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# Synthesis and biological study of a new series of bifunctional organoiron thio- and seleno-terephthalate derivatives $(C_5H_5)Fe(CO)_2ECO(C_6H_4)COX$ (E = S, X = $R_2N$, RNH, $NH_2$, OH, Cl; E = Se, X = RNH, RS, RCOO, $NH_2$, OH, Cl)

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**A new series of bifunctional organoiron thio- and seleno-terephthalate complexes — $(\eta\text{-}C_5H_5)Fe(CO)_2ECO(C_6H_4)COX$ [E = S; X = $C_6H_{11}NH$, $(C_2H_5)_2N$; and E = Se; X = $P-CH_3-C_6H_4-NH$, $C_6H_5-C_2N_2O-S$, $m-NO_2-C_6H_4-CH{=}CH-COO$] — has been synthesized *via* the organic transformation reactions of the terephthaloyl chloride precursors $\eta\text{-}(C_5H_5)Fe(CO)_2ECO(C_6H_4)COCl$ with the desired nucleophiles. These new complexes were characterized by elemental analysis, IR and $^1H$ NMR spectra. The above complexes, in addition to some other selected analogues, were tested for their antifungal, antibacterial and mutagenic activity. Our results show that all the selenium-containing compounds have antifungal activity on *Candida albicans* and antibacterial effects against *Bacillus subtilis* and *Staphylococcus aureus*. Four of the six selenium-containing derivatives exhibited growth inhibitory effects against *Pseudomonas aeruginosa* and/or *Escherichia coli*. Sulfur-containing derivatives elicited activity against *C. albicans*, and each one of them showed activity against at least one of the bacterial strains that have been used in this investigation. Two selenium- and two sulfur-containing derivatives showed mutagenic activity against one or more than one strain of the *Salmonella typhimurium* using the Ames test. Copyright © 2001 John Wiley & Sons, Ltd.**

**KEYWORDS:** bifunctional complexes; selenium; sulfur; mutagenicity; antibacterial; antifungal

Although much attention has been focused on the synthetic and structural aspects of transition metal chalcogen complexes, the understanding of their reactivity is still at an early stage.[1–6] Organometallic complexes containing sulfur or selenium are nowadays of special interest owing to their important biological and catalytic applications.[7–10] X-ray Crystal diffraction analyses have clearly defined a metal cysteinate coordination in a large number of metalloproteins.[11–14] Moreover, selenium has recently been found to occur in a surprising number of proteins.[15]

It has been demonstrated that selenium is incorporated in the enzyme glutathione peroxidase (GPX), which is a vital enzyme that protects red blood cells, cell membranes and sub-cellular components against undesirable reactions with soluble peroxides.[16] Now, more scientific interest is being generated with the recent finding that selenium is also a vital constituent of other mammalian enzymes, such as phospholipid hydroxyperoxide glutathione peroxidase (PHGPX), which blocks formation of harmful alkoxy radicals and inhibits peroxidative chain branching. This activity is of even more potential importance in the prevention of cancer, heart disease and accelerated aging.[16]

The biochemistry and pharmacology of selenium compounds are subjects of current research, because of evidence that deficiency of trace selenium in the body may play a role

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in diseases such as cancer, heart disease, arthritis and AIDS.[17]

It was found that some newly synthesized selenium compounds, p-methoxy benzyl selenocyanate and 1,4-phenylene bis(methylene) selenocyanate (PXSC), prevented both precancerous cell growth and tumor growth in animals after they had received a compound known to induce colorectal cancer, and without inducing toxic side effects.[18] Moreover, studies on some patented phenylamino alkyl selenide compounds showed that these compounds are active antihypertensive systems that decrease blood pressure and increase blood velocity, without increasing heart rate in the experimental animals.[17]

These recent discoveries on some selenide complexes have pointed the way toward other selenium-based therapeutic agents that might help in expand knowledge of the role of this element in human health.[15–20]

During our synthetic work on organotransition-metal chalcogen complexes we were able to prepare a new class of organotransition-metal sulfur and selenium-bonded thio carboxylate complexes $\eta$-Cp′M(CO)$_2$ECOR ($\eta$-Cp′ = $C_5H_5$, $^t$Bu t-$C_5H_4$, 1,3-$^t$Bu$_2$-$C_5H_3$; M = Fe, Ru; E = S, Se; R = alkyl, aryl).[21–23] Recently, we reported a convenient synthesis of organoiron thio- and seleno-terephthaloyl chloride complexes $\eta$-Cp′Fe(CO)$_2$ECO($C_6H_4$)COCl *via* reaction of organoiron sulfides and selenides [$\eta$-Cp′Fe(CO)$_2$]$_2$($\mu$-E$_x$); (E = S, Se; $x$ = 1–5) with terephthaloyl chloride ClCO($C_6H_4$)COCl.[24]

These terephthaloyl chloride complexes are interesting organometallic compounds that possess a reactive center, namely the acid chloride group. Thus the reaction of $\eta$-Cp′Fe(CO)$_2$ECO($C_6H_4$)COCl with organic nucleophiles facilitates synthesis of a large variety of interesting bifunctional complexes.[25]

In view of the biological importance of transition-metal chalcogen complexes and the facile synthesis of a wide range of bifunctional complexes, we report here the synthesis of some new organoiron thio- and seleno-terphthalate complexes ($\eta$-$C_5H_5$)Fe(CO)$_2$ECO($C_6H_4$)COX and the study of some selected bifunctional complexes as an exploration of the biological activity of these systems.

## EXPERIMENTAL

### A Synthesis of organoiron thio- and seleno-terephthalate complexes

All reactions were conducted under dinitrogen using Schlenk techniques. The terephthaloyl chloride complexes ($\eta$-$C_5H_5$)Fe(CO)$_2$SCO($C_6H_4$)COCl (**1a**) and ($\eta$-$C_5H_5$)Fe(CO)$_2$-SeCO($C_6H_4$)COCl (**1b**) were prepared as previously reported.[24] The acid derivatives ($\eta$-$C_5H_5$)Fe(CO)$_2$ SCO($C_6H_4$)COOH (**2a**) ($\eta$-$C_5H_5$)Fe(CO)$_2$SeCO($C_6H_4$)COOH (**2b**) and the amide derivatives ($\eta$-$C_5H_5$)Fe(CO)$_2$SCO($C_6H_4$)-CONH$_2$ (**3a**) and ($\eta$-$C_5H_5$)Fe(CO)$_2$SeCO($C_6H_4$)CONH$_2$ (**3b**) were prepared as reported.[25]

The imide bridged dinuclear complex [($\eta$-$C_5H_5$)Fe(CO)$_2$ SCO($C_6H_4$)CO]$_2$NH (**9**) was prepared as reported.[26] IR spectra were recorded on a Nicolet Impact 400 FTIR spectrophotometer and $^1$H NMR spectra on a Bruker WP 80 SY spectrometer with Me$_4$Si as internal standard. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ, USA.

#### *Synthesis of ($\eta$-$C_5H_5$)Fe(CO)$_2$SCO($C_6H_4$)CONH($C_6H_{11}$) (**4**)*

A benzene solultion (80 ml) containing compound **1a** (0.40 g, 1.1 mmol), cyclohexylamine (0.20 ml, 1.8 mmol) and five drops of pyridine was refluxed for 3 h. The reaction mixture was cooled to room temperature and filtered. The solvent was evaporated *in vacuo* at 20 °C and the residue was transferred to a chromatography column made up in *n*-hexane.

An orange band was eluted with $CH_2Cl_2$–ether (9:1). The solvent was evaporated *in vacuo* and the remaining solid was washed with hexane to give the analytically pure orange powder of compound ***4***. Yield 85%; m.p. (decomposition) 155–157 °C. Found: C, 57.32; H, 4.80; N, 3.17; S, 7.10. Calc. for $C_{21}H_{21}FeNO_4S$: C, 57.40; H, 4.78; N, 3.18; S, 7.29%.

#### *Synthesis of ($\eta$-$C_5H_5$)Fe(CO)$_2$SCO($C_6H_4$)CON($C_2H_5$)$_2$ (**5**)*

In a similar procedure to that described above, a benzene solution (80 ml) containing compound ***1a***, (0.40 g, 1.1 mmol), diethylamine (0.20 ml, 1.9 mmol) and five drops of pyridine was refluxed for 3 h. Column chromatography afforded an orange band which was eluted with $CH_2Cl_2$–ether (10:1) and from which compound **5** was obtained. Yield 65%; m.p. (decomposition) 150–152 °C. Found: C, 55.31; H, 4.68; N, 3.30. Calc. for $C_{19}H_{19}FeNO_4S$: C, 55.20, H, 4.60; N, 3.39%.

#### *Synthesis of ($\eta$-$C_5H_5$)Fe(CO)$_2$SeCO($C_6H_4$)CONH (4-$CH_3-C_6H_4$) (**6**)*

A benzene solution (100 ml) containing compound ***1b*** (10.50 g, 1.18 mmol), toluidine (0.13 g, 1.2 mmol) and five drops of pyridine was refluxed for 2 h. The mixture was cooled to room temperature and filtered. Silica gel (~3g) was added and the solvent was evaporated *in vacuo* at 20 °C. The residue was transferred to a chromatography column made up in *n*-hexane. An orange band was eluted with $CH_2Cl_2$–ether (9:1), from which an orange powder of compound ***6*** was obtained. Yield 62%; m.p. (decomposition) 55–57 °C. Found: C, 53.56; H, 3.48; N, 3.00. Calc. for $C_{22}H_{17}FeNO_4Se$: C, 53.44; H, 3.44; N, 2.83%.

#### *Synthesis of ($\eta$-$C_5H_5$)Fe(CO)$_2$SeCO($C_6H_4$)CO$_2$COCH=CH(3-$NO_2-C_6H_4$) (**7**)*

A tetrahydrofuran (THF) solution (100 ml) containing compound ***1b*** (0.50 g, 1.18 mmol), *m*-nitrocinnamic acid (0.23, 1.19 mmol) and five dorps of pyridine was refluxed for 3 h. The reaction mixture was cooled to room temperature and the solvent was evaporated *in vacuo* at 20 °C. The residue was dissolved in benzene (50 ml) and filtered. Silica gel (~3 g) was added and the solvent was evaporated *in vacuo*. The residue was transferred to a chromatography column made up in *n*-hexane. An orange–red band was eluted with $CH_2Cl_2$–ether (8:2). The solvent was evaporated and the residue was dissolved in $CH_2Cl_2$. Addition of hexane precipitated a yellow powder that was recrystallized from $CH_2Cl_2$–hexane to give organe crystals of compound **7**. Yield 85%; m.p. (decomposition) 129–131 °C. Found: C, 49.50; H, 2.62; N, 2.38. Calc. for $C_{24}H_{15}FeNO_8Se$: C, 49.66; H, 2.59; N, 2.41%.

### *Synthesis of ($\eta$-$C_5H_5$)Fe(CO)$_2$SeCO($C_6H_4$)COS($C_2N_2O$) – $C_6H_5$ (8)*

A THF solution (100 ml) containing compound ***1b*** (0.50 g, 1.18 mmol), 2-phenyl-5-mercapto-1,3,4-oxadiazole (0.22 g, 1.2 mmol) and five drops of pyridine was refluxed for 2 h. The mixture was cooled to room temperature and the solvent was evaporated *in vacuo* at 20 °C. The residue was dissolved in benzene (50 ml) and filtered. Silica gel (~3 g) was added and the solvent was evaporated *in vacuo*. The residue was transferred to a chromatography column made up in *n*-hexane. An orange–red band was eluted with $CH_2Cl_2$–ether (10:1). The solvent was evaporated *in vacuo* and the remaining solid was washed with hexane to give the analytically pure orange–red powder of compound ***8***. Yield 75%; m.p. (decomposition) 70–72 °C. Found: C, 48.67; H, 2.44; N, 5.03; S, 5.86. Calc. for $C_{23}H_{14}FeN_2O_7SSe$: C, 48.85; H, 2.48; N, 4.96; S, 5.66%.

## Biological activity

The following bacterial strains were used in the antimicrobial study: *Bacillus subtilis* ATCC 6633, *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* and *Candida albicans*. For the mutagenicity tests the *Salmonella typhimurium* strains TA98, TA100 and TA102 were used. These strains were kindly supplied by Professor B. N. Ames (Department of Biochemistry, University of California, Berkeley, USA).

## Antimicrobial activity

### *Preparation of the test chemicals*

The test chemicals were disssolved in dimethyl sulfoxide (DMSO). Dextrose broth was then added to obtain a starting concentration of 4 mg ml$^{-1}$ for each compound. Serial dilutions were made until final test concentrations of 450, 300, 200, 100, 50 and 25 $\mu$g ml$^{-1}$ were reached. Nalidixic acid (an antibacetrial drug) and miconazole (an antifungal drug) were used as positive controls.

### *Antimicrobial assay*

The microorganisms were grown overnight in dextrose broth at 35 °C and diluted to $10^{-3}$ just before being used. Plates were prepared by mixing one part of each solution of chemicals with nine parts of melted nutrient agar to obtain the desired final concentrations. The mixtures were poured into Petri dishes and allowed to harden at room temperature. Each plate, including positive and negative controls, was inoculated with a single streak using a 10 $\mu$l calibrated loop. The plates were examined after 20 h incubation at 35 °C for the presence or absence of bacterial growth.[27]

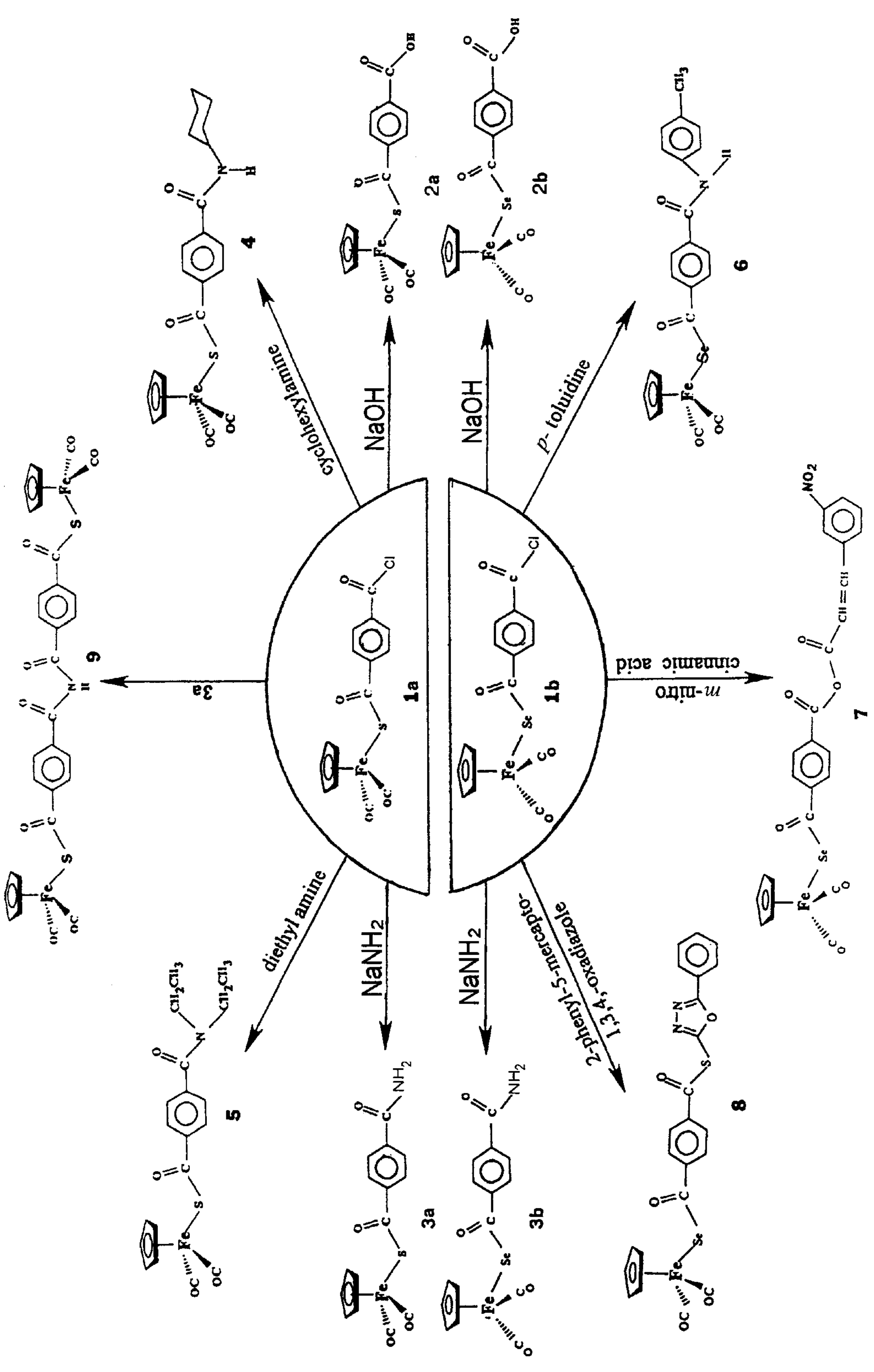
### *Mutagenic studies*

Stock solutions of the test chemicals were prepared by dissolving 10 mg of the compound in DMSO. Serial dilutions ranging from 4 to 0.01 mg ml$^{-1}$ were made. Vogel–Bonner medium E(SOX), histidine–biotin solution (0.5 M), top agar, minimal glucose plates, histidine–biotin plates and ampicillin plates were prepared as described by Maron and Ames.[28] The plate incorporation test as described by Maron and Ames[28] was followed. The top agar was distributed into capped culture tubes, which were held at 45 °C in a water bath. To each tube, 0.1 ml of a fresh overnight culture of the tester strain was added, followed by the addition of 0.1 ml of the test compound solution. Sodium azide, nitrophenylene diamine and methylmethane sulfonate were used as positive controls. The test components were mixed by vortexing the tube for about 3 s at low speed and directly poured onto a minimal glucose agar plate. After 45 min the plates were inverted and placed in a dark 37 °C incubator. The revertant colonies on the treated and on the positive and negative control plates were counted.

## RESULTS AND DISCUSSION

The reaction of the ($\eta$-$C_5H_5$)Fe(CO)$_2$SCO($C_6H_4$)COCl (**1a**) and the ($\eta$-$C_5H_5$)Fe(CO)$_2$SeCO($C_6H_4$)COCl (**1b**) thio- and seleno-terephthaloyl chloride complexes with organic nucleophiles in the presence of pyridine as a catalyst is a straightforward reaction that affords the expected bifunctional complexes ($\eta$-$C_5H_5$)Fe(CO)$_2$ECO($C_6H_4$)COX (E = S, Se; X = nucleophile) in fairly good yields (Scheme 1). The resulting bifunctional complexes of this reaction can be easily characterized from their IR, $^1$H NMR spectra and elemental analysis. The IR spectra of these systems was a reliable tool that elucidated their structure analysis.[26] There are two very strong bands in the ranges 2010–2060 and 1960–2000 cm$^{-1}$, corresponding to the stretching frequencies of the two terminal carbonyl groups bonded to the iron center. The strong band in the range 1580–1600 cm$^{-1}$ is assigned to the thiocarboxylate part (SC=O)[29] and that in the range 1600–1630 cm$^{-1}$ to the selenocarboxylate part (SeC=O).[26]

The other strong band in the range 1630–1750 cm$^{-1}$ is assigned to the second carbonyl of the terephthalate moiety (COX).[25] Moreover, the IR spectra data can also differentiate between thio- and the seleno-terephthalate complexes of the same functional groups.[26] The IR and the $^1$H NMR spectra of the complexes synthesized in this work are presented in


1a
1b
NaOH
NaOH
2a
2b
cyclohexylamine
4
p- toluidine
6
m-nitro cinnamic acid
7
2-phenyl-5-mercapto-1,3,4,-oxadiazole
8
NaNH2
NaNH2
3a
3b
diethyl amine
5
3a
9

Scheme 1.

**Table 1.** IR and $^1$H NMR spectra of the synthesized bifunctional complexes ($\eta$-$C_5H_5$)Fe(CO)$_2$ECO($C_6H_4$)COX (**4**–**8**)

| Complex | X, E | IR[a] (KBr) (cm$^{-1}$) | $^1$H NMR/$CDCl_3$ $\delta$ (ppm) |
|---|---|---|---|
| **4** | NH($C_6H_{11}$), S | 3249 m, $\nu$(N–H)<br>2050 vs, 2000 $\nu$(CO)<br>1634 s, $\nu$(NC=O)<br>1600 s, $\nu$(SC=O)<br>928 s, $\nu$(C–S) | 2.10 (m, 11H, $C_6H_{11}$)<br>5.07 (s, 5H, $C_5H_5$)<br>7.90 (m, 4H, Ar-H) |
| **5** | N($C_2H_5$)$_2$, S | 2051 vs, 2000 vs, $\nu$(CO)<br>1634 s, $\nu$(NC=O)<br>1583 s, $\nu$(SC=O)<br>936 s, $\nu$(C–S) | 1.14 (m, 6H, $CH_3$)<br>3.33 (m, 4H, $CH_2^-$)<br>5.07 (s, 5H, $C_5H_5$)<br>7.70 (m, 4H, Ar-H) |
| **6** | NH(4-$CH_3$–$C_6H_4$), Se | 3333 m, $\nu$(N–H)<br>2021 vs, 1984, $\nu$(CO)<br>1653 s, $\nu$(NC=O)<br>1621 s, $\nu$(C–Se) | 2.34 (s, 3H, $CH_3$)<br>5.08 (s, 5H, $C_5H_5$)<br>7.36 (m, 8H, Ar-H) |
| **7** | $O_2C$–CH=CH–(3-$NO_2$–$C_6H_4$), Se | 2030 vs, 1984, $\nu$(CO)<br>1703 s, $\nu$(COO)<br>1630 s, $\nu$(SeC=O)<br>889 s, $\nu$(C–Se) | 5.08 (s, 5H, $C_5H_5$)<br>7.50 (m, 10H, Ar-H and CH=CH) |
| **8** | S($C_2N_2O$)–$C_6H_5$, Se | 2031 vs, 1983 vs, $\nu$(CO)<br>1691 s, $\nu$(SC=O)<br>1617 s, $\nu$(SeC=O)<br>897 s, $\nu$(C–Se) | 5.10 (s, 5H, $C_5H_5$)<br>7.84 (m, 9H, Ar-H) |

[a] vs: very strong; s: strong; m: medium.

Table 1. The $^1$H NMR spectra show the characteristic protons in their expected chemical shift regions (Table 1).

In the biological study included in this work, we chose three systems of the thio- and the seleno-terephthalate complexes (**1a**, **b**, **2a**, **b** and **3a**, **b**) that differ only in one atom (i.e the chalcogen atom) for comparison in addition to three other different systems to explore their biological activity.

**Table 2.** Antibacterial and antifungal activity of the organoiron thio- and seleno-terephthalate complexes ($\eta$-$C_5H_5$)Fe(CO)$_2$ECO($C_6H_4$)COX[a]

| | MIC ($\mu$g ml$^{-1}$) | | | | |
|---|---|---|---|---|---|
| Compound | *B. subtilis* | *S. aureus* | *E. coli* | *P. aeruginosa* | *C. albicans* |
| **1a** | 300 | 300 | N.A. | 400 | 400 |
| **1b** | 300 | 300 | 400 | 400 | 300 |
| **2a** | 300 | N.A. | N.A. | N.A. | 400 |
| **2b** | 300 | 300 | N.A. | N.A. | 300 |
| **3a** | 300 | N.A. | 400 | N.A. | 300 |
| **3b** | 250 | 250 | 400 | N.A. | 250 |
| **4** | 300 | N.A. | N.A. | N.A. | 400 |
| **5** | 300 | N.A. | N.A. | N.A. | 400 |
| **6** | 300 | 300 | 400 | 400 | 300 |
| **7** | 300 | 300 | N.A. | N.A. | 300 |
| **8** | 300 | 300 | 400 | N.A. | 300 |
| **9** | 300 | N.A. | N.A. | N.A. | 400 |

[a] N.A.: no activity at a concentration of $\leq$450 $\mu$g ml$^{-1}$ could be detected.

The antimicrobial studies revealed that compounds **1b**, **2b**, **3a**, **6**, **7** and **8** are active as antifungal agents at a minimum inhibitory concentration MIC of 300 $\mu$g ml$^{-1}$ (table 2). Compound **3b** was found to be active at an MIC of 250 $\mu$g ml$^{-1}$. All of the above compounds, except **3a**, are seleno-containing derivatives (Scheme 1). Moreover, compounds **1b**, **2b**, **3b**, **6**, **7**, **8** and **1a** showed antibacterial activity against both *B. Subtilis* and *S. aureus* at an MIC of 300 $\mu$g ml$^{-1}$.

The results presented in Table 2 show that the sulfur-containing derivatives **2a**, **3a**, **4**, **5** and **9** are also effective against *B. subtilis* at an MIC of 300 $\mu$g ml$^{-1}$. However, the antifungal activity of **1a**, **2a**, **4**, **5** and **9**, which are all sulfur-containing derivatives, occurs at an MIC of 400 $\mu$g ml$^{-1}$. Activity against *P. aeruginosa* is only exhibited by compounds **1a**, **1b** and **6** at an MIC of 400 $\mu$g ml$^{-1}$.

The above results indicate that the selenium-containing derivatives are generally more potent as antimicrobial agents than their sulfur analogues. Comparing the antimicrobial activity of compounds **3a** and **3b**, which differ only in the type of chalcogen atom present, the selenium-containing derivative **3b** proved to be more potent than the sulfur-containing analogue. It seems that the selenium compounds

**Table 3.** Results of mutagenicity studies of the organoiron thio- and seleno-terephthalate complexes ($\eta$-$C_5H_5)Fe(CO)_2ECO(C_6H_4)COX$[a]

| Compound | TA 98 ($\mu$g/plate) | TA 100 ($\mu$g/plate) | TA 102 ($\mu$g/plate) |
|---|---|---|---|
| **1a** | 5 | 1 | – |
| **1b** | 250 | 200 | – |
| **5** | – | 40 | – |
| **7** | 650 | – | – |

[a] The figures in each column represent the concentration at which the compound shows mutagenic action.

exhibit a stronger effect on the mode of the metabolic pathway and/or the metabolic products of these compounds. Recent studies on the role of metal-based drugs and metal compounds in therapy and in the transport and storage of metal ions,[30] the recent proposal stating that the reduction of selenium and its methylation to dimethyl selenol by purple non-sulfur bacteria might well represent the basis for the resistance of these bacteria to metalloid oxyanions,[31] and the fact that selenium forms organic compounds *in vivo* that are metabolized and transformed[32,33] suggest that further studies on the metabolism of the test compounds in a mammalian system are highly recommended.

The present investigation showed clearly that the potency of these bifunctional organoiron complexes is influenced markedly by the two functional groups present in these systems. For example, compound **3b**, which has the seleno carboxylate (SeCO) on one side and the primary amide ($CONH_2$) on the other, proved to be the most active antimicrobial agent in terms of its MIC. Moreover, compound **1b**, which has (SeCO) and (COCl) as functional groups, and compound **6**, which has (SeCO) and (CONH tolyl) as functional groups, were found to be active against all test organisms.

The Ames test using different strains of *S. typhimurium* was used throughout this investigation for mutagenicity studies. The results are presented in Table 3. They show that four compounds of the test chemicals, namely **1a**, **1b**, **5** and **7**, have mutagenic properties. Compounds **1a** and **1b** showed both base-pair and frameshift mutagenic activity. Compound **5** exhibited a base-pair substitution activity, and compound **7** was found to be a frameshift mutagen.

It is worth noting that the mutagenicity of compounds **1b** and **7**, which are selenium-containing derivatives, was found at a relatively high concentration in comparison with **1a** and **5**, which are sulfur-containing derivatives. Moreover, if one considers the relationship between mutagenicity and carcinogenicity,[34–36] one should handle these mutagenic compounds with special care. Chemical modification of these mutagenic compounds is needed in order to increase their biological benefits and to overcome their mutagenicity. Recently, a benzyl selenocyanate glutathione conjugate was shown to be a promising colon anticarcinogenic compound.[37] It has also been demonstrated that benzyl selenocyanate and 1,4-phenylene bis(methylene) selenocyanate inhibit the activity of DNA cytosine methyltransferase. The authors suggested that an inhibition could be an important mechanism of chemoprevention by organoselenium compounds at the post-initiation stage of carcinogenesis.[38] These investigations provoke us to explore further biological activities of the nonmutagenic selenium-containing bifunctional complexes. Such activities include antiviral, including anti-HIV, cytotoxicity, antimutagenicity and anticarcinogenicity. Some of these studies are being carried out in our laboratories.

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## REFERENCES

1. Roof LC and Kolis JW. *Chem. Rev.* 1993; **93**: 1937.
2. Wachter J. *Angew. Chem. Int. Ed. Engl.* 1989; **28**: 1613.
3. Herrmann WA, Bohrmann J and Hecht C. *J. Organomet. Chem.* 1985; **290**: 53.
4. Herrmann WA. *Angew. Chem. Int. Ed. Engl.* 1986; **25**: 56.
5. Draganjac M and Rauchfuss TB. *Angew. Chem. Int. Ed. Engl.* 1985; **24**: 742.
6. Ansari MA and Ibers JA. *Coord. Chem. Rev.* 1990; **100**: 223.
7. Holm RH, Ciurli S and Weigel JA. *Prog. Inorg. Chem.* 1986; **25**: 56.
8. Coucouvanis D. *Acc. Chem. Res.* 1991; **24**: 1.
9. Chianelli RR. *Catal. Rev. Sci. Eng.* 1984; **26**: 361.
10. Toposoe H and Calusen BS. *Catal. Rev. Sci. Eng.* 1984; **26**: 395.
11. Stout DC. *Iron–Sulfur Proteins.* John Wiley, New York, 1982.
12. Monaco HL, Crawford JL and Lipscomb WN. *Proc. Natl. Acad. Sci. U.S.A.* 1978; **5**: 5276.
13. Ghosh D, Donnell SO, Furey W, Robbins AH and Stout CD. *J. Mol. Biol.* 1982; **158**: 73.
14. Powers L, Chance B, Ching Y and Angiolillo P. *Biophys. J.* 1981; **33**: 95a.
15. Standtman TC. *Annu. Rev. Biochem.* 1990; **59**: 111.
16. Ursini F. *Biochim. Biophys. Acta* 1985; **839**: 62.
17. Mag SW, Wang LG, Gillwoznichak MM, Browner RF, Oganowski AA and Pollock S. *J. Pharmacol. Exp. Ther.* 1997; **283**: 470.
18. El-Bayoumy K. *J. Natl. Cancer Inst.* 1997; **89**: 907.
19. Clarck LC, Combs GF, Turnball BW, State EH and Chalker DK. *J. Am. Med. Assoc.* 1996; **276**: 1957.
20. Hartman TJ, Albanes D, Pietnen P, Hartman AM, Rautalahti M, Tangred JA and Taylor PR. *Cancer Epidemiol. Biomark. Prev.* 1998; **7**: 335.
21. El-Hinnawi MA, El-Khatib MA, Jibril I and Abu-Orabi ST. *Synth. React. Inorg. Met. Org. Chem.* 1989; **19**: 809.
22. Jibril I, Esmadi FT, Al-Massri H, Zsolnai L and Huttner G. *J. Organomet. Chem.* 1996; **510**: 109.
23. Jibril I and Abu-Nimreh O. *Synth. React. Inorg. Met. Org. Chem.* 1996; **26**: 1409.
24. Jibril I and Ali AK. *Indian J. Chem.* 1997; **36A**: 987.
25. Jibril I, Ali AK and Omar JT. *Polyhedron* 1997; **16**: 3327.

26. Jibril I, Abd-Alhadi E and Hamadah Z. *Transit. Met. Chem.* 2000; **25**: 407.
27. (a) Mandell GI and Sande MA. Antimicrobial agents. In *The Pharmacological Basis of Therapeutics*, Gilman AG, Goodman LS, Gilman A (eds). 6th edn. Macmillan Publishing Co., Inc. New York, 1980; (b) Harvey SC. Antiseptics, disinfectants, fungicides and ectoparasiticides. In *The Pharmacological Basis of Therapeutics*, Gilman AG, Goodman LS, Gilman A (eds). 6th edn. Macmillan Publishing Co., Inc. New York, 1980.
28. Maron DM and Ames BN. *Mutat. Res.* 1983; **113**: 173.
29. El-Hinnawi MA and Al-Ajlouni AM. *J. Organomet. Chem.* 1987; **332**: 321.
30. Templeton DM. *Analusis* 1998; **26**: 68.
31. Van-Fleet SV and Chasteen TG. *J. Photochem. Photobiol. B. Biol.* 1998; **43**: 193.
32. Tsai JH, Hiserodt RD, Tang HC, Hartman TG and Rosen RT. *J. Agric. Food Chem.* 1998; **46**: 2541.
33. Heninger I. *Chem. Spec. Bioavailab.* 1998; **10**: 1.
34. Rosenkranz HS and Poirier LA. *J. Natl. Cancer Inst.* 1979; **62**: 873.
35. Schaaper RM, Glickman BW and Roeb LA. *Cancer Res.* 1982; **42**: 3480.
36. Simon VF. *J. Natl. Cancer Inst.* 1979; **62**: 901.
37. Kawamori T, El-Bayoumy K, Ji-Ben Y, Rodriguez JGR, Rao RC and Reddy BS. *Int. J. Oncol.* 1998; **13**: 29.
38. Fiala ES, Staretz ME, Pandya GA, El-Bayoumy K and Hamilton SR. *Carcinogeous Oxford* 1998; **19**: 597.