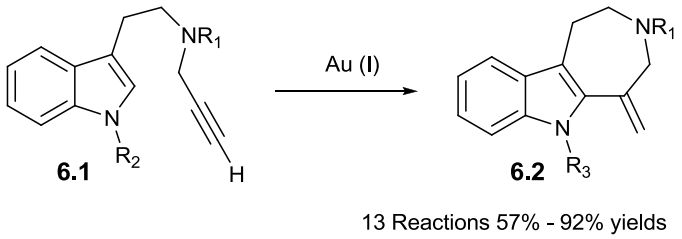
Chapter 6 – Gold(I)-Catalysed Addition of Indoles to Cyclopropenes

Acknowledgment: *The author would like to reserve special thanks once more for Dr. Alan Boyd who helped with the identification of the initial products through NMR analysis. I would also like to thank Paul Young and the Lee group for their endeavours in finishing and publishing the work started by the author and developing the optimised reactions (Scheme 8).*

6.1 Introduction

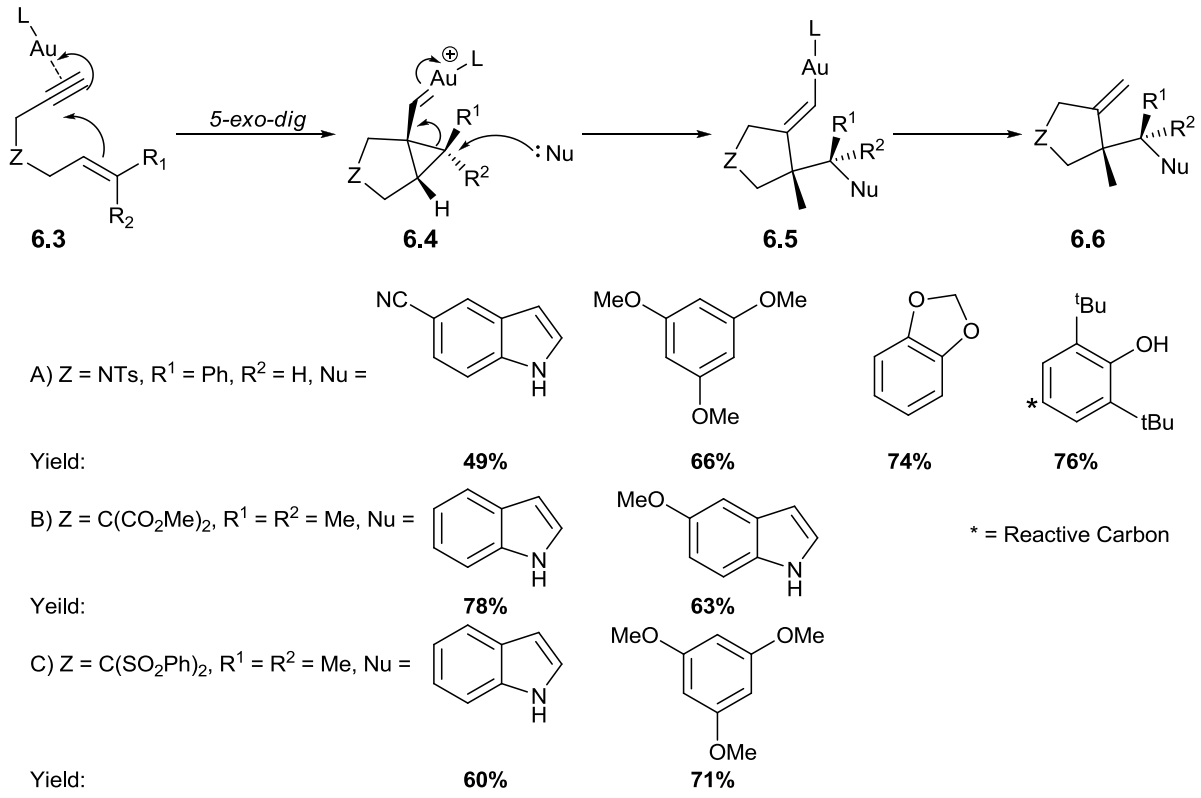
Indoles and their chemistry have been studied for many decades,[1] they can be found in various natural products such as serotonin.[2] Considering the vast array of literature published on this subject and the various metal catalysed reactions observed (for example Pt[3] and Pd[4]), we shall focus on the gold(I)-catalysed nucleophilic additions of indoles for the purpose of this brief introduction.

The majority of work in this area has been carried out by the Echavarren group who first observed the gold(I)-catalysed intramolecular addition of indoles towards alkynes (Scheme 1).[5] The reaction proceeds by gold(I) activating the alkyne π-system in **6.1** towards nucleophilic attack of the indole. This is then followed by 1,2 migration, elimination to re-aromatise and protodemetalation to give the 7-membered cyclic product **6.2**.



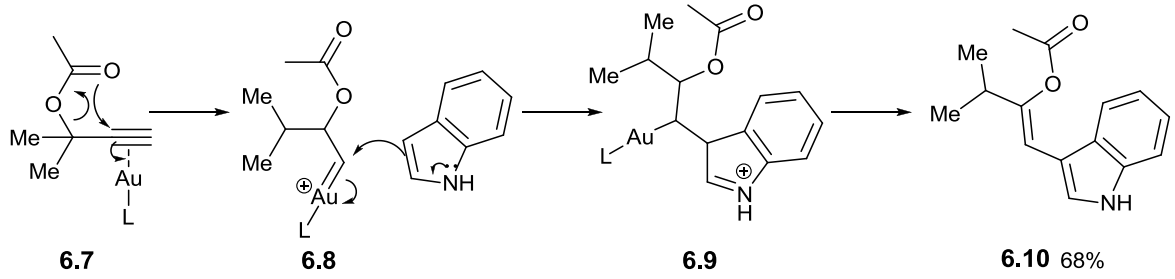
Scheme 1 7-exo-dig Cyclisation of Alkynyl Indoles

Intermolecular additions of indoles, and other carbon based nucleophiles, were shown to react with 1,6-enynes *via* a gold(I) carbene intermediate (Scheme 2).[6] Later, the mechanism was examined in great depth and it was shown that 1,3 dicarbonyls give rise to similar products.[7]



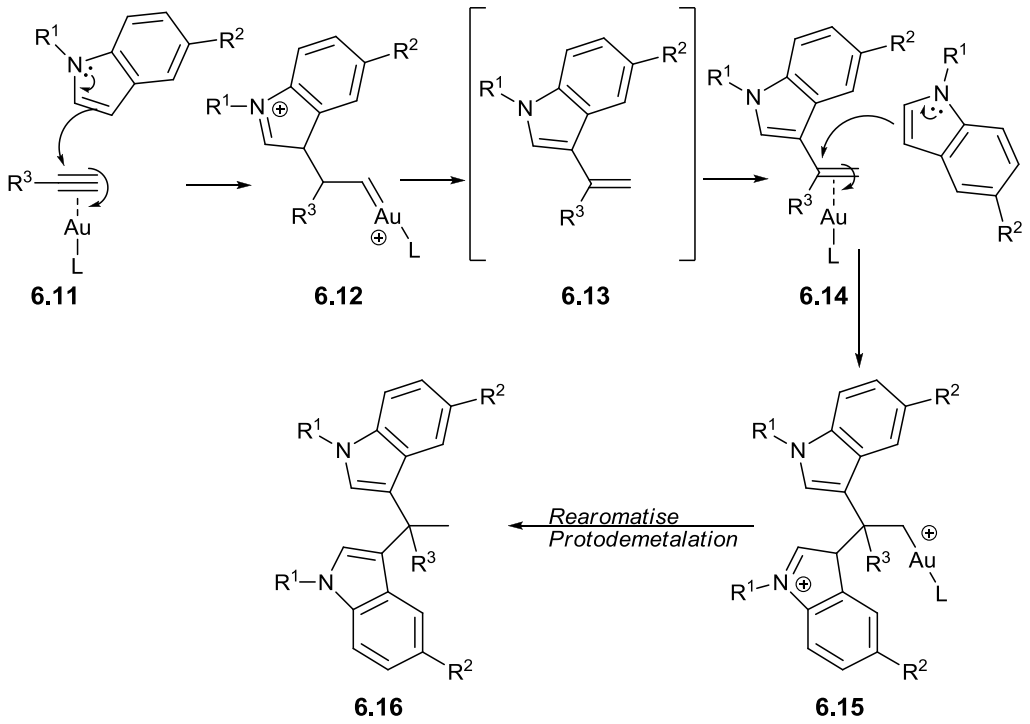
Scheme 2 Gold(I)-Catalysed Additions to 1,6-enynes

Attack of carbon nucleophiles to gold carbenes (**6.8**) formed from rearrangement of propargyl carboxylates can also be achieved.[8] Scheme 3 shows one example of such a reaction with indole as the nucleophile.



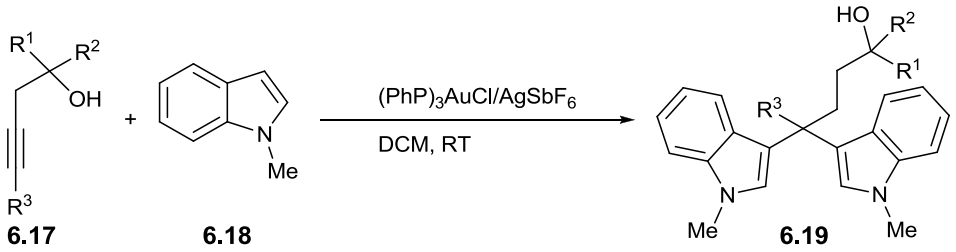
Scheme 3 Indole Attack of Gold(I) Activated Propargyl Acetate

Indole additions to gold(I) activated terminal alkynes can give rise to *bis*(indolyl) alkanes (**6.16**, Scheme 4).[9] The double addition products arise due to reactivation of the key intermediate (**6.13**) allowing another equivalent of indole to add.



Scheme 4 Double Addition of Indole to Terminal Alkynes

Expanding the functionality of the alkynes was achieved by gold(I)-catalysed addition of indoles to butynol derivatives (Scheme 5).[10]



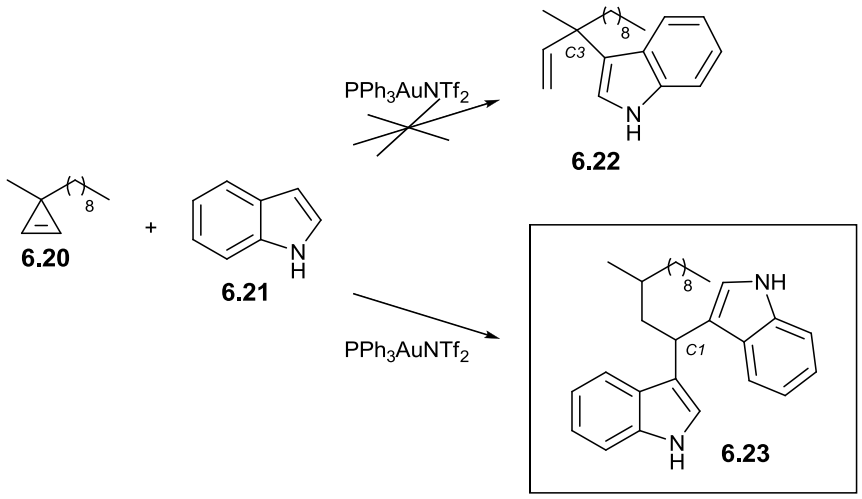
Scheme 5 Bis(indolyl) Alkanes from Butynol Derivatives

The *bis*(indolyl) alkanes are not a new class of compounds and have been shown posses various properties, for example, the first isolation of a hallucinogenic *bis*(indolyl) alkane was from a fungus in 1977.[11] They have now been isolated from a variety of natural sources, marine and terrestrial, with wide ranging biological activities such as anti-bacterial[12] and anti-carcinogenic.[13] Due to their potentially important properties in medicine, the synthesis of these *bis*(indolyl) alkanes with a variety of functionalities is of current interest.[14]

6.2 Results and Discussion

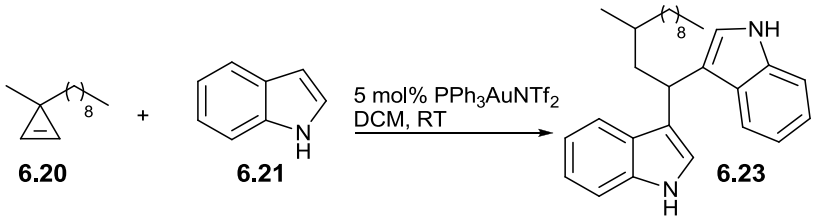
It has been shown that indoles can undergo nucleophilic attack on activated π-systems to form carbon-carbon bonds.[9] After observing good reactivity of alcohols towards gold(I) activated cyclopropenes we wanted to test the scope of nucleophiles and see if we could extend this to indoles.

We hypothesised that the reaction may produce similar products to that observed for the addition of alcohols where the nucleophile attacks at the C3 position to give **6.22** (Scheme 6). However the resulting structure was confirmed to be the addition of two indole species bonded to the C1 carbon to give the *bis*(indolyl) alkane **6.23** (Scheme 6).



Scheme 6 Bis(indolyl) Alkane Observed as Major Product

This chapter describes our observations as we attempted to optimise the reaction. We began by increasing the equivalents of indole (Table 1). One equivalent of indole (Entry 1) gave a moderate yield (62%) however there was very little difference when the amount of indole was increased from two equivalents (53%) to 6 equivalents (51%, Entries 2 and 3). This suggests that the reaction performs best with an excess of cyclopropene, which is not an ideal scenario being that the indole is a far cheaper material and hence for the rest of this study two equivalents of indole were used.

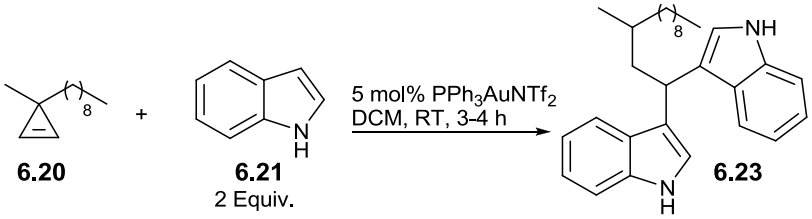


Entry	Equivalents of Indole **6.21**	Yield (%)
1	1[a]	62
2	2[b]	53
3	6[c]	51

[a] 0.14 M, 5 h. [b] 0.14 M, 2 h. [c] 0.37M, 1 h.

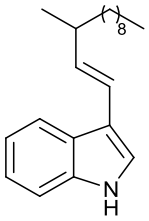
Table 1 Indole Equivalents Screen

In an effort to improve the reaction, a short solvent screen was carried out (Table 2). The reaction with THF (Entry 1) as a solvent produced a complex mixture of products, while the reaction in toluene (Entry 2) gave a comparatively clean reaction with the *bis*(indolyl) alkane **6.23** as the major product (52%). When acetonitrile is used (Entry 3) the isolation of the product **6.23** was difficult resulting in an inaccurate yield (<30%). However, analysis of the crude ^{1}H NMR shows that vinylindole **6.24** (Figure 1) is the major product (0.2:1/**6.23**:**6.24**) when acetonitrile is the solvent.



Entry	Solvent	Yield of **6.23** (%)	Comment
1	THF	25	Complex Mixture
2	Toluene	52	*Bis*(indolyl) alkane is major product
3	MeCN	<30	Vinylindole is major product (crude ^{1}H NMR)

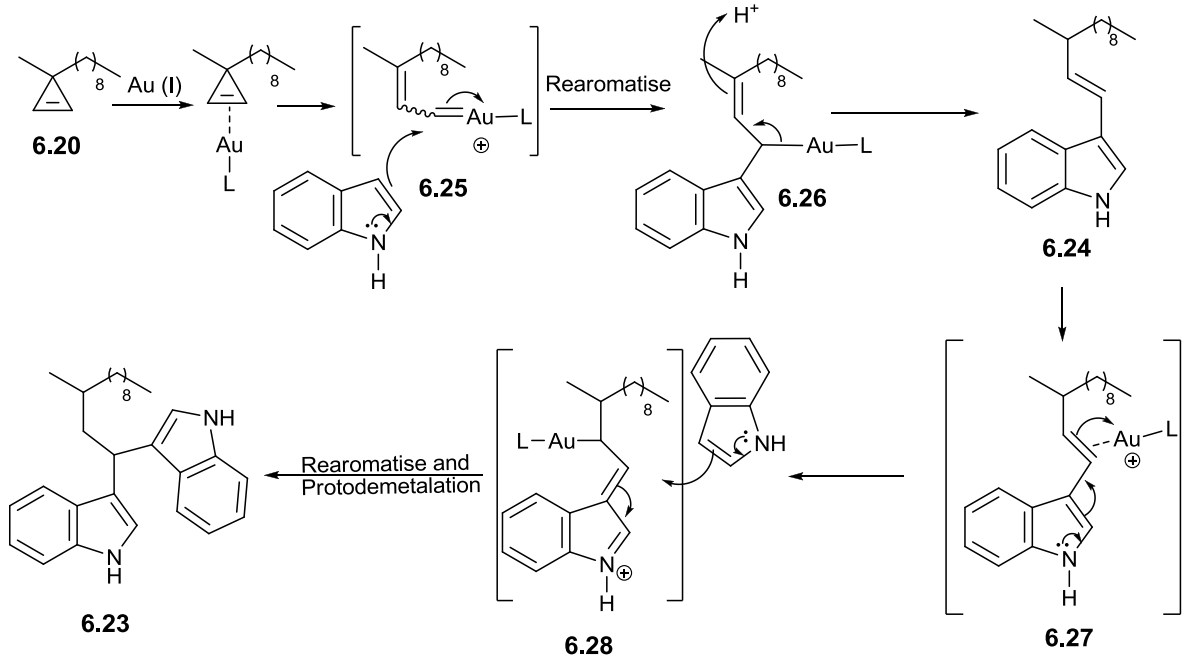
Table 2 Solvent Screen



6.24

Figure 1 Vinylindole

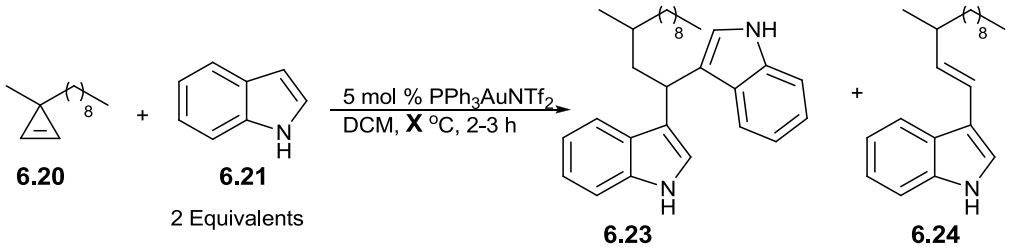
We hypothesise that attack of indole to the intermediate **6.25** forms vinlyindole **6.24** (Scheme 7). Activation of the intermediate vinyl species (**6.27**) and addition of another indole to intermediate **6.28** forms the product *bis*(indolyl) alkane (Scheme 7). However it appears that when a polar aprotic solvent is used (acetonitrile) it drastically slows the second addition of indole.



Scheme 7 Proposed Mechanism

Variations in temperature often affect the reaction mechanism and so a temperature screen was carried out and the crude products analysed by ^{1}H NMR to see if we could form the *bis*(indolyl) alkane **6.23** more selectively (Table 3). Refluxing the reaction (Entry 1) appears to produce the *bis*(indolyl) alkane **6.23**, however an unknown by-product is also present. As we lower the temperature we start to observe the vinylindole

6.24 (Figure 1, Entries 2, 3 and 4). At 0 ^{o}C (Entry 2) we start to observe the vinylindole **6.24** and as the energy in the system drops we see less of the "double addition" product **6.23**. When the reaction is carried out at – 40 ^{o}C (Entry 4) the reactivation of the vinyl bond is so sluggish that the second indole is unable to attack and the product **6.24** is favoured.

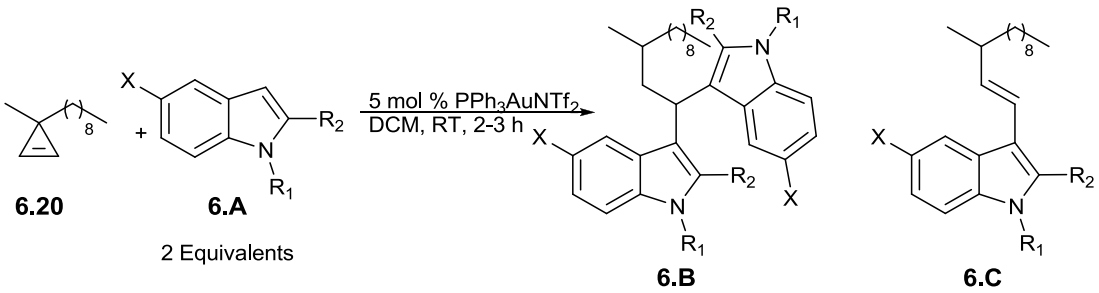


Entry	Temperature **X**/^{o}C	Observed product (ratio **6.23**/**6.24**)[a]
1	Reflux	**6.23**/**6.24** (1:0)
2	0	**6.23**/**6.24** (1:0.3)
3	-15	**6.23**/**6.24** (0.7:1)
4	-40	**6.23**/**6.24** (0.3:1)

[a]Determined through ^{1}H NMR analysis of the crude mixture

Table 3 Temperature Screen

Next, we decided to examine the scope of the indole nucleophile (Table 4). When the substituents in the 5 position on the indole is either electron donating (Entry 1) or electron withdrawing (Entry 2) it has little effect on the reaction. When the properties on the nitrogen were altered, e.g. 1-methyl indole in entry 3, the reactivity switches. However when the indole is 1,2-dimethyl indole, this renders the nucleophile unreactive under these conditions and the reaction does not occur (Entry 4).

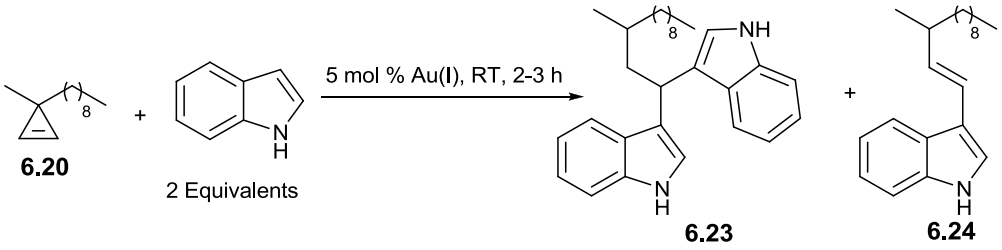


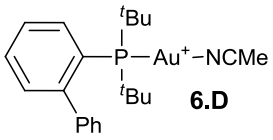
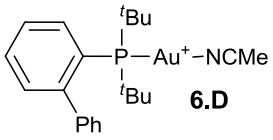
Entry	X	R_1	R_2	Product Yield	(ratio **6.B**/**6.C**)
1	OMe	H	H	**6.25** (46%)	>99:1
2	F	H	H	**6.26** (46%)	98:2
3	H	Me	H	**6.27** (6%)[a]	0.4:1
4	H	Me	Me	0 %	0 %

[a] Isolated yield; Extremely difficult purification.

Table 4 Indole Screen

In previous chapters we have observed that varying the gold(I) catalyst can have profound effects on the reaction and hence the product, this catalyst effect is also seen here (Table 5). When the catalyst is changed to the cationic catalyst **6.D** in DCM (Entry 3), a complete switch in the product is observed from **6.23** to **6.24** (3:97). Catalyst **6.D** favours the formation of product **6.24** (Entry 3), however the non-chlorinated solvent, toluene, (Entry 2) forms **6.23** preferentially with PPh_3AuNTf_2. When catalyst **6.D** is used in conjunction with toluene neither product **6.23** nor **6.24** is favoured and a 1:1 mixture is observed.

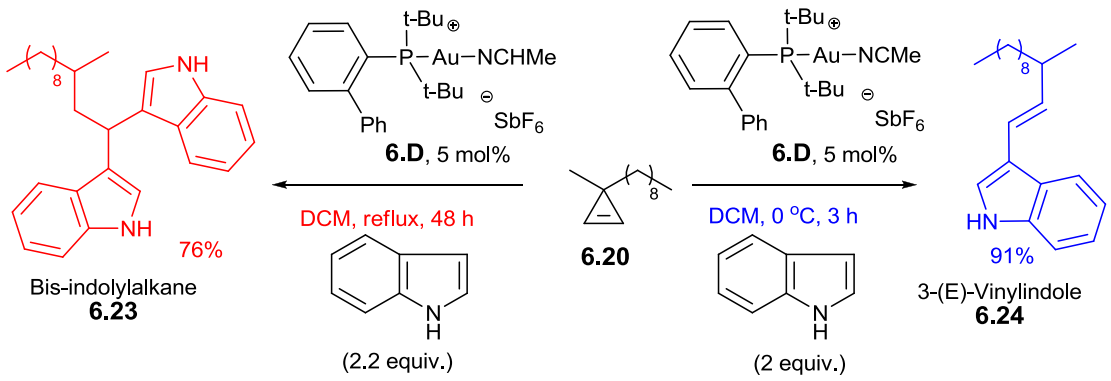


Entry	Solvent	Catalyst	Product	Yield	(ratio **6.23**/**6.24**)
1	DCM	PPh_3AuNTf_2	**6.23**	53 %	80:20
2	Toluene	PPh_3AuNTf_2	**6.23**	52 %	96:4
3	DCM	 **6.D**	**6.24**	42 %	3:97
4	Toluene	 **6.D**	**6.23/6.24**	n/a[a]	50:50

[a] Products not isolated

Table 5 Catalyst Screen

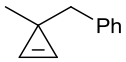
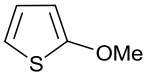
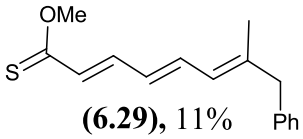
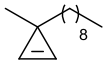
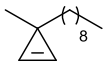
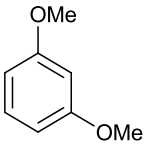
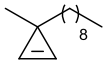
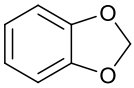
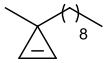
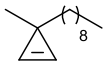
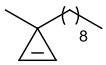
The preliminary results presented in this chapter have since been expanded and optimised by other members of the Lee Group. After extensive screening, the following conditions were found to be optimal (Scheme 8).[15]



Scheme 8 Optimised Reaction

6.3 Miscellaneous Nucleophiles

Regrettably some nucleophiles did not perform as well as others (alcohols, furans and indoles) in gold(I) catalysed reactions with cyclopropenes (Table 6). When 2-methoxythiophene (Entry 1) was reacted with the cyclopropene **6.28** it produced a complex mixture of products but an inseparable mixture of two *E/Z* trienethioester isomers (1.6/1) were isolated, however, the resulting yield was low (11%). Pyrrole (Entry 2) proved to be perhaps too reactive or the product was unstable as a complex mixture of products was observed. The electron rich aromatic nucleophiles in Entry 3 and Entry 4 were not nucleophilic enough as they remained largely unreacted. Finally when the nucleophiles are protected amines or TBAF (Entries 5, 6 and 7) the reaction also does not proceed. The cause of the lack of reactivity may be due to the nucleophile binding to the catalyst which inhibits the activation of the cyclopropene.

Entry	Cyclopropene	Nucleophile	Catalyst	Product / Observation[a]
1	 **(6.28)**		Catalyst **6.D**	 **(6.29),** 11%
2	 **(6.20)**		PPh_3AuNTf_2	Complex Mixture of Products
3	 **(6.20)**		PPh_3AuNTf_2	Products not observed, mainly unreacted nucleophile
4	 **(6.20)**		PPh_3AuNTf_2	Products not observed, mainly unreacted nucleophile
5	 **(6.20)**	H_2NBoc	PPh_3AuNTf_2	Products not observed, mainly unreacted nucleophile
6	 **(6.20)**	H_2NTs	PPh_3AuNTf_2	No Reaction
7	 **(6.20)**	TBAF	PPh_3AuNTf_2	No Reaction[b]

[a] Observation made by ^1H NMR analysis of crude mixture. [b] Monitored by TLC

Table 6 Unsuccessful Nucleophilic Additions to Cyclopropenes

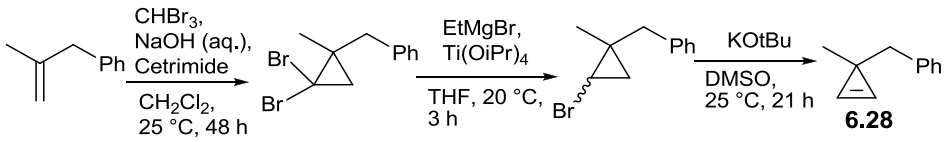
6.4 Experimental

General Experimental

^{1}H NMR spectra were recorded on Bruker AC200, AV 300, DPX 400 and AV 400 spectrometers at 200, 300 and 400 MHz respectively and referenced to residual solvent. ^{13}C NMR spectrum were recorded using the same spectrometers at 50, 75 and 100 MHz respectively. Chemical shifts (δ in ppm) were referenced to tetramethylsilane (TMS) or to residual solvent peaks ($CDCl_3$ at δ 7.26). *J* values are given in Hz and s, d, dd, t, q and m abbreviations correspond to singlet, doublet, doublet of doublet, triplet, quartet and multiplet. Mass spectra were obtained at the EPSRC National Mass Spectrometry Service Centre in Swansea. Infrared spectra were obtained on Perkin-Elmer Spectrum 100 FT-IR Universal ATR Sampling Accessory, deposited neat or as a chloroform solution to a diamond/ZnSe plate.

Flash column chromatography was carried out using Matrix silica gel 60 from Fisher Chemicals and TLC was performed using Merck silica gel 60 F254 precoated sheets and visualised by UV (254 nm) or stained by the use of aqueous acidic $KMnO_4$ or aqueous acidic ammonium molybdate as appropriate. Reactions that were kept at 0 ^{o}C overnight used a jacketed reaction vessel attached to a Julabo FP40 Bohdan mini block temperature controlled recirculator with a Julabo temperature regulator. Tetrahydrofuran was dried by distillation from sodium – benzophenone under nitrogen, dimethylsulfoxide, acetonitrile and toluene were dried over calcium hydride. Petrol ether refers to petroleum ether (40 – 60 %). Dichloromethane (DCM) was purchased from Fisher and used without further purification. All indole substrates were purchased from Aldrich and used without further purification. The gold(I)-catalysed reactions were carried out without the need for dry solvents or inert atmosphere, unless stated otherwise. All other reactions were carried out under an atmosphere of N_2 unless otherwise stated.

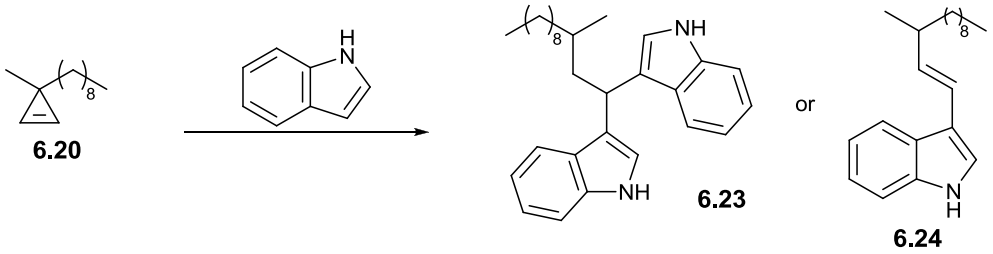
Cyclopropenes **6.20 and 6.28** were synthesised following procedures reported in earlier chapters (Scheme 9).



Scheme 9 General Cyclopropene Synthesis

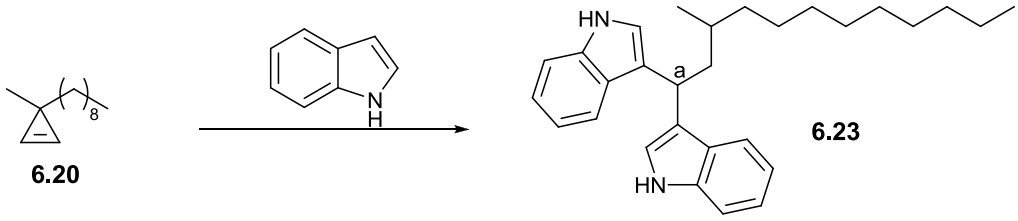
***Bis*-indolylalkane general synthetic procedure:**

The general procedure described below was used to carry out the reactions described in this chapter, the details of each reaction is shown in **Tables 1** to **5** or stated in the discussions regarding those tables.



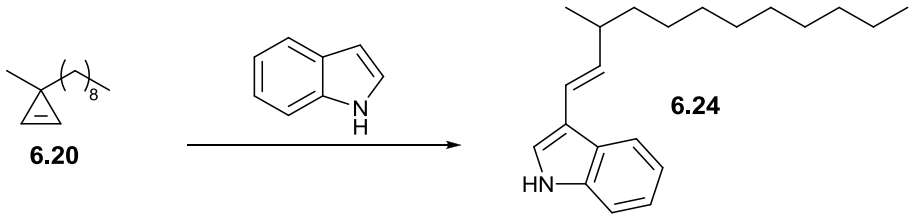
To a solution of cyclopropene (1 equiv.) and indole (2.2 equiv.) in a solvent (0.14 M), 5 mol% of catalyst was added. The solution was allowed to stir for described time and temperature. The reaction was allowed to cool to room temperature, concentrated under reduced pressure and purified by flash column chromatography.

6.23, 3,3'-(3-Methyldodecane-1,1-diyl)*bis*(1H-indole)



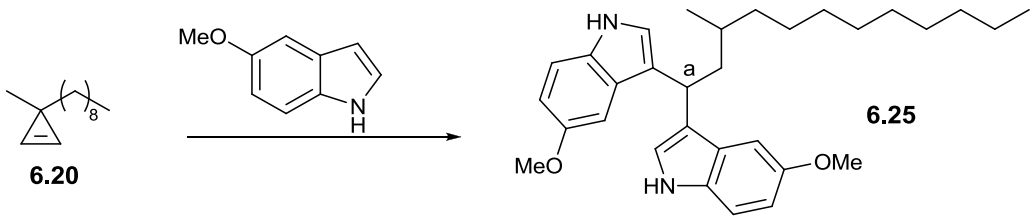
Purified using a gradient eluent system of 5:1 → 2:1 hexane:diethyl ether. Pale yellow oil obtained. R_f 0.18 (2:1 hexane:diethyl ether); ν_{max}/cm^{-1} 3413 s (N-H), 2954 m 2924 s 2853 s (C-H) 1456 s (Aromatic C=C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, H, N<u>H</u>), 7.84 (s, H, N<u>H</u>), 7.72 – 7.57 (m, 2H, Ar-H), 7.33 (dd, *J* = 8.0, 5.5 Hz, 2H, Ar-H), 7.17 (t, *J* = 7.3 Hz, 2H, Ar-H), 7.06 (m, 3H, Ar-H), 6.91 (s, 1H, Ar-H), 4.70 – 4.59 (m, 1H, <u>H$_a$</u>), 2.33 – 1.94 (m, 2H, CHC<u>H$_2$</u>CH), 1.67 – 1.10 (m, 17H, long chain alkyl H), 1.00 (d, *J* = 6.6 Hz, 3H, CHC<u>H$_3$</u>), 0.90 (t, *J* = 6.8 Hz, 3H, CH_2C<u>H$_3$</u>); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.8 (2xC), 127.4 (C), 127.2 (C), 121.9 (2xCH), 121.6 (CH), 121.5 (CH), 121.3 (C), 120.3 (C_t), 119.9 (CH), 119.7 (CH), 119.2 (2xCH), 111.2 (2xCH), 43.5 (CH_2), 37.5 (CH_2), 32.1 (CH_2), 31.6 (CH), 30.8 (CH), 30.2 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 27.1 (CH_2), 22.9 (CH_2), 20.1 (CH_3), 14.3 (CH_3); Found (APCI) $[M]^+$ 414.3018, $C_{29}H_{38}N_2$ requires 414.3030.

6.24, *(E)*-3-(3-Methyldodec-1-enyl)-1H-indole



Purified using an eluent system of neat hexane → 5:1 hexane:diethyl ether. R_f 0.20 (5:1 hexane:diethyl ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (s, 1H, NH), 7.87 (d, J = 7.9 Hz, 1H, Ar-H), 7.36 (dd, J = 6.9, 1.2 Hz, 1H, Ar-H), 7.25 – 7.12 (m, 3H, Ar-H), 6.52 (d, J = 16.1 Hz, 1H, CH=CHC), 6.08 (dd, J = 16.1, 7.9 Hz, 1H, CHCH=CH), 2.29 (m, 1H, CH_3CHCH_2), 1.49 – 1.16 (m, 16H, alkyl CH_2), 1.11 (d, J = 6.7 Hz, 3H, $CHCH_3$), 0.87 (t, J = 6.7 Hz, 3H, CH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.9 (C), 134.7 (CH), 125.9 (C), 122.5 (CH), 122.2 (CH), 120.3 (CH), 120.2 (CH), 120.1 (CH), 115.9 (C), 111.3 (CH), 38.0 (CH), 37.7 (CH_2), 32.1 (CH_2), 30.0 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 27.7 (CH_2), 22.9 (CH_2), 21.2 (CH_3), 14.3 (CH_3). Found (ESI) [M+H]+ 298.2526, $C_{21}H_{32}N$ requires 298.2529.

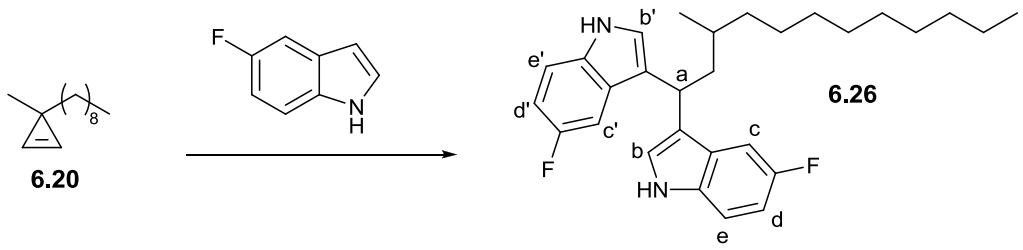
3,3'-(3-Methyldodecane-1,1-diyl)*bis*(5-methoxy-1H-indole)



Purified using a gradient eluent system of 10:1 → 2:1 hexane:diethyl ether. Colourless oil obtained.

R_f 0.12 (2:1 hexane:diethyl ether); ν_{max}/cm^{-1} 3413 s (N-H), 2922 s 2852 s (C-H), 1624 s 1581 s 1482 s 1454 s 1438 s (Aromatic C=C), 1208 s (C-O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (s, H, NH), 7.75 (s, H, NH), 7.22 (d, *J* = 8.8 Hz, H, Ar-H), 7.21 (d, *J* = 8.8 Hz, H, Ar-H), 7.10 (d, *J* = 2.4 Hz, H, Ar-H), 7.08 (d, *J* = 2.4 Hz, H, Ar-H), 7.00 (d, *J* = 2.4 Hz, 1H, Ar-H), 6.90 (d, *J* = 2.4 Hz, 1H, Ar-H), 6.83 (dd, *J* = 8.8, 2.4 Hz, 2H, Ar-H), 4.52 (dd, *J* = 8.8, 6.4 Hz, 1H, H_a), 3.81 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 2.31 – 1.92 (m, 2H, $CHCH_2CH$), 1.62 – 1.13 (m, 17H, long alkyl chain H), 1.01 (d, *J* = 6.5 Hz, 3H, $CHCH_3$), 0.90 (t, *J* = 6.8 Hz, 3H, CH_2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.7 (2xC), 132.0 (C), 131.9 (C), 127.8 (C), 127.6 (C), 122.4 (CH), 122.4 (CH), 120.9 (C), 119.8 (C), 111.8 (CH), 111.8 (CH), 111.6 (2xCH), 102.0 (CH), 102.0 (CH), 56.0 ($2xCH_3$), 43.1 (CH_2), 37.6 (CH_2), 32.1 (CH_2), 31.6 (CH), 30.8 (CH), 30.2 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 27.1 (CH_2), 22.8 (CH_2), 20.2 (CH_3), 14.3 (CH_3); Found (APCI) $[M]^+$ 474.3236, $C_{31}H_{42}N_2O_2$ requires 474.3241.

6.26, 3,3'-(3-Methyldodecane-1,1-diyl)*bis*(5-fluoro-1H-indole)



Purified using an eluent system of 2:1 hexane:diethyl ether. Pale yellow oil obtained. R_f 0.15 (2:1 hexane:diethyl ether); ν_{max}/cm^{-1} 3473 m 3429 m (N-H), 2954 m 2923 s 2853 s (C-H), 1627 m 1580 m (Ar C=C) 1167 s (C-F); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (s, 1H, N<u>H</u>), 7.89 (s, 1H, N<u>H</u>), 7.19 – 7.05 (m, 4H, $H_{c/c'}/H_{e/e'}$), 7.02 (d, *J* = 2.4 Hz, 1H, $H_b/H_{b'}$), 6.93 (d, *J* = 2.3 Hz, 1H, $H_b/H_{b'}$), 6.80 (app. td, *J* = 9.1, 2.6 Hz, 2H, $H_{d/d'}$), 4.37 (dd, *J* = 8.9, 6.5 Hz, 1H, H_a), 2.19 – 1.78 (m, 2H, CHC<u>H$_2$</u>CH), 1.55 – 0.97 (m, 17H, long alkyl chain H), 0.89 (d, *J* = 6.5 Hz, 3H, CHC<u>H$_3$</u>), 0.80 (t, *J* = 6.8 Hz, 3H, CH_2C<u>H$_3$</u>); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.4 (d, *J* = 233.8 Hz, 2xC-F), 133.15 (2xC), 127.4 (d, *J* = 9.4 Hz, C), 127.2 (d, *J* = 9.4 Hz, C), 123.2 (CH), 123.1 (CH), 120.7 (d, *J* = 4.8 Hz, C), 119.7 (d, *J* = 4.8 Hz, C), 111.7 (d, *J* = 9.7 Hz, 2xCH), 110.4 (CH), 110.0 (CH), 104.6 (d, *J* = 23.5 Hz, CH), 104.4 (d, *J* = 23.5 Hz, CH), 42.7 (CH_2), 37.4 (CH_2), 32.1 (CH_2), 31.8 (CH), 30.7 (CH), 30.1 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 27.0 (CH_2), 22.8 (CH_2), 20.0 (CH_3), 14.3 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ -124.9 (td, *J* = 9.6, 4.4 Hz); Found (APCI) $[M]^+$ 450.2829, $C_{29}H_{36}F_2N_2$ requires 450.2841.

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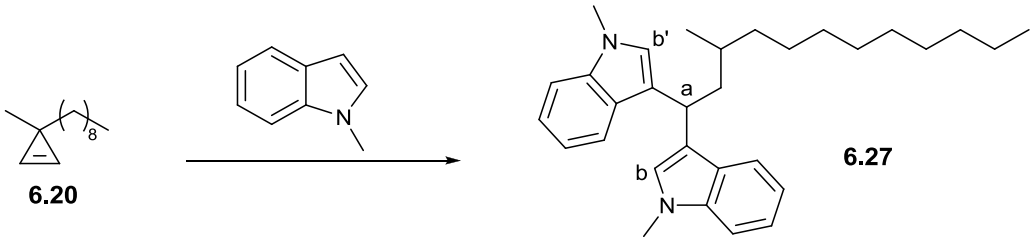
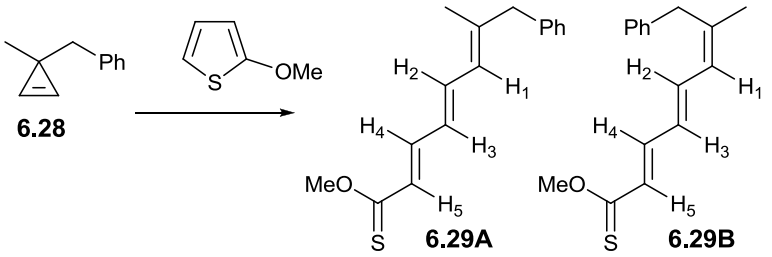
6.27, 3,3'-(3-Methyldodecane-1,1-diyl)*bis*(1-methyl-1H-indole)



Purified using a gradient eluent system of 10:1 → 4:1 hexane:diethyl ether. Yellow oil obtained.

R_f 0.52 (2:1 hexane:diethyl ether); ν_{max}/cm^{-1} 2953 s 2923 s 2853 s (C-H) 1615 w 1548 w (C=C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 – 7.50 (m, 2H, Ar-H), 7.21 – 7.15 (m, 2H, Ar-H), 7.15 – 7.05 (m, 2H, Ar-H), 6.96 (m, 2H, Ar-H), 6.89 (s, 1H, H_b), 6.79 (s, 1H, $H_{b'}$), 4.53 (dd, *J* = 8.9, 6.5 Hz, 1H, H_a), 3.64 (s, 3H, NC$\underline{H}_3$), 3.60 (s, 3H, NC$\underline{H}_3$), 2.23 (ddd, *J* = 14.2, 8.9, 5.4 Hz, 1H, CHC$\underline{H}$HCH), 2.06 – 1.92 (m, 1H, CHCH$\underline{H}$CH), 1.56 – 1.01 (m, 17H, long alkyl chain), 0.90 (d, *J* = 6.5 Hz, 3H, CHC$\underline{H}_3$), 0.80 (t, *J* = 6.8 Hz, 3H, $CH_2C\underline{H}_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.4 (2xC), 127.8 (C), 127.5(C), 126.4 (CH), 126.3 (CH), 121.4 (2xCH), 120.0 (C), 119.9(CH), 119.7 (CH), 118.9 (C), 118.5 (2xCH), 109.2 (CH), 109.2 (CH), 44.0 (CH_2), 37.5 (CH_2), 32.8(CH_3), 32.7 (CH_3), 32.1 (CH_2), 31.4 (CH), 30.8 (CH), 30.2 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 27.0 (CH_2), 22.9 (CH_2), 20.1 (CH_3), 14.3 (CH_3). Found (APCI) $[M+H]^+$ 443.3418, $C_{31}H_{42}N_2$ requires 443.3421.

6.29A, (2*E*,4*E*,6*E*)-O-methyl 7-methyl-8-phenylocta-2,4,6-trienethioate, 6.29B (2*E*,4*E*,6*Z*)-O-methyl 7-methyl-8-phenylocta-2,4,6-trienethioate



Catalyst **6.D** (10.8 mg, 1.4 x 10^{-5} mol) was added to a solution of ((1-methylcycloallyl)methyl)benzene **6.28** (40.3 mg, 0.28 mmol) and 2-methoxythiophene (42.0 μL, 0.42 mmol) in dichloroethane (0.5 mL). The reaction mixture was allowed to stir for 24 h at 40 °C. A crystal of iodine was added and the reaction allowed to stir for a further 6 h. The reaction mixture was filtered through a plug of silica and washed with diethyl ether (1% triethylamine). The solvent was evaporated and the residue was purified by flash column chromatography (20:1 n-pentane/diethyl ether, 1% triethylamine) to yield an inseparable mixture (2*E*,4*E*,6*E*)-O-methyl 7-methyl-8-phenylocta-2,4,6-trienethioate **6.29A,** (2*E*,4*E*,6*Z*)-O-methyl 7-methyl-8-phenylocta-2,4,6-trienethioate **6.29B** (8 mg, 0.031 mmol, 11%) as a yellow oil.

R_f 0.70 (20:1 hexane:diethyl ether); ν_{max}/cm^{-1} 3027 w (Ar C-H), 2938 m (C-H) 1596 s (C=C), 1494 w, 1439 m (Ar C=C), 1232 s (C-O), 1113 s (C=S); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (1H, dd, *J* = 14.3, 11.3, H-4 **6.29B**), 7.47 (1H, dd, *J* = 14.7, 11.5, H-4 **6.29A**), 7.38-7.17 (10H, m, Ar-H **6.29A** + **6.29B**), 7.08 (1H, dd, *J* = 14.3, 11.3, H-2 **6.29B**), 6.93 (1H, dd, *J* = 14.7, 11.5, H-2 **6.29A**), 6.51 (1H, d, *J* = 14.3, H-5 **6.29B**), 6,48 (1H, d, *J* = 14.7, H-5 **6.29A**), 6.33 (1H, dd, *J* = 14.3, 11.3, H-3 **6.29B**), 6.28 (1H, dd, *J* = 14.7, 11.5, H-3 **6.29A**), 6.18 (1H, d, *J* = 11.3, H-1 **6.29B**), 6.07 (1H, d, *J* = 11.5, H-1 **6.29A**), 4.17 (3H, s, OC$\underline{H}_3$ **6.29B**), 4.17 (3H, s, OC$\underline{H}_3$ **6.29A**), 3.59 (2H, s, CC$\underline{H}_2$ **6.29B**), 3.45 (2H, s, CC$\underline{H}_2$ **6.29A**), 1.82 (3H, s, CC$\underline{H}_3$ **6.29A**), 1.81 (3H, s, CC$\underline{H}_3$ **6.29B**); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.0 (C=S), 211.0 (C=S), 144.7 (C), 144.2 (C), 142.2 (C), 142.2 (C), 138.8 (2xCH), 138.3 (CH), 138.0 (CH), 130.8 (CH), 130.6 (CH), 129.4 (CH), 129.3 (CH), 129.0 (CH), 128.9 (CH), 128.5 (CH), 128.4 (CH), 127.0 (CH), 126.6 (CH), 126.4 (CH), 126.3 (CH), 58.3 (2 x CH_3), 46.6 (CH_2), 38.7 (CH_2), 24.2 (CH_3), 17.2 (CH_3).

6.5 References

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