] as well as more abundant metals such as nickel[24] or copper.[25] In these systems, carbon nanotubes offer several advantages including large surface area, stability, and potential stabilization of transient oxidation states of the catalytic metals.

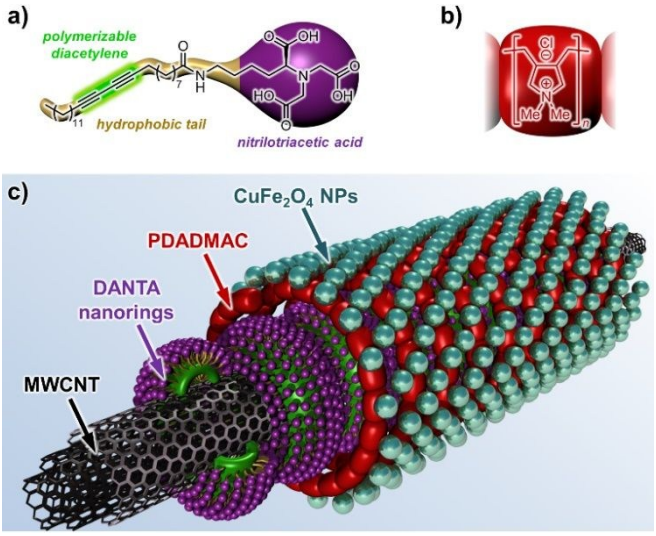


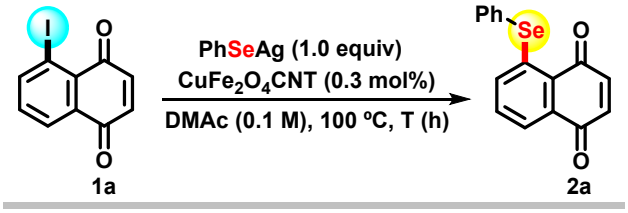
Fig. 3 Structures of a) DANTA and b) PDADMAC; c) Overview of the $CuFe_2O_4$ catalyst.

Considering the catalytic efficiency of the CNT-based nanocatalysts, we used $CuFe_2O_4$CNT to efficiently promote the selenation of naphthoquinones and anthraquinones, since its use for click reactions has been recently described.[25] Initially, the reaction of

View Article Online DOI: 10.1039/C9NJ02026H

1a and PhSeAg with 0.3 mol% of $CuFe_2O_4$CNT as the catalyst was conducted at 100 °C in dimethylacetamide (DMAc) but, under these conditions, we did not observe any transformation after 1 h with stirring (Table 3, entry 1). Following our attempts to prepare **2a**, we increased the reaction time to 2, 4, 8 and 12 h (entries 2-5), which led to a concomitant increase in the yield. Finally, after 18 h of reaction, **2a** was prepared in 74% yield (entry 6). The use of 0.4 or 0.5 mol% of the catalyst did not generate significant changes in the formation of **2a** (entry 7 and 8). The application of a higher temperature (120 °C) also had no effect on the synthesis of **2a** (entry 9). It should be noted that while the "classical" selenation reaction was carried out with 10 mol% of CuTC or 2.5 mol% of $Cu(PPh_3)_3Br$ (Tables 1 and 2), here only 0.3 mol% of $CuFe_2O_4$CNT is required for the preparation of **2a** in comparable yield.

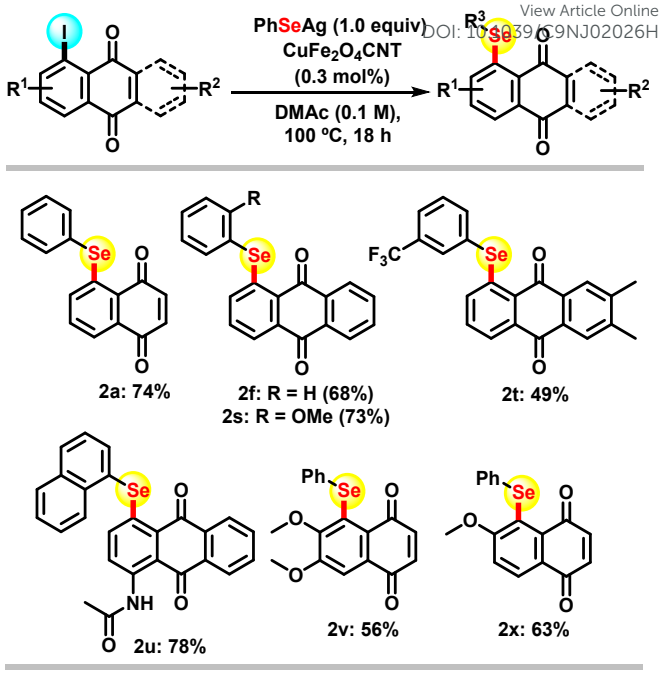
Table 3 Selected optimization results for the selenation reaction using $CuFe_2O_4$CNT as catalyst.



Entry	$CuFe_2O_4$CNT (mol %)	Time (h)	Yield (%)[b]
1	0.3	1	NR
2	0.3	2	NR
3	0.3	4	Traces
4	0.3	8	10
5	0.3	12	26
6	**0.3**	**18**	**74**
7	0.4	18	73
8	0.5	18	51
9	0.3	18	70[c]
10	-	18	NR

[a]General reaction conditions: **1a** (0.2 mmol), $CuFe_2O_4$CNT (0.3 mol%, 157 µL of 1.9 mM aqueous suspension). [b]Isolated yields. [c]120 °C. NR = for all cases starting material **1a** was recovered.

Subsequently, we applied the optimized method for the preparation of selenium-containing quinones using the $CuFe_2O_4$CNT nanocatalyst as an activator. Compounds **2a** and **2f** were prepared in moderate 74 and 65% yield, respectively, respectively. To verify the efficiency of the nanocatalyst, we also prepared the quinonoid compound **2s**-**2x**. This robust and potent catalyst allowed the synthesis of the selenated derivatives in similar yields with very low metal loading. In addition to the superior activity of the $CuFe_2O_4$CNT nanocatalyst, a second advantage is the combination of catalytically active copper with magnetically active iron. If recycling of the catalyst is required, the latter key feature can be exploited for easy magnetic recovery, as previously shown by some of us.[25]



Scheme 4 Scope of the selenation protocol involving 1,4-naphthoquinones and 9,10-anthraquinones using $CuFe_2O_4$CNT as catalyst.

Trypanocidal evaluation of the selenoquinones

Chagas disease, described by the Brazilian Carlos Chagas more than a century ago, is a parasitic disease caused by the hemoflagellate protozoan *Trypanosoma cruzi* (*T. cruzi*). This illness is considered a neglected tropical disease, leading to more than 10,000 deaths each year. The World Health Organization estimates that almost 8 million people are infected worldwide.[26] In Latin American countries where it is endemic, low-income populations are the most severely affected, and the relation between considerable morbidity/mortality and poverty can be clearly observed. Recently, globalization has led to an intensification of the movement of infected individuals to well-developed areas such as Europe and North America and consequently the number of Chagas disease cases has increased in non-endemic countries.[27] Clinically, Chagas disease shows an acute phase evidenced by the high number of the parasites in the bloodstream, with unspecific symptoms, and an asymptomatic chronic stage characterized by reduced parasitemia in spite of the positive serology.[28] During the course of the infection, 20-30% of the patients will develop cardiac and digestive symptoms, or more rarely, polyneuropathy.[29] Treatment is currently based on only two drugs, benznidazole and nifurtimox, nitroderivatives active on acute cases that present notable limitations in chronic patients.[30] Controversial efficacy and severe side effects reinforce the need for new trypanocidal drugs to be developed.[31]

To this end, over the past few years, we have evaluated the trypanocidal potential of various naphthoquinoidal compounds containing, for example, hydroxyl,[13] imidazole,[32] 1,2,3-triazole,[33] alkyl[34] and aryl[35] groups. Here, compounds **2a**-**2e** presented potent trypanocidal activity with IC_{50} values in the range of 13.3 to 37.0 µM. Of particular remark are compounds **2c** and **2d**, which were almost eight times more active than benznidazole, the positive control and one of the drugs used against the parasite that causes Chagas'

View Article Online DOI: 10.1039/C9NJ03086H

disease. Naphthoquinones **2k**-**2n** were also active against the parasite with emphasis on compound **2k** (IC_{50} = 23.9 µM) which is four times more active than the positive control, benznidazole. Anthraquinones **2f**-**2j** and **2o**-**2t** were inactive against *T. cruzi* (Table 4). Compounds **2u**-**2x** were obtained in small amount and were not evaluated against the parasite.

Table 4 Activity of naphthoquinones on trypomastigote forms of *T. cruzi*.

Compounds	IC_{50}/24 h[a] (µM)	Compounds	IC_{50}/24 h[a] (µM)
2a	14.4 ± 0.6	**2k**	23.9 ± 1.5
2b	23.5 ± 1.1	**2l**	39.0 ± 7.6
2c	13.3 ± 1.4	**2m**	37.7 ± 4.6
2d	13.4 ± 2.3	**2n**	40.0 ± 4.6
2e	37.0 ± 3.7	**2o**	>4000.0
2f	>4000.0	**2p**	>4000.0
2g	>4000.0	**2q**	>4000.0
2h	>4000.0	**2r**	>4000.0
2i	>4000.0	**2s**	>4000.0
2j	>4000.0	**2t**	>4000.0
Bz	103.6 ± 0.6[36]	**Bz**	103.6 ± 0.6[36]

[a]Mean ± SD of at least three independent experiments.

3. Conclusions

In conclusion, we developed an efficient and reliable method for preparing selenated naphthoquinones and anthraquinones. The copper complexes and carbon nanotube-copper ferrite were found to efficiently catalyze the reaction and provide the desired products in high yield. In addition, the compounds showed action against *T. cruzi* and potent trypanocidal compounds were identified. These new derivatives open up new avenues for the design of potent compounds that could be used against the parasite that causes Chagas disease. In broader terms, the strategy described herein represents a promising approach to the synthesis of A-ring selenated quinones and may guide the synthesis of redox compounds based on chalcogen chemistry.

4. Experimental Section

Starting materials obtained from commercial suppliers were used as received unless otherwise stated. For reagents requiring purification, standard laboratory techniques based on methods published by Perrin, Armarego, and Perrin (Pergamon Press, 1966) were employed. Zinc powder was previously washed with HCl solution (1 M), water and acetone, dried under reduced pressure and stored under argon. Flash column chromatography (FCC) was performed using silica gel (Aldrich 40-63 µm, 230-400 mesh). Thin layer chromatography (TLC) was performed using aluminum-backed 60 F254 silica plates. Visualization was achieved by UV fluorescence. Proton nuclear magnetic resonance (NMR) spectra were recorded using a Bruker DRX 400 or a Bruker AVANCE 400 spectrometer. ^{13}C NMR spectra were recorded at 100 MHz as stated. Chemical shifts (δ) are given in parts per million (ppm). Peaks are described as singlets (s), doublets (d), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of triplet of doublets (dtd), triplets (t), doublet of triplets (dt), quintets (quint), sextets (sext) and multiplets (m). The ^{1}H and ^{13}C NMR spectra were referenced to the appropriate residual solvent peak or TMS peak. Coupling constants (*J*) were quoted to the nearest 0.5 Hz. Mass spectra were recorded using a Brüker Daltonics micrOTOF-Q II ($APPI^+$ and ESI^+ mode). Infrared spectra were recorded on a Perkin Elmer Spectrum One FTIR spectrometer as thin films or solids compressed on a diamond plate. IR bands are described by the wavenumber ($\bar{\nu}$, cm^{-1}). Melting points were determined using the Stuart SMP30 melting point apparatus and are uncorrected.

Synthesis of catalysts and substrates: $Cu(PPh_3)_3Br$ and $Cu(DMPHEN)_2Cl$ were synthesized following previously reported procedures.[37] $CuFe_2O_4CNT$ was prepared according to the method described by Gravel and Doris.[24] Diselenides were synthesized via the Grignard reaction followed by transmetalation with Se powder (200 mesh).[38] 1,2-dibutyldiselane was synthesized through the reaction of *N*-butyllithium with Se powder (200 mesh).[39] Phenyl hypochloroselenoites were synthesized by reaction of the corresponding diselenides with SO_2Cl_2 in hexane under reflux, followed by the recrystallization in hexane as previously described in the literature with minor modifications.[40] Iodinated naphthoquinones and anthraquinones were prepared via the rhodium C-H iodination protocol previously reported by our research group[12] or by the methodology reported by Shvartsberg and co-workers.[41] Substrate (**1p**) was synthesised by acetylation of 1-amino-4-iodoanthracene-9,10-dione (**1o**) with acetic anhydride and pyridine under reflux.[42] Substrate (**1q**) was synthesised by Diels-Alder reaction of 5-iodo-1,4-naphthoquinone (**1a**) with 2,3-dimethylbuta-1,3-diene followed by oxidation with 5% ethanolic potassium hydroxide solutionand oxygen flux for 16 hours.[43]

General procedure for the selenation reactions (CuTC as catalyst), Method A

An oven dried re-sealable reaction tube was loaded with the corresponding iodinated quinone (0.10 mmol), the corresponding phenyl hypochloroselenoite (0.20 mmol), copper 2-thiophene carboxylate (1.9 mg, 10 mol %) and anhydrous DMAc (1.0 mL). The Zn powder (2.5-5.0 eq.) was then added and the tube was sealed. The mixture was kept at 100 °C for 18 h. After cooling and solvent removal by reduced pressure the residue was purified by FCC, under the conditions noted.

General procedure for the selenation reactions ($Cu(PPh_3)_3Br$ as catalyst), Method B

An oven dried re-sealable reaction tube was loaded with the corresponding iodinated quinone (0.10 mmol), AgSeR-salts (0.10 mmol) and $Cu(PPh_3)_3Br$ (2.3 mg, 2.5 mol %). Anhydrous DMAc (1.0 mL) was added and the tube was sealed. The mixture was kept at 100 °C for 18 h. After cooling and solvent removal by reduced pressure the residue was purified by FCC, under the conditions noted.

General procedure for the selenation reactions ($CuFe_2O_4CNT$ as catalyst), Method C

View Article Online DOI: 10.1039/C9NJ02041H

An oven dried re-sealable reaction tube was loaded with the corresponding iodinated quinone (0.10 mmol), AgSeR-salts (0.10 mmol) and $CuFe_2O_4$CNT (suspension in H_2O 1.9 mM, 157 µL, 0.3 mol %). DMAc (1.0 mL) was then added and the tube was sealed. The mixture was kept at 100 °C for 18 h. After cooling, the crude product was extracted with ethyl acetate (3 x 10 mL) and the organic phase was dried with $MgSO_4$. After solvent removal by reduced pressure, the residue was purified by FCC, under the conditions noted. (Note: catalyst suspension was submitted to vigorous stirring for 10 minutes prior to the beginning of the reaction).

General procedure for the synthesis of AgSeR-salts: A 100 mL round-bottom flask was loaded with the corresponding diselenide (2.0 mmol), 10 mL of an HCl solution (3.0 mol/L) and 10 mL of Et_2O. The mixture was submitted to vigorous stirring until the solution became colorless. The organic phase was separated and added dropwise to a 100 mL round-bottom flask containing Et_3N (2.0 mmol, 279 µL), $AgNO_3$ (679.4 mg, 4.0 mmol) and acetonitrile (15 mL). A precipitate was formed, and the mixture was kept under vigorous stirring for 30 min. The precipitate was filtered and washed with acetonitrile (3 x 10 mL) and Et_2O (3 x 10 mL). The resulting solid was dried under reduced pressure to afford the corresponding AgSeR-salts in quantitative yields.

***N*-(4-iodo-9,10-dioxo-9,10-dihydroanthracen-1-yl)acetamide (1p).** Orange solid, 99% yield. Solvent for flash chromatography: toluene; mp: 238.1-240.3 °C; IR (solid, cm^{-1}) v: 2962, 1677, 1485, 1249, 1094, 800; ^1H NMR (400 MHz, $CDCl_3$) δ: 12.50 (s, 1H), 8.78 (d, *J* = 9.1 Hz, 1H), 8.35 (d, *J* = 9.1 Hz, 1H), 8.30-8.25 (m, 1H), 8.25-8.20 (m, 1H), 7.84-7.77 (m, 2H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 186.6, 181.6, 170.0, 150.0, 143.1, 134.7, 134.2, 133.1, 133.0, 133.0, 127.4, 126.9, 126.2, 86.1, 25.9; HRMS (APPI$^+$): 390.9689 $[M]^+$. Cald. for $[C_{16}H_{10}INO_3]^+$: 390.9700.

1-iodo-6,7-dimethylanthracene-9,10-dione (1q). Yellow solid, 98% yield. Solvent for flash chromatography: toluene; mp: 245.1-246.3 °C; IR (solid, cm^{-1}) v: 1677, 1314, 1212, 732; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.38 (ddd, *J* = 13.2, 7.8, 1.2 Hz, 2H), 8.06 (s, 1H), 7.98 (s, 1H), 7.35 (t, *J* = 7.8 Hz, 1H), 2.43 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 181.9, 181.6, 148.4, 144.6, 144.0, 136.0, 133.6, 132.3, 131.8, 130.6, 128.7, 128.2, 127.6, 93.0, 20.3, 20.2; HRMS (APPI$^+$): 361.9798 $[M]^+$. Cald. for $[C_{16}H_{11}IO_2]^+$: 361.9804.

5-(phenylselanyl)-1,4-naphthoquinone (2a). Red solid, 25.4 mg, 81% yield (Method A), 30.0 mg, 96% yield (Method B), 23.1 mg, 74% yield (Method C). Solvent system for flash chromatography: hexane/THF: 99/1; mp: 152.3-154.0 °C; IR (solid, cm^{-1}) v: 2922, 1661, 1633, 1265, 738; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.90 (d, *J* = 7.3 Hz, 1H), 7.71 (d, *J* = 6.7 Hz, 2H), 7.53-7.43 (m, 3H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 1H), 7.07 (d, *J* = 10.3 Hz, 1H), 6.97 (d, *J* = 10.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.8, 185.1, 142.7, 139.4, 137.7, 137.7, 134.3, 134.0, 132.9, 130.2, 129.9, 128.6, 128.5, 124.5; HRMS (APPI$^+$): 330.9868 $[M+OH]^+$. Cald. for $[C_{16}H_{11}O_3Se]^+$: 330.9868.

5-((4-methoxyphenyl)selanyl)-1,4-naphthoquinone (2b). Red solid, 19.9 mg, 58% yield (Method A), 25.4 mg, 74% yield (Method B). Solvent system for flash chromatography: hexane/THF: 99/1; mp: 107.6-111.0 °C; IR (solid, cm^{-1}) v: 2922, 1639, 1568, 1240, 819; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.89 (d, *J* = 8.3 Hz, 1H), 7.60 (d, *J* = 8.7 Hz, 2H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 8.9 Hz, 1H), 7.06 (d, *J* = 10.3 Hz, 1H), 7.02-6.93 (m, 3H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.8, 185.1, 161.1, 143.5, 139.5, 139.2, 137.7, 134.2, 134.0, 132.8, 128.4, 124.4, 118.9, 115.9, 55.6; HRMS (APPI$^+$): 360.9974 $[M+OH]^+$. Cald. for $[C_{17}H_{13}O_4Se]^+$: 360.9974.

5-((4-chlorophenyl)selanyl)-1,4-naphthoquinone (2c). Red solid, 14.6 mg, 42% yield (Method A), 27.1 mg, 78% yield (Method B). Solvent system for flash chromatography: hexane/THF: 99/1; mp: 138.1-141.3 °C; IR (solid, cm^{-1}) v: 2925, 1664, 1639, 1298, 788; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.92 (d, *J* = 7.4 Hz, 1H), 7.64 (d, *J* = 8.3 Hz, 2H), 7.47-7.37 (m, 3H), 7.19 (d, *J* = 8.1 Hz, 1H), 7.07 (d, *J* = 10.3 Hz, 1H), 6.97 (d, *J* = 10.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.8, 184.9, 142.1, 139.3, 139.1, 137.8, 136.5, 134.1, 133.1, 130.5, 128.5, 126.8, 124.7; HRMS (APPI$^+$): 364.9476 $[M+OH]^+$. Cald. for $[C_{16}H_{10}ClO_3Se]^+$: 364.9478.

5-((4-fluorophenyl)selanyl)-1,4-naphthoquinone (2d). Red solid, 19.9 mg, 60% yield (Method A), 30.8 mg, 93% yield (Method B). Solvent system for flash chromatography: hexane/THF: 99/1; mp: 157.9-161.1 °C; IR (solid, cm^{-1}) v: 2919, 1646, 1575, 1219, 825; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.91 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.68 (dd, *J* = 8.6, 5.5 Hz, 2H), 7.40 (t, *J* = 8.2Hz, 1H), 7.18-7.12 (m, 3H), 7.07 (d, *J* = 10.3 Hz, 1H), 6.97 (d, *J* = 10.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.6, 184.7, 165.1, 162.6, 142.3 (d, *J* = 0.9 Hz), 139.6 (d, *J* = 8.1 Hz), 139.1, 137.6, 133.9, 133.8, 132.8, 128.3, 124.4, 123.3 (d, *J* = 3.6 Hz), 117.3 (d, *J* = 21.3 Hz); HRMS (APPI$^+$): 348.9776 $[M+OH]^+$. Cald. for $[C_{16}H_{10}FO_3Se]^+$: 348.9774.

5-(*p*-tolylselanyl)-1,4-naphthoquinone (2e). Red solid, 18.3 mg, 56% yield (Method A), 23.5 mg, 72% yield (Method B). Solvent system for flash chromatography: hexane/THF: 99/1; mp: 128.9-130.6 °C; IR (solid, cm^{-1}) v: 2912, 1646, 1289, 788; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.88 (d, *J* = 7.4 Hz, 1H), 7.58 (d, *J* = 7.9 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 1H), 7.28-7.20 (m, 3H), 7.06 (d, *J* = 10.3 Hz, 1H), 6.96 (d, *J* = 10.3 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.5, 184.9, 142.9, 139.9, 139.2, 137.4, 136.8, 134.1, 133.8, 132.6, 130.8, 126.1, 124.7, 124.2, 21.5; HRMS (APPI$^+$): 327.9996 $[M]^+$. Cald. for $[C_{17}H_{12}O_2Se]^+$: 327.9997.

1-(phenylselanyl)-9,10-anthraquinone (2f). Orange solid, 28.6 mg, 79% yield (Method A), 31.2 mg, 86% yield (Method B), 24.6 mg, 68% yield (Method C). Solvent system for flash chromatography: hexane/ethyl acetate: 99/1; mp: 167.5-169.1 °C; IR (solid, cm^{-1}) v: 2922, 1670, 1571, 1265, 704; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.39 (d, *J* = 7.1 Hz, 1H), 8.29 (d, *J* = 7.8 Hz, 1H), 8.13 (d, *J* = 7.4 Hz, 1H), 7.88-7.77 (m, 2H), 7.75 (d, *J* = 6.7 Hz, 2H), 7.54-7.44 (m, 3H), 7.41 (t, *J* = 7.8 Hz, 1H), 7.27 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 184.0, 183.2, 143.3, 137.8, 135.7, 134.6, 134.2, 133.9, 133.0, 133.0, 130.2, 129.8, 129.8, 129.3, 127.7, 127.3, 125.1. Data are consistent with those reported in the literature.[17]

1-((4-methoxyphenyl)selanyl)-9,10-anthraquinone (2g). Orange solid, 25.9 mg, 66% yield (Method A), 34.2 mg, 87% yield (Method B).

Solvent for flash chromatography: toluene; mp: 226.9-229.0 °C; IR (solid, cm^{-1}) v: 2928, 1661, 1565, 1249, 701; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.39 (d, *J* = 7.5 Hz, 1H), 8.29 (d, *J* = 7.0 Hz, 1H), 8.12 (d, *J* = 7.3 Hz, 1H), 7.86-7.77 (m, 2H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.28 (d, *J* = 11.5 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.8, 183.1, 160.8, 143.9, 139.0, 135.5, 134.3, 134.2, 134.1, 133.9, 133.7, 132.8, 132.7, 129.6, 127.5, 127.2, 127.0, 124.8, 119.4, 115.6, 55.4. Data are consistent with those reported in the literature.[17]

1-((4-chlorophenyl)selanyl)-9,10-anthraquinone (2h). Orange solid, 29.4 mg, 74% yield (Method A), 35.3 mg, 89% yield (Method B). Solvent system for flash chromatography: hexane/ ethyl acetate: 99/1; mp: 230.1-233.0 °C; IR (solid, cm^{-1}) v: 2922, 1568, 1469, 1271, 704; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.38 (d, *J* = 6.8 Hz, 1H), 8.30 (d, *J* = 7.9 Hz, 1H), 8.15 (d, *J* = 7.4 Hz, 1H), 7.82 (quint, *J* = 7.3 Hz, 2H), 7.67 (d, *J* = 8.1 Hz, 2H), 7.44 (d, *J* = 7.9 Hz, 3H), 7.26 (d, *J* = 3.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.8, 182.9, 142.5, 138.9, 136.2, 135.5, 134.4, 134.1, 133.6, 133.0, 132.8, 130.3, 129.7, 127.5, 127.3, 127.1, 125.1. Data are consistent with those reported in the literature.[17]

1-((4-fluorophenyl)selanyl)-9,10-anthraquinone (2i). Orange solid, 28.2 mg, 74% yield (Method A), 34.3 mg, 90% yield (Method B). Solvent system for flash chromatography: hexane/ethyl acetate: 99/1; mp: 207.2-210.0 °C; IR (solid, cm^{-1}) v: 2922, 1664, 1568, 1271, 800, 707; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.37 (d, *J* = 6.9 Hz, 1H), 8.29 (d, *J* = 8.5 Hz, 1H), 8.13 (d, *J* = 7.3 Hz, 1H), 7.86-7.77 (m, 2H), 7.71 (dd, *J* = 8.3, 5.7 Hz, 2H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.16 (t, *J* = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 184.05, 183.13, 165.23, 162.75, 143.11, 139.8 (d, *J* = 8.1 Hz), 135.69, 134.59, 134.3 (d, *J* = 2.5 Hz), 133.80, 133.13, 132.96, 129.86, 127.71, 127.31, 125.21, 124.2 (d, *J* = 3.7 Hz), 117.5 (d, *J* = 21.2 Hz). Data are consistent with those reported in the literature.[17]

1-(*p*-tolylselanyl)-9,10-anthraquinone (2j). Orange solid, 28.7 mg, 76% yield (Method A), 34.8 mg, 91% yield (Method B). Solvent for flash chromatography: toluene; mp: 195.6-197.0 °C; IR (solid, cm^{-1}) v: 2926, 1636, 1133, 744; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.39 (d, *J* = 7.0 Hz, 1H), 8.29 (d, *J* = 7.0 Hz, 1H), 8.12 (d, *J* = 7.4 Hz, 1H), 7.87-7.75 (m, 2H), 7.62 (d, *J* = 7.8 Hz, 2H), 7.41 (t, *J* = 7.8 Hz, 1H), 7.27 (d, *J* = 8.1 Hz, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.8, 183.1, 143.5, 139.8, 137.5, 135.4, 134.3, 133.9, 133.7, 132.8, 132.7, 130.8, 129.6, 127.5, 127.0, 125.4, 124.8, 21.4. Data are consistent with those reported in the literature.[17]

5-(naphthalen-1-ylselanyl)-1,4-naphthoquinone (2k). Deep red solid, 35.5 mg, 98% yield (Method B). Solvent system for flash chromatography: hexane/ethyl acetate: 19/1; mp: 114.9-116.2 °C; IR (solid, cm^{-1}) v: 1642, 1574, 1286, 769; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.25 (d, *J* = 8.4 Hz, 1H), 8.09-8.00 (m, 2H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.58-7.44 (m, 3H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.12 (d, *J* = 10.3 Hz, 1H), 6.99 (d, *J* = 10.3 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.75, 184.82, 141.81, 139.22, 137.56, 135.36, 134.49, 134.20, 133.91, 132.70, 131.22, 128.87, 128.50, 128.20, 127.65, 127.60, 126.72, 126.35, 124.25; HRMS ($APPI^+$): 363.9999 $[M]^+$. Cald. for $[C_{20}H_{12}O_2Se]^+$: 364.0003.

5-(butylselanyl)-1,4-naphthoquinone (2l). Red solid, 14.9 mg, 51% yield (Method B). Solvent system for flash chromatography: hexane/ethyl acetate: 10/1; mp: 68.3-70.0 °C; IR (solid, cm^{-1}) v: 2919, 1664, 1646, 1255, 772; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.94 (d, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.02 (d, *J* = 10.2 Hz, 1H), 6.94 (d, *J* = 10.2 Hz, 1H), 2.94 (t, *J* = 7.5 Hz, 2H), 1.80 (quint, *J* = 7.5 Hz, 2H), 1.56 (sext, *J* = 7.5 Hz, 2H), 1.00 (t, *J* = 7.3 Hz, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.4, 184.9, 141.1, 139.5, 137.5, 137.0, 134.2, 132.7, 132.6, 129.1, 126.1, 123.7, 30.5, 24.8, 23.4, 13.7; HRMS ($APPI^+$): 295.0233 $[M+H]^+$. Cald. for $[C_{14}H_{15}O_2Se]^+$: 295.0232.

5-((3-(trifluoromethyl)phenyl)selanyl)-1,4-naphthoquinone (2m). Orange solid, 32.0 mg, 84% yield (Method B). Solvent system for flash chromatography: hexane/ethyl acetate: 10/1; mp: 159.1-160.9 °C; IR (solid, cm^{-1}) v: 1649, 1571, 1305, 1122, 769; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.99 (s, 1H), 7.92 (t, *J* = 8.7 Hz, 2H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.60 (t, *J* = 7.7 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.13 (d, *J* = 8.2 Hz, 1H), 7.09 (d, *J* = 10.3 Hz, 1H), 6.99 (d, *J* = 10.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.6, 184.6, 141.2, 140.9, 139.1, 137.7, 134.1 (q, *J* = 7.7 Hz), 133.9, 133.8, 133.0, 132.4, 132.1, 130.3, 129.5, 128.3, 126.5 (q, *J* = 3.3 Hz), 124.6; HRMS ($APPI^+$): 381.9713 $[M]^+$. Cald. for $[C_{17}H_9F_3O_2Se]^+$: 381.9720.

5-((2-methoxyphenyl)selanyl)-1,4-naphthoquinone (2n). Orange solid, 22.3 mg, 65% yield (Method B). Solvent system for flash chromatography: hexane/ethyl acetate: 10/1; mp: 185.9-187.2 °C; IR (solid, cm^{-1}) v: 2922, 1642, 1568, 1243, 760; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.89 (d, *J* = 7.4 Hz, 1H), 7.71 (d, *J* = 7.3 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.18 (d, *J* = 8.1 Hz, 1H), 7.09-7.01 (m, 3H), 6.95 (d, *J* = 10.3 Hz, 1H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.6, 184.9, 160.6, 141.8, 139.3, 139.2, 137.4, 134.1, 133.9, 132.4, 132.1, 128.5, 124.2, 121.9, 117.0, 111.3, 56.0; HRMS ($APPI^+$): 343.9949 $[M]^+$. Cald. for $[C_{17}H_{12}O_3Se]^+$: 343.9952.

1-amino-4-(phenylselanyl)-9,10-anthraquinone (2o). Purple solid, 32.1 mg, 85% yield (Method B). Solvent system for flash chromatography: hexane/ethyl acetate: 5/1; mp: 203.9-205.0 °C; IR (solid, cm^{-1}) v: 3414, 1587, 1633, 1268, 726; ^1H NMR (400 MHz, DMSO) δ: 8.24 (t, *J* = 7.0 Hz, 2H), 7.96-7.86 (m, 2H), 7.70 (d, *J* = 7.0 Hz, 2H), 7.58-7.46 (m, 3H), 7.04 (d, *J* = 9.2 Hz, 1H), 6.91 (d, *J* = 9.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ: 183.7, 183.2, 151.8, 137.7, 135.2, 134.8, 134.3, 134.0, 132.9, 130.6, 130.2, 130.1, 129.9, 129.1, 127.1, 126.9, 125.2, 112.8; HRMS ($APPI^+$): 380.0179 $[M+H]^+$. Cald. for $[C_{20}H_{14}NO_2Se]^+$: 380.0184.

***N*-(9,10-dioxo-4-(phenylselanyl)-9,10-dihydroanthracen-1-yl)acetamide (2p).** Deep red solid, 36.1 mg, 86% yield (Method B). Solvent system for flash chromatography: hexane/ethyl acetate: 5/1; mp: 233.2-234.0 °C; IR (solid, cm^{-1}) v: 3052, 1577, 1481, 1258, 719; ^1H NMR (400 MHz, $CDCl_3$) δ: 12.51 (s, 1H), 8.83 (d, *J* = 9.4 Hz, 1H), 8.42 (d, *J* = 8.5 Hz, 1H), 8.32 (d, *J* = 8.6 Hz, 1H), 7.87 (quint, *J* = 7.6 Hz, 2H), 7.77 (d, *J* = 6.8 Hz, 2H), 7.60-7.45 (m, 3H), 7.32 (d, *J* = 8.0 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 187.1, 183.1, 169.9, 140.7, 138.1, 137.4, 136.5, 134.5, 134.0, 133.3, 132.8, 129.9, 129.6, 129.1, 127.3, 127.1, 125.4, 118.6, 77.4, 77.0, 76.7, 25.8; HRMS ($APPI^+$): 421.0216 $[M]^+$. Cald. for $[C_{22}H_{15}NO_3Se]^+$: 421.212.

View Article Online
DOI: 10.1039/C9NJ02026H

2-iodo-1-(phenylselanyl)-9,10-anthraquinone (2q). Red solid, 42.5 mg, 87% yield (Method B). Solvent for flash chromatography: toluene; mp: 117.9-120.0 °C; IR (solid, cm^{-1}) v: 3058, 1667, 1302, 710; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.29-8.24 (m, 2H), 8.19-8.10 (m, 1H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.82-7.77 (m, 2H), 7.29-7.20 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.0, 182.5, 145.6, 140.9, 137.7, 134.7, 134.5, 134.4, 134.3, 133.8, 132.3, 131.7, 129.4, 127.7, 127.4, 127.1, 126.8, 117.1; HRMS (APPI$^+$): 489.8972 $[M]^+$. Cald. for $[C_{20}H_{11}IO_2Se]^+$: 489.8964.

6,7-dimethyl-1-(phenylselanyl)-9,10-anthraquinone (2r). Deep yellow solid, 37.1 mg, 95% yield (Method B). Solvent system for flash chromatography: hexane/ethyl acetate: 5/1; mp: 198.6-199.8 °C; IR (solid, cm^{-1}) v: 3067, 1673, 1336, 741; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.14 (d, *J* = 8.0 Hz, 2H), 8.05 (s, 1H), 7.79 (d, *J* = 6.7 Hz, 2H), 7.58-7.46 (m, 3H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.29 (t, *J* = 6.5 Hz, 1H), 2.49 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 184.0, 183.1, 144.3, 143.9, 142.6, 137.5, 135.6, 134.1, 132.6, 131.7, 130.8, 129.9, 129.8, 129.5, 129.3, 128.4, 128.0, 124.7, 20.3, 20.2; HRMS (APPI$^+$): 392.0322 $[M]^+$. Cald. for $[C_{22}H_{16}O_2Se]^+$: 392.0310.

1-((2-methoxyphenyl)selanyl)anthracene-9,10-dione (2s). Orange solid, 28.7 mg, 73% yield (Method C). Solvent for flash chromatography: toluene; mp: 188.1-190.8 °C; IR (solid, cm^{-1}) v: 2925, 1664, 1568, 1271, 757; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.44 (d, *J* = 8.9 Hz, 1H), 8.33 (dd, *J* = 7.5, 1.4 Hz, 1H), 8.17 (d, *J* = 6.8 Hz, 1H), 7.84 (dtd, *J* = 22.5, 7.5, 1.4 Hz, 3H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 1H), 7.13-7.04 (m, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 183.8, 183.1, 160.6, 142.4, 139.3, 135.5, 134.3, 134.3, 133.9, 133.7, 132.8, 132.6, 132.0, 129.9, 127.5, 127.0, 124.8, 121.9, 117.7, 111.3, 56.0; HRMS (APPI$^+$): 394.0102 $[M]^+$. Cald. for $[C_{21}H_{14}O_3Se]^+$: 394.0103.

6,7-dimethyl-1-((3-(trifluoromethyl)phenyl)selanyl)anthracene-9,10-dione (2t). Deep yellow solid, 22.5 mg, 49% yield (Method C). Solvent for flash chromatography: toluene; mp: 232.2-234.1 °C; IR (solid, cm^{-1}) v: 1670, 1323, 1116, 797; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.18-8.10 (m, 2H), 8.04 (s, 2H), 7.95 (d, *J* = 7.6 Hz, 1H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.60 (t, *J* = 7.7 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.16 (d, *J* = 9.1 Hz, 1H), 2.47 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 184.1, 182.9, 144.4, 144.2, 141.4, 140.9, 135.7, 134.1 (q, *J* = 3.8 Hz), 133.7, 132.9, 132.4, 132.1, 131.5, 130.8, 130.5, 130.2, 129.9, 128.5, 128.1, 126.3 (q, *J* = 3.8 Hz), 125.1, 122.3, 20.3, 20.2; HRMS (APPI$^+$): 477.0213 $[M+OH]^+$. Cald. for $[C_{23}H_{16}F_3O_3Se]^+$: 477.0211.

***N*-(4-(naphthalen-1-ylselanyl)-9,10-dioxo-9,10-dihydroanthracen-1-yl)acetamide (2u).** Deep red solid, 36.7 mg, 78% yield (Method C). Solvent system for flash chromatography: toluene; mp: 285.2-286.0 °C; IR (solid, cm^{-1}) v: 3061, 1581, 1478, 1258, 766; ^1H NMR (400 MHz, $CDCl_3$) δ: 12.47 (s, 1H), 8.63 (d, *J* = 9.4 Hz, 1H), 8.45 (d, *J* = 8.7 Hz, 1H), 8.31 (d, *J* = 7.0 Hz, 1H), 8.27 (d, *J* = 8.4 Hz, 1H) 8.09 (d, *J* = 6.9 Hz, 1H), 8.04 (d, *J* = 8.2 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.86 (dt, *J* = 13.0, 6.6 Hz, 2H), 7.54 (t, *J* = 7.5 Hz 2H), 7.47 (t, *J* = 7.9 Hz, 1H), 7.00 (d, *J* = 9.3 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 188.0, 183.3, 169.9, 140.7, 137.6, 137.4, 136.8, 135.4, 134.5, 134.2, 134.1, 133.3, 132.8, 131.2, 129.3, 128.9, 128.8, 128.2, 127.6, 127.3, 127.1, 126.7, 126.3, 125.4, 118.7, 25.7; HRMS (APPI$^+$): 472.0448 $[M+H]^+$. Cald. for $[C_{26}H_{17}NO_3Se]^+$: 472.0446.

6,7-dimethoxy-5-(phenylselanyl)naphthalene-1,4-dione (2v). Deep red solid, 20.9 mg, 56% yield (Method C). Solvent system for flash chromatography: hexane/ethyl acetate: 99/1; mp: 103.2-105.1 °C; IR (solid, cm^{-1}) v: 2937, 1565, 1308, 732; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.57 (s, 1H), 7.57-7.52 (m, 2H), 7.28-7.23 (m, 3H), 6.97 (d, *J* = 10.2 Hz, 1H), 6.87 (d, *J* = 10.2 Hz, 1H), 3.96 (s, 3H), 3.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 184.4, 156.5, 153.6, 139.9, 136.3, 133.3, 133.1, 132.0, 130.3, 128.8, 127.5, 126.7, 109.1, 59.6, 56.3; HRMS (APPI$^+$): 391.0111 $[M+OH]^+$. Cald. for $[C_{18}H_{15}O_5Se]^+$: 391.0079.

6-methoxy-5-(phenylselanyl)naphthalene-1,4-dione (2x). Deep red solid, 21.6 mg, 63% yield (Method C). Solvent system for flash chromatography: hexane/ethyl acetate: 99/1; mp: 98.6-99.8°C; IR (solid, cm^{-1}) v: 2919, 1655, 1280, 1026, 831; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.06 (d, *J* = 8.5 Hz, 1H), 7.55-7.39 (m, 2H), 7.27-7.19 (m, 3H), 7.03 (d, *J* = 10.3 Hz, 1H), 6.99 (d, *J* = 8.5 Hz, 1H), 6.91 (d, *J* = 10.2 Hz, 1H), 3.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.4, 184.0, 163.1, 139.5, 137.3, 133.8, 132.6, 128.6, 128.2, 127.1, 126.9, 126.8, 114.5, 55.6; HRMS (APPI$^+$): 360.9982 $[M+OH]^+$. Cald. for $[C_{17}H_{13}O_4Se]^+$: 360.9974.

Trypanocidal assays: Stock solutions of the compounds were prepared in dimethylsulfoxide (DMSO), with the final concentration of the latter in the experiments never exceeding 0.1%. Preliminary experiments showed that at concentrations up to 0.5% DMSO has no deleterious effect on the parasites. Bloodstream trypomastigotes of the Y strain were obtained at the peak of parasitemia from infected albino mice, isolated by differential centrifugation and resuspended in Dulbecco's modified Eagle medium (DME) to give a parasite concentration of 10^7 cells mL^{-1} in the presence of 10% of mouse blood. This suspension (100 mL) was added in the same volume of each compound previously prepared at twice the desired final concentrations. Cell counts were performed in a Neubauer chamber and the trypanocidal activity was expressed as IC_{50}, corresponding to the concentration that leads to lysis of 50% of the parasites.[36]

Crystal structure and refinement: X-ray diffraction data for single crystals of **2a**, **2b**, **2d** and **2e** were collected with an Oxford-Diffraction GEMINI-Ultra diffractometer using Mo-Kα radiation (0.71073 Å). Measurements were performed at 250 K. Data integration and scaling of the reflections for all compounds were performed with the CRYSALIS suite.[44] Final unit cell parameters were based on the fitting of all reflection positions. Analytical absorption corrections and the space group identification were also performed using the CRYSALIS suite.[44] The structures of the compounds were solved by direct methods using the SUPERFLIP program.[45] The positions of all atoms could be unambiguously assigned on consecutive difference Fourier maps. Refinements were performed using SHELXL[46] based on F^2 through the full-matrix least squares routine. All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. All hydrogen atoms were located on difference maps and included as fixed contributions according to the riding model.[47] Values were C—H = 0.97 Å and U_{iso}(H) = 1.2 U_{eq}(C) for the aromatic carbon atoms. Molecular graphs were obtained with ORTEP-3[48] in association with the POV-Ray software.[49] ORTEP-3

View Article Online
DOI: 10.1039/C9NJ02034H

diagrams of the molecules are shown in Scheme 1. CCDC 1906753 (**2a**), 1906752 (**2c**), 1906751 (**2d**) and 1906750 (**2e**), 1921236 (**2h**), 1921235 (**2i**) and 1921237 (**2q**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

Acknowledgements

This research was funded by grants from CNPq (404466/2016-8 and PQ 305741/2017-9), FAPEMIG (PPM-00638-16, PPM-00635-18 and Rede de Pesquisa e Inovação para Bioengenharia de Nanossistemas-RED-00282-16), FAPERJ, CAPES and INCT-Catálise. ENSJ would also like to thank the SeSRedCat and Capes-Humboldt research fellowship program for experienced researchers (Proc. No. 88881.145517/2017-01). G.A.M. Jardim acknowledges CNPq for post-doctoral financial support (Project no. 151150/2018-4). The "Service de Chimie Bioorganique et de Marquage" belongs to the Laboratory of Excellence in Research on Medication and Innovative Therapeutics (ANR-10-LABX-0033-LERMIT).

Conflicts of interest

There are no conflicts to declare.

Notes and References

1. (a) D. de Souza, D. O. C. Mariano, F. Nedel, E. Schultze, V. F. Campos, F. Seixas, R. S. da Silva, T. S. Munchen, V. Ilha, L. Dornelles, A. L. Braga, J. B. T. Rocha, T. Collares and O. E. D. Rodrigues, *J. Med. Chem.*, 2015, **58**, 3329-3339; (b) S. F. Fonseca, N. B. Padilha, S. Thurow, J. A. Roehrs, L. Savegnago, M. N. de Souza, M. G. Fronza, T. Collares, J. Buss, F. K. Seixas, D. Alves and E. J. Lenardão, *Ultrason Sonochem.*, 2017, **39**, 827-836; (c) Y. Pang, B. An, L. Lou, J. Zhang, J. Yan, L. Huang, X. Li and S. Yin, *J. Med. Chem.*, 2017, **60**, 7300-7314; (d) Z. Chen, D. Li, N. Xu, J. Fang, Y. Yu, W. Hou, H. Ruan, P. Zhu, R. Ma, S. Lu, D. Cao, R. Wu, M. Ni, W. Zhang, W. Su and B. H. Ruan, *J. Med. Chem.*, 2019, **62**, 589-603.
2. V. Gandin, P. Khalkar, J. Braude and A. P. Fernandes, *Free Radic. Biol. Med.*, 2018, **127**, 80-97.
3. (a) *Organoselenium Compounds in Biology and Medicine: Synthesis, Biological and Therapeutic Treatments*, Ed. V. K. Jain and K. I. Priyadarsini, Royal Society of Chemistry, UK, 2018; (b) C. M. Weekley and H. H. Harris, *Chem. Soc. Rev.*, 2013, **42**, 8870-8894; (c) I. L. Martins, C. Charneira, V. Gandin, J. L. F. da Silva, G. C. Justino, J. P. Telo, A. J. S. C. Vieira, C. Marzano and A. M. M. Antunes, *J. Med. Chem.*, 2015, **58**, 4250-4265; (d) E. E. Alberto and A. L. Braga, *Selenium and Tellurium Chemistry – From Small Molecules to Biomolecules and Materials*, ed. W. J. Derek and L. Risto, Springer-Verlag, Berlin, 2011; (e) A. L. Braga and J. Rafique, *Synthesis of biologically relevant small molecules containing selenium. Part A. Antioxidant compounds, The Chemistry of Organic Selenium and Tellurium Compounds*, ed. Z. Rappoport, John Wiley & Sons, Ltd, Chichester, UK, 2013, vol. 4; (f) A. L. Braga and J. Rafique, *Synthesis of biologically relevant small molecules containing selenium. Part B. Anti-infective and anticancer Compounds, The Chemistry of Organic Selenium and Tellurium Compounds*, ed. Z. Rappoport, John Wiley & Sons, Ltd, Chichester, UK, 2013, vol. 4; (g) A. L. Braga and J. Rafique, *Synthesis of biologically relevant small molecules containing selenium. Part C. Miscellaneous biological activities, The Chemistry of Organic Selenium and Tellurium Compounds*, ed. Z. Rappoport, John Wiley & Sons, Ltd, Chichester, UK, 2013, vol. 4; (h) C. Jacob, G. I. Giles, N. M. Giles and H. Sies, *Angew. Chem., Int. Ed.*, 2003, **42**, 4742-4758.
4. G. S. Bates, M. D. Fryzuk and C. Stone, *Can. J. Chem.*, 1987, **65**, 2612-2617.
5. M.-D. Ruan, Z.-J. Wu, W.-Q. Fan and X.-J. Zhou, Heterocycles, 1994, 37, 323-329.
6. (a) S. Mecklenburg, S. Shaaban, L. A. Ba, T. Burkholz, T. Schneider, B. Diesel, A. K. Kiemer, A. Röseler, K. Becker, J. Reichrath, A. Stark, W. Tilgen, M. Abbas, L. A. Wessjohann, F. Sasse and C. Jacob, *Org. Biomol. Chem.*, 2009, **7**, 4753-4762; (b) M. Doering, L. A. Ba, N. Lilienthal, C. Nicco, C. Scherer, M. Abbas, A. A. P. Zada, R. Coriat, T. Burkholz, L. Wessjohann, M. Diederich, F. Batteux, M. Herling and C. Jacob, *J. Med. Chem.*, 2010, **53**, 6954-6963.
7. S. Shaaban, A. Negm, A. M. Ashmawy, D. M. Ahmed and L. A. Wessjohann, *Eur. J. Med. Chem.*, 2016, **122**, 55-71.
8. (a) A. A. Vieira, J. B. Azeredo, M. Godoi, C. Santi, E. N. da Silva Júnior and A. L. Braga, *J. Org. Chem.*, 2015, **80**, 2120-2127; (b) A. A. Vieira, I. R. Brandão, W. O. Valença, C. A. de Simone, B. C. Cavalcanti, C. Pessoa, T. R. Carneiro, A. L. Braga and E. N. da Silva Júnior, *Eur. J. Med. Chem.*, 2015, **101**, 254-265; (c) E. H. G. da Cruz, M. A. Silvers, G. A. M. Jardim, J. M. Resende, B. C. Cavalcanti, I. S. Bomfim, C. Pessoa, C. A. de Simone, G. V. Botteselle, A. L. Braga, D. K. Nair, I. N. N. Namboothiri, D. A. Boothman and E. N. da Silva Júnior, *Eur. J. Med. Chem.*, 2016, **122**, 1-16.
9. (a) W.-Q. Fan, J. Wang, J. Jiang and Y.-M. Zhang, *Synth. Commun.*, 1992, **22**, 3061-3066; (b) K. Selvakumar, H. B. Singh, N. Goel, U. P. Singh and R. J. Butcher, *Dalton Trans.*, 2011, **40**, 9858-9867; (c) S. Shaaban, D. Vervandier-Fasseur, P. Andreoletti, A. Zarrouk, P. Richard, A. Negm, G. Manolikakes, C. Jacob and M. Cherkaoui-Malki, *Bioorg. Chem.*, 2018, **80**, 43-56.
10. (a) W.-M. Zhou, H. Liu and D.-M. Du, *Org. Lett.*, 2008, **10**, 2817-2820; (b) R. Wu, X. Chang, A. Lu, Y. Wang, G. Wu, H. Song, Z. Zhou and C. Tanga, *Chem. Commun.*, 2011, **47**, 5034-5036; (c) B. V. Subba Reddy, S. M. Reddy and M. Swain, *RSC Adv.*, 2013, **3**, 930-936; (d) For a review see: B. Hosamani, M. F. Ribeiro, E. N. da Silva Júnior and I. N. N. Namboothiri, *Org. Biomol. Chem.*, 2016, **14**, 6913-6931.
11. (a) Q. Wang, B. Wang, H. Deng, Y. Shangguan, Y. Lin, Y. Zhang, Z. Zhang, Y. Xiao, H. Guo and C. Zhang, *J. Org. Chem.*, 2019, **84**, 1006-1014; (b) N. O. Ilchenko, P. G. Janson and K. J. Szabó, *Chem. Commun.*, 2013, **49**, 6614-6616.
12. G. A. M. Jardim, E. N. da Silva Júnior and J. F. Bower, *Chem. Sci.*, 2016, **7**, 3780-3784.
13. G. G. Dias, T. Rogge, R. Kuniyil, C. Jacob, R. F. S. Menna-

Barreto, E. N. da Silva Júnior and L. Ackermann, *Chem. Commun.*, 2018, **54**, 12840-12843.

14. (a) G. G. Dias, T. A. do Nascimento, A. K. A. de Almeida, A. C. S. Bombaça, R. F. S. Menna-Barreto, C. Jacob, S. Warratz, E. N. da Silva Júnior and L. Ackermann, *Eur. J. Org. Chem.*, 2019, 2344-2353; (b) E. N. da Silva Júnior, G. A. M. Jardim, R. S. Gomes, Y.-F. Liang and L. Ackermann, *Chem. Commun.*, 2018, **54**, 7398-7411.
15. G. A. M. Jardim, W. X. C. Oliveira, R. P. de Freitas, R. F. S. Menna-Barreto, T. L. Silva, M. O. F. Goulart and E. N. da Silva Júnior, *Org. Biomol. Chem.*, 2018, **16**, 1686-1691.
16. (a) C. Santi, S. Santoro, B. Battistelli, L. Testaferri and M. Tiecco, *Eur. J. Org. Chem.*, 2008, 5387-5390; (b) B. Battistelli, T. Lorenzo, M. Tiecco and C. Santi, *Eur. J. Org. Chem.*, 2011, 1848-1851.
17. W. Nakanishi, S. Hayashi, D. Shimizu and M. Hada, *Chem. Eur. J.*, 2006, **12**, 3829-3846.
18. (a) C. Santi, S. Santoro, B. Battistelli, L. Testaferri and M. Tiecco, *Eur. J. Org. Chem.*, 2008, 5387-5390; (b) B. Battistelli, T. Lorenzo, M. Tiecco and C. Santi, *Eur. J. Org. Chem.*, 2011, 1848-1851.
19. (a) J. John, E. Gravel, I. N. N. Namboothiri and E. Doris. *Nanotechnol. Rev.*, 2012, **1**, 515-539; (b) E. Gravel, I. N. N. Namboothiri and E. Doris, *Synlett*, 2016, **27**, 1179-1186; (c) J. John, E. Gravel, I. N. N. Namboothiri and E. Doris, *Nanotechnol. Rev.*, 2012, **1**, 515-539.
20. (a) J. John, E. Gravel, A. Hagège, H. Li, T. Gacoin and E. Doris, *Angew. Chem. Int. Ed.*, 2011, **50**, 7533-7536; (b) R. Kumar, E. Gravel, A. Hagège, H. Li, D. V. Jawale, D. Verma, I. N. N. Namboothiri and E. Doris, *Nanoscale*, 2013, **5**, 6491-6497; (c) D. V. Jawale, E. Gravel, V. Geersten, H. Li, N. Shah, I. N. N. Namboothiri and E. Doris, *Tetrahedron*, 2014, **70**, 6140-6145; (d) S. Donck, E. Gravel, N. Shah, D. V. Jawale, E. Doris and I. N. N. Namboothiri, *RSC Advances*, 2015, **5**, 50865-50868; (e) P. Basu, N. Shah, P. Prakash, S. Donck, E. Gravel, I. N. N. Namboothiri and E. Doris, *Nanomaterials*, 2016, **6**, 37; (f) P. Prakash, E. Gravel, H. Li, H. Y. Li, F. Miserque, A. Habert, M. den Hertog, W. L. Ling, I. N. N. Namboothiri and E. Doris, *Catal. Sci. Technol.*, 2016, **6**, 6476-6479; (g) E. Gopi, E. Gravel and E. Doris, *Nanoscale Adv.*, 2019, **1**, 1181-1185.
21. (a) D. V. Jawale, E. Gravel, N. Shah, V. Dauvois, H. Li, I. N. N. Namboothiri and E. Doris, *Chem. Eur. J.*, 2015, **21**, 7039-7042; (b) S. Donck, E. Gravel, A. Li, P. Prakash, N. Shah, J. Leroy, I. N. N. Namboothiri and E. Doris, *Catal. Sci. Technol.*, 2015, **5**, 4542-4546; (c) P. Prakash, E. Gravel, D. V. Nguyen, I. N. N. Namboothiri and E. Doris, *ChemCatChem*, 2017, **9**, 2091-2094; (d) R. L. de Carvalho, G. A. M. Jardim, A. C. C. Santos, M. H. Araujo, W. X. C. Oliveira, A. C. S. Bombaça, R. F. S. Menna-Barreto, E. Gopi, E. Gravel, E. Doris and E. N. da Silva Júnior, *Chem. Eur. J.*, 2018, **24**, 15227-15235.
22. (a) D. V. Jawale, E. Gravel, C. Boudet, N. Shah, V. Geertsen, H. Li, I. N. N. Namboothiri and E. Doris, *Chem. Commun.*, 2015, **51**, 1739-1742; (b) P. Basu, P. Prakash, E. Gravel, N. Shah, K. Bera, E. Doris and I. N. N. Namboothiri, *ChemCatChem*, 2016, **8**, 1298-1302.
23. D. V. Jawale, E. Gravel, C. Boudet, N. Shah, V. Geertsen, H. Li, I. N. N. Namboothiri and E. Doris, *Catal. Sci. Technol.*, 2015, **5**, 2388-2392.
24. P. Prakash, V. Geertsen, F. Miserque, I. N. N. Namboothiri, E. Gravel and E. Doris, *ChemistrySelect*, 2017, **2**, 5891-5894.
25. P. Prakash, R. A. Kumar, F. Miserque, V. Geertsen, E. Gravel and E. Doris, *Chem. Commun.*, 2018, **54**, 3644-3647.
26. WHO. Chagas disease – Epidemiology. http://www.who.int/chagas/epidemiology/en/ (2017), Accessed July 2018.
27. (a) Q. Liu Q and X. N. Zhou, *Infect. Dis. Poverty.*, 2015, **4**, 60; (b) A. Rassi Júnior and A. Rassi, J. A. Marin-Neto, *Lancet.*, 2010, **375**, 1388; (c) G. Schmunis and Z. E. Yadon, *Acta Tropica*, 2010, **115**, 14-21.
28. (a) WHO. Expert Committee. Control of Chagas Disease. Brasilia, Brazil: World Health Organization, 2002. WHO technical report series 905; (b) A. Prata, *Lancet Infect. Dis.*, 2001, **1**, 92.
29. C. Bern, *N. Engl. J. Med*., 2015, **373**, 456.
30. C. A. Morillo, J. A. Marin-Neto, A. Avezum, S. Sosa-Estani, A. Rassi Júnior, F. Rosas, E. Villena, R. Quiroz, R. Bonilla, C. Britto, F. Guhl, E. Velazquez, L. Bonilla, B. Meeks, P. Rao-Melacini, J. Pogue, A. Mattos, J. Lazdins, A. Rassi, S. J. Connolly and S. Yusuf, *N. Engl. J. Med.*, 2015, **373**, 1295.
31. (a) R. F. Menna-Barreto and S. L. de Castro, *Curr. Top. Med. Chem.*, 2017, **17**, 1212; (b) S. B. Scarim, D. H. Jornada, R. C. Chelucci, L. de Almeida, J. L. dos Santos, M. C. Chung, *Eur. J. Med. Chem.*, 2018, **155**, 824.
32. E. N. da Silva Júnior, T. T. Guimarães, R. F. S. Menna-Barreto, M. C. F. R. Pinto, C. A. de Simone, C. Pessoa, B. C. Cavalcanti, J. R. Sabino, C. K. Z. Andrade, M. O. F. Goulart, S. L. de Castro and A. V. Pinto, *Bioorg. Med. Chem.*, 2010, **18**, 3224-3230.
33. (a) E. B. T. Diogo, G. G. Dias, B. L. Rodrigues, T. T. Guimarães, W. O. Valença, C. A. Camara, R. N. de Oliveira, M. G. da Silva, V. F. Ferreira, Y. G. de Paiva, M. O. F. Goulart, R. F. S. Menna-Barreto, S. L. de Castro and E. N. da Silva Júnior, *Bioorg. Med. Chem.*, 2013, **21**, 6337-6348; (b) S. L. de Castro, F. S. Emery and E. N. da Silva Júnior, *Eur. J. Med. Chem.*, 2013, **69**, 678-700; (c) E. N. da Silva Júnior, G. A. M. Jardim, R. F. S. Menna-Barreto and S. L. de Castro, *J. Braz. Chem. Soc.*, 2014, **25**, 1780-1798; (d) S. B. B. B. Bahia, W. J. Reis, G. A. M. Jardim, F. T. Souto, C. A. de Simone, C. C. Gatto, R. F. S. Menna-Barreto, S. L. de Castro, B. C. Cavalcanti, C. Pessoa, M. H. Araujo and E. N. da Silva Júnior, *Med. Chem. Commun.*, 2016, **7**, 1555-1563.
34. G. A. M. Jardim, T. L. Silva, M. O. F. Goulart, C. A. de Simone, J. M. C. Barbosa, K. Salomão, S. L. de Castro, J. F. Bower and E. N. da Silva Júnior, *Eur. J. Med. Chem.*, 2017, **136**, 406-419.
35. G. A. M. Jardim, W. J. Reis, M. F. Ribeiro, F. M. Ottoni, R. J. Alves, T. L. Silva, M. O. F. Goulart, A. L. Braga, R. F. S. Menna-Barreto, K. Salomão, S. L. de Castro and E. N. da Silva Júnior, *RSC Adv.*, 2015, **5**, 78047-78060.
36. E. N. da Silva Júnior, R. F. S. Menna-Barreto, M. C. F. R. Pinto, R. S. F. Silva, D. V. Teixeira, M. C. B. V. de Souza, C. A.

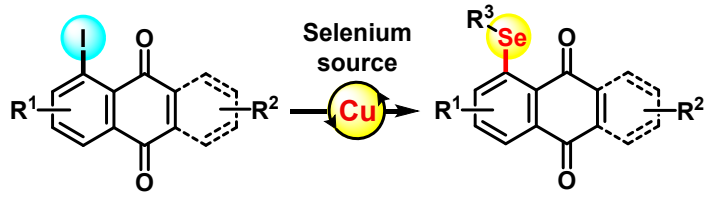
View Article Online
DOI: 10.1039/C9NJ02026H

de Simone, S. L. de Castro, V. F. Ferreira and A. V. Pinto, *Eur. J. Med. Chem.*, 2008, **43**, 1774.

37. (a) For the synthesis of $Cu(PPh_3)_3Br$ see: R. Gujadhur, D. Venkataraman and J. T. Kintigh, *Tetrahedron Lett.*, 2001, **42**, 4791-4793; (b) For the synthesis of $Cu(DMPHEN)_2Cl$ see: A. J. Pallenberg, K. S. Koenig and D. M. Barnhart, *Inorg. Chem.*, 1995, **34**, 2833-2840.
38. H. J. Reich, J. M. Renga and leva L. Reich, *J. Am. Chem. Soc.*, 1975, **97**, 5434-5447.
39. A. Krief, T. V. Wemmel, M. Redon, W. Dumont and C. Delmotte, *Angew. Chem. Int. Ed.*, 1999, **38**, 2245-2248.
40. M. Tiecco, L. Testaferri, C. Santi, C. Tomassini, S. Santoro, F. Marini, L. Bagnoli, A. Temperini and F. Costantino, *Eur. J. Org. Chem.*, 2006, 4867-4873.
41. N. V. Ivashkina, V. S. Romanov, A. A. Moroz and M. S. Shvartsberg, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1984, **33**, 2345-2348.
42. J. Weinstein, R. C. Clapp, M. Nakashima and J. A. Sousa, *J. Chem. Eng. Data*, 1979, **24**, 74-75.
43. C. F. H. Allen, A. Bell, *Org. Synth.* 1942, **22**, 37-40.
44. CrysAlisPro Software system; Rigaku Corporation, Oxford, UK, 2015.
45. L. Palatinus, G. Chapuis, *J. Appl. Crystallogr.*, 2007, 40, 786-790.
46. G. M. Sheldrick, *Acta Crystallogr. C* 2015, **71**, 3-8.
47. C. K. Johnson in ORTEP, Crystallographic Computing, (Ed.: F. R. Ahmed), Copenhagen, Denmark, 1971, pp. 217-219.
48. L. J. Farrugia, *J. Appl. Crystallogr.*, 2012, **45**, 849-854.
49. Persistence of Vision Raytracer, Persistence of Vision Pty. Ltd., Williams town, Australia, 2004.

Table of Contents

Copper complexes and carbon nanotube-copper ferrite-catalyzed benzenoid A-ring selenation of quinones: An efficient method for the synthesis of trypanocidal agents



Application of three different synthetic strategies for the preparation of selenium derivatives:
- CuTC + Santi reagent
- Copper complex + AgSeR-Salts
- Carbon nanotube-copper ferrite + AgSeR-Salts
23 new selenium-containing quinoidal derivatives

Compounds evaluated against *Trypanosoma cruzi*
9 compounds with potent trypanocidal activity

A-ring selenation of naphthoquinones and anthraquinones are reported. The reaction was accomplished in the presence of copper complexes and carbon nanotube-supported copper ferrite as catalysts and provides an efficient and general method for preparing selenium-based quinones with trypanocidal activity.