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ON THE COUPLING REACTION OF 1-BENZOTHIAZOLYL-2-AZA-PENTADIENYL METALS WITH C-ELECTROPHILES

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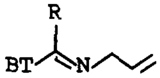
Summary: The coupling reaction of 1-benzothiazolyl-2-aza-pentadienyl metals 3 with carbonyl compounds has been investigated. The reaction of 3 with aldehydes leads to α and/or γ-regioisomeric homoallylic alcohols 8, 9 and 10 depending upon the experimental conditions. The coupling of 3 with α,β-unsaturated carbonyl compounds was highly α-1,4-regioselective. The reaction of 3b and 3e with chalcone afforded small amount of pyrrolidine 13, while the coupling of 3b and 3c with 2-cyclopentenone provided mainly pyrrolidines 18a and 18b respectively.

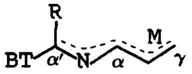
2-Aza-pentadienyl anions 1 deserve consideration for their synthetic potential as polyfunctional reactive intermediates for C-C bond forming reactions. The electronic perturbation of such anions due to the position of nitrogen along the aza-diene chain makes them usefully reactive.[1] Their electrocyclization reactions deserve exploration as a useful strategy to functionalized heterocyclic sistems.[2] 2-Azapentadienyl anions, however, have not been sufficiently studied so far. In the present paper, as part of our continuing interest in the coupling reactions of stabilized carbanions,[3] we wish to report our results concerning the reactions of benzothiazolyl substituted 2-aza-pentadienyl metals 3 with C-electrophiles. 2-Aza-diene precursors 2a-c were prepared from 2-formyl-, 2-acetyl-, and 2-benzoyl-benzothiazole respectively and allylamine in benzene/$TiCl_4$. Lithiated dienes 3a-c were obtained by lithiation of 2a-c with lithium diisopropylamide (LDA) in THF at -78°C under nitrogen atmosphere. 2-Aza-pentadienyl potassium 3d was prepared upon treatment of 2b with potassium t-butoxide and 2-aza-pentadienyl magnesium bromide 3e by transmetallation of 3b with magnesium bromide.

Attempts to trap 2-aza-pentadienyllithium 3a with C-electrophiles failed. Indeed, treatment of 3a with MeI and with benzaldehyde led to complex mixtures of polar compounds (TLC) that could not be separated and characterized. Similarly, 2-aza-dienyllithium 3b did not couple with MeI and upon quenching with an aqueous solution of NH_4Cl furnished a 1:1 mixture of aza-dienes 4a and 5, which are isomers of the precursor 2b.

1



2a R=H
2b R=Ph
2c R=Me



3a R=H; M=Li
3b R=Ph; M=Li
3c R=Me; M=Li
3d R=Ph, M=K
3e R=Ph; M=MgBr

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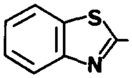
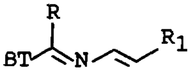
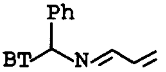




4a R=Ph; R_1=Me
4b R=R_1=Me
4c R=Ph;R_1=Et
4d R=Me;R_1=Et
4e R=R_1= Et
4f R=Me; R_1=*n*-Pr



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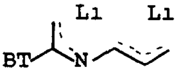
$R_3SiOOSiR_3$

6a R=Me
6b R=Et



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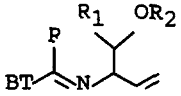
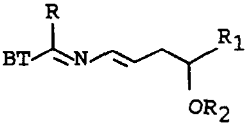
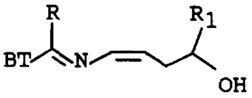


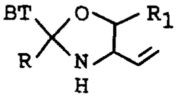
8a R=R_1=Ph;R_2=H
8b R=R_1=Ph;R_2=Ac
8c R=Ph;R_1=Cl_2Ph;R_2=H
8d R=Me;R_1=Cl_2Ph;R_2=H



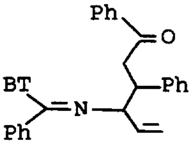
9a R=R_1=Ph;R_2=H
9b R=R_1=Ph;R_2=Ac
9c R=Ph;R_1=Cl_2Ph,R_2=H
9d R=Me;R_1=Cl_2Ph;R_2=H



10 R=R_1=Ph



11a R=Ph;R_1=Cl_2Ph
11b R=Me;R_1=Cl_2Ph



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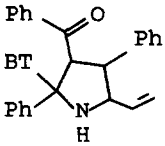

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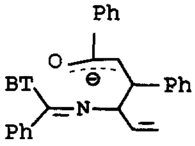

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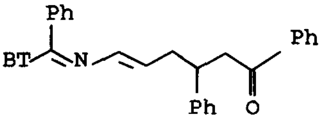

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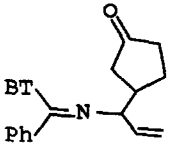

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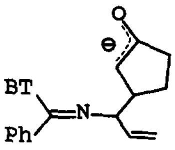

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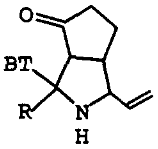


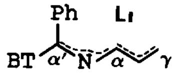
18a R=Ph
18b R=Me

Interestingly, 3b could be regio- and stereo-selectively methylated upon treatment with bistrimethylsilylperoxide 6a yielding 2-aza-diene 4c.[4] Similarly, 3c reacted with 6a to give the monomethylated aza-diene 4d and the dimethylated aza-diene 4e[4] likely arising from the dilithiated species 7. Yet regio- and stereo-selectively, 3c underwent ethylation upon treatment with bistriethylsilylperoxide 6b providing aza-diene 4f.[4]

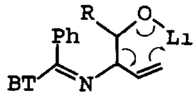
Aza-dienes 4a and 5 were recovered as main compounds when 3b was treated with cyclopentanone or acetophenone or benzophenone. 3c Furnished aza-diene 4b upon treatment with cyclopentanone.

The reactions of aza-dienyl metals 3 with aldehydes turned out to be heavily influenced by the experimental conditions and the nature of the counterion. Indeed, the reaction of 3b with benzaldehyde proceeded with poor regio- and stereo-selectivity to give the regioisomeric homoallylic alcohols 8a and 9a when carried out under kinetic conditions (at -78°C and quenching of the reaction medium with aqueous NH_4Cl after 1h). In contrast, the coupling reaction of 3b with benzaldehyde appeared to be regio- and diastereo-selective to give a 3:1 mixture of the alcohols 9a and 10 when carried out under thermodynamic conditions (-78°C for 0.5h, then 16h at RT and quenching with NH_4Cl). The allylic alcohol 8a tends to decompose during chromatographic purification but can be trapped through acetylation with acetic anhydride/pyridine to give 8b (a 1:1 mixture of separable threo (J = 8 Hz) and erythro (J = 7 Hz) diastereomers). Similarly, the coupling reaction of 3b with 2,6-dichlorobenzaldehyde took place in a poorly regio- and stereo-selective manner yielding a 1:1 mixture of the alcohols 8c and 9c under kinetic conditions. As a matter of fact, 8c tends to equilibrate to the oxazolidine 11a that can be envisaged as the result of the intramolecular nucleophilic attack of the OH function of 8c on the C-N double bond. Under thermodynamic conditions (-78°C, 0.5h; 4h at RT and then addition of aqueous NH_4Cl) the reaction of 3b with 2,6-dichlorobenzaldehyde was highly regio- and diastero-selective providing the trans (with respect to C-C double bond) homoallylic alcohol 9c.

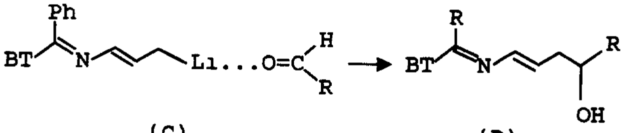
A rationalization of the results of the coupling of 3b with aldehydes might come from the assumption that the organolithium 3b adopts the all-trans-W-conformation (A),[5] that would react reversibly through the α-carbon to give the alkoxide (B)



(A)



(B)



(C) (D)

that then reverses to the aldehyde-organolithium complex (C), likely via a cyclic transition state, to afford finally the -regioisomer (D).

Yet highly regioselective was the coupling of 3b with 2,6-dichlorobenzaldehyde carried out in THF in the presence of HMPA as well as the reaction of aza-pentadienylpotassium 3d with the same aldehyde to give the homoallylic alcohol 9c.

The coupling reaction of 3c with 2,6-dichlorobenzaldehyde was highly regioselective under kinetic conditions to give a 4:1 mixture of the regioisomeric alcohols 8d and 9d. When the same reaction was performed under thermodynamic conditions the alcohol 9d formed exclusively. It is worthy noting that the alcohol 8d, particularly in $CDCl_3$ solution, tends to equilibrate with the oxazolidine 11b.

The coupling of the aza-dienylmagnesium bromide 3e with chalcone was very highly α-regioselective both with reference to 3e and to the unsatured carbonyl compound furnishing mainly the 1,4-addition product 12, having an exclusive erythro configuration, as proved by X-Ray analysis (see Fig.1), together with a small amount of the pyrrolidine 13, likely arising from the cyclization of the enolate 14, resulting from the 1,4 addition of 3e to the chalcone, on the C=N bond. The structure of compound 13 was ascertained by X-ray analysis (see Fig.2)

Less regioselective was the reaction of 3b with the same chalcone leading to a 4:1 mixture of 12 and 15. Also in this case 12 was mixed with a small percentage of 13.

Completely α-1,4-regioselective was the coupling reaction of 3b with 2-cyclopentenone leading to a mixture of two compounds 18a and 16 (ratio 18a/16 = 97/3).

Here again we may assume that 18a derives from the cyclization of the enolate intermediate 17.

Similarly, the coupling of 3c with 2-cyclopentenone led to the pyrrolidine 18b.

No reaction took place when 3b was treated with 3-methyl-2-cyclopentenone. The methyl group on the position 3 of the carbonyl compound may hamper the approach of 3b for the coupling process.

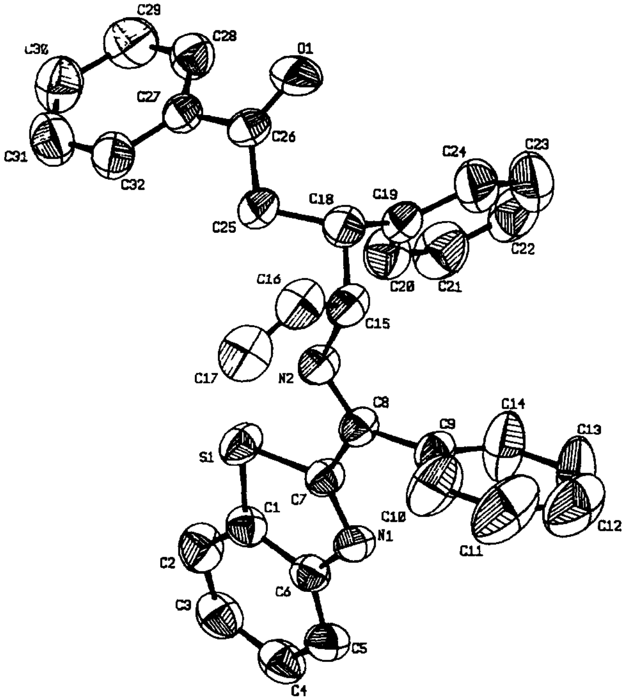


Fig. 1
Atom numbering and molecular structure of compound 12

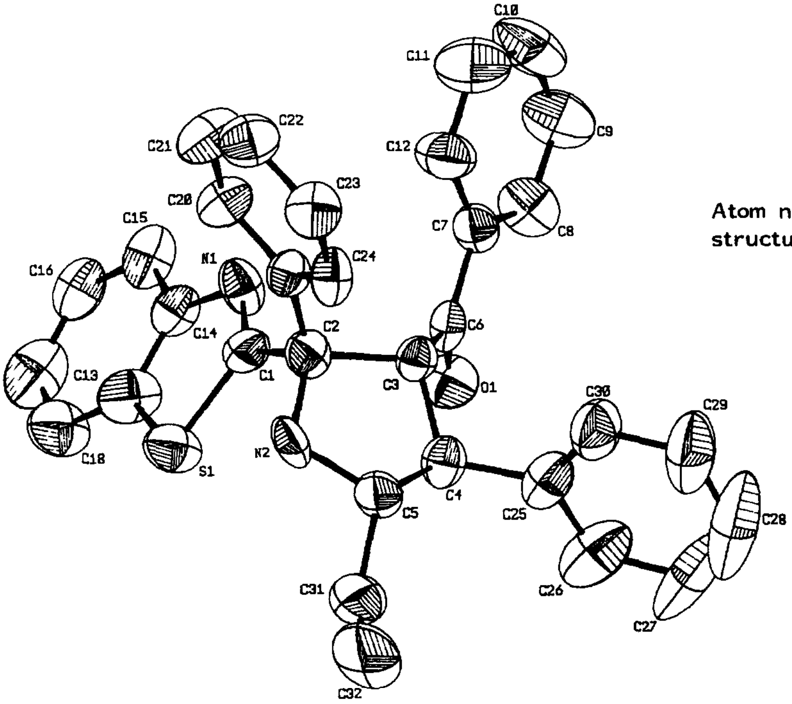


Fig.2
Atom numbering and molecular structure of compound 13

Table. Reaction of aza-dienyl metals 3b,c with electrophiles.

Aza-dienyl metal	Reaction conditions	E^+	Reaction products (% yield)[a]
3b	THF/-78°C,1h	CH_3I	4a (10) 5 (10)
"	THF/-78°C,2h R.T., 1h	6a	4c (38)[4]
3c 7	"	"	4d (13)[4] 4e (14)[4]
3c	"	6b	4f (40)[4]
3b	"	cyclopentanone	4a (10) 5 (10)
"	"	CH_3COPh	" "
"	"	PH_2CO	" "
3c	"	cyclopentanone	4b (17)
3b	THF/-78°C,1h	PhCHO	8a (16) 9a (18)
"	THF/-78°C,1h R.T.,16h	"	10 (10) 9a (32)
"	THF/-78°C,1h	1) PhCHO/ 2) Ac_2O(Py)	threo8b (8) erythro8b (8) 9b (10)
3b	"	2,6-Cl_2PhCHO	8c 11a 9c (36)
"	THF/-78°C,1h R.T.,16h	"	9c (b)
"	THF/HMPA/-78°C,1h	"	" "
3d[c]	THF/-78°C,2h R.T.,1h	"	" "
3c	THF/-78°C,1h	"	8d (26) 11b (26) 9d (14)
"	THF/-78°C,1h R.T.,24h	"	9d (b)
3b	THF/-78°C,1h	PhCOCH=CHPh	13 (13) 12 (42) 15 (11)
3e[d]	THF/-78°C,2h	"	13 (6) 12 (36)
3b	"	2-cyclopentenone	16 (3) 18a (36)
3c	"	"	18b (21)

a) Yields are on isolated compounds. b) Unknown global yield, reaction was monitored only by T.L.C.. c) 3d was prepared by reaction of 2b with Me_3COK. d) 3e was prepared in situ by transmetallation of 3b with $MgBr_2$

The present results concerning the coupling reaction of 3 with C-electrophiles suggest the following considerations:

a) 2-aza-pentadienyl metals 3 never react through the α' carbon of the aza dienyl chain (A), the reacting sites being the α and γ position.

b) the coupling of 3 through the α-carbon with aldehyde is reversible so that at low temperature and short reaction time (kinetic conditions) the α-regioisomer forms together with the γ-regioisomer but under thermodynamic conditions the α-regioisomer reverses completely to the γ-isomer.

c) the coupling of 3 with α,β-unsaturated carbonyl compounds is highly regioselective yielding irreversibly mainly the α-1,4-regioisomers.

In conclusion the results here presented on the coupling reactions of benzothiazolyl 2-azapentadienyl anions are in our view of remarkable interest either because reveal some aspects of the reactivity of such species and from the synthetic viewpoint as their coupling permits the preparation of a number of new benzothiazolyl substituted aza-dienes which in turn are of outstanding synthetic potential either for open-chain polyenic substances and for new heterocyclic systems.

EXPERIMENTAL

Melting points were measured on a Electrothermal apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 598 spectrophotometer. ^{1}H-NMR spectra were recorded on a Varian EM-360 A or a Varian XL-200 spectrometers and chemical shifts are reported in parts per million (δ) from internal Me_4Si. Thin-layer chromatography (TLC) was performed on silica gel sheets with fluorescent indicator (DC-Alufolien Kieselgel 60 F_{254}, Merck). Column chromatography was carried out by using Merck 70-230 mesh silica gel. For the flash chromatographies Merck 230-400 mesh silica gel was used. GC/mass spectrometry analyses were performed on a Hewlett-Packard 5890A Gas Chromatograph equipped with SE-30 capillary column, 30 m and Hewlett Packard Mass Selective Detector MSD 5970B. All new compounds showed satisfactory microanalytical data.

Materials: Tetrahydrofuran (THF), benzene and diethyl ether (Et_2O) from commercial sources (RS, Carlo Erba) were purified by distillation (twice) from sodium wire in a N_2 atmosphere. Petroleum ether (RS, C.E.) refers to the 40-60°C boiling fraction. 2-Formyl-[6] and 2-acetylbenzothiazole[7] were prepared as reported. All other chemicals were commercial grade and were used without further purification.

Preparation of 1-(2-Benzothiazolyl)-2-aza-1,4-pentadiene 2a.

To a benzene (60 ml) solution of 2-formylbenzothiazole (6.24 g, 38.3 mmol) was added allylamine (2.2 g, 38.3 mmol). The reaction mixture was refluxed for 1h 30' then cooled to room temperature and added of anydrous Na_2SO_4. Filtration and solvent evaporation under reduced pressure left a solid residue which was crystallized from ethanol to give 2a (64% yield), m.p. 26-27°C. IR (nujol) 1640 cm^{-1} (C=N). ^{1}H-NMR ($CDCl_3$): δ 4.4-4.6 (m, 2H), 5.15-5.6 (m, 2H), 5.8-6.5 (m, 1H) 7.4-7.8 (m, 2H), 7.9-8.3 (m, 2H), 8.7 (s, 1H).

Preparation of 2-benzoylbenzothiazole

To a Et_2O (100 ml) solution of 2-formylbenzothiazole (25 mmol) was added a Et_2O (31 ml) solution of phenylmagnesium bromide (27.5 mmol) under N_2 at 0-5° C. The reaction mixture was kept at that temperature for 20' and at R.T. for 30', then quenched with aq. saturated NH_4Cl. Extraction with diethyl ether (3x25 ml), drying over anydrous Na_2SO_4 and solvent evaporation under reduced pressure left the crude (2-benzothiazolyl)phenylcarbinol (95% yield). IR (nujol) 3400-3040 cm^{-1} (OH). ^1H-NMR (CCl_4): δ 4.8 (broad s, 1H, exchange with D_2O), 6.4 (s, 1H), 7.5-8.3 (m, 9H). The alcohol, without purification, was oxidized with aq. $K_2Cr_2O_7/H_2SO_4$ in acetone solution to 2-benzoylbenzothiazole (73% yield), m.p. 99-100.5°C (petroleum ether). IR (nujol) 1635 cm^{-1} (C=O). ^1H-NMR (CCl_4): δ 7.4-7.8 (m, 5H) 8.0-8.4 (m, 2H), 8.7-8.9 (m, 2H).

Preparation of 1-(2-benzothiazolyl)-2-aza-1-phenyl-1,4-pentadiene 2b and 2-(2-benzothiazolyl)-3-aza-2,5-hexadiene 2c.

The preparation of 2b is here described.

To a benzene (70 ml) solution of 2-benzoylbenzothiazole (11.28 mmol) was added allylamine (11.28 mmol) and after cooling to 0-5°C a benzene solution of $TiCl_4$ (8.7 mmol). The reaction mixture was kept at room temperature for 5h. After filtration under reduced pressure on florisil column (10 cm hight, 2.5 cm diameter) the solvent was evaporated under reduced pressure to afford 2b, oil (98% yield). IR (neat) 1615 cm^{-1} (C=N). ^1H-NMR (CCl_4): δ 4.2-4.4 (m, 2H), 5.1-5.5 (m, 2H), 5.9-6.5 (m, 1H), 7.3-7.8 (m, 7H), 7.9-8.2 (m, 2H).
Similarly was prepared 2c (94% yield), m.p. 56-57 °C (Et_2O-petroleum ether). IR ($CHCl_3$) 1635 cm^{-1} (C=N). ^1H-NMR (CCl_4): δ 2.48 (s, 3H), 4.2-4.4 (m, 2H), 5.1-5.5 (m, 2H), 5.8-6.5 (m, 1H), 7.3-7.75 (m, 2H), 7.8-8.2 (m, 2H).

Preparation of lithiated dienes 3a-c

To a THF solution of LDA (1.2 mmol of the commercial hexane solution of 2.5 M BuLi, 1.2 mmol of diisopropylamine) was added a 10% THF solution of 2a-c (1.0 mmol), under N_2, at -78°C. Then the reaction mixture was warmed to -30°C for 30'.

Preparation of potassium and magnesium bromide dienes 3d and 3e.

The dienyl potassium 3d was prepared by addition of the phenylbenzothiazolylazadiene 2b (1.0 mol) in THF to potassium t-butoxide (1.2 mol) in THF at -78°C under N_2 (20 min).
The dienyl magnesium bromide 3e was prepared in situ through addition of $MgBr_2 \cdot Et_2O$ (1.2 mole) to the THF solution of lithium derivative 3b (1.0 mol) at -78°C under N_2 (20 min).

Reaction of 1-(2-benzothiazolyl)-1-phenyl-2-aza-pentadienyllithium 3b with benzaldehyde.

To a stirred solution of 3b (1.08 mmol) a THF (10 ml) solution of benzaldehyde (1.3 mmol) was added dropwise at -78° C under N_2. The reaction was monitored by TLC using 1:1 diethyl ether/petroleum ether mixture as eluting system. The mixture was kept at -78° C for 1h and then warmed to room temperature and quenched with aqueous saturated NH_4Cl. Extraction with diethyl ether (3x25 ml), drying over Na_2SO_4 and solvent evaporation under reduced pressure left an oily residue of two main compounds. They were separated by TLC on 2 mm silica gel sheet using Et_2O-petroleum ether (1:1) as eluent. The upper band product was a diastereomeric mixture of 2-aza-1-(2-benzothiazolyl)-1-phenyl-3-(α-hydroxybenzyl)-1,4-pentadiene 8a, oil (0.07 g, 16% yield). ^1H-NMR ($CDCl_3$): δ 3.0 (broad s, exchange with D_2O, 1H), 4.1-4.45 (m, 1H), 4.7-5.4 (m, 3H), 5.7-6.4 (m. 1H), 6.8-8.3 (m, 14H).
The lower band product was trans-2-aza-1-(2-benzothiazolyl)-1,6-diphenyl-6-hydroxy-1,3-hexadiene 9a (0.08 g, 18% yield), m.p. 148-149° C (benzene). IR (nujol) 3500-3060 cm^{-1} (OH). ^1H-NMR (DMSO-d_6+D_2O): δ 2.4-2.7 (dd, 2H, J=7, J=7 Hz), 4.75 (t, 1H, J= 7 Hz,), 6.4 (dt,1H,J=7, J=13 Hz),

6.95 (d, 1H, J=13 Hz). 7.2-8.3 (m, 14 H).

When the reaction was carried out under different experimental conditions (30 min at -78° C, 16 h at room temperature) usual workup led to an oily residue that was chromatographed on silica gel column using Et_2O-petroleum ether mixture of increasing polarity starting from 1:9 as eluting system. The first eluted compound was cis-2-aza-1-(2-benzothiazolyl)-1,6-diphenyl-6-hydroxy-1,3-hexadiene 10, oil (0.04 g, 10% yield), IR (neat) 3530-3050 cm^{-1} (OH). ^{1}H-NMR (CCl_4+D_2O): δ 3.0 (dd, 2H, J=6, J=7 Hz), 4.8 (t, 1H, J=6 Hz), 5.6 (dt, 1H, J=7, J=8 Hz), 7.1 (d, 1H, J=8 Hz), 7.1-8.1 (m, 14H).

The second eluted compound was 9a (0,13 g, 32% yield).

Acetylation of alcohol 8a

To the residue (0.68 g) of the reaction of 3b with benzaldhyde was added pyridine (11.3 ml) and acetic anhydride (11.3 ml). The resulting mixture was kept at room temperature overnight with stirring. The mixture was then poured into water and extracted with CH_2Cl_2. The organic extracts were washed several times with diluted HCl and dried over Na_2SO_4. Removal of the solvent in vacuo gave an oily residue wich was a mixture of three main compounds which were separated by column chromatography using Et_2O-petroleum ether mixture of increasing polarity starting from petroleum ether as eluting system. The first eluted compound was threo-2-aza-1-(2-benzothiazolyl)-3-(α-acetoxybenzyl)-1-phenyl-1,4-pentadiene 8b, oil (0.06 g, 8% yield). IR (CCl_4) 1750 (C=O), 1230 cm^{-1} (C-O). ^{1}H-NMR ($CDCl_3$, 200 MHz): δ 2.05 (s, 3H), 4.37 (dd, 1 H, J=7, J=8 Hz), 5.08-5.25 (m, 2 H), 6.04 (d, 1 H, J=8 Hz), 6.0-6.16 (m, 1 H), 6.87-6.92 (m, 2 H), 7.2-7.3 (m, 5 H), 7.37-7.43 (m, 5 H), 7.88-7.96 (m, 2H). The second compound was erythro-2-aza-1-(2-benzothiazolyl)-3-(α-acetoxybenzyl)-1-phenyl-1,4-pentadiene 8b (0.06 g, 8% yield), m.p. 141-142 °C (Et_2O-petroleum ether). IR (CCl_4) 1745 (C=O), 1230 cm^{-1} (C-O). ^{1}H-NMR ($CDCl_3$, 200 MHz): δ 2.05 (s, 3 H), 4.44 (dd, J=6, J=7 Hz), 4.9-5.1 (m, 2 H), 5.7-5.8 (m, 1 H), 6.04 (d, 1 H, J=7 Hz), 7.2-7.5 (m, 12 H), 7.2-8.0 (m, 2H). The third eluted compound was trans-2-aza-1,6-diphenyl-6-(α-acetoxybenzyl)-1,3-hexadiene 9b (0.08 g, 10%), m.p. 154-155° C (Et_2O-petroleum ether). IR (CCl_4) 1735 (C=O), 1220 cm^{-1} (C-O). ^{1}H-NMR ($CDCl_3$, 200 MHz): δ 2.08 (s, 3 H), 2.6-2.8 (m, 2 H). 5.82 (dd, 1 H, J=7, J=7 Hz), 6.28 (dt, 1 H, J=7.7, J=13 Hz), 6.9 (d, J=13 Hz, 1 H), 7.2-7.5 (m, 12 H), 7.8-8.0 (m, 2 H).

Reaction of 3b and 3c with 2,6-dichlorobenzaldehyde.

To a solution of 3b (1.8 mmol) a THF (10 ml) solution of 2,6-dichlorobenzaldehyde (0.38 g, 2.16 mmol), was added dropwise at -78° C under N_2. After stirring at -78° C for 1 h the reaction mixture was warmed to R.T. and quenched with aq. sat. NH_4Cl. Usual workup afforded an oily residue of three main compounds which were separated by flash chromatography using Et_2O-petroleum ether mixture of increasing polarity starting from 10% of Et_2O as eluent. The first eluted product was a mixture of 2-aza-1-(2-benzothiazolyl)-3-(α-hydroxy-2,6-dichlorobenzyl)-1-phenyl-1,4-pentadiene 8c and 2-(2-benzothiazolyl)-2-phenyl-4-vinyl-5-(2,6-dichlorophenyl)-oxazolidine 11a [(8c+11a) 0.21 g, 33% yield) which after crystallization from ethanol afforded the pure 11a, m.p. 164-165° C. IR ($CHCl_3$) 3600-3500 cm^{-1} (NH). ^{1}H-NMR ($CDCl_3$, 200 MHz): δ 3.25 (broad s, 1 H, exchange with D_2), 4.5 (dd, 1 H, J=7.9, J=8 Hz), 5.0-5.2 (m, 2 H), 5.7 (d, 1H, J=8 Hz), 5.8-6.0 (m, 1 H), 7.1-8.1 (m, 12 H). The second eluted compound was 2-aza-1-(2-benzothiazolyl)-6-hydroxy-6-(2,6-dichlorophenyl)-1-phenyl-1,3-hexadiene 9c (0.25 g, 36%), m.p. 129-130 (ethanol). IR ($CHCl_3$) 3620-3520 cm^{-1} (OH). ^{1}H-NMR ($CDCl_3$+D_2O): δ 2.8-3.1 (m, 2 H), 5.63 (t, 1H, J=7 Hz), 6.5 (dt, 1 H, J=7, J=13 Hz), 7.15 (d, 1 H, J=13 Hz), 7.3-8.3 (m, 12 H).

Similarly reaction of 3c afforded a crude residue consisting of a mixture of 3-aza-2-(2-benzothiazolyl)-4-(α-hydroxy-2,6-dichlorobenzyl)-2,5-hexadiene 8d, 2-(2-benzothiazolyl)-2-methyl-4-vinyl-5-(2,6-dichlorobenzyl)-oxazolidine 11b and 3-aza-2-(2-benzothiazolyl)-7-hydroxy-7-(2,6-dichlorophenyl)-2,4-heptadiene 9d. 8d was separated by crystallization from Et_2O-petroleum ether (0.23 g, 26%), m.p. 161-162° C. IR (nujol) 3500-3040 (OH). ^1H-NMR ($CDCl_3$): δ 2.5 (s, 3 H), 3.4 (d, 1 H, J=7 Hz, exchange with D_2O), 4.9-5.4 (m, 3 H), 5.7-6.0 (m, 2 H), 7.1-8.3 (m, 7 H). The other two compounds were separated by flash chromatography (Et_2O-petroleum ether mixture of increasing polarity starting from 90% of petroleum ether). The first eluted compound was 11b, oil (0.24 g, 26% yield). ^1H-NMR ($CDCl_3$+D_2O, 200 MHz): δ 2.0 (s, 1H), 4.49 (dd, 1 H, J=7.4, J=7.4 Hz), 4.9-5.2 (m, 2 H), 5.55 (d, 1H, J=8.1 Hz), 5.7-6.0 (m, 1 H), 7.1-8.1 (m, 7 H). The second compound was 9d, oil (0.13 g,14%). IR (neat) 3560-3040 cm^{-1} (OH). ^1H-NMR ($CDCl_3$+D_2O): δ 2.5 (s, 3 H), 2.7-3.2 (m, 2 H), 5.4-5.9 (m, 1 H), 5.9-6.6 (m, 1 H), 6.8-7.55 (m, 6 H), 7.6-8.2 (m, 2 H).

Reaction of 3b with CH_3I

To a stirred solution of 3b (1.08 mmol) a THF (2 ml) solution of CH_3I (1.3 mmol) was added dropwise at -78°C, under N_2. Quenching after 1h and usual workup of the reaction left a crude oily residue of 2-aza-1-(2-benzothiazolyl)-1-phenyl-1,3-pentadiene 4a and 2-aza-1-(2-benzothiazolyl)-1-phenyl-2,4-pentadiene 5 which were separated by column chromatography using Et_2O-petroleum ether (2:8) as eluent. The first eluted compound was 4a (0.03g, 0.11 mmol). ^1H-NMR ($CDCl_3$): δ 1.9 (d, 3H, J=7 Hz), 6.8 (dq, 1H, J=7, J=13 Hz), 7.25 (d, 1H, J=13 Hz), 7.3-7.7 (m, 7H). The second eluted compound was 5, oil (0.03 g, 0.11 mmol). ^1H-NMR (CCl_4) δ 5.5-6.0 (m, 3H), 6.35-7.1 (m, 1H), 7.2-8.3 (m, 10 H).

Reaction of 3c with cyclopentanone

To a stirred solution of 3c (1.39 mmol) a THF (2 ml) solution of cyclopentanone (1.67 mmol) was added dropwise at -78°C, under N_2. Quenching after 1h at -78°C and 48h at R.T. and usual workup of the reaction left a crude oily residue of 3-aza-1-(2-benzothiazolyl)-2,4-hexadiene 4b which was purified by flash chromatography using Et_2O-petroleum ether 1:1 mixture as eluent. 4b (0.05 g, 0.23 mmol), m.p. 153-155°C (Et_2O-petroleum ether). ^1H-NMR (CCl_4): δ 1.95 (d, 3H, J=6 Hz), 2.5 (s, 3H), 6.3 (dq, 1H, J=6, J=13 Hz), 7.3 (dd, 1H, J=13 Hz), 7.35-8.4 (m, 4H).

Reaction of 3b with chalcone

To a stirred solution of 3b (2.5 mmol) a THF (5 ml) solution of chalcone (0.62 g, 3.0 mmol) was added dropwise at -78° C under N_2. After 1 h at -78° C the reaction mixture was worked up as described above for the analogous reaction with benzaldehyde. The crude oily residue was made of three main compounds which were separated by flash chromatography (Et_2O-petroleum ether mixture of increasing polarity starting from 90% of petroleum ether. The first eluted compound was 2-(2-benzothiazolyl)-3-benzoyl-2,4-diphenyl-5-vinylpyrrolidine 13 (0.04 g, 3% yield), m.p. 148-149° C (MeOH). IR ($CHCl_3$) 3420-3160 (NH), 1675 cm^{-1} (C=O). ^1H-NMR ($CDCl_3$+D_2O): δ 3.4-3.9 (m, 2H), 4.1-4.4 (m, 1H), 5.1-5.5 (m,2H), 5.8-6.5 (m, 1H), 6.8-8.1 (m, 19H).
The second eluted compound was 2-aza-1-(2-benzothiazolyl)-1,4-diphenyl-3-vinyl-5-benzoyl-1-pentene 12 (0.51 g, 42%), m.p. 94-95° C (petroleum ether). IR (CCl_4) 1685 cm^{-1} (C=O). ^1H-NMR ($CDCl_3$, 200 MHz): δ 3.7-3.8 (m, 2H), 3.8-4.0 (m, 1H), 4.3-4.4 (m, 1H; such a multiplet by irradiation of the signal at 5.1 ppm became a doublet centered at 4.34 ppm, J=4 Hz), 5.0-5.2 (m, 2H), 5.9-6.1 (m, 1H), 6.8-7.6 (m, 15 H), 8.0-8.1 (m, 4H).
The third eluted compound was 2-aza-1-(2-benzothiazolyl)-1,6-diphenyl-7-benzoyl-1,3-heptadiene 15 (0.14 g, 11%), m.p. 120-121°C (petroleum ether). IR (CCl_4) 1685 cm^{-1} (C=O). ^1H-NMR ($CDCl_3$, 200 MHz): δ

2.5-2.6 (m, 2 H), 3.31 (d, 2H, J= 6.8 Hz), 3.5-3.6 (m, 1H), 6.3 (dt, 1H, J= 12.8, J= 7.8 Hz), 6.8 (d, 1H, J= 12.8 Hz), 7.2-7.6 (m, 15 H), 7.86-8.0 (m, 4H).

Reaction of 3e with chalcone.

To a stirred THF (5 ml) solution of 3e (1.8 mmol), prepared as above, a THF (3 ml) solution of chalcone (0.45 g, 2.16 mmol) was added dropwise at -78° C, under N_2. After 2 h at -78°C the reaction mixture was allowed to warm at RT and quenched with aq.sat. NH_4Cl. Usual work up gave an oil residue that was a mixture of two compounds which were separated by column chromatography (ether-petroleum ether mixture of increasing polarity starting from 0.5:9.5 as eluting system). The first eluted compound was pyrrolidine 13 (0.05 g, 6% yield); the second eluted compound was ketone 12 (0.32 g, 36% yield).

Reaction of 3b and 3c with cyclopentenone.

To a THF solution of 3b (1.8 mmol) a THF (3 ml) solution of cyclopentenone (0.18 ml, 2.16 mmol) was added dropwise at -78° C, under N_2. After stirring for 1 h at -78 ° C the reaction mixture was worked up as previously described for the analogous reaction with benzaldehyde. The crude oily residue of two main compounds was flash chromatographed (Et_2O-petroleum ether 2:8 mixture) to give in order of elution the 2-aza-1-(2-benzothiazolyl)-1-phenyl-3-(3-oxocyclopentyl)-1,4-pentadiene 16, oil (0.02 g, 3%). IR (CCl_4) 1745 cm^{-1} (C=O). ^1H-NMR ($CDCl_3$): δ 1.6-2.7 (m, 7H), 3.9-4.3(m, 1H), 4.9-5.4 (m,2H), 5.8-6.45 (m, 1H), 7.2-8.3 (m, 9H); and the 3-aza-2-(2-benzothiazolyl)-2-phenyl-4-vinylbicyclo[3.3.0]octan-8-one 18a (0.22 g, 36%), m.p. 128-129° C (MeOH). IR (CCl_4) 3313 (N-H), 1735 cm^{-1} (C=O). ^1H-NMR ($CHCl_3$, 200 MHz): δ 1.7-2.1 (m, 2H), 2.16-2.3 (m, 2H), 2.88-3.0 (m, 1H; irradiation of the signal at 1.9 ppm showed a double doublet centered at 2.94 ppm, J=8.1, J=10 Hz), 3.1 (s, 1H, exchange with D_2O), 3.9 (d, 1H, J= 8.1 Hz), 4.0 (dd, 1H, J=6.6, J=10.0 Hz), 5.17-5.47 (m, 2H), 5.8-5.96 (m, 1H), 7.24-7.49 (m, 5H), 7.59-7.65 (m, 2H), 7.8-8.0 (m, 2H). Ms m/e (rel. int.): 360 (M^+, 2), 278 (100), 263 (24), 224 (11), 143 (67), 77 (18), 55 (14).

Similarly the reaction of 3c with cyclopentenone afforded 3-aza-2-(2-benzothiazolyl)-2-methyl-4-vinylbicyclo[3.3.0]octan-8-one 18b, oil (0.09 g, 21%). IR ($CHCl_3$) 3500-3220 (NH), 1735 cm^{-1} (C=O). ^1H-NMR ($CDCl_3$+D_2O, 200 MHz): δ 1.75 (s, 3H), 1.9-2.8 (m, 4H), 2.9-3.1 (m, 1H), 3.4 (d, 1H, J=7.0 Hz), 4.1-4.3 (m, 1H), 5.1-5.5 (m, 2H), 5.8-6.0 (m, 1H), 7.1-8.3 (m, 4H).

X-ray crystallographic data of 12

Crystal data: $C_{32}H_{26}N_2OS$; triclinic, P 1; a = 14.126 (2), b = 11.399 (2), c = 9.753 (2) Å; α = 79.1 (2)°, β = 84.8 (2),° = 87.5 (2)°; V = 1535 (1) Å^3; D_c = 1.05 gr cm^{-3}.
Colourless crystals, 0.4 x 0.7 x 0.7 mm was monitored on a Philips PW 1100 four-circles diffractometer, 6009 independent reflections were read -2 scan mode to 2 = 52° using MoKα radiation, h = 0.7107 Å. LP correction, no absorption and secondary extinction were applied.
The structure was phased by direct methods of Multan 80 programs and refined by blocked least-squares with the thermal parameters of all non hydrogen atoms anisotropic. The hydrogen atoms were calculated and not refined. The final conventional R factor for 3719 reflections with $I \geq 2.5\ \sigma$ (I) was 0.09 and Rw = 0.097 with w = $1/[\sigma^2$ (F) + 0.025 $F^2]$. The highest map residual = 0.54 $\bar{e}$ Å^{-3}.

The C(8)-N(2) bond is almost coplanar to benzothiazole ring, C(7)-C(8)-N(2)-C(15) torsion angle = 6° and N(2)-S(1) distance = 2.88 Å.

X-ray crystallographic data of 13

Crystal data: $C_{32}H_{24}N_2OS$; monoclinic, P $2_{1/c}$ (N.14), a = 16.516 (2), b = 11.065 (2), c = 14.867 (2) Å; ß = 109.6 (2)°; V = 2559 (3) $Å^3$; Z=4; Dc = 1.26 gr cm^{-3}; h = 0.7107 Å.
Colourless crystal 0,5 x 0,5 x 0,4 mm was mounted on a Philips PW 1100 four-circles diffractometer; 6126 (6032 independent) reflections were read -2 scan mode to 2 = 56°.
The stability of the crystal and the electronic was checked, LP correction, no absorption and secondary extinction were applied. The structure was phased by direct methods of Multan 80 programs and refined by blocked least-squares. The thermal parameters of all the non hydrogen atoms were anisotropic; only two hydrogen atoms were located on a DF-map, the other were calculated and not refined. The final conventional R factor for 1927 reflections with $I \geq 3\sigma(I)$ was 0.085; w = 1.
The highest map residual = 0.44 e $Å^{-3}$.

Data affected by the bad quality of crystals give high standard deviations to the results.
The pyrrolidine ring makes an angle of 122° with benzothiazole ring and coplanar to this stands the C(2)-N(2) bond with a possible hydrogen bond, 270 Å, between N(2)-S(1) atoms.

Tables of atom coordinates, isotropic temperature factors, bond lengthts and angles for compounds 12 and 13 are available on request.

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