

REGIOCHEMISTRY AND STEREOCHEMISTRY OF THE COUPLING OF  
PHENYLTHIOPENTADIENYL METALS WITH C-ELECTROPHILES

S. Florio\*, L. Ronzini, R. Sgarra

Laboratorio di Chimica Organica, Dipartimento di Biologia,  
Università di Lecce, Via Monteroni, 73100 Lecce, Italy.

**Abstract.** Phenylthiopentadienyl anions 2 couple with MeI and cyclopentanone either regioselectively and stereoselectively to give 3a and 4a respectively. With aldehydes the regiochemistry and stereochemistry is affected by the counterion of 2, furnishing  $\alpha$ -,  $\gamma$ - or  $\epsilon$ -regioisomeric alcohols.

While thioallylic anions represent as an increasingly important tool in synthetic organic chemistry,<sup>1</sup> heteroatom stabilized dienylanions have been much less explored notwithstanding the potential of such reagents as precursors of functionalized dienes, which are of great interest either as such and in Diels-Alder cyclization.

Specifically, the regiochemistry and the stereochemistry of the coupling of phenylthiopentadienyl anions with C-electrophiles have been very little studied.<sup>2</sup>

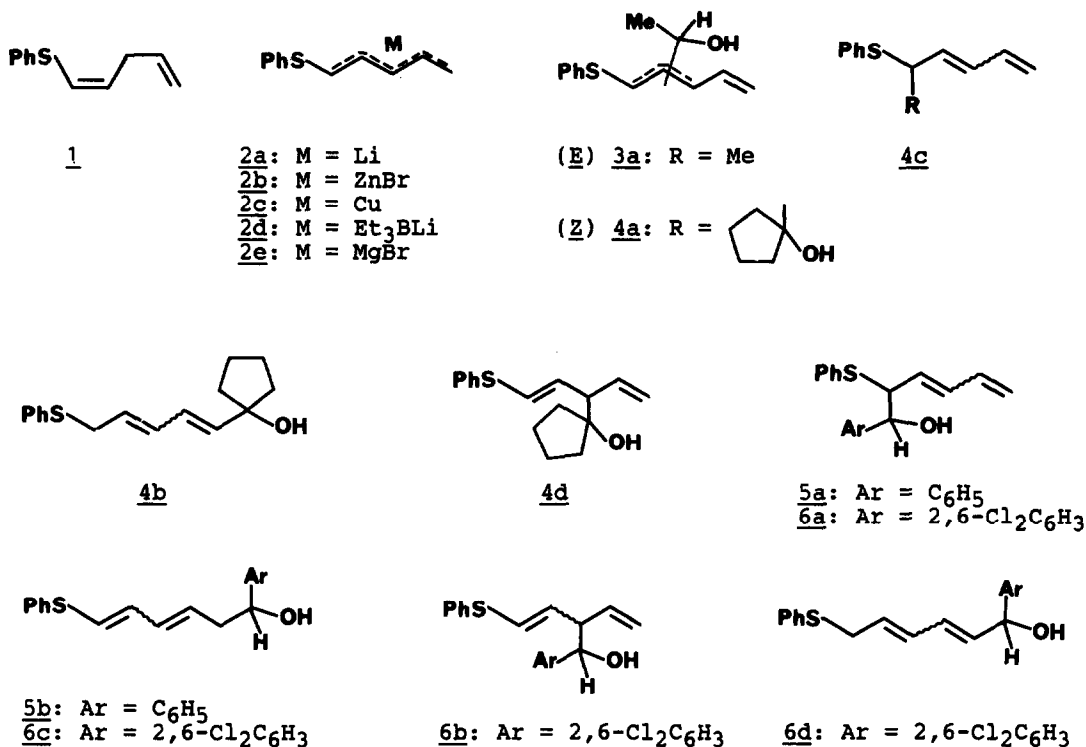
As part of our researches<sup>3</sup> regarding the C-C bond forming reaction of heteroarylmethyl metal compounds, we have undertaken a detailed investigation of the coupling reaction of phenylthiopentadienyl anions 2 with C-electrophiles paying particular attention to the involved regiochemistry and stereochemistry.

Phenylthiopentadienyllithium 2a was readily prepared through lithiation (BuLi, THF, -78°C) of (2)-phenyl-pentadienyl sulfide 1 which in turn was synthesized by Nickel-complex activated cross-coupling of (2)-1-bromo-2-phenylthio-ethene with allylmagnesium bromide.<sup>4</sup>

Treatment of phenylthiopentadienyllithium 2a with methyl iodide in THF at -78°C and subsequent quenching with aqueous sat NH<sub>4</sub>Cl furnished the (E)- $\alpha$ -regioisomer 3a in a regioselective and stereoselective fashion.

Completely  $\alpha$ -regioselective was also the reaction of 2a with cyclopentanone leading to the alcohol 4a.<sup>2</sup> This is noteworthy as phenylthioallyllithium is known to react with ketones at the  $\alpha$ - and  $\gamma$ -position<sup>5</sup> and alkylthioallyllithiums mainly at the  $\gamma$ -position.<sup>6</sup> Moreover, this reaction turned out to be also stereoselective as the alcohol 4a adopted a (Z) geometry.<sup>7</sup>

Similarly, cyclopentanone reacted with phenylthiopentadienyl copper 2c<sup>8</sup>



and phenylthiopentadienyltriethyl lithium borate<sup>8</sup>  $\underline{2d}$  in a regioselective and stereoselective manner leading to the alcohol  $\underline{4a}$  (Z). (See table) It must be noticed that alcohol (Z)- $\underline{4a}$  showed a propensity to undergo a 1,5-isomerization to give  $\underline{4b}$ .

Surprisingly, the reaction of the cyclopentanone with phenylthiopentadienylzinc bromide<sup>8</sup>  $\underline{2b}$  afforded the alcohol  $\underline{4c}$  as the major product together with the  $\gamma$ -regioisomeric alcohol (E)- $\underline{4d}$ . It is reasonable to think that compound  $\underline{4c}$  comes from a coupling reaction of  $\underline{2b}$  with acetaldehyde that likely arises from the ring cleavage of THF.<sup>9</sup>

The regiochemistry and the stereochemistry of the coupling reaction of the phenylthiopentadienyl metals  $\underline{2}$  with aldehydes turned out to be dependent either upon the counterion of  $\underline{2}$  and the aldehyde.

Indeed, the reaction of  $\underline{2a}$  with benzaldehyde occurred with very poor regioselectivity affording an almost 1:1 mixture of the  $\alpha$ - and  $\epsilon$ -regioisomers  $\underline{5a}$  and  $\underline{5b}$ .

The reaction of 2,6-dichlorobenzaldehyde with  $\underline{2a}$  was still not regioselective, but afforded the  $\gamma$ - and  $\epsilon$ -regioisomers  $\underline{6b}$  and  $\underline{6c}$ .

The reaction of 2,6-dichlorobenzaldehyde with phenylthiopentadienyl-

zinc bromide 2b was highly  $\gamma$ -regioselective leading to the regioisomeric alcohols 6a of exclusive (E)-geometry and 6b (E + Z).

No reaction took place when 2,6-dichlorobenzaldehyde was treated with phenylthiopentadienylmagnesium bromide<sup>8</sup> 2e, but a satisfactory  $\alpha$ -regioselective coupling occurred with phenylthiopentadienyl copper 2c furnishing the alcohols 6a (E) and 6b (E + Z).

Very poor regioselectivity was observed in the case of the reaction of 2,6-dichlorobenzaldehyde with phenylthiopentadienyltriethyl lithium borate 2d leading to the  $\alpha$ -,  $\gamma$ - and  $\epsilon$ -regioisomers 6a (Z), 6b (Z + E) and 6c. This reaction was highly stereoselective in the  $\alpha$ -regioisomer, as it was of (Z) geometry exclusively. (Z)-6a appeared to be very prone to give 1,5-isomerization yielding (Z,Z)-6d.

In conclusion, the present paper shows that the coupling of phenylthiopentadienyl anions 2 is  $\alpha$ -regioselective with cyclopentanone whatever the counterion. The reaction is also stereoselective as only the Z-isomers form.<sup>10</sup> In contrast, the coupling of 2 with aldehydes can be made regioselective depending upon the counterion.

Our results are, in our opinion, of considerable importance from the synthetic standpoint as we can prepare phenylthiopentadienyl carbinols of a given geometry and stereochemistry of potential application in synthetic organic chemistry.

**Acknowledgements:** we thank Italian Consiglio Nazionale delle Ricerche (CNR) and Ministero Pubblica Istruzione (Rome) for financial support of this research.

Table. Reactions of pentadienyl metals 2 with electrophiles in THF at  $-78^{\circ}\text{C}$

Pentadienyl metal	Electrophile	Reaction product (%)	Overall yield (%)
<u>2a</u>	MeI	( <u>E</u> )- <u>3a</u> (100)	88
<u>2a</u>	Cyclopentanone	( <u>Z</u> )- <u>4a</u> (100)	73
<u>2c</u>	"	( <u>Z</u> )- <u>4a</u> (95)	68
<u>2d</u>	"	( <u>Z</u> )- <u>4a</u> (100)	30
<u>2b</u>	"	<u>4c</u> (83)	30
		( <u>E</u> )- <u>4d</u> (17)	
<u>2a</u>	PhCHO	<u>5a</u> (45)	57
		<u>5b</u> (55)	
<u>2a</u>	2,6-dichlorobenzaldehyde	( <u>Z</u> )- <u>6b</u> (46)	67
		<u>6c</u> (54)	
<u>2b</u>	"	( <u>E</u> )- <u>6a</u> (11)	73
		( <u>E</u> + <u>Z</u> )- <u>6b</u> (89)	
<u>2c</u>	"	( <u>E</u> )- <u>6a</u> (66)	84
		( <u>Z</u> + <u>E</u> )- <u>6b</u> (34)	
<u>2d</u>	"	( <u>Z</u> )- <u>6a</u> (41)	76
		( <u>Z</u> + <u>E</u> )- <u>6b</u> (18)	
		<u>6c</u> (41)	
<u>2e</u>	"	-	-

## References

- 1) J.F.Biellman and J.B.Ducep, Org. Reaction, **27**, 1 (1982).
- 2) T.Kauffmann and K.R.Gaydoul, Tetrahedron Lett., **26**, 4071 (1985).
- 3) E.Epifani, S.Florio and G.Ingrosso, Tetrahedron Lett., **26**, 6385 (1987); Tetrahedron, **44**, 5869 (1988).
- 4) According to the procedure described for the cross-coupling of 1-bromo-2-phenylthioethene with Grignard reagents: V.Fiandanese, G.Marchese, F.Naso, and L.Ronzini, J. Chem. Soc. Perkin Trans. I, 1115 (1985).
- 5) M.R.Binns and R.K.Haines, J. Org. Chem., **46**, 3790 (1981)
- 6) P.L.Slotter and R.E.Hornish, J. Am. Chem. Soc., **95**, 4444 (1973); S.Torii, H.Tanaka and J.Tomotaki, Chem. Lett. 1541 (1974); P.Atlani, J.F.Biellman, S.Dube and J.J.Vicens, Tetrahedron Lett., 2665 (1974).
- 7) All the new compounds were characterized by IR and NMR spectroscopy. Physical data are here given: **1**:  $^1\text{H-NMR}$  (60 MHz,  $\text{CCl}_4$ , TMS),  $\delta$  7.5-7.2 (m, 5H), 6.4-5.6 (m, 3H), 5.3-4.9 (m, 2H), 3.2-2.8 (m, 2H). **3a** (E):  $^1\text{H-NMR}$  (200 MHz,  $\text{CDCl}_3$ ),  $\delta$  7.44-7.24 (m, 5H), 6.28 (dt,  $J = 10$  Hz and 17 Hz, 1H), 5.94 (dd,  $J = 10$  Hz and 15 Hz, 1H), 5.70 (dd,  $J = 7.9$  Hz and 15.1 Hz, 1H), 5.14-5.00 (m, 2H), 3.84-3.77 (m, 1H), 1.42 (d,  $J = 6.8$  Hz, 3H). This compound has been characterized as the  $\alpha$ -regioisomer and has been assigned the E configuration by  $^1\text{H-NMR}$  through a decoupling experiment. Irradiation of the proton  $\alpha$  to the phenylthio group causes the methyl group to become a singlet and the adjacent vinylic proton becomes a clear doublet with a  $J = 15.1$  Hz which suggests a E geometry around the central double bond. This is supported by the failure of **3a** to undergo 1,5-isomerisation as  $\alpha$ -regioisomers with Z configuration do (see Ref 10). **4a** (Z):  $^1\text{H-NMR}$  (60 MHz,  $\text{CDCl}_3$ , TMS),  $\delta$  7.6-7.3 (m, 5H), 6.7-5.8 (m, 3H), 5.4-4.9 (m, 2H), 3.9-3.6 (m, 1H), 2.3 (s, 1H), 2.0-1.5 (br. s, 8H). **4b**:  $^1\text{H-NMR}$  (200 MHz,  $\text{CDCl}_3$ ),  $\delta$  7.53-7.16 (m, 5H), 6.31-6.05 (m, 2H), 5.81-5.64 (m, 2H), 3.68 (d,  $J = 7.3$  Hz, 2H), 1.89-1.63 (m, 8H). **4c**:  $^1\text{H-NMR}$  (60 MHz,  $\text{CCl}_4$ , TMS),  $\delta$  7.5-7.1 (m, 5H), 6.5-5.6 (m, 3H), 5.4-4.9 (m, 2H), 3.9-3.6 (m, 1H), 3.1-2.6 (m, 1H), 2.3 (s, 1H), 1.3-1.0 (m, 3H). **4d** (E):  $^1\text{H-NMR}$  (200 MHz,  $\text{CDCl}_3$ ),  $\delta$  7.34-7.17 (m, 5H), 6.25 (d,  $J = 15.2$  Hz, 1H), 6.07-5.82 (m, 2H), 5.21-5.10 (m, 2H), 3.00-2.92 (m, 1H), 1.84-1.53 (m, 9H). **5a**:  $^1\text{H-NMR}$  (200 MHz,  $\text{CDCl}_3$ ),  $\delta$  7.44-7.18 (m, 10H), 6.43-5.65 (m, 3H), 5.29-5.00 (m, 2H), 4.00-3.93 (dd,  $J = 4.4$  Hz and 9 Hz, 1H), 2.93-2.68 (br. s, 1H). **5b**:  $^1\text{H-NMR}$  (200 MHz,  $\text{CDCl}_3$ ),  $\delta$  7.54-7.21 (m, 10H), 6.61-6.13 (m, 2H), 5.87-5.65 (m, 1H), 5.41-5.08 (m, 1H), 4.75-4.69 (m, 1H), 2.63-2.50 (m, 2H), 2.37 (br. s, 1H). **6a** (E):  $^1\text{H-NMR}$  (200 MHz,  $\text{CDCl}_3$ ),  $\delta$  7.38-7.14 (m, 8H), 6.10-5.92 (m, 2H), 5.66 (dd,  $J = 8.8$  Hz and 15 Hz, 1H), 5.39-5.24 (m, 3H), 3.93-3.79 (m, 1H), 2.82 (d,  $J = 8.7$  Hz, 1H). **6b** (E):  $^1\text{H-NMR}$  (200 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40-7.19 (m, 8H), 6.36 (d,  $J = 15.1$  Hz, 1H), 6.09 (dd,  $J = 7.6$  Hz and 15.1 Hz, 1H), 5.72-5.54 (m, 1H), 5.43-5.30 (m, 1H), 5.00-4.87 (m, 2H), 3.82 (ddd,  $J = 7.0$  Hz, 7.6 Hz and 8.3 Hz, 1H), 2.98-2.85 (m, 1H). **6b** (Z):  $^1\text{H-NMR}$  (200 MHz,  $\text{CDCl}_3$ ),  $\delta$  7.41-7.21 (m, 8H), 6.51 (d,  $J = 9.3$  Hz, 1H), 6.16-5.92 (m, 1H), 5.78-5.27 (m, 2H), 5.04-4.87 (m, 2H), 4.40-4.26 (m, 1H), 3.05 (d,  $J = 10.5$  Hz, 1H). **6c**:  $^1\text{H-NMR}$  (60 MHz,  $\text{CCl}_4$ , TMS),  $\delta$  7.5-7.1 (m, 8H), 6.5-5.2 (m, 5H), 3.1-2.5 (m, 3H). **6d**:  $^1\text{H-NMR}$  (60 MHz,  $\text{CCl}_4$ , TMS),  $\delta$  7.4-7.1 (m, 8H), 6.2-5.2 (m, 5H), 3.6 (d,  $J = 6.5$  Hz, 2H), 3.0-2.65 (m, 1H).
- 8) Borate **2d** was prepared by transmetalation of **2a** with  $\text{Et}_3\text{B}$ . Similarly organometals **2b**, **2c**, **2e** were prepared by transmetalation of **2a** with  $\text{ZnBr}_2$ ,  $\text{CuI}$  and  $\text{MgBr}_2$  respectively.
- 9) F.Babudri, L.Di Nunno, S.Florio and S.Valzano, Tetrahedron, **40**, 1731 (1984) and Refs therein.
- 10) It is worthy noticing that  $\alpha$ -regioisomers of E configuration do not give 1,5-isomerization while  $\alpha$ -regioisomers of Z configuration promptly undergo 1,5-isomerization probably because a cyclic transition state is allowed in this case.