FULL PAPER

Trifluoromethylpyridine-Substituted *N*-Heterocyclic Carbenes Related to Natural Products: Synthesis, Structure, and Potential Antitumor Activity of some Corresponding Gold(I), Rhodium(I), and Iridium(I) Complexes

by **Elena Maftei**[a])[b]), **Catalin V. Maftei**[a])[b]), **Peter G. Jones**[a]), **Matthias Freytag**[a]), **M. Heiko Franz**[b])[c]), **Gerhard Kelter**[d]), **Heinz-Herbert Fiebig**[d]), **Matthias Tamm***[a]), and **Ion Neda***[a])[b])

[a]) Institut für Anorganische und Analytische Chemie, Technische Universität Carola Wilhelmina, Hagenring 30, DE-38106 Braunschweig (phone: +49(0)5313915309, e-mail: m.tamm@tu-bs.de)

[b]) Institutul National de Cercetare Dezvoltare pentru Electrochimie si Materie Condensata, Str. Dr. A. Paunescu Podeanu Nr. 144, RO-300569 Timisoara (phone: +49(0)5313915276, fax: (+)495313915387, e-mail: i.neda@tu-bs.de)

[c]) InnoChemTech GmbH, Hagenring 30, DE-38106 Braunschweig

[d]) Oncotest GmbH, Am Flughafen 12-14, DE-79108 Freiburg

This work presents the synthesis, characterization, and application of several new metal(I) complexes with trifluoromethylpyridine-containing *N*-heterocyclic carbene (NHC) ligands. The metal of choice was gold(I) for compounds **7** – **10**, rhodium(I) for **11** – **12**, and iridium(I) for **13** – **14**, respectively. The trifluoromethylpyridine moiety was incorporated, along with other biologically active moieties, with the intention of modifying the lipophilicity of the complexes, so that the transport of the active units (M–NHC) through the cell wall barrier is facilitated. The biological activity of the complexes was investigated. *In vitro* assessment of antitumor activity in a panel of 12 human tumor cell lines by a monolayer assay revealed good potency (mean IC_{50} 12.6 μM) and tumor selectivity for one compound. The solid-state structures of two solvates of compound **7**, one with MeOH and one with THF, were determined by X-ray diffraction analysis.

Keywords: Trifluoromethylpyridine, Imidazoles, Gold–NHC, Rhodium–NHC, Iridium–NHC, Antitumor activity.

Introduction

N-heterocyclic carbene (NHC)-gold complexes are nowadays one of the most promising classes of substances for drug development [1][2]. The starting point for the pharmacological application of gold complexes was when auranofin, a triethylphosphine gold(I) glucose-thiolate, was marketed in 1982 as an antirheumatic substance [3]. The oral administration of this compound, together with its different pharmacological behavior from that of the well-established platinum species ('cisplatin') [2][4], represented a major breakthrough in this area.

An important characteristic of gold(I)–NHC complexes is their antimitochondrial activity [5 – 7], which is necessary for the development of these substances as antitumor agents. The imidazole core facilitates variation of the *N*-substituents and of the backbone in order to modify properties, such as lipophilicity, steric demand and donor strength of the NHC. Several complexes have been presented in the last few years and their biological activity is often impressive. Some were tested against protein tyrosine phosphatases and were found to exhibit potency in the low micromolar range [5][8]. Others were targeted in the inhibition of thioredoxin reductase [9 – 12]. Some simple gold–NHC complexes, such as imidazolin-2-ylidene (chloro)gold(I), were shown to have very good anticancer activity based on their antiproliferative properties against *cis*-platin-resistant cell lines [13].

Since the beginning of the century, pyridine derivatives have played an important role in drug discovery programs. Many compounds based on the pyridine core are of commercial interest, having application in domains where the biological activity is relevant. This important motif can be found in the structure of many natural products and in important bioactive compounds with a large range of activities [14 – 16]. For example, some are strong antitumor agents [17][18], others have strong antimicrobial properties [19][20], or potent antiviral activity [21][22]; many pyridine-based products are good herbicides [23][24]; many form part of a wide variety of organic ligands [25][26].

The incorporation of fluorine into biologically active molecules confers major modifications in their molecular properties (chemical, physical, and biological). Our substrate has the trifluoromethyl group attached at the *meta*-position of the pyridine moiety. This is an important

DOI: 10.1002/hlca.201500529

motif from a medicinal point of view because of its stereoelectronic properties. This group tends to increase the lipophilicity of the molecule and thus improves the transport *in vivo*. At the same time, because of the strong C–F bond, the secondary metabolic transformations are reduced.

In *Figs. 1* and *2*, we present some examples of known bioactive substances involving a pyridine unit. Compound A was described as a γ-secretase modulator and was able to improve the treatment of *Alzheimer*'s disease [27]. Other derivatives, such as B, were reported to be active as phosphodiesterase subtype-10 inhibitors [28]. Product C was reported by a Canadian research group as a thumb pocket 1 NS5B polymerase inhibitor with antiviral activity in patients infected with genotype 1 Hepatitis C virus [29]. *Khanapure et al.* synthesized and tested compound D as a cyclooxygenase-2 selective inhibitor candidate [30]. The substance was found to have strong activity and it could be an analog for etoricoxib, an approved drug in the European market as a COX-2 selective inhibitor containing a pyridyl ring.

Anchoori et al. reported compound E to be a powerful antitumoral agent against paclitaxel-sensitive and paclitaxel-resistant ovarian cells (SKOV3) [17]. Another example of cytostatic derivatives is F, which was described as an excellent growth inhibitor, having GI_{50} values in the low micromolar to nanomolar range of concentration [31]. The same research group also reported compound G to have growth inhibition activity with the GI_{50} value as a nanomolar concentration [32].

Results and Discussions

In our previous work, we reported the synthesis of 2-(3-chloro-5-(trifluoromethyl)pyridin-2-*yl*)ethan-1-amine (**1**) [33]. Having this molecule as starting material, we wished to generate a new library of NHC–metal complexes and tested them *in vitro* for antitumor activity toward a panel of 12 cell lines using a monolayer cell survival and proliferation assay. The first step in building the NHC complexes was the synthesis of the imidazolium salts. Despite having a large number of literature protocols, the task was not as easy as it seemed. In order to increase the cytostatic activity and the transport of the molecule to the target, we wanted to introduce a wide variety of bioactive residues as second substituents to the imidazolium ring. Unfortunately, all attempts to generate the imidazolium salt failed if the protocol required a temperature higher than 50 °C, because the ethylene bridge between the trifluoropyridine and imidazole was unstable at this temperature. Accordingly, we generated and tested a smaller library of compounds. *Scheme 1* presents the synthesis of the imidazolium salts. The symmetrical imidazolium salt, 1,3-bis[2-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)ethyl]-imidazolium chloride (**3**) was obtained directly from the amine **1** [34][35]. The other three salts were generated in two steps. First, 2-[2-(1*H*-imidazol-1-yl)ethyl]-3-chloro-5-(trifluoromethyl)pyridine (**2**) was obtained from the amine derivative **1** [36]. Using different protocols under mild conditions, the Me, benzyl, and 2,3,4,5-tetra-*O*-acetyl-D-galactocopyranosyl groups were inserted as second substituents [37 – 44].

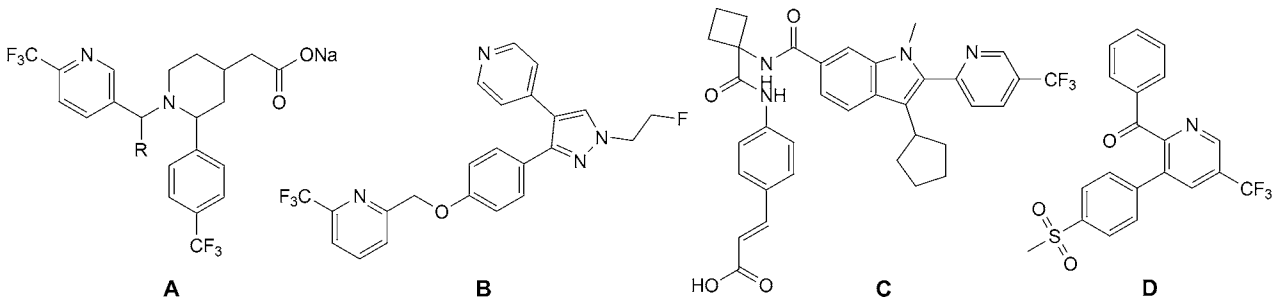


Fig. 1. Example of bioactive compounds having a CF_3-pyridine core.

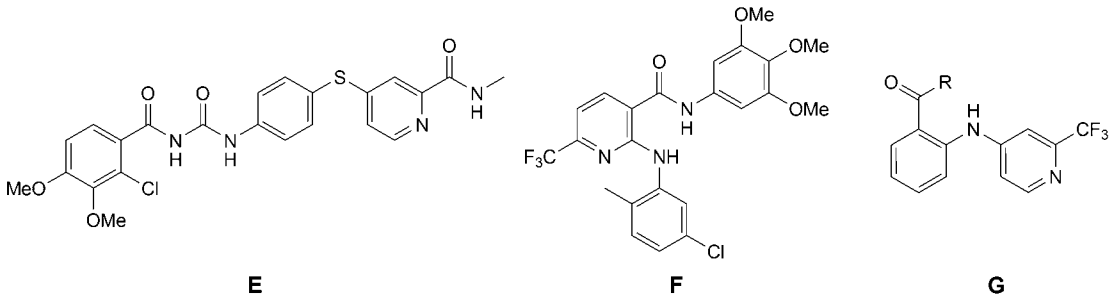
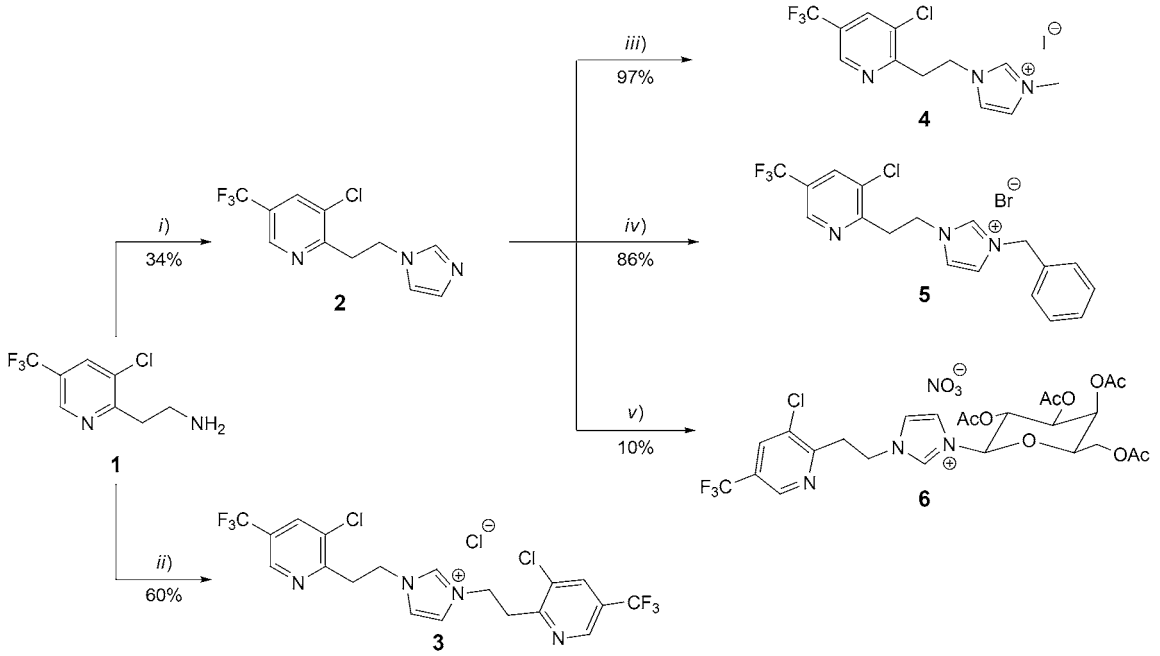


Fig. 2. Examples of antitumor pyridine-based active compounds.

Scheme 1. Synthesis of imidazolium salts starting from 2-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)ethanamine (**1**).



i) Glyoxal, NH_4Cl, 37% aq. formaldehyde, H_3PO_4, MeOH, reflux; *ii*) paraformaldehyde, glyoxal, HCl, toluene, reflux; *iii*) MeI, THF, r.t.; *iv*) Benzyl bromide, CH_2Cl_2, r.t.; *v*) 2,3,4,5-tetra-*O*-acetyl-D-galactopyranosylbromide, $AgNO_3$, MeCN, 50°.

After generating the imidazolium salts, the next step was the introduction of the metal core. The metals chosen were gold, ruthenium, and iridium, in view of their previously reported antitumor activities; a large number of protocols for the insertion of these metals are presented in the literature [10][45 – 55]. For the gold–NHC complexes, we began using the silver transmetalation route, which involves a silver complex as intermediate, but we achieved higher yields (58%) by generating the free carbene *in situ* and reacting it immediately with the gold precursor $Au(Me_2S)Cl$ (*Fig 3*, *Scheme 2*).

The rhodium– and iridium–NHC complexes were obtained through the silver transmetalation route. The imidazolium salts were deprotonated by Ag_2O as a

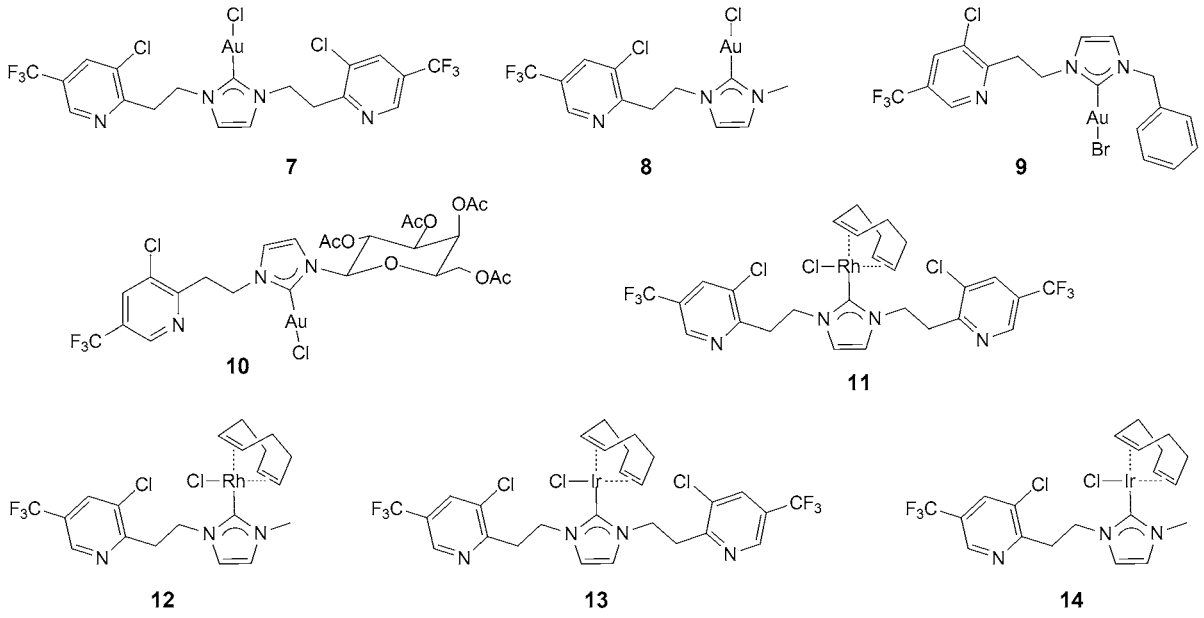
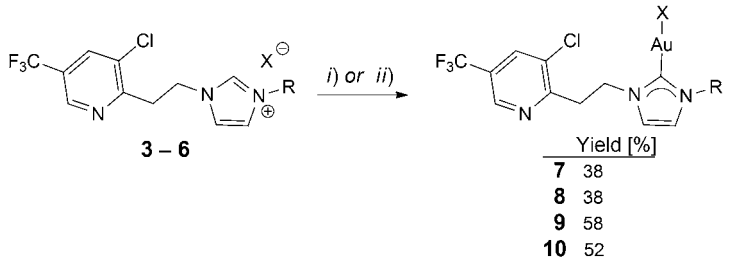


Fig. 3. Structures of the NHC derivatives based on trifluoromethylpyridines[a]).

Scheme 2. Synthesis of NHC–Au(I)X (X = Cl, Br) with different substituents.



i) Ag_2O, THTAuCl, CH_2Cl_2, r.t.; *ii*) KO^{t}Bu, Au(Me_2S)Cl, THF, r.t.

weak base in CH_2Cl_2, and after filtration through *Celite* the solution was treated with the corresponding [M(cod)Cl]$_2$.

The NHC–chlorogold(I) complex **7** was analyzed by X-ray diffraction analysis from two different samples, the MeOH solvate **7a** and the THF solvate **7b**. Solvate **7a** crystallizes in the triclinic space group $P\bar{1}$ with one molecule of **7** and one MeOH in the asymmetric unit (*Fig. 4*). The two trifluoromethylpyridine groups are connected through the ethylene bridges, which show extended conformations (torsion angles 170, −171°), to the imidazolium core. The two pyridine rings are almost parallel (interplanar angle 6°). The imidazole ring is perpendicular to the pyridine rings (angles 87, 83°). This leads to approximate mirror symmetry of the molecule (rms deviation 0.25 Å). The gold coordination, through the NHC C-atom and the chloride ligand, is as expected close to linearity, with C–Au–Cl angle 178.65(8)° and bond lengths Au–C 1.986(3) and Au–Cl 2.2940(8), which can be considered typical for NHC–Au–Cl complexes. The MeOH molecule is connected to the gold complex *via* a H-bond O–H···ClAu (*Scheme 3*).

The THF solvate **7b** crystallizes in the monoclinic space group $P2_1/n$ with one molecule of **7** and one badly disordered THF in the asymmetric unit (*Fig. 5*). Clearly, the overall molecular conformation is completely different from **7a**, with an angle of 42° between the pyridinic rings, which in turn subtend angles of 13° and 40° to the imidazole ring. Major differences in torsion angle are observed for C(4)–C(5)–C(6)–N(3) (−13° for **7a**, −81° for **7b**; values for **7b** inverted), N(2)–C(12)–C(13)–C(14) (−161, 66°), and C(12)–C(13)–C(14)–N(4) (5, 80°). The coordination at gold shows similar values to **7a** for the C–Au–Cl angle 178.84(11)°, and for the bond lengths Au–C 1.982 (3) and Au–Cl 2.2847(9) Å.

NMR Spectra of the Compounds

In their ^{1}H- and ^{13}C-NMR spectra, the imidazolium salts display specific resonances for imidazolium protons located between 9.15 and 10.22 ppm, and the corresponding imidazolium carbons in the range 137.2 – 138.3 ppm (*Table 1*).

The NMR spectra confirm the generation of the new NHC–metal complexes; the resonance attributed to the N–C*H*–N in the ^{1}H-NMR is no longer visible, and the resonance of the carbene C-atoms is shifted upfield (170.6 – 183.6 ppm), confirming that the trifluoromethylpyridine

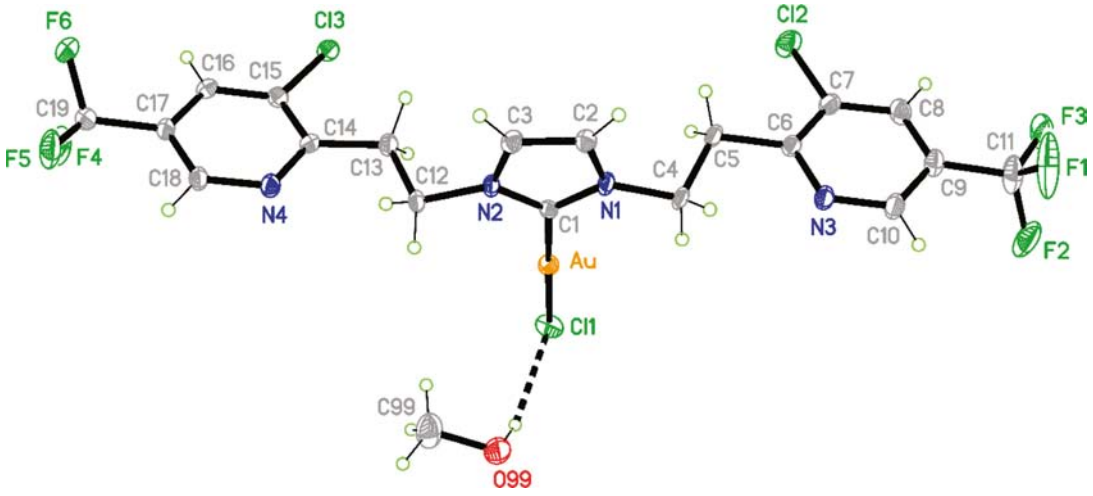
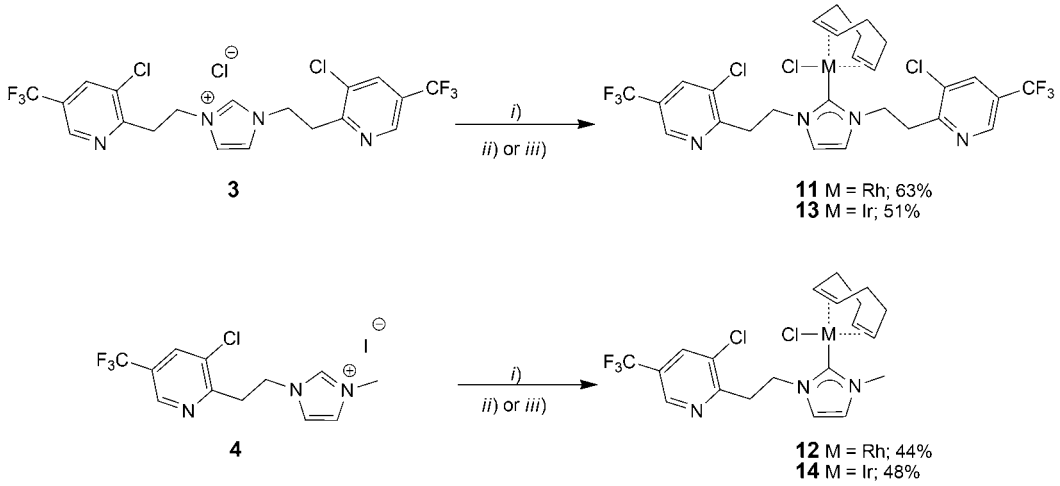


Fig. 4. Molecular structure of chloro{1,3-bis[(2-ethyl)-3-chloro-5-(trifluoromethyl)pyridine)]-1*H*-imidazolin-2(3*H*)-ylidene)}gold(I) (MeOH solvate, **7a**). Atoms are drawn as 50% thermal ellipsoids.

Scheme 3. Synthesis of NHC-Rh and NHC-Ir complexes



i) Ag_2O, CH_2Cl_2, r.t.; *ii*) $[Rh(COD)Cl]_2$, CH_2Cl_2, r.t.; *iii*) $[Ir(COD)Cl]_2$, CH_2Cl_2, r.t.

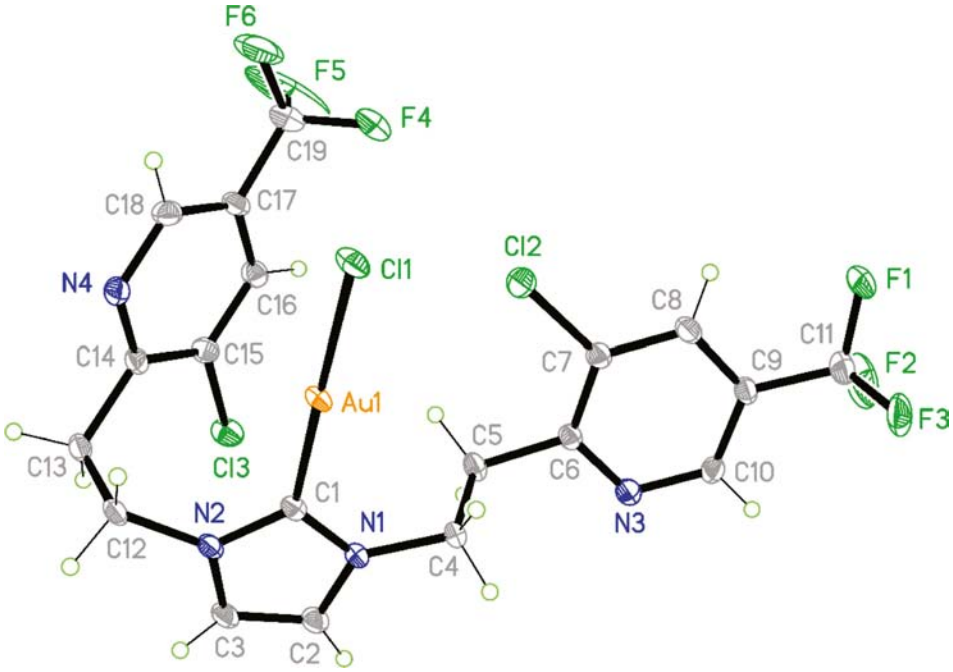


Fig. 5. Molecular structure of chloro{1,3-bis[(2-ethyl)-3-chloro-5-(trifluoromethyl)pyridine)]-1*H*-imidazolin-2(3*H*)-ylidene)}gold(I) (THF solvate, **7b**, solvent omitted). Atoms are drawn as 30% thermal ellipsoids.

Table 1. Notable features in the ^{1}H- and ^{13}C-NMR spectra of the imidazolium salts and the corresponding NHC–metal complexes

NHC–metal complex	δ(C) (NHC–Au)[a]) [ppm]	Imidazolium salt	Solvent	δ(H) (NHC*HX) [ppm]	δ(C) (NHC*HX) [ppm]	$\Delta\delta$ (C)
7	170.6	**3**	(D_6)DMSO	9.15	137.4	33.2
8	171.2	**4**	$CDCl_3$	10.04	137.3	33.9
9	174.4	**5**	(D_4)MeOH	9.23	138.3	36.1
10	171.2	**6**	$CDCl_3$	10.22	137.9	33.3
11	183.6	**3**	(D_6)DMSO	9.15	137.4	33.2
12	183.4	**4**	$CDCl_3$	10.04	137.3	33.9
13	181.3	**3**	(D_6)DMSO	9.15	137.4	33.2
14	181.5	**4**	$CDCl_3$	10.04	137.3	33.9

[a]) ^{13}C-NMR Spectra were recorded using $CDCl_3$ as solvent.

imidazolium salts have been successfully deprotonated and that the C-metal bonds formed. These values are consistent with reported values for M–NHC complexes.

In vitro *Antitumor Activity Toward Human Tumor Cell Lines*

The *in vitro* antitumor activity of the compounds **2, 4** – **14** was assessed in a panel of 12 human tumor cell lines using a monolayer cell survival and proliferation assay. In order to show the change in the antitumor activity after the insertion of the metal center (Au, Rh, or Ir), we tested also the imidazolium salts **4** – **6**. In addition, there are some recent publications [55 – 57], in which the imidazolium salts are described as antitumorals. Although the incorporation of metal into an imidazolium salt via a metal–NHC bond generally increases its activity, in our case, only the Au(I)–NHC complexes **7** – **9** showed a higher activity that the corresponding imidazolium salts; the Rh and Ir complexes showed less activity that their imidazolium precursors.

As shown in *Fig. 6*, six compounds (**7**, **8**, **9**, **4**, **12**, **11**) exhibited antitumor activity with geometric mean IC_{50} values in the range from 12.6 μM (**7**) to 43.3 μM (**11**). The other compounds (**5**, **2**, **14**, **13**, **6**, **10**) showed no *in vitro* anticancer activity.

Fig. 7 shows the individual IC_{50} values as a heatmap presentation. The most active compound **7** displayed individual IC_{50} values in the range from 4.95 μM (22RV1) to 28.6 μM (OVXF 899), corresponding to a 5.8-fold difference between the most sensitive and the least sensitive cell line. The highest level of tumor selectivity was detected for **4**, with IC_{50} values in the range from 6.17 μM to > 100 μM (16-fold difference).

Comparing the *in vitro* activity of the compounds with established platinum compounds approved for cancer therapy revealed a similar potency for one compound (*Fig. 8*). Five platinum compounds of the first and second generation exhibited geometric mean IC_{50} values across the 12 cell line panel in the range from 0.96 μM (satraplatin) to 11.68 μM (carboplatin). With a geometric mean IC_{50} value of 12.6 μM, compound **7** is clearly in the same area of potency as the marketed compound Carboplatin.

Conclusions

A series of novel Au(I)–, Rh(I)–, and Ir(I)–NHC linked to trifluoromethylpyridine derivatives were generated from the corresponding imidazolium salts. All derivatives were designed, isolated, characterized, and tested for antitumor activity *in vitro* toward a panel of 12 cell lines using a monolayer cell survival and proliferation assay. One compound revealed good potency with a mean IC_{50} value 12.6 μM.

All derivatives were obtained in high purity (at least 95%) and good to moderate yields. The structural assignment was corroborated by the X-ray structure analysis for compound **7**.

This work was supported by the *Romanian National Authority for Scientific Research* through the (EXPLORATORY RESEARCH PROGRAM IDEI-PCE-PROJECT NR. 341-/05.10.2011 – Immunomodulatory Fluoroglycopeptide Molecular Architectures (*I. Neda*).

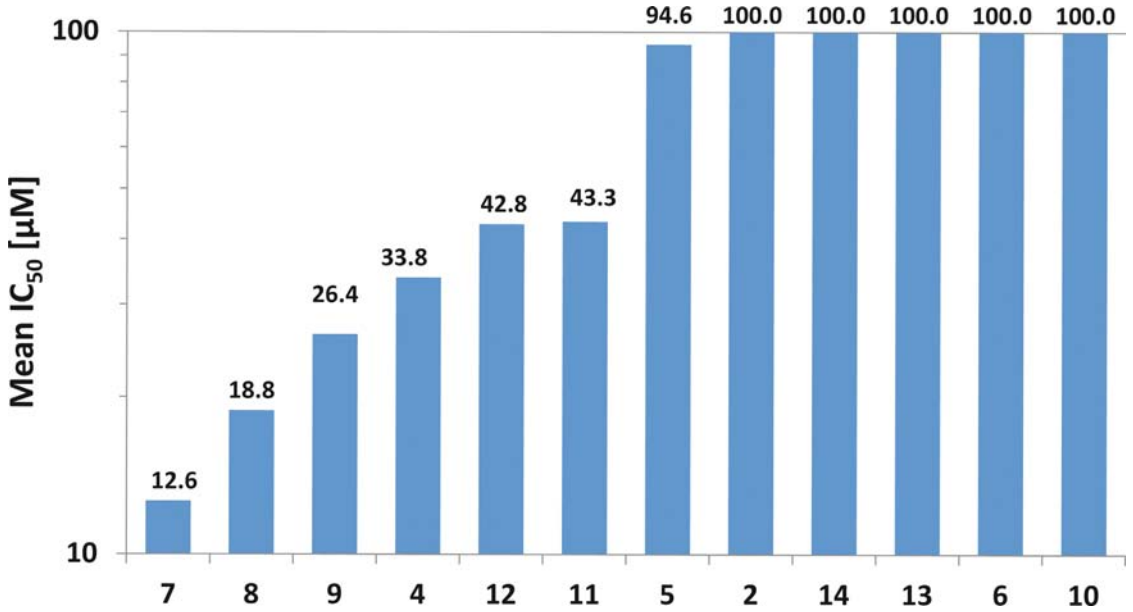


Fig. 6. *In vitro* antitumor potency of compounds **2, 4** – **14** in a panel of 12 human tumor cell lines (geometric mean IC_{50} values in a panel of 12 tumor cell lines).

compound	unit	Cell lines											Geom. mean IC_{50} [μM]
		CXF HT-29	GXF 251	LXFA 629	LXFL 529	MAXF 401	MEXF 462	OVXF 899	PAXF 1657	PRXF 22Rv1	PXF 1752	RXF 486	UXF 1138	
7	μM	24.06	17.59	23.40	9.55	9.27	9.56	28.18	7.89	4.95	26.65	9.25	7.28	**12.6**
8	μM	32.68	35.40	37.05	10.74	14.03	14.54	31.68	9.62	10.28	29.76	13.44	17.02	**18.8**
9	μM	32.8	28.9	16.1	100	13.7	12.5	100	100	12.5	21.6	13.8	11.9	**26.4**
4	μM	33.22	21.98	62.21	6.17	25.28	51.86	60.92	100.00	13.66	56.27	100.00	12.87	**33.8**
12	μM	79.45	31.24	31.27	41.29	13.73	48.49	100	45.34	34.25	40.25	95.31	29.96	**42.8**
11	μM	75.73	31.59	31.68	36.66	19.61	46.38	100	52.28	31.56	46.38	100	22.21	**43.3**
5	μM	100	51.4	100	100	100	100	100	100	100	100	100	100	**94.6**
2	μM	100	100	100	100	100	100	100	100	100	100	100	100	**100**
14	μM	100	100	100	100	100	100	100	100	100	100	100	100	**100**
13	μM	100	100	100	100	100	100	100	100	100	100	100	100	**100**
6	μM	100	100	100	100	100	100	100	100	100	100	100	100	**100**
10	μM	100	100	100	100	100	100	100	100	100	100	100	100	**100**

1/32 1/16 1/8 1/4 1/2 1 2 4 8 16 32 -fold mean IC_{50}
sensitive cell lines resistant cell lines

Fig. 7. Heatmap presentation of individual IC_{50} values for compounds **2, 4** – **12** in a panel of 12 human tumor cell lines.

compound	unit	Cell lines											Geom. mean IC_{50} [μM]
		CXF HT-29	GXF 251	LXFA 629	LXFL 529	MAXF 401	MEXF 462	OVXF 899	PAXF 1657	PRXF 22Rv1	PXF 1752	RXF 486	UXF 1138	
Satraplatin	μM	2,07	1,11	1,32	0,82	0,27	0,75	0,57	1,11	0,46	3,07	2,83	0,47	**0,96**
Tetraplatin	μM	1,29	0,43	18,27	0,84	0,40	2,33	0,46	2,69	0,70	8,10	1,05	2,11	**1,49**
Oxaliplatin	μM	1,28	1,55	12,13	3,37	0,60	5,32	0,21	4,77	0,71	15,34	0,69	3,36	**2,08**
Cisplatin	μM	14,55	4,97	4,71	0,83	0,68	0,73	2,54	7,62	3,57	38,58	8,79	2,77	**3,80**
Carboplatin	μM	26,16	9,19	19,65	4,69	1,98	4,04	8,01	36,61	9,99	52,31	27,68	8,53	**11,68**

1/32 1/16 1/8 1/4 1/2 1 2 4 8 16 32 -fold mean IC_{50}
sensitive cell lines resistant cell lines

Fig. 8. Heatmap presentation of individual IC_{50} values for approved platinum compounds in a panel of 12 human tumor cell lines (historical data of Oncotest).

Experimental Part

General Procedures

All reagents were purchased from commercial sources (*Sigma–Aldrich*, Taufkirchen, Germany or *Fisher-Scientific*, Schwerte, Germany) and used without further purification. Solvents were of analytical grade. All complexes reported in the manuscript have a purity of > 95%. The purity of compounds **2** – **6** was assessed to be > 95% by HPLC on *Shimadzu CBM-10A* instrument (*Shimadzu*, Hannover, Germany) with a *Pinnacle DB C18* (5 μm, 250 × 4.6 mm, *Restek*, Bellefont, PA, USA) column using $(NEt_3H)H_2PO_4$ buffer (0.08M in H_2O)/95% MeCN with $(NEt_3H)H_2PO_4$ buffer (0.08M in H_2O) gradients as the eluents. Reactions were monitored by TLC, performed on silica gel plates 40 × 80 mm *Polygram Sil G/UV*$_{254}$ (*Machery-Nagel*, Düren, Germany). Visualization on TLC was achieved by UV light. Column chromatography was performed with silica gel *60* (70 – 200 mesh, *Merck*, Darmstadt, Germany). IR Spectra: *Bruker Vertex 70* ATR (*Bruker*, Karlsruhe, Germany). ^{1}H-NMR, ^{13}C-NMR spectra: *Bruker Avance 300* (*Bruker*, Karlsruhe, Germany) operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C;

chemical shifts (δ) are reported relative to the TMS peak set at 0.00 ppm. MS: *Finnigan MAT 95 XP* (*Thermofinnigan*, Bremen, Germany). HR-MS: *LTQ-Orbitrap Velos* (*ThermoFisher Scientific*, Bremen, Germany) Elemental C, H, N analysis: *VarioMICRO V3.1.1* (*Elementar Analysensysteme*, Hanau, Germany).

In Vitro *Antitumor Activity Toward Human Tumor Cell Lines*

Antitumor activity of these compounds was tested in a monolayer cell survival and proliferation assay using human tumor cell lines. Studies using panels of human tumor cell lines of different origin/histotype allow for analysis of potency and tumor selectivity of test compounds.

Ten out of the twelve cell lines as tested were established at Oncotest from patient-derived human tumor xenografts passaged subcutaneously in nude mice [58]. The origin of the donor xenografts has been described [59][60]. The cell line 22RV1 was supplied by ATCC (Rockville, MD, USA), HT-29 was kindly provided by the National Cancer Institute (Bethesda, MA, USA). Cells were cultured in RPMI 1640 medium, supplemented with 10% fetal calf serum, and 0.1 mg/ml gentamicin under standard conditions (37 °C, 5% CO_2). The authenticity of all cell lines was proven by STR analysis at the DSMZ (Braunschweig, Germany).

A modified propidium iodide assay was used to assess activity of the compounds toward human tumor cell lines [61]. Briefly, cells were harvested from exponential phase cultures by trypsinization, counted, and plated in 96-well flat-bottom microtiter plates at a cell density dependent on the cell line (4000 – 20 000 cells/well). After a 24 h recovery period to allow the cells to adhere and resume exponential growth, compounds were added at 10 concentrations in half-log increments and left for a further 4 days. The inhibition of proliferation was determined by measuring the DNA content using an aqueous propidium iodide solution (7 μg/ml). Fluorescence was measured using the Enspire Multimode-Plate Reader (excitation λ = 530 nm, emission λ = 620 nm), providing a direct relationship to the total viable cell number. In each experiment, all data points were determined in duplicates. Antitumor activity was reported as the absolute IC_{50} value, which reflects the concentration of the test compound that achieves test/control values of 50%. Calculation was performed using a four-parameter nonlinear curve fit (Oncotest Data Warehouse Software, Freiburg, Germany). The overall potency of a compound was determined by the geometric mean IC_{50} values of all individual IC_{50} values. In the heatmap representation of IC_{50} values, the distribution of the IC_{50} values obtained for a test compound in the individual tumor models is given in relation to the geometric mean IC_{50} value, obtained over all cell lines tested.

The individual *IC* values are highlighted in colors ranging from dark green (≤ 1/32-fold geometric mean IC_{50}, corresponds to very potent compound activity or high-tumor sensitivity) to dark red (≥ 32-fold geometric mean IC_{50}, corresponds to lack of compound activity or tumor resistance). The heatmap presentation, therefore, represents an antiproliferative 'fingerprint' profile of a test compound.

1,3-Bis{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl}-1*H*-imidazol-3-ium Chloride (**3**). To a solution of paraformaldehyde (0.5 g, 15 mmol) in toluene (20 ml) was added 2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl] ethanamine (6.5 g, 31 mmol) and 40% (*v*/*v*) aqueous glyoxal (0.87 g, 15 mmol) followed by the dropwise addition of 37% (*v*/*v*) HCl (1.14 ml, 15 mmol). The mixture was heated to reflux and the water was removed from reaction using a water separator. The solvent was removed under reduced pressure, and the resulting residue was triturated with acetone, after which a white solid appeared. Yield: 60% (4.51 g, 8.68 mmol). ^{1}H-NMR (300.1 MHz, (D_6) DMSO): 9.51 (*s*, 1 H, NC*H*N); 8.88 – 8.84 (*m*, 2 H, CH_{Im}); 8.47 (*d*, *J*(H,H) = 1.7, 2 H, CH_{Py}); 7.89 (*d*, *J*(H,H) = 1.4, 2 H, CH_{Py}); 4.73 (*t*, ^{3}*J*(H,H) = 6.6, 4 H, CH_2); 3.57 (*t*, ^{3}*J*(H,H) = 6.6, 4 H, CH_2). ^{13}C-NMR (75.47 MHz, $CDCl_3$): 158.75 (*C*$_{Py}$); 143.82 (*q*, ^{3}*J*(C,F) = 4.2, *C*H$_{Py}$); 137.39 (N*C*HN); 133.91 (*q*, ^{3}*J*(C,F) = 3.3, *C*H$_{Py}$); 131.75 (*C*$_{Py}$); 124.88 (*q*, ^{2}*J*(C,F) = 33.4 *C*$_{Py}$); 122.83 (*q*, ^{1}*J*(C,F) = 272.9, *C*F$_3$); 122.61 (*C*H$_{Im}$); 46.05 (Im–*C*H$_2$); 34.38 (Py–*C*H$_2$). HR-ESI-MS: 483.0573 (M^+), $C_{19}H_{15}Cl_2F_6N_4^+$; calc. 483.0572.

1-{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl}-3-methyl-1*H*-imidazol-3-ium Iodide (**4**). A solution of 3-chloro-2-[2-(1*H*-imidazol-1-yl)ethyl]-5-(trifluoromethyl) pyridine (**2**; 2.5 g, 9.08 mmol) and MeI (1.42 g, 0.621 ml, 9.98 mmol) in dry THF (20 ml) was stirred under Ar atmosphere at r.t. for 24 h. The precipitate was collected by filtration, washed with Et_2O, and dried in vacuum, giving an off-white solid. Yield: 97% (3.6 g, 8.79 mmol). ^{1}H-NMR (300.1 MHz, $CDCl_3$): 10.04 (*s*, 1 H, NC*H*N); 8.82 (*d*, ^{3}*J*(H,H) = 1.9, 1 H, CH_{Im}); 7.91 (*d*, ^{3}*J*(H,H) = 1.9, 1 H, CH_{Im}); 7.68 (*dd*, *J*(H,H) = 1.8, *J*(H,H) = 1.8, 1 H, CH_{Py}); 7.57 (*dd*, *J*(H,H) = 1.8, *J*(H,H) = 1.7, 1 H, CH_{Py}); 4.99 (*t*, ^{3}*J*(H,H) = 6.2, 2 H, CH_2); 4.12 (*s*, 3 H, CH_3); 3.68 (*t*, ^{3}*J*(H,H) = 6.2, 2 H, CH_2). ^{13}C-NMR (75.47 MHz, $CDCl_3$): 157.19 (*C*$_{Py}$); 143.83 (*q*, ^{3}*J*(C,F) = 4.0, *C*H$_{Py}$); 137.28 (NC*H*N); 133.91 (*q*, ^{3}*J*(C,F) = 3.5, *C*H$_{Py}$); 131.75 (*C*$_{Py}$); 126.29 (*q*, ^{2}*J*(C,F) = 33.8 *C*$_{Py}$); 123.36 (*C*H$_{Im}$); 122.82 (*C*H$_{Im}$); 122.38 (*q*, ^{1}*J*(C,F) = 273.1, *C*F$_3$); 46.25 (Im–*C*H$_2$); 37.05 (Im–*C*H$_3$); 34.78 (Py–*C*H$_2$). HR-ESI-MS: 290.0665 (M^+), $C_{12}H_{12}ClF_3N_3^+$; calc. 290.0666.

3-Benzyl-1-{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl] ethyl}-1*H*-imidazol-3-ium Bromide (**5**). A solution of 2-[2-(1*H*-imidazol-1-yl)ethyl]-3-chloro-5-(trifluoromethyl)pyridine (0.5 g, 1.81 mmol) and 0.22 ml of benzyl bromide (0.310 g, 1.81 mmol) in dry CH_2Cl_2 (10 ml) was stirred under an inert atmosphere for 48 h. After cooling, the

imidazolium salt was precipitated by adding Et_2O (50 ml). After filtration and drying under vacuum, a white solid was obtained. Yield: 86% (0.695 g, 1.56 mmol).

^{1}H-NMR (300.1 MHz, (D_4)MeOD): 9.23 (*s*, 1 H, NC*H*N); 8.71 (*d*, ^3J(H,H) = 1.5, 1 H, CH_{Im}); 8.20 (*d*, ^3J(H,H) = 1.5, 1 H, CH_{Im}); 7.76 (*dd*, *J*(H,H) = 1.8, *J*(H,H) = 1.8, 1 H, CH_{Py}); 7.64 (*dd*, *J*(H,H) = 1.8, *J*(H,H) = 1.7, 1 H, CH_{Py}); 7.46 – 7.39 (*m*, 5 H, Ar–H_{Bn}); 5.43 (*s*, 2 H, CH_2); 4.85 (*t*, ^3J(H,H) = 6.25, 2 H, CH_2); 3.65 (*t*, ^3J(H,H) = 6.25, 2 H, CH_2). ^{13}C-NMR (75.47 MHz, $CDCl_3$): 159.63 (C_{Py}); 145.01 (*q*, ^3J(C,F) = 4.1, *C*H$_{Py}$); 138.30 (NC*H*N); 135.54 (*q*, ^3J(C,F) = 3.6, *C*H$_{Py}$); 135.45 (C_{Bn}); 133.15 (C_{Py}); 130.37 (2 *C*H$_{Bn}$); 130.33 (*C*H$_{Bn}$); 129.62 (2 *C*H$_{Bn}$); 126.01 (*q*, ^2J(C,F) = 34.2 C_{Py}); 124.23 (*C*H$_{Im}$); 123.75 (*C*H$_{Im}$); 123.29 (*q*, ^1J(C,F) = 271.3, *C*F$_3$); 54.09 (Im–*C*H$_2$–Ph); 47.90 (Im-*C*H$_2$); 35.45 (Py–*C*H$_2$). HR-ESI-MS: 366.0970 (M^+), $C_{18}H_{16}ClF_3N_3^+$; calc. 366.0979.

1-{2-[3-Chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl}-3-{(2*R*,3*R*,4*S*,5*S*,6*R*)-3,4,5-tris(acetyloxy)-6-[(acetyloxy)methyl]tetrahydro-2*H*-pyran-2-yl}-1*H*-imidazol-3-ium Nitrate (**6**). To a solution of 2,3,4,5-tetra-*O*-acetyl-D-galactopyranosylbromide (1.63 g, 3.99 mmol) in MeCN (20 ml) were added silver nitrate (0.68 g, 3.99 mmol) and 2-(2-(1*H*-imidazol-1-yl)ethyl)-3-chloro-5-(trifluoromethyl)pyridine (1 g, 3.63 mmol). The reaction mixture was stirred at 50 °C for 24 h. Insoluble material was removed by filtration through *Celite*, and then the solution was concentrated under reduced pressure. The resulting solid was dissolved in CH_2Cl_2 and stirred over Na_2CO_3 for 30 min. After filtration, the product was recrystallized several times from CH_2Cl_2/^{t}BuOMe to give a white solid. Only the β-isomer was observed in NMR spectra. Yield: 10% (0.24 g, 0.369 mmol).

^{1}H-NMR (300.1 MHz, $CDCl_3$): 10.22 (*s*, 1 H, NC*H*N); 8.77 (*d*, *J*(H,H) = 1.9, 1 H, CH_{Im}); 7.91 (*d*, *J*(H,H) = 1.9, 1 H, CH_{Im}); 7.92 (*s*, 1 H, CH_{Py}); 7.63 (*s*, 1 H, CH_{Py}); 6.26 (*d*, *J*(H,H) = 8.3, 1 H, N–C*H*–O); 5.55 (*d*, *J*(H,H) = 2.2 Hz, 1 H, C$H_{carbohydrate}$); 5.41–5.28 (*m*, 2 H, C$H_{carbohydrate}$); 4.99 (*dd*, *J*(H,H) = 5.9, *J*(H,H) = 5.7, 2 H, CH_2); 4.48 (*dd*, *J*(H,H) = 6.3 *J*(H,H) = 6.2, 1 H, C$H_{carbohydrate}$); 4.22 (*dd*, *J*(H,H) = 11.5, *J*(H,H) = 5.6, 1 H, CH_2, C$H_{carbohydrate}$); 4.14 (*dd*, *J*(H,H) = 11.5, *J*(H,H) = 7.0, 1 H, CH_2, C$H_{carbohydrate}$); 3.67 (*dd*, *J*(H,H) = 13.7, *J*(H,H) = 9.8, 2 H, CH_2); 2.22 (*s*, 3 H, CH_3); 2.03 (*s*, 3 H, CH_3); 1.98 (*s*, 3 H, CH_3); 1.93 (*s*, 3 H, CH_3). ^{13}C-NMR (75.47 MHz, $CDCl_3$): 170.19 (CH_3–*C*=O); 169.78 (CH_3–*C*=O); 169.54 (CH_3–*C*=O); 169.32 (CH_3–*C*=O); 157.42 (C_{Py}); 143.65 (*q*, ^3J(C,F) = 4.0, *C*H$_{Py}$); 137.91 (N*C*HN); 133.80 (*q*, ^3J(C,F) = 3.5, *C*H$_{Py}$); 131.58 (C_{Py}); 126.22 (*q*, ^2J(C,F) = 33.7 C_{Py}); 123.69 (*C*H$_{Im}$); 122.37 (*q*, ^1J(C,F) = 272.9, *C*F$_3$); 119.35 (*C*H$_{Im}$); 84.48 (N–*C*H$_{carbohydrate}$–O); 73.86 (O–*C*H$_{carbohydrate}$–C); 70.09 (*C*H$_{carbohydrate}$); 68.27 (*C*H$_{carbohydrate}$); 66.80 (*C*H$_{carbohydrate}$); 61.04 (C–*C*H$_{2carbohydrate}$–OAc); 46.69 (Im–*C*H$_2$); 34.37 (Py–*C*H$_2$); 20.38 (CO–*C*H$_3$); 20.34 (CO–*C*H$_3$); 20.19 (CO–*C*H$_3$); 19.91(CO–*C*H$_3$). HR-ESI-MS: 606.1464 (M^+), $C_{25}H_{28}ClF_3O_9N_3^+$; calc. 606.1461.

Chloro{1,3-bis[2-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)ethyl]-1*H*-imidazolin-2(3*H*)-ylidene)}gold(I) (**7**). A mixture of 1,3-bis{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl}-1*H*-imidazol-3-ium chloride (**3**; 102.89 mg, 0.198 mmol) and silver(I) oxide (27.5 mg, 0.118 mmol) in dry CH_2Cl_2 (10 ml) was stirred for 24 h at r.t. in the absence of light. The mixture was filtered through *Celite,* and chloro(tetrahydrothiophene)gold(I) (63.47 mg, 0.198 mmol) was added. The resulting mixture was stirred for 12 h and filtered through *Celite*. The solvent was removed in vacuum, and CH_2Cl_2 (2 ml) was added. The product was precipitated as a white solid upon addition of pentane, and purified by column chromatography (CH_2Cl_2/AcOEt, 3:1). Yield: 38% (53 mg, 0.075 mmol). Single crystals suitable for X-ray analysis were obtained from MeOH (**7a**) or THF/pentane (**7b**). ^{1}H-NMR (300.1 MHz, $CDCl_3$): 8.69 (*d*, *J*(H,H) = 1.7, 2 H, CH_{Py}); 7.89 (*d*, *J*(H,H) = 2.0, 2 H, CH_{Py}); 6.93 (*s*, 2 H, CH_{Im}); 4.67 (*t*, ^3J(H,H) = 6.8, 4 H, CH_2); 3.55 (*t*, ^3J(H,H) = 6.8, 4 H, CH_2). ^{13}C-NMR (75.47 MHz, $CDCl_3$): 170.59 (Au$C_{Carbene}$); 158.29 (*q*, ^5J(C,F) = 1.1, C_{Py}); 143.69 (*q*, ^3J(C,F) = 4.0, *C*H$_{Py}$); 133.84 (*q*, ^3J(C,F) = 3.5, *C*H$_{Py}$); 131.77 (C_{Py}); 126.22 (*q*, ^2J(C,F) = 33.7 C_{Py}); 122.43 (*q*, ^1J(C,F) = 272.9, *C*F$_3$); 121.10 (*C*H$_{Im}$); 48.47 (Im–*C*H$_2$); 36.26 (Py–*C*H$_2$). EI-MS: 718.0 [8, $M(^{37}Cl_2{}^{35}Cl)^+$], 716.0 [25, $M(^{37}Cl^{35}Cl_2)^+$], 714.0 [24, $M(^{35}Cl_3)^+$], 680.0 [67], 678.0 [100], 645.0 [11], 643.0 [32].

Chloro{1-[2-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)ethyl]-3-methyl-1*H*-imidazolin-2(3*H*)-ylidene)}gold(I) (**8**). A mixture of 1-{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl}-3-methyl-1*H*-imidazol-3-ium iodide (**4**; 100 mg, 0.24 mmol) and silver(I) oxide (35 mg, 0.15 mmol) in dry CH_2Cl_2 (15 ml) was stirred for 24 h at r.t. in the absence of light. The mixture was filtered through *Celite*, and (dimethyl sulfide)gold(I)chloride (71 mg, 0.24 mmol) was added. The resulting mixture was stirred for 12 h and filtered through *Celite*. The solvent was removed *in vacuo*, and CH_2Cl_2 (2 ml) was added. The product was precipitated as a white solid upon addition of pentane and purified by column chromatography (CH_2Cl_2/AcOEt, 3:1). Yield: 38% (47.5 mg, 0.091 mmol). ^{1}H-NMR (300.1 MHz, $CDCl_3$): 8.63 (*d*, *J*(H,H) = 1.1, 1 H, CH_{Py}); 7.83 (*d*, *J*(H,H) = 1.5, 1 H, *CH*$_{Py}$); 6.95 (*d*, ^3J(H,H) = 1.9, 1 H, *CH*$_{Im}$); 6.85 (*d*, ^3J(H,H) = 1.9, 1 H, CH_{Im}); 4.63 (*t*, ^3J(H,H) = 6.8, 2 H, CH_2); 3.75 (*s*, 3 H, CH_3); 3.49 (*t*, ^3J(H,H = 6.8, 2 H, CH_2). ^{13}C-NMR (75.47 MHz, $CDCl_3$): 171.19 (Au$C_{Carbene}$); 158.36 (*C*Py); 143.79 (*q*, ^3J(C,F) = 4.0, *C*H$_{Py}$); 134.01 (*q*, ^3J(C,F) = 3.6, *C*H$_{Py}$); 131.92 (C_{Py}); 126.42 (*q*, ^2J(C,F) = 33.6 C_{Py}); 123.42 (*q*, ^1J(C,F) = 272.7, *C*F$_3$); 121.54 (*C*H$_{Im}$); 121.31 (*C*H$_{Im}$); 48.35 (Im–*C*H$_2$); 38.31 (Im–*C*H$_3$); 36.42 (Py–*C*H$_2$). EI-MS: 525.0 [5, $M(^{37}Cl_2)^+$], 523.0 [26, $M(^{37}Cl^{35}Cl)^+$], 521.0 [40, $M(^{35}Cl_2)^+$], 488.0 [8], 487.0 [14], 486.0 [27], 485.0 [36], 254.1 [100].

Bromo{1-[(2-ethyl)-3-chloro-5-(trifluoromethyl)pyridine)]-3-(benzyl)-1*H*-imidazolin-2(3*H*)-ylidene)}gold(I) (**9**). To a mixture of 3-benzyl-1-{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl}-1*H*-imidazol-3-ium bromide (**5**; 89 mg,

0.2 mmol), potassium *tert*-butoxide (22.6 mg, 0.2 mmol) and (dimethyl sulfide)gold(I)chloride (59.5 mg, 0.2 mmol) was added under an inert atmosphere dry THF (5 ml), and the suspension was stirred for 24 h at r.t. in the absence of light. The resulting mixture was filtered over *Celite*. The solvent was removed *in vacuo*, and CH_2Cl_2 (2 ml) was added. The product was precipitated as a white solid upon addition of hexane and purified by column chromatography (CH_2Cl_2/AcOEt, 3:1). Yield: 58% (74 mg, 0.116 mmol). ^{1}H-NMR (300.1 MHz, $CDCl_3$): 8.65 (*dd*, *J*(H,H) = 1.1, *J*(H,H) = 0.95, 1 H, C*H*$_{Py}$); 7.87 (*dd*, *J* (H,H) = 1.2, *J*(H,H) = 0.7, 1 H, C*H*$_{Py}$); 7.39 – 7.28 (*m*, 5 H, Ar–*H*$_{Bn}$); 7.01 (*d*, ^{3}*J*(H,H) = 2.0, 1 H, C*H*$_{Im}$); 6.87 (*d*, ^{3}*J*(H,H) = 2.0 Hz, 1 H, C*H*$_{Im}$); 5.32 (*s*, 2 H, C*H*$_2$); 4.71 (*t*, ^{3}*J*(H,H) = 6.7, 2 H, C*H*$_2$); 3.57 (*t*, ^{3}*J*(H,H) = 6.7, 2 H, C*H*$_2$). ^{13}C-NMR (75.47 MHz, $CDCl_3$): 174.40 (Au*C*$_{Carbene}$); 158.34 (C$_{Py}$); 143.85 (*q*, ^{3}*J*(C,F) = 4.1, *C*H$_{Py}$); 134.91 (*C*$_{Bn}$); 134.54 (*q*, ^{3}*J*(C,F) = 3.6, *C*H$_{Py}$); 131.96(C$_{Py}$); 128.95 (2 *C*H$_{Bn}$); 128.66 (*C*H$_{Bn}$); 128.01 (2 *C*H$_{Bn}$); 126.30 (*q*, ^{2}*J* (C,F) = 33.8 *C*$_{Py}$); 122.30 (*q*, ^{1}*J*(C,F) = 273.0, *C*F$_3$); 121.58 (*C*H$_{Im}$); 120.58 (*C*H$_{Im}$); 55.01 (Bn–*C*H$_2$); 48.62 (Im–*C*H$_2$); 36.48 (Py-*C*H$_2$). HR-EI-MS: 640.9743 (M^+), $C_{18}H_{15}Au^{79}Br^{35}ClF_3N_3^+$; calc. 640.9755. EI-MS: 642.8 [2.5], 640.8 [2], 562.0 [2], 207.0 [45], 158.1 [40], 91.0 [100].

Chloro{1-[2-(3-chloro-5-(trifluoromethyl)pyridin-2-yl) ethyl]-3-(2,3,4,5-tetra-*O*-acetyl-D-galactopyranosyl)-1*H*-imidazolin-2(3*H*)-ylidene}gold(I) (**10**). To a mixture of 1-{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl}-3-{(2*R*,3*R*, 4*S*,5*S*,6*R*)-3,4,5-tris(acetyloxy)-6-[(acetyloxy)methyl]tetrahydro-2*H*-pyran-2-yl}-1*H*-imidazol-3-ium nitrate (**6**; 132 mg, 0.2 mmol), potassium *tert*-butoxide (22.6 mg, 0.2 mmol) and (dimethyl sulfide)gold(I)chloride (59.5 mg, 0.2 mmol) was added under an inert atmosphere dry THF (5 ml), and the suspension was stirred for 24 h at r.t. in the absence of light. The resulting mixture was filtered through *Celite.* The solvent was removed in vacuo, and CH_2Cl_2 (2 ml) was added. The product was precipitated as a white solid upon addition of hexane and purified by column chromatography (CH_2Cl_2/AcOEt, 3:1). Yield: 52% (85 mg, 0.104 mmol). ^{1}H-NMR (300.1 MHz, $CDCl_3$): 8.71 (*dd*, *J*(H,H) = 2.0, *J*(H,H) = 1.1, 1 H, C*H*$_{Py}$); 7.92 (*dd*, *J*(H,H) = 2.0, *J*(H,H) = 0.9, 1 H, C*H*$_{Py}$); 7.21 (*d*, *J*(H,H) = 2.0, 1 H, C*H*$_{Im}$); 7.01 (*d*, *J*(H,H) = 2.0, 1 H, C*H*$_{Im}$); 5.96 (*d*, *J*(H,H) = 8.5, 1 H, N–C*H*–O); 5.54 (*d*, *J*(H,H) = 2.4, 1 H, C*H*$_{carbohydrate}$); 5.30 (*dd*, *J*(H, H) = 10.3, *J*(H,H) = 3.2, 1 H, C*H*$_{carbohydrate}$); 5.23 (*dd*, *J* (H,H) = 10.3, *J*(H,H) = 8.4, 1 H, C*H*$_{carbohydrate}$); 4.71 (*t*, ^{3}*J*(H,H) = 6.9, 2 H, C*H*$_2$); 4.26 – 4.11 (*m*, 3 H, C*H*$_{carbohydrate}$); 3.56 (*t*, ^{3}*J*(H,H) = 6.9, 2 H, C*H*$_2$); 2.18 (*s*, 3 H, C*H*$_3$); 2.06 (*s*, 3 H, C*H*$_3$); 2.01 (*s*, 3 H, C*H*$_3$); 1.99 (*s*, 3 H, C*H*$_3$). ^{13}C-NMR (75.47 MHz, $CDCl_3$): 171.24 (Au*C*$_{Carbene}$); 170.31 (CH$_3$-*C*=O); 169.71 (CH$_3$-*C*=O); 169.51 (CH$_3$-*C*=O); 169.44 (CH$_3$-*C*=O); 157.95 (*C*$_{Py}$); 143.88 (*q*, ^{3}*J*(C,F) = 4.1, *C*H$_{Py}$); 134.05 (*q*, ^{3}*J*(C,F) = 3.5, *C*H$_{Py}$); 131.82 (*C*$_{Py}$); 126.42 (*q*, ^{2}*J*(C,F) = 33.6 *C*$_{Py}$); 122.46 (*C*H$_{Im}$); 122.22 (*q*, ^{1}*J*(C,F) = 272.7, *C*F$_3$); 117.72 (*C*H$_{Im}$); 87.05 (N–*C*H$_{carbohydrate}$–O); 73.84 (O–*C*H$_{carbohydrate}$–CH$_2$); 70.33 (*C*H$_{carbohydrate}$); 68.46 (*C*H$_{carbohydrate}$); 66.82 (*C*H$_{carbohydrate}$); 61.22 (CH–*C*H$_{2carbohydrate}$–OAc); 48.76 (Im–*C*H$_2$); 36.26 (Py–*C*H$_2$); 20.75 (CO–*C*H$_3$); 20.64 (CO–*C*H$_3$); 20.57 (CO–*C*H$_3$); 20.40 (CO–*C*H$_3$). HR-ESI-MS: 860.0635 [*M*+Na]$^+$, $C_{25}H_{27}AuCl_2N_3O_9F_3Na^+$; calc. 860.0634.

Chloro(η^4-1,5-cyclooctadiene){1,3-bis-[1-(2-(3-chloro-5-(trifluoromethyl))pyridin-2-yl)ethyl-]-1*H*-imidazolin-2(3*H*)-ylidene)}rhodium(I) (**11**). A mixture of 1,3-bis{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl}-1*H*-imidazol-3-ium chloride (**3**; 52 mg, 0.1 mmol) and silver(I) oxide (14 mg, 0.06 mmol) in dry CH_2Cl_2 (10 ml) was stirred for 24 h at r.t. in the absence of light. The mixture was filtered through *Celite* and $[Rh(COD)Cl]_2$ (25 mg, 0.05 mmol) was added. The resulting mixture was stirred for 12 h and filtered through *Celite*. The solvent was removed in vacuum, and CH_2Cl_2 (2 ml) was added. The product was precipitated as a white solid upon addition of pentane and purified by column chromatography (CH_2Cl_2/AcOEt, 3:1). Yield: 63% (51 mg, 0.063 mmol). IR (ATR): 3091, 2936, 2916, 2878, 2831, 1603, 1555, 1453, 1397, 1322, 1221, 1129, 1090, 1062, 997, 959, 912, 884, 865, 816, 747, 728, 700, 624. UV/Vis (CH_2Cl_2): 393 (0.160), 271 (0.946), 228 (1.341). ^{1}H-NMR (300.1 MHz, $CDCl_3$): 8.75 (*d*, *J*(H, H = 1.0, 2 H, C*H*$_{Py}$); 7.93 (*d*, *J*(H,H) = 1.6, 2 H, C*H*$_{Py}$); 6.93 (*s*, 2 H, C*H*$_{Im}$); 5.15 (*ddd*, *J*(H,H) = 13.6, *J*(H, H) = 9.5, *J*(H,H) = 5.9, 2 H, C*H*$_2$); 5.06 – 5.00 (*m*, 2 H, *COD*$_{vinyl}$); 4.87 (*ddd*, *J*(H,H) = 13.6, *J*(H,H) = 9.3, *J*(H, H) = 6.2, 2 H, C*H*$_2$); 3.93 (*ddd*, *J*(H,H) = 15.5, *J*(H, H) = 9.2, *J*(H,H) = 5.9, 2 H, C*H*$_2$); 3.55 (*ddd*, *J*(H, H) = 15.5, *J*(H,H) = 9.4, *J*(H,H) = 6.2, 2 H, C*H*$_2$); 3.39 – 3.331 (*m*, 2 H, *COD*$_{vinyl}$); 2.52 – 2.32 (*m*, 4 H, *COD*$_{allyl}$); 1.99 – 1.90 (*m*, 4 H, *COD*$_{allyl}$). ^{13}C-NMR (75.47 MHz, $CDCl_3$): 183.63 (*d*, ^{1}*J*(C,Rh) = 51.0, Rh*C*$_{Carbene}$); 159.67 (*C*HPy, 2 C); 143.75 (*q*, ^{3}*J*(C,F) = 4.1, *C*H$_{Py}$, 2 C); 133.87 (*q*, ^{3}*J*(C,F) = 3.6, *C*H$_{Py}$, 2 C); 131.88 (*C*$_{Py}$, 2 C); 126.30 (*C*H$_{Im}$); 126.22 (*q*, ^{2}*J*(C,F) = 33.6 *C*$_{Py}$, 2 C); 122.43 (*q*, ^{1}*J*(C,F) = 272.9, *C*F$_3$, 2 C); 120.97 (*C*H$_{Im}$); 98.85 (*COD*$_{vinyl}$), 98.76 (*COD*$_{vinyl}$), 68.38 (*COD*$_{vinyl}$); 68.19 (*COD*$_{vinyl}$); 48.14 (Im–*C*H$_2$, 2 C); 36.63 (Py–*C*H$_2$, 2 C); 32.92 (*COD*$_{allyl}$, 2 C); 28.81 (*COD*$_{allyl}$, 2 C). ESI-MS: 693.0489 [*M* – Cl]$^+$. EI-MS: 733.0 [3], 732.0 [8, *M*(^{37}Cl$_2$)$^+$], 731.0 [5], 730.0 [14, *M*(^{37}Cl^{35}Cl)$^+$], 729.0 [5], 728.0 [17, *M*(^{35}Cl$_2$)$^+$], 713.0 [8], 711.0 [17], 709.0 [15], 695.10 [27], 693.1 [38], 667.9 [25], 665.9 [50], 663.9 [31], 623.9[30], 621.9 [96], 619.9 [100], 240.1 [80], 207.0 [85].

Chloro(η^4-1,5-cyclooctadiene){[1-[2-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)ethyl]-3-methyl-1*H*-imidazolin-2(3*H*)-ylidene)}rhodium(I) (**12**). A mixture of 1-{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl}-3-methyl-1*H*-imidazol-3-ium iodide (**4**; 100 mg, 0.24 mmol) and silver(I) oxide (35 mg, 0.15 mmol) in dry CH_2Cl_2 (15 ml) was stirred for 24 h at r.t. in the absence of light. The mixture was filtered through *Celite* and $[Rh(COD)Cl]_2$ (59 mg, 0.12 mmol) was added. The resulting mixture was stirred for 12 h and filtered through *Celite*. The solvent was removed in vacuum, and CH_2Cl_2 (2 ml) was added. The product was precipitated as a white solid upon addition of

pentane and purified by column chromatography (CH_2Cl_2/AcOEt, 3:1). Yield: 44% (57 mg, 107 mmol). IR (ATR): 3095, 2934, 2916, 2877, 2829, 1603, 1556, 1456, 1396, 1322, 1223, 1130, 1091, 1062, 996, 958, 911, 884, 865, 816, 790, 725, 697, 624. UV/Vis (CH_2Cl_2): 393 (0.022), 272 (0.101), 227 (0.195). ^{1}H-NMR (300.1 MHz, $CDCl_3$): (*d*, *J*(H,H) = 1.0, 1 H, CH_{Py}); 7.86 (*d*, *J*(H,H) = 1.7, 1 H, CH_{Py}); 6.84 (*d*, ^{3}*J*(H,H) = 1.9, 1 H, CH_{Im}); 6.73 (*d*, ^{3}*J*(H,H) = 1.89, 1 H, CH_{Im}); 5.05 (*ddd*, *J*(H,H) = 13.6, *J*(H,H) = 9.4, *J*(H,H) = 6.0, 1 H, CH_2); 4.98 – 4.94 (*m*, 2 H, COD_{vinyl}); 4.76 (*ddd*, *J*(H,H) = 13.5, *J*(H,H) = 9.0, *J*(H,H) = 6.2, 1 H, CH_2); 4.02 (*s*, 3 H, CH_3); 3.85 (*ddd*, *J*(H,H) = 14.6, *J*(H,H) = 8.9, *J*(H,H) = 6.0, 1 H, CH_2); 3.49 (*ddd*, *J*(H,H) = 15.7, *J*(H,H) = 9.5, *J*(H,H) = 6.4, 1 H, CH_2); 3.41 – 3.26 (*m*, 2 H, COD_{vinyl}); 2.46 – 2.42 (*m*, 4 H, COD_{allyl}); 2.01 – 1.92 (*m*, 4 H, COD_{allyl}). ^{13}C-NMR (75.47 MHz, $CDCl_3$): 183.42 (*d*, ^{1}*J*(C,Rh) = 50.3, Rh$C_{Carbene}$); 160.35 (*C*Py); 143.25 (*q*, ^{3}*J*(C,F) = 4.0, *C*H_{Py}); 133.57 (*q*, ^{3}*J*(C,F) = 3.6, *C*H_{Py}); 132.58 (*C*$_{Py}$); 126.31 (*q*, ^{2}*J*(C,F) = 33.2 *C*$_{Py}$); 122.24 (*q*, ^{1}*J*(C,F) = 273.2, *C*F_3); 122.05 (*C*H_{Im});120.86 (*C*H_{Im}); 98.74 (COD_{vinyl}); 98.52 (COD_{vinyl}); 68.86 (COD_{vinyl}); 68.47 (COD_{vinyl}); 48.88 (Im–*C*H_2); 37.79 (*C*H_3); 36.78 (Py–*C*H_2); 33.31 (COD_{allyl}); 32.52 (COD_{allyl}); 29.18 (COD_{allyl}); 28.47 (COD_{allyl}). EI-MS: 535.0/537.0 (M^+), 500.1/502.1 (M^+-Cl). ESI-MS: 500.18 (100), 501.11 (30), 501.98 (40).

Chloro(η^4-1,5-cyclooctadiene){[1,3-bis[2-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)ethyl]-1*H*-imidazolin-2(3*H*)-ylidene)}iridium(I) (13). A mixture of 1,3-bis{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl}-1*H*-imidazol-3-ium chloride (**3**; 52 mg, 0.1 mmol) and silver(I) oxide (14 mg, 0.06 mmol) in dry CH_2Cl_2 (10 ml) was stirred for 24 h at r.t. in the absence of light. The mixture was filtered through *Celite* and $[Ir(COD)Cl]_2$ (33.6 mg, 0.05 mmol) was added. The resulting mixture was stirred for 12 h and filtered through *Celite*. The solvent was removed in vacuum, and CH_2Cl_2 (2 ml) was added. The product was precipitated as a white solid upon addition of pentane and purified by column chromatography (CH_2Cl_2/AcOEt, 3:1). Yield: 51% (41 mg, 0.051 mmol). IR (ATR): 3898, 2927, 2880, 2832, 1603, 1556, 1451, 1397, 1322, 1223, 1130, 1090, 1062, 970, 912, 884, 865, 818, 781, 740, 705, 689, 623. UV/Vis (CH_2Cl_2): 481 (0.019), 419 (0.108), 269 (0.797), 227 (0.857). ^{1}H-NMR (300.1 MHz, $CDCl_3$): 8.73 (*d*, *J*(H,H) = 1.1, 2 H, CH_{Py}); 7.92 (*d*, *J*(H,H) = 1.4, 2 H, CH_{Py}); 6.92 (*s*, 2 H, CH_{Im}); 5.00 (*ddd*, *J*(H,H) = 13.5, *J*(H,H) = 9.2, *J*(H,H) = 6.0, 2 H, CH_2); 4.74 (*ddd*, *J*(H,H) = 13.5, *J*(H,H) = 9.0, *J*(H,H) = 6.2, 2 H, CH_2); 4.66 – 4.57 (*m*, 2 H, COD_{vinyl}); 3.81 (*ddd*, *J*(H,H) = 15.3, *J*(H,H) = 8.9, *J*(H,H) = 6.0, 2 H, CH_2); 3.51 (*ddd*, *J*(H,H) = 15.4, *J*(H,H) = 9.2, *J*(H,H) = 6.3, 2 H, CH_2); 2.96 – 2.88 (*m*, 2 H, COD_{vinyl}); 2.31 – 2.05 (*m*, 4 H, COD_{allyl}); 1.59 – 149 (*m*, 4 H, COD_{allyl}). ^{13}C-NMR (75.47 MHz, $CDCl_3$): 181.33 (Ir$C_{Carbene}$); 159.61(*C*$_{Py}$, 2 C); 143.79 (*q*, ^{3}*J*(C,F) = 4.0, *C*H_{Py}, 2 C); 133.93 (*q*, ^{3}*J*(C,F) = 3.6, *C*H_{Py}, 2 C); 131.92(*C*$_{Py}$, 2 C); 126.33 (*q*, ^{2}*J*(C,F) = 33.2 *C*$_{Py}$, 2 C); 122.42 (*q*, ^{1}*J*(C,F) = 273.4, *C*F_3, 2 C); 120.68 (*C*H_{Im}, 2 C); 85.03 (COD_{vinyl}, 2 C); 51.86 (COD_{vinyl}, 2 C); 47.81 (Im–*C*H_2, 2 C); 36.67 (Py–*C*H_2, 2 C); 33.68 (COD_{allyl}, 2 C); 29.56 (COD_{allyl}, 2 C). ESI-MS: 783.0 ($[M - Cl]^+$).

Chloro(η^4-1,5-cyclooctadiene){1-[2-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)ethyl]-3-methyl-1*H*-imidazolin-2(3*H*)-ylidene)}iridium(I) (14). A mixture of 1-{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl}-3-methyl-1*H*-imidazol-3-ium iodide (**4**; 100 mg, 0.24 mmol) and silver(I) oxide (35 mg, 0.15 mmol) in dry CH_2Cl_2 (15 ml) was stirred for 24 h at r.t. in the absence of light. The mixture was filtered through *Celite* and $[Ir(COD)Cl]_2$ (80 mg, 0.12 mmol) was added. The resulting mixture was stirred for 12 h and filtered through *Celite*. The solvent was removed in vacuum, and CH_2Cl_2 (2 ml) was added. The product was precipitated as a white solid upon addition of pentane and purified by column chromatography (CH_2Cl_2/AcOEt, 3:1). Yield: 48% (72 mg, 115 mmol). IR (ATR): 3101, 2925, 2877, 2831, 1603, 1455, 1397, 1322, 1224, 1131, 1091, 1062, 999, 969, 910, 883, 865, 818, 706, 688, 624. UV/Vis (CH_2Cl_2): 483 (0.017), 419 (0.089), 373 (0.058), 268 (0.598), 227 (0.718). ^{1}H-NMR (300.1 MHz, $CDCl_3$): 8.73 (*d*, *J*(H,H) = 1.0, 1 H, CH_{Py}); 7.91 (*d*, *J*(H,H) = 1.6, 1 H, CH_{Py}); 6.91 (*d*, *J*(H,H) = 1.95, 1 H, CH_{Im}); 6.80 (*d*, *J*(H,H) = 1.95, 1 H, CH_{Im}); 4.94 (*ddd*, *J*(H,H) = 13.5, *J*(H,H) = 9.0, *J*(H,H) = 6.0, 1 H, CH_2); 4.74 (*ddd*, *J*(H,H) = 13.5, *J*(H,H) = 8.9, *J*(H,H) = 6.3, 1 H, CH_2); 4.64 – 4.57 (*m*, 2 H, COD_{vinyl}); 3.96 (*s*, 3 H, CH_3); 3.81 (*ddd*, *J*(H,H) = 15.2, *J*(H,H) = 8.5, *J*(H,H) = 5.9, 1 H, CH_2); 3.52 (*ddd*, *J*(H,H) = 15.5, *J*(H,H) = 9.0, *J*(H,H) = 6.5, 1 H, CH_2); 3.05 – 2.83 (*m*, 2 H, COD_{vinyl}); 2.29 – 2.12 (*m*, 4 H, COD_{allyl}); 1.52 – 1.42 (*m*, 4 H, COD_{allyl}). ^{13}C-NMR (75.47 MHz, $CDCl_3$): 181.45 (Ir$C_{Carbene}$); 160.25 (*C*$_{Py}$); 142.25 (*q*, ^{3}*J*(C,F) = 4.0, *C*H_{Py}); 133.47 (*q*, ^{3}*J*(C,F) = 3.6, *C*H_{Py}); 132.34 (*C*$_{Py}$); 126.23 (*q*, ^{2}*J*(C,F) = 33.2 *C*$_{Py}$); 122.32 (*q*, ^{1}*J*(C,F) = 273.2, *C*F_3); 121.69 (*C*H_{Im});120.62 (*C*H_{Im}); 85.08 (COD_{vinyl}); 84.39 (COD_{vinyl}); 51.91 (COD_{vinyl}); 51.20 (COD_{vinyl}); 47.56 (Im–*C*H_2); 37.53 (Im–*C*H_3); 36.79 (Py–*C*H_2); 34.02 (COD_{allyl}); 33.12 (COD_{allyl}); 29.96 (COD_{allyl}); 29.12 (COD_{allyl}). ESI-MS: 590.08 ($[M - Cl]^+$).

X-ray Diffraction Studies

Data were recorded at 100(2) K using an *Oxford Diffraction Xcalibur E diffractometer* with monochromated Mo Kα radiation (*Oxford Diffraction*, Yarnton, UK). Absorption corrections were based on multiscans. The structures were refined anisotropically using the SHELXL-97 program [62]. Some F-atoms displayed large and irregular thermal ellipsoids, but no disorder model of the corresponding CF_3 groups could be refined. The OH hydrogen of **7a** was refined freely; other H-atoms were included as idealized Me groups allowed to rotate but not tip, or placed geometrically and allowed to ride on their attached C-atoms. For **7b**, the THF solvent was severely disordered; the effects of the solvent were removed mathematically using the program SQUEEZE [63].

Table 2. Crystallographic data of compounds **7a** and **7b**

	7a (MeO solvate)	7b (THF solvate)
Empirical formula	$C_{20}H_{18}AuCl_3F_6N_4O$	$C_{23}H_{22}AuCl_3F_6N_4O$
Formula weight	747.70	787.76
Temperature (K)	100(2)	100(2)
Wavelength λ (Å)	0.71073	0.71073
Crystal system	Triclinic	Monoclinic
Space group	$P\bar{1}$	$P2_1/n$
a [Å]	7.9891(3)	9.5502(2)
b [Å]	9.1311(3)	21.7082(6)
c [Å]	16.5465(6)	12.8858(3)
α [°]	92.938(3)	90
β [°]	96.362(3)	104.446(3)
γ [°]	92.392(3)	90
Volume [Å^3]	1196.68	2586.99
Z	2	4
ρ_{calcd} [g cm^{-3}]	2.075	2.023
μ [mm^{-1}]	6.6	6.1
$2\theta_{max}$	62	61.6
Reflections collected	67595	93992
Independent reflections	7149 [R_{int} = 0.064]	7783 [R_{int} = 0.056]
Parameters	321	298
$R(F_o)$, [$I > 2\sigma(I)$]	0.029	0.034
R_w (F_o^2)	0.050	0.071
Goodness of fit on F^2	1.05	1.07
$\Delta\rho$ [e Å^{-3}]	1.2/–1.1	1.4/–1.0

Crystallographic Data

Crystallographic data (excluding structure factors) have been deposited with the *Cambridge Crystallographic Data Centre* as supplementary publications no. CCDC-1442026 (**7a**), and CCDC-1442027 (**7b**) (see *Table 2*). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ (fax: (+44) 1223-336-033; e-mail: www.ccdc.cam.ac.uk/data_request/cif.

REFERENCES

[1] I. Ott, *Coord. Chem. Rev.* **2009**, *253*, 1670.
[2] G. Gasser, I. Ott, N. Metzler-Nolte, *J. Med. Chem.* **2011**, *54*, 3.
[3] *The Pharmaceutical Journal* **1987**, *239*.
[4] S. J. Berners-Price, *Angew. Chem., Int. Ed.* **2011**, *50*, 804.
[5] D. Krishnamurthy, M. R. Karver, E. Fiorillo, V. Orrú, S. M. Stanford, N. Bottini, A. M. Barrios, *J. Med. Chem.* **2008**, *51*, 4790.
[6] P. J. Barnard, M. V. Baker, S. J. Berners-Price, D. A. Day, *J. Inorg. Biochem.* **2004**, *98*, 1642.
[7] P. J. Barnard, A. Y. Y. Ho, M. V. Baker, D. A. Day, S. J. Berners-Price, *Proc. Gold* **2003**, *1*.
[8] M. R. Karver, D. Krishnamurthy, R. A. Kulkarni, N. Bottini, A. M. Barrios, *J. Med. Chem.* **2009**, *52*, 6912.
[9] R. Rubbiani, I. Kitanovic, H. Alborzinia, S. Can, A. Kitanovic, L. A. Onanbele, M. Stefanopoulou, Y. Geldmacher, W. S. Sheldrick, G. Wolber, A. Prokop, S. Wölfl, I. Ott, *J. Med. Chem.* **2010**, *53*, 8608.
[10] E. Schuh, C. Pflüger, A. Citta, A. Folda, M. P. Rigobello, A. Bindoli, A. Casini, F. Mohr, *J. Med. Chem.* **2012**, *55*, 5518.
[11] C.-H. Wang, W.-C. Shih, H. C. Chang, Y.-Y. Kuo, W.-C. Hung, T.-G. Ong, W.-S. Li, *J. Med. Chem.* **2011**, *54*, 5245.
[12] W. Liu, K. Bensdorf, M. Proetto, U. Abram, A. Hagenbach, R. Gust, *J. Med. Chem.* **2011**, *54*, 8605.
[13] L. Messori, L. Marchetti, L. Massai, F. Scaletti, A. Guerri, I. Landini, S. Nobili, G. Perrone, E. Mini, P. Leoni, M. Pasquali, C. Gabbiani, *Inorg. Chem.* **2014**, *53*, 2396.
[14] G. D. Henry, *Tetrahedron* **2004**, *60*, 6043.
[15] D. O'Hagan, *Nat. Prod. Rep.* **2000**, *17*, 435.
[16] M. Balasubramanian, J. G. Keay, 'Pyridines and their Benzo Derivatives: Applications', in 'Comprehensive Heterocyclic Chemistry II', Eds. A. R. Katritzky, C. W. Rees and E. F. V. Scriven, Pergamon, Oxford, 1996, Vol. 5, p. 245.
[17] R. K. Anchoori, M. S. Q. Kortenhorst, M. Hidalgo, T. Sarkar, G. Hallur, R. Bai, P. J. Van Diest, E. Hamel, S. R. Khan, *J. Med. Chem.* **2008**, *51*, 5953.
[18] G.-H. Kuo, C. Prouty, A. Wang, S. Emanuel, A. DeAngelis, Y. Zhang, F. Song, L. Beall, P. J. Connolly, P. Karnachi, X. Chen, R. H. Gruninger, J. Sechler, A. Fuentes-Pesquera, S. A. Middleton, L. Jolliffe, W. V. Murray, *J. Med. Chem.* **2005**, *48*, 4892.
[19] Y. Wang, X. Dong, R. C. Larock, *J. Org. Chem.* **2003**, *68*, 3090.
[20] G. A. Wächter, M. C. Davis, A. R. Martin, S. G. Franzblau, *J. Med. Chem.* **1998**, *41*, 2436; J. A. Tucker, D. A. Allwine, K. C. Grega, M. R. Barbachyn, J. L. Klock, J. L. Adamski, S. J. Brickner, D. K. Hutchinson, C. W. Ford, G. E. Zurenko, R. A. Conradi, P. S. Burton, R. M. Jensen, *J. Med. Chem.* **1998**, *41*, 3727.
[21] Y.-W. Kim, J. C. Hackett, R. W. Brueggemeier, *J. Med. Chem.* **2004**, *47*, 4032.
[22] R. T. Skerlj, Y. Zhou, T. Wilson, G. J. Bridger, *J. Org. Chem.* **2002**, *67*, 1407.
[23] Q. Ren, W. Mo, L. Gao, H. He, Y. Gu, *J. Heterocycl. Chem.* **2010**, *47*, 171.
[24] G. Li, X. Qian, J. Cui, Q. Huang, R. Zhang, H. Guan, *J. Agric. Food Chem.* **2006**, *54*, 125.
[25] T. J. Anderson, G. D. Jones, D. A. Vicic, *J. Am. Chem. Soc.* **2004**, *126*, 8100.
[26] A. Tsuboyama, H. Iwawaki, M. Furugori, T. Mukaide, J. Kamatani, S. Igawa, T. Moriyama, S. Miura, T. Takiguchi, S. Okada, M. Hoshino, K. Ueno, *J. Am. Chem. Soc.* **2003**, *125*, 12971.
[27] A. Hall, R. L. Elliott, G. M. P. Giblin, I. Hussain, J. Musgrave, A. Naylor, R. Sasse, B. Smith, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 1306.
[28] J.-I. Andrés, M. De Angelis, J. Alcázar, L. Iturrino, X. Langlois, S. Dedeurwaerdere, I. Lenaerts, G. Vanhoof, S. Celen, G. Bormans, *J. Med. Chem.* **2011**, *54*, 5820.
[29] P. L. Beaulieu, M. Bos, M. G. Cordingley, C. Chabot, G. Fazal, M. Garneau, J. R. Gillard, E. Jolicoeur, S. LaPlante, G. McKercher, M. Poirier, M.-A. Poupart, Y. S. Tsantrizos, J. Duan, G. Kukolj, *J. Med. Chem.* **2012**, *55*, 7650.
[30] S. P. Khanapure, M. E. Augustyniak, R. A. Earl, D. S. Garvey, L. G. Letts, A. M. Martino, M. G. Murty, D. J. Schwalb, M. J. Shumway, A. M. Trocha, D. V. Young, I. S. Zemtseva, D. R. Janero, *J. Med. Chem.* **2005**, 3930.
[31] V. Onnis, M. T. Cocco, R. Fadda, C. Congiu, *Bioorg. Med. Chem.* **2009**, *17*, 6158.
[32] C. Congiu, M. T. Cocco, V. Lilliu, V. Onnis, *J. Med. Chem.* **2005**, *48*, 8245.
[33] E. Fodor, C. V. Maftei, I. Mangalagiu, P. G. Jones, C. G. Daniliuc, H. M. Franz, I. Neda, *Rev. Roum. Chim.* **2010**, *55*, 557.
[34] R. S. Crees, M. L. Cole, L. R. Hanton, C. J. Sumby, *Inorg. Chem.* **2010**, *49*, 1712.
[35] D. A. J. Harding, E. G. Hope, K. Singh, G. A. Solan, *Organometallics* **2012**, *31*, 1518.
[36] J. Liu, J. Chen, J. Zhao, Y. Zhao, L. Li, H. Zhang, *Organometallics* **2003**, *17*, 2661.
[37] J. Berding, J. A. van Paridon, V. H. S. van Rixel, E. Bouwman, *Eur. J. Inorg. Chem.* **2011**, *15*, 2450.

[38] A. Flahaut, S. Roland, P. Mangeney, *J. Organomet. Chem.* **2007**, *692*, 5754.
[39] J. J. Concepcion, J. W. Jurss, M. R. Norris, Z. Chen, J. L. Templeton, T. J. Meyer, *Inorg. Chem.* **2010**, *49*, 1277.
[40] A. K. Ghosh, V. J. Catalano, *Eur. J. Inorg. Chem.* **1832**, *2009*, 13.
[41] S. Gründemann, A. Kovacevic, M. Albrecht, J. W. Faller, R. H. Crabtree, *J. Am. Chem. Soc.* **2002**, *124*, 10473.
[42] F. Tewes, A. Schlecker, K. Harms, F. Glorius, *J. Organomet. Chem.* **2007**, *692*, 4593.
[43] B. K. Keitz, R. H. Grubbs, *Organometallics* **2010**, *29*, 403.
[44] M. Micksch, T. Strassner, *Eur. J. Inorg. Chem.* **2012**, *35*, 5872.
[45] A. Collado, A. Gómez-Suárez, A. R. Martin, A. M. Z. Slawin, S. P. Nolan, *Chem. Commun.* **2013**, *49*, 5541.
[46] S. P. Nolan, *Acc. Chem. Res.* **2011**, *44*, 91.
[47] P. de Frémont, N. M. Scott, E. D. Stevens, S. P. Nolan, *Organometallics* **2005**, *24*, 2411.
[48] P. de Frémont, N. Marion, S. P. Nolan, *Coord. Chem. Rev.* **2009**, *253*, 862.
[49] M. R. L. Furst, C. S. J. Cazin, *Chem. Commun.* **2010**, *46*, 6924.
[50] S. Zhu, R. Liang, H. Jiang, *Tetrahedron* **2012**, *68*, 7949.
[51] B. Landers, O. Navarro, *Eur. J. Inorg. Chem.* **2012**, *18*, 2980.
[52] M. Fèvre, J. Pinaud, A. Leteneur, Y. Gnanou, J. Vignolle, D. Taton, K. Miqueu, J.-M. Sotiropoulos, *J. Am. Chem. Soc.* **2012**, *134*, 6776.
[53] R. Visbal, A. Laguna, M. C. Gimeno, *Chem. Commun.* **2013**, *49*, 5642.
[54] M. Pažický, A. Loos, M. J. Ferreira, D. Serra, N. Vinokurov, F. Rominger, C. Jäkel, A. S. K. Hashmi, M. Limbach, *Organometallics* **2010**, *29*, 4448.
[55] W.-C. Wan, W. Chen, L.-X. Liu, Y. Li, L.-J. Yang, X.-Y. Deng, H.-B. Zhang, X.-D. Yang, *Med. Chem. Res.* **2014**, *23*, 1599.
[56] M. A. Iqbal, R. A. Haque, S. A. Ahamed, S. F. Jafari, M. B. K. Ahamed, A. M. S. A. Majid, *Med. Chem.* **2015**, *11*, 473.
[57] C. V. Maftei, E. Fodor, P. G. Jones, M. Freytag, H. M. Franz, G. Kelter, H.-H. Fiebig, M. Tamm, I. Neda, *Eur. J. Med. Chem.* **2015**, *101*, 431.
[58] T. Roth, A. M. Burger, W. Dengler, H. Willmann, H. H. Fiebig, 'Human tumor cell lines demonstrating the characteristics of the patient tumors as useful models for anticancer drug screening', in: 'Relevance of Tumor Models for Anticancer Drug Development', Vol. 54, Eds. H. H. Fiebig and A. M. Burger, Karger, Basle, Switzerland, 1999, pp. 15 – 27.
[59] H. H. Fiebig, W. A. Dengler, T. Roth, 'Human tumor xenografts: predictivity, characterization, and discovery of new anticancer agents', in: 'Relevance of Tumor Models for Anticancer Drug Development', Vol. 54, Eds. H. H. Fiebig and A. M. Burger, Karger, Basle, Switzerland, 1999, pp. 29 – 50.
[60] H. H. Fiebig, D. P. Berger, W. A. Dengler, E. Wallbrecher, B. R. Winterhalter, *Strahlenther. Onkol.* **1992**, *42*, 321.
[61] W. A. Dengler, J. Schulte, D. P. Berger, R. Mertelsmann, H. H. Fiebig, *Anti-Cancer Drugs* **1995**, *6*, 522.
[62] G. M. Sheldrick, *Acta Crystallogr., Sect. A* **2008**, *64*, 112.
[63] A. L. Spek, Part of the PLATON program suite, University of Utrecht, Netherlands.

Received December 17, 2015
Accepted February 22, 2016

