

"CROSS-COUPLING" OF 2-CHLOROBENZOTHAZOLE WITH BENZOTHAZOLYLALKYL-MAGNESIUM BROMIDE: SYNTHESIS OF BIS(2-BENZOTHAZOLYL)ALKANES

Francesco Babudri,^a Saverio Florio,*^b Giovanni Ingrosso,^b
and Anna Maria Turco^b

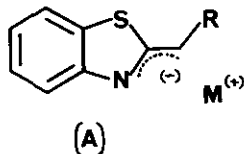
^aDipartimento di Chimica, Università, via Amendola 173, 70126 Bari, Italy

^bLaboratorio di Chimica Organica del C.d.L. in Scienze Biologiche,
Università, via Monteroni, 73100 Lecce, Italy

Abstract - Bis(2-benzothiazolyl)alkanes have been prepared via cross-coupling of 2-chlorobenzothiazole with benzothiazolylalkylmagnesium bromide.

As reported in a previous paper¹ 2-halogenobenzothiazoles are reluctant to undergo "cross-coupling" reaction with alkyl and aryl Grignard reagents. For such a reaction nickel-complex activated Grignard reagents must be used. However, we recently have also disclosed that allylic Grignard reagents give clean "cross-coupling" with some 2-heterosubstituted benzothiazoles.²

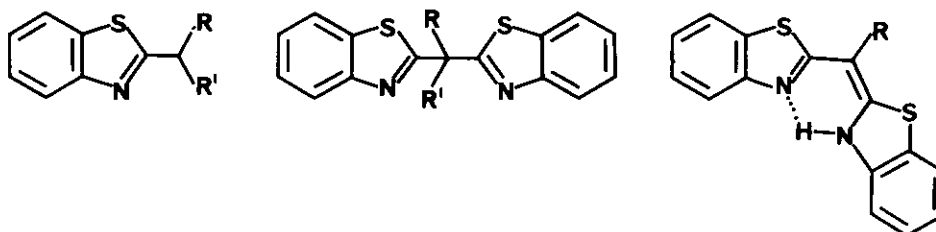
Metallated species of the type (A), easily available from 2-alkylbenzothiazoles,^{3,4} are considered to be as aza-allyl organometallic reagents. Therefore we reasoned that they could be used for the "cross-coupling" with 2-chlorobenzothiazole to give the bis(2-benzothiazolyl)alkanes 3, which are useful fluorimetric reagents⁵ and lubricating oil antioxidants.⁶ Bis(2-benzothiazolyl)alkanes are normally prepared from o-aminobenzenethiol and dicarboxylic acids in polyphosphoric acid at 150°C.⁷



Reflux the 2-methylbenzothiazole 1a (1 mole) overnight with 2-chlorobenzothiazole (1 mole) in tetrahydrofuran (THF) in the presence of n-butylmagnesium bromide (1.5 moles), and quenching with aqueous ammonium chloride afforded a mixture of some unreacted 1a and a new product that was characterised as the "cross-coupling" compound 3a. In a similar fashion 2-alkylbenzothiazoles 1b-f reacted with 2-chlorobenzothiazole and n-BuMgBr providing satisfactory yields of the bis(2-benzothiazolyl)-alkanes 3b-f.⁸ In all cases appreciable amounts of the unreacted starting 2-alkylbenzothiazole were recovered.

It appears to be likely that the formation of the above-mentioned bis(2-benzothi-

azolyalkylmagnesium bromide 2, which, as aza-allyl Grignard reagent, may add to the C-N double bond of the 2-chlorobenzothiazole to give the benzothiazolebenzothiazoline derivatives 5 via the six-membered cyclic transition state 6 according to a S_Ei' -like mechanism.⁹ Subsequent elimination would produce the cross-coupled products 3, as shown in the Scheme.



1a: R = R' = H

1b: R = H; R' = Me

1c: R = H; R' = Et

1d: R = R' = Me

1e: R = H, R' = Prⁿ

1f: R = H; R' = Ph

3a: R = R' = H

3b: R = H; R' = Me

3c: R = H; R' = Et

3d: R = R' = Me

3e: R = H; R' = Prⁿ

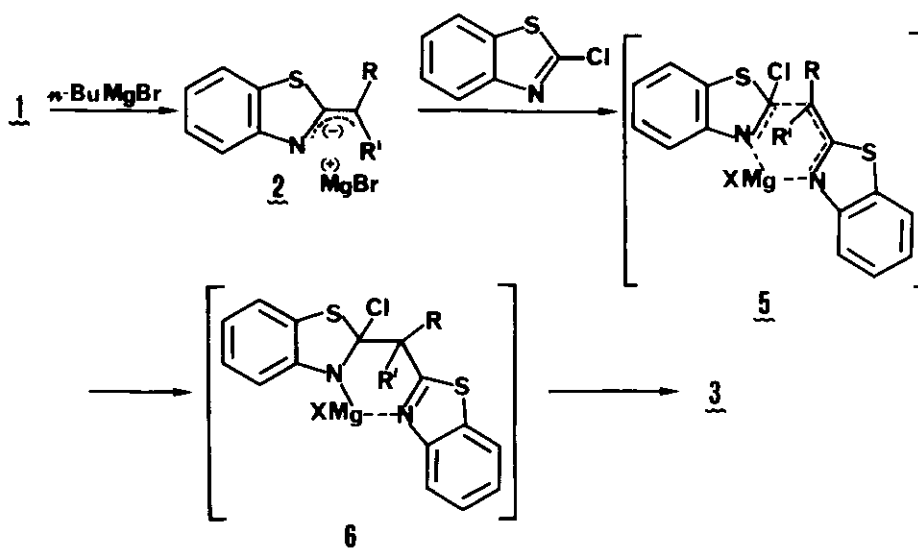
3f: R = H; R' = Ph

4a: R = Et

4b: R = Prⁿ

4c: R = Ph

SCHEME



In accordance with the mechanism is the fact mentioned above that part of the starting material 2-alkylbenzothiazole is recovered unchanged. This is likely due to the competitive reversible condensation of 2 with 1. The condensation product, as reported,⁹ slowly goes back to the starting alkylbenzothiazole 1 during the workup of the reaction mixture.

It is worthy to note that some of the bis(2-benzothiazolyl)alkanes 3 in deuterio-chloroform (CDCl_3) have been found to convert slowly to the enamine forms 4. The tautomers can be separated and isolated by column chromatography.

In summary, this paper describes a mild and new route to the useful bis(2-benzothiazolyl)alkanes 3 starting from easily or commercially available 2-alkylbenzothiazoles and 2-chlorobenzothiazole under basic conditions using $n\text{-BuMgBr}$.

EXPERIMENTAL

Reaction of 2-chlorobenzothiazole with 2-alkylbenzothiazole 1 and $n\text{-BuMgBr}$.

General procedure.

The reaction of 1a is described as an example. A THF solution of 0.87 N $n\text{-BuMgBr}$ (8.7 ml, 7.5 mmole) was added dropwise to a stirred solution containing 1a (0.75 g, 5.01 mmole) and 2-chlorobenzothiazole (0.852 mmole) in 50 ml of dry tetrahydrofuran. The reaction mixture was refluxed until the disappearance of 2-chlorobenzothiazole (~8 h) and then cooled to room temperature and quenched with an aqueous solution of ammonium chloride. Extraction with ether (3 x 30 ml), drying over MgSO_4 and removal of the solvent under reduced pressure left a solid residue that was crystallised from petroleum ether (60-80°C boiling fraction) to give the bis(2-benzothiazolyl)-methane 3a. IR, ^1H - and ^{13}C -NMR and physical data for 3a-e and 4a-e are given in ref. 10.

ACKNOWLEDGEMENTS

We thank C.N.R. and Ministero Pubblica Istruzione (Roma) for financial support.

REFERENCES

- 1) F. Babudri, S. Florio, L. Ronzini, and M. Aresta, Tetrahedron, **39**, 1515 (1983).
- 2) S. Florio, E. Epifani, and G. Ingrosso, Tetrahedron, **40**, 4527 (1984).
- 3) E.J. Corey and D.L. Boger, Tetrahedron Lett., **5** (1978).
- 4) F. Babudri, F. Ciminale, and S. Florio, Tetrahedron Lett., **25**, 2051 (1984).
- 5) R. Douglas Earl and B.K. Afghan, Anal. Chim. Acta, **44**, 115 (1969); R.R. Trenholm and D.E. Ryan, ibid., **32**, 317 (1965).
- 6) C. Rai and J.B. Braunwarth, Chem. Abstr., **62**, 1500e (1965).
- 7) J.J. D'Amico, J. Org. Chem., **26**, 3434 (1961).
- 8) The bis(2-benzothiazolyl)phenylmethane 3f was obtained as the enamine form 4c.
- 9) E.A. Hill, J. Organomet. Chem., **91**, 123 (1975).

10) All of the products gave satisfactory elemental analysis. Yields are based on the converted 2-alkylbenzothiazole.

3a: yield 55%; mp 96-97°C from ethanol (Lit. 96-97°C see ref. 9); $^1\text{H-NMR}$ (CDCl_3 , TMS int.), δ 5.0 (s, 2H), 7.4-8.3 (m, 8H); $^{13}\text{C-NMR}$ (CDCl_3), δ 38.9, 121.6, 123.1, 125.3, 126.2, 135.8, 153.1, 165.6.

3b: yield 45%; oil; $^1\text{H-NMR}$ (CDCl_3 , TMS int.), δ 2.1 (d, 3H, $J = 7$ Hz), 5.2 (q, 1H, $J = 7$ Hz), 7.2-8.5 (m, 8H).

Tautomers 3c and 4a were separated by column chromatography on silica gel using acetone/petroleum ether (1/9) as eluent.

3c: yield 28%; oil; $^1\text{H-NMR}$ (CDCl_3 , TMS int.), δ 1.1 (t, 3H), 2.1-2.8 (m, 2H), 4.85 (t, 1H), 7.2-8.1 (m, 8H); $^{13}\text{C-NMR}$ (CDCl_3), δ 12.2, 29.6, 51.5, 121.6, 123.2, 125.1, 126.1, 135.3, 151.9, 170.8.

4a: yield 28%; oil; ir (NaCl), 3490 cm^{-1} (NH); $^1\text{H-NMR}$ (CDCl_3 , TMS int.), δ 1.0 (t, 3H), 2.6 (q, 2H), 5.7 (s, 1H, exchange with D_2O), 7.2-8.1 (m, 8H); $^{13}\text{C-NMR}$ (CDCl_3), δ 6.8, 36.1, 78.9, 121.0, 122.2, 124.4, 125.2, 135.2, 151.5, 174.2.

3d: yield 48%; mp 132-134°C from ethanol; $^1\text{H-NMR}$ (CDCl_3 , TMS int.), δ 2.1, (s, 6H), 7.2-8.0 (m, 8H); $^{13}\text{C-NMR}$ (CDCl_3), δ 29.4, 47.5, 121.5, 123.2, 125.1, 126.0, 135.5, 152.9, 176.6.

Tautomers 3e and 4b were separated by column chromatography on silica gel using acetone/petroleum ether (1/4) as eluent.

3e: yield 38%; oil; $^1\text{H-NMR}$ (CDCl_3 , TMS int.), δ 1.9 (t, 3H), 1.1-1.6 (m, 2H), 2.4 (q, 2H), 4.9 (t, 1H), 7.0-8.0 (m, 8H); $^{13}\text{C-NMR}$ (CDCl_3), δ 14.0, 20.8, 38.2, 49.7, 121.6, 123.1, 125.2, 126.1, 135.3, 153.0, 171.0.

4b: yield 35%; oil; ir (NaCl), 3480 cm^{-1} (NH); $^1\text{H-NMR}$ (CDCl_3 , TMS int.), δ 0.9 (t, 3H), 1.1-1.6 (m, 2H), 2.5 (t, 2H), 5.5 (s, 1H, exchange with D_2O), 7.1-8.0 (m, 8H); $^{13}\text{C-NMR}$ (CDCl_3), δ 14.0, 16.8, 45.9, 79.6, 121.8, 123.1, 125.2, 126.1, 136.1, 152.3, 175.2.

4c: yield 65%; mp 148.5-149.5°C from ethanol; ir 3380 cm^{-1} (NH); $^1\text{H-NMR}$ (CDCl_3 , TMS int.), δ 6.3 (s, 1H, exchange with D_2O), 7.3-8.3 (m, 13H); $^{13}\text{C-NMR}$ (CDCl_3), δ 80.1, 121.8, 123.4, 126.1, 126.6, 128.5, 128.7, 136.1, 142.4, 152.2, 174.6.

Received, 24th March, 1986