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Synthesis of a (thienylethenyl)benzimidazole platinum acetylide complex

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ABSTRACT

A new platinum acetylide complex based on 6-dialkylaminobenzimidazol-2-yl-vinyl-2-thiophene-5-ylethyne was synthesized in seven steps and 2% overall yield.

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Platinum σ–acetylide complexes (commonly referred to as platinum acetylides) are π–electron conjugated molecules with platinum(II) bonded to two ethynyl groups typically in the *trans* configuration along with two phosphorus, nitrogen, or arsine containing ligands, Figure 1.[1] Platinum acetylides have shown interesting photophysical properties such as two-photon absorption and nonlinear optical effects.[2] As part of a project to identify new materials for optical power limiting devices,[3,4] several group VIII metal acetylides were prepared for evaluation. This Letter will describe the synthesis of a new platinum acetylide (**1**), Figure 1.

Starting with 2,4-difluoronitrobenzene, selective nucleophilic aromatic substitution of the *ortho* fluorine atom with ethylamine gave intermediate **2** in good yield, Scheme 1. Substitution of the second fluorine with 2-(methylamino)ethanol gave diaminonitrobenzene **3** in excellent yield. To make the overall synthesis more convergent, acryloyl chloride **7** was prepared in three steps as shown in Scheme 2. Initial samples of 2-iodothiophene-5-carboxaldehyde (**8**)[5] were prepared by the iodination of thiophene-2-carboxaldehyde using the procedure of Wu et al.[6] This reaction was capricious to scale-up and later batches of 8 were prepared consistently in good yield by adapting the iodination conditions of Barrios Sosa et al.[7] A minor impurity observed by ^{1}H nuclear magnetic resonance (NMR) in this reaction was thiophene-2-carboxylic acid, presumably formed by the oxidation of the aldehyde by the periodic/persulfuric acids present. Doebner-modification[8] of the Perkin reaction of aldehyde **8** with malonic acid in hot pyridine gave the unreported acrylic acid **9**. Typically these condensation reactions are performed at reflux temperature (pyridine boiling point

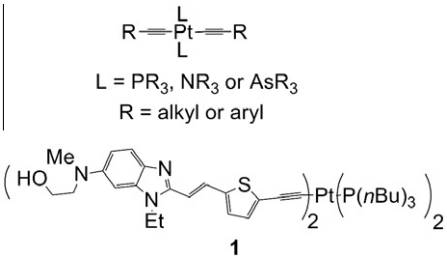
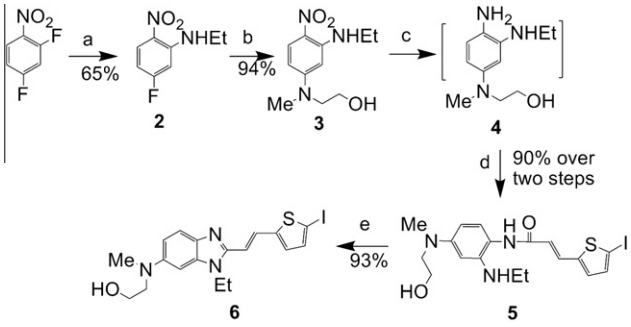


Figure 1. Generic platinum acetylide complex and structure of new molecule **1** synthesized.



Scheme 1. Reagents and conditions: (a) $EtNH_3Cl$, H_2O, TEA; (b) $MeNH(CH_2)_2OH$, K_2CO_3, *N*,*N*-dimethylacetamide; (c) H_2, Pd/C, HOAc, THF; (d) **6**, TEA, THF; (e) $(HOCH_2)_2$, HOAc, reflux.

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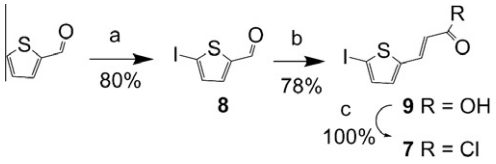
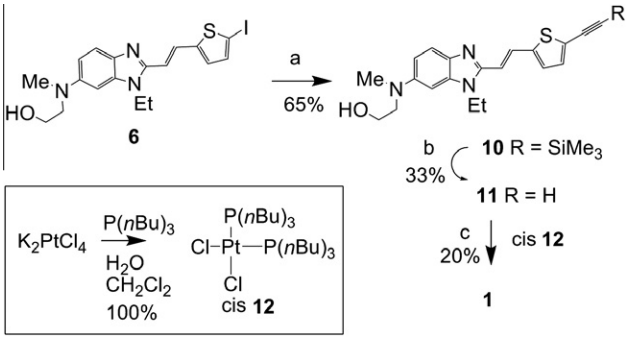


Scheme 2. Reagents and conditions: (a) $NaIO_4$, I_2, H_2O, CCl_4, HOAc, H_2SO_4; (b) $CH_2(CO_2H)_2$, pyridine, piperidine, reflux; (c) $SOCl_2$.

118 °C) however it was found to occur even at 60 °C, although with significant accumulation of the intermediate ylidenemalonic acid as observed by ^{1}H NMR spectroscopy. Increasing the temperature to 75 °C brought the reaction to completion overnight and resulted in higher quality product. The acrylic acid **9** was converted into acryloyl chloride **7** with thionyl chloride.[9–11] Returning to Scheme 1, it was found that a two-step sequence of reduction followed by the amidation of **3** could be combined efficiently. Following catalytic hydrogenation of **3**, the reaction mixture was blanketed with nitrogen and triethylamine was added followed by the addition of acryloyl chloride **7**. In this way, the isolation of air-sensitive **4** was avoided and the yield of amide **5** was markedly improved. Proton NMR analysis confirmed that the acylation event occurred at the primary amine due to the amide proton resonance at 9.17 ppm. Cyclization of **5** in refluxing ethylene glycol containing 2 equiv of acetic acid gave the benzimidazole **6**.[12] Single crystal X-ray analysis of **6** confirmed the desired constitution, Figure 2.[13]

The synthesis was completed by the sequence shown in Scheme 3. Sonogashira reaction of **6** with trimethylsilylacetylene gave the protected acetylene **10**.[14] The latter was deprotected to give the terminal acetylene **11** with tetrabutylammonium fluoride in tetrahydrofuran. The low yield of this deprotection may be due to the sensitivity of the benzimidazole ring to the basic nature of this reagent. The *cis* dichlorobis(tri-*n*-butylphosphine)platinum(II) (**12**) was prepared according to the method of Kauffman and Teter.[15] The value obtained for $^1J(^{195}Pt–^{31}P)$ of 3517 Hz agrees perfectly with the previously reported value.[16,17] Sonogashira reaction of **12** with an excess of **11** in the presence of diisopropylamine base and catalyzed



Scheme 3. Reagents and conditions: (a) Me_3SiCCH, $Pd(OAc)_2$, PPh_3, CuI, DIPA, THF, reflux; (b) TBAF, THF; (c) CuI, $HN(CH(Me)_2)_2$, THF.

Table 1
Comparison of ^{31}P and ^{195}Pt NMR spectroscopy of complex **1** with *cis* and *trans* $PtCl_2(PnBu_3)_2$ (**12**) in $CDCl_3$ at 25 °C

Compound	^{31}P (ppm)	J_{PtP} (Hz)
cis **12**	+1.6	3517
trans **12**	+5.1	2388
1	+4.2	2330

by copper(I) iodide gave the platinum acetylide complex **1**[18] in low and unoptimized yield to complete the synthesis.[19] Combustion analysis proved that the substance contained only mononuclear platinum(II) rather than symmetrical dinuclear platinum(I).[20]

Although the initial platinum species **12** had the *cis* configuration, the complex **1** appears to be the more thermodynamically favored *trans* isomer, a facile isomerization previously reported.[21,22] Phosphorus-31 and ^{13}C NMR spectroscopy showed the characteristic values for the chemical shift of phosphorus as well as the coupling of $^{195}Pt–^{31}P$ signifying *trans* orientation in **1**, Table 1.[23–26] Experiments are underway to obtain crystals of **1** suitable for

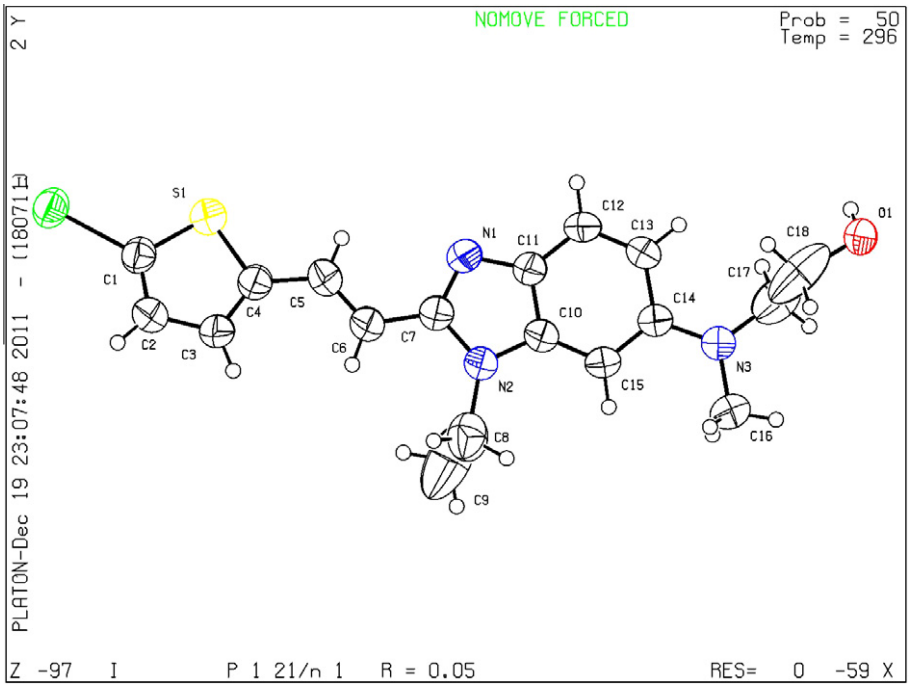


Figure 2. X-ray crystal structure of compound **6**.

X-ray structural analysis to provide further evidence for this conclusion. In summary, the synthesis of a new platinum acetylide complex (**1**) containing a heterocyclic alkyne was completed in seven linear steps and 2% overall yield. Photophysical studies of **1** along with some of its derivatives will be the subject of future communication.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2012.01.023.

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18. Data for bis[*trans* 1-ethyl-2-(2-(5-ethynylthiophen-2-yl)vinyl)-6-(*N*-methyl-*N*-(2-hydroxyethyl)amino)benzimidazole]bis(tri-*n*-butylphosphine)platinum (II) **1**: Mp 210–212 °C. ^{1}H {^{31}P} NMR (300 MHz, $CDCl_3$): 7.9 (d, J = 15.2 Hz, 2H), 7.6 (d, J = 8.7 Hz, 2H), 6.9 (d, J = 3.5 Hz, 2H), 6.9 (d, J = 8.8 Hz, 2H), 6.8 (d, J = 3.5 Hz, 2H), 6.7 (d, J = 15.3 Hz, 2H), 6.6 (m, 2H), 4.2 (q, J = 7.0 Hz, 4H), 3.9 (t, J = 5.2 Hz, 4H), 3.5 (t, J = 5.6 Hz, 4H), 3.0 (s, 6H), 2.1 (m, 12H), 1.7–1.4 (m, 30 H), 1.3 (s, 2 OH), 0.9 (t, J = 7.0 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.2, 147.6, 138.8, 136.6, 136.3, 130.6, 129.2, 128.9, 128.5, 119.5, 118.4, 111.9, 110.7, 102.5, 93.2, 60.1, 56.9, 39.8, 38.1, 26.6, 24.6 (t, $J_{C\gamma P}$ = 7.0 Hz), 24.2 (t, $J_{C\alpha P}$ = 17.1 Hz), 15.4, 14.0; ^{31}P {^{1}H} NMR (121 MHz, $CDCl_3$): δ +4.2 (pseudo t, $^{1}J_{(P\text{-}Pt)}$ = 2327 Hz); ^{195}Pt NMR (64.3 MHz, $CDCl_3$): δ −4689.4 (t, $^{1}J_{Pt\text{-}P}$ = 2330 Hz). Elemental analysis calculated for $C_{64}H_{94}N_6O_2P_2PtS_2$: C, 59.10; H, 7.28; N, 6.46. Found: C, 59.17; H, 7.28; N, 6.56.
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