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# Esters of Isoxazole- and Isothiazolecarboxylic Acids and Oximes of β-Isatin, Isoxazole- and Ferrocene-Containing Ketones and Carborane Alcohols

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**Abstract—**Oximes of β-isatin, isoxazole- and ferrocene-containing ketones, *o*- and *m*-carborane alcohols react with isoxazol- and isothiazolecarboxylic acid chlorides in the presence of triethylamine to afford the corresponding esters.

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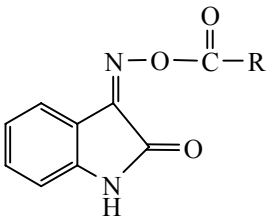
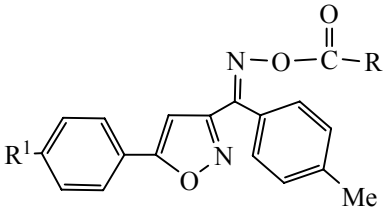
The synthesis of esters of 1,1'-diacetylferrocene dioxime has been previously reported [1]. 4,5-Dichloroisothiazol-, *o*- and *m*-carboranecarboxylic acids esters possess a high antimicrobial and fungicidal activity [2, 3].

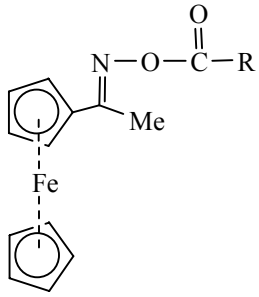
In this work we describe the synthesis of new potentially pharmacophore esters of isoxazole- and 4,5-dichloroisothiazolecarboxylic acids and oximes of β-isatin, isoxazole- and ferrocene-containing ketones, *o*- and *m*-carborane alcohols **I**–**XXIX**. The esterification was carried out in anhydrous diethyl ether in the presence of triethylamine to obtain the functionally substituted esters **I**–**XXIX** in a 85–90% yield.



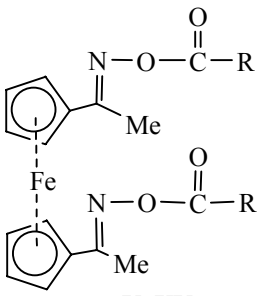
**I, XI, XXI**



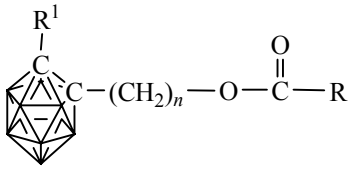
**II, III, XII, XIII, XXII, XXIII**



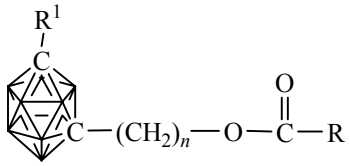
**IV, XIV, XXIV**



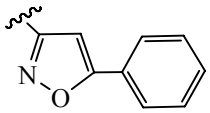
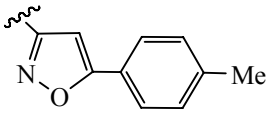
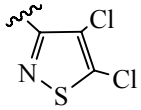
**V, XV**



**VI–VIII, XVI–XVIII, XXV–XXVII**



**IX, X, XIX, XX, XXVIII, XXIX**

R =  (**I–X**);  (**XI–XX**);  (**XXI–XXIX**); $R^1$ = H (**II, IX, XII, XXII, XXVIII**), Me (**III, VI, XIII, XVI, XXII, XXV**), $Me_2CH$ (**VII, X, XVII, XX, XXVI, XXIX**), $CH_2$=C(Me) (**VIII, XVIII, XXVII**); *n* = 1 (**VI, XVI, XXV**), 2 (**VII–X, XVII–XX, XVI–XXIX**).

The initial oximes of isoxazole- (**XXX**, **XXXI**) and ferrocene-containing ketones (**XXXII**, **XXXIII**) were prepared by the reaction of the corresponding ketones with hydroxylamine hydrochloride in the presence of sodium hydrogen carbonate in ethanol according to the standard procedure [4]. Yield of oximes **XXX**–**XXXIII** was 77–82%.

The resulting esters **I**–**XXIX** and oximes **XXX**–**XXXIII** are colorless or colored crystalline substances,

Yields, melting points, and the elemental analysis data of compounds **I**–**XXXIII**

| Comp. no. | Yield, % | mp, °C | Found, % | | | | | | Formula | Calculated, % | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | C | H | N | B (Fe) | Cl | S | | C | H | N | B (Fe) | Cl | S |
| **I** | 85 | 198–199 | 65.12 | 3.49 | 12.21 | – | – | – | $C_{18}H_{11}N_3O_4$ | 64.86 | 3.33 | 12.61 | – | – | – |
| **II** | 86 | 157–158 | 72.58 | 4.18 | 8.95 | – | – | – | $C_{27}H_{18}N_3O_4$ | 72.31 | 4.05 | 9.37 | – | – | – |
| **III** | 86 | 167–168 | 73.10 | 4.50 | 8.81 | – | – | – | $C_{28}H_{20}N_3O_4$ | 72.72 | 4.36 | 9.09 | – | – | – |
| **IV** | 90 | 124–125 | 64.07 | 4.30 | 6.25 | 13.04 | – | – | $C_{22}H_{18}FeN_2O_3$ | 63.79 | 4.38 | 6.76 | 13.48 | – | – |
| **V** | 88 | 165–166 | 63.94 | 4.17 | 8.32 | 6.16 | – | – | $C_{34}H_{26}FeN_4O_6$ | 63.56 | 4.08 | 8.72 | 8.69 | – | – |
| **VI** | 87 | 92–93 | 47.02 | 6.08 | 3.59 | 29.88 | – | – | $C_{14}H_{21}B_{10}NO_3$ | 46.78 | 5.89 | 3.90 | 30.08 | – | – |
| **VII** | 87 | 138–139 | 51.08 | 6.93 | 3.20 | 26.57 | – | – | $C_{17}H_{27}B_{10}NO_3$ | 50.85 | 6.78 | 3.49 | 26.93 | – | – |
| **VIII** | 89 | 133–134 | 51.40 | 6.21 | 3.17 | 26.75 | – | – | $C_{17}H_{25}B_{10}NO_3$ | 51.11 | 6.31 | 3.51 | 27.06 | – | – |
| **IX** | 88 | 95–96 | 47.03 | 6.04 | 3.55 | 29.84 | – | – | $C_{14}H_{21}B_{10}NO_3$ | 46.78 | 5.89 | 3.90 | 30.08 | – | – |
| **X** | 85 | 75–76 | 51.12 | 6.97 | 3.16 | 26.63 | – | – | $C_{17}H_{27}B_{10}NO_3$ | 50.58 | 6.78 | 3.49 | 26.93 | – | – |
| **XI** | 86 | 186–187 | 66.06 | 3.92 | 11.88 | – | – | – | $C_{19}H_{13}N_3O_4$ | 65.70 | 3.77 | 12.10 | – | – | – |
| **XII** | 89 | 164–165 | 73.10 | 4.55 | 8.67 | – | – | – | $C_{28}H_{20}N_3O_4$ | 72.72 | 4.36 | 9.09 | – | – | – |
| **XIII** | 88 | 182–183 | 73.45 | 4.21 | 8.54 | – | – | – | $C_{29}H_{22}N_3O_4$ | 73.10 | 4.65 | 8.82 | – | – | – |
| **XIV** | 88 | 150–151 | 64.91 | 4.57 | 6.25 | 12.58 | – | – | $C_{23}H_{20}FeN_2O_3$ | 64.50 | 4.71 | 6.54 | 13.04 | – | – |
| **XV** | 87 | 168–169 | 64.84 | 4.36 | 7.93 | 7.90 | – | – | $C_{36}H_{30}FeN_4O_6$ | 64.49 | 4.51 | 8.36 | 8.33 | – | – |
| **XVI** | 86 | 128–129 | 48.80 | 6.43 | 3.27 | 28.49 | – | – | $C_{15}H_{23}B_{10}NO_3$ | 48.24 | 6.21 | 3.75 | 28.95 | – | – |
| **XVII** | 86 | 133–134 | 52.42 | 7.19 | 3.01 | 25.62 | – | – | $C_{18}H_{29}B_{10}NO_3$ | 52.03 | 7.03 | 3.37 | 26.02 | – | – |
| **XVIII** | 87 | 137–138 | 52.55 | 6.50 | 2.98 | 25.77 | – | – | $C_{18}H_{27}B_{10}NO_3$ | 52.28 | 6.58 | 3.39 | 26.14 | – | – |
| **XIX** | 88 | 155–156 | 48.69 | 6.42 | 3.44 | 28.50 | – | – | $C_{15}H_{23}B_{10}NO_3$ | 48.24 | 6.21 | 3.75 | 28.95 | – | – |
| **XX** | 85 | 22–23 | 52.46 | 7.24 | 3.03 | 25.88 | – | – | $C_{18}H_{29}B_{10}NO_3$ | 52.03 | 7.03 | 3.37 | 26.02 | – | – |
| **XXI** | 90 | 167–168 | 42.65 | 1.28 | 11.89 | – | 20.46 | 9.04 | $C_{12}H_5Cl_2N_3O_3S$ | 42.12 | 1.47 | 12.28 | – | 20.72 | 9.37 |
| **XXII** | 86 | 137–138 | 55.41 | 2.66 | 8.85 | – | 15.05 | 6.62 | $C_{21}H_{13}Cl_2N_3O_3S$ | 55.03 | 2.86 | 9.17 | – | 15.47 | 7.00 |
| **XXIII** | 85 | 144–145 | 56.20 | 3.37 | 8.72 | – | 14.64 | 6.42 | $C_{22}H_{15}Cl_2N_3O_3S$ | 55.94 | 3.20 | 8.90 | – | 15.01 | 6.79 |
| **XXIV** | 88 | 124–125 | 45.87 | 3.00 | 6.28 | 12.86 | 16.22 | 7.60 | $C_{16}H_{12}FeCl_2N_2O_2S$ | 45.42 | 2.86 | 6.62 | 13.20 | 16.76 | 7.58 |
| **XXV** | 88 | 118–119 | 26.42 | 4.24 | 3.55 | 18.97 | 18.99 | 8.22 | $C_8H_{15}B_{10}Cl_2NO_2S$ | 26.09 | 4.11 | 3.80 | 29.35 | 19.25 | 8.71 |
| **XXVI** | 90 | 134–135 | 32.05 | 5.29 | 3.04 | 26.04 | 16.80 | 7.17 | $C_{11}H_{21}B_{10}Cl_2NO_2S$ | 32.19 | 5.16 | 3.41 | 26.34 | 17.28 | 7.81 |
| **XXVII** | 87 | 123–124 | 32.64 | 4.40 | 3.17 | 26.10 | 16.95 | 7.32 | $C_{11}H_{19}B_{10}Cl_2NO_2S$ | 32.35 | 4.69 | 3.43 | 26.47 | 17.36 | 7.85 |
| **XXVIII** | 88 | oil | 26.43 | 4.25 | 3.46 | 28.88 | 18.86 | 8.62 | $C_8H_{15}B_{10}Cl_2NO_2S$ | 26.09 | 4.11 | 3.80 | 29.35 | 19.25 | 8.71 |
| **XXIX** | 86 | 47–48 | 32.38 | 5.24 | 3.20 | 25.90 | 16.99 | 7.58 | $C_{11}H_{21}B_{10}Cl_2NO_2S$ | 32.19 | 5.16 | 3.41 | 26.34 | 17.28 | 7.81 |
| **XXX** | 82 | 119–120 | 73.81 | 5.22 | 9.70 | – | – | – | $C_{17}H_{14}N_2O_2$ | 73.37 | 5.07 | 10.07 | – | – | – |
| **XXXI** | 80 | 135–136 | 74.19 | 5.38 | 9.14 | – | – | – | $C_{18}H_{16}N_2O_2$ | 73.95 | 5.52 | 9.58 | – | – | – |
| **XXXII** | 77 | 172–173 | 59.63 | 5.15 | 5.43 | 22.51 | – | – | $C_{12}H_{13}FeNO$ | 59.29 | 5.39 | 5.76 | 22.97 | – | – |
| **XXXIII** | 78 | 141–142 | 56.34 | 5.44 | 9.02 | 18.12 | – | – | $C_{14}H_{16}FeN_2O_2$ | 56.02 | 5.37 | 9.33 | 18.61 | – | – |

which may be used without additional purification. Their structure was proved by the elemental analysis (see the table), IR and $^1$H NMR spectroscopy.

In the IR spectra of esters **I–XXIX** the following characteristic absorption bands were observed ($\nu$, cm$^{-1}$): 1766–1729 (C=O, ester, **I–XXIX)**, 1784–1778 (C=O, **I**, **XI**, **XXI**); 1230–1210 and 1135–1095 (C–O, **I–XXIX),** 2650–2530 (B–H, **VI–X**, **XVI–XX**, **XXV–XXIX**). The $^1$H NMR spectra of esters **I–XXIX** and oximes **XXX–XXXIII** contain the signals corresponding to the structural fragments of these compounds. The synthesized compounds **I–XXXIII** are interesting as potential ligands for metal complexes and objects of biological testing [2, 3, 5].

## EXPERIMENTAL

The IR spectra were recorded on a Nicolet Protégé-460 FTIR spectrophotometer from thin layers or KBr pellets. The $^1$H NMR spectra were registered on a Tesla BS-587A spectrometer (100 MHz) using $CDCl_3$ as a solvent and TMS as an internal reference.

**Esters I–XXIX.** To a mixture of 10 mmol of oxime or alcohol and 10 mmol of anhydrous triethylamine in 50 ml of anhydrous diethyl ether was added in portions 10 mmol of the appropriate isoxazole- or 4,5-dichloroisothiazolecarboxylic acid chloride. In all cases the reagents ratio was 1:1:1 except for the synthesis of compounds **V**, **XV (**1:2:2). The reaction mixture was kept at 20–23°C for 24 h. The formed precipitate was filtered off, washed successively with ether, water (3×200 ml), and saturated $NaHCO_3$ solution (3×200 ml). The resulting compounds **I–XXIX** were dried in air at 25–30°C for 2–3 days.

## ACKNOWLEDGMENTS

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