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THIAZOLYLMETHYLENETRIPHENYLPHOSPORANE AND ITS BENZO DERIVATIVE: STABLE AND PRACTICAL WITTIG REAGENTS FOR THE SYNTHESIS OF VINYLTHIAZOLES AND VINYLBENZOTHIAZOLES. TWO-CARBON HOMOLOGATION OF ALDEHYDES.

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Abstract: The title thiazolyl phosphorane is a stable yet quite reactive Wittig-type reagent which upon reaction with various aldehydes affords vinylthiazoles, mainly or exclusively as E-isomers, in very good yields. Also the benzothiazolyl phosphorane derivative, unlike a literature report, prove to react with aldehydes. Vinylthiazoles subjected to formyl deblocking from thiazole nucleous afford two-carbon homologated satured aldehydes. As an example, one of these vinylthiazoles, viz. the β-phenyl derivative **8f**, proves to add n-butyl lithium cuprate to give after the formyl deblocking 3-phenylheptanal.

Formyl phosphoranes[1,2] **1** are precious tools in the arsenal of the Wittig reagents since they perform a tactical useful operation in synthesis such as the conversion of an aldehyde into its α,β-unsaturated vinylogue.[3] Synthetically useful variants of phosphoranes **1** are the formyl protected derivative **2a**[4] and the masked formyl equivalent **2b**.[5] Wittig reactions with these phosphoranes lead to protected α,β-unsaturated aldehydes which are suitable for carbon-carbon double bond elaborations without interference of the carbonyl group.[6] Closely related entries to masked equivalents of α,β-enals in the form of vinylbenzothiazoles and vinyloxazines employ the Horner[5,7] [reagent, $YCH_2P(O)(OC_2H_5)_2$] or the Peterson[8] (reagent, YCH_2TMS) olefination methodologies. These approaches overcome the low yield syntheses of α,β-enals[9] from Wittig reactions with **1** and/or the quite often necessary formyl group protection[10]

$Ph_3\overset{+}{P}-\overset{-}{C}(R)CHO$

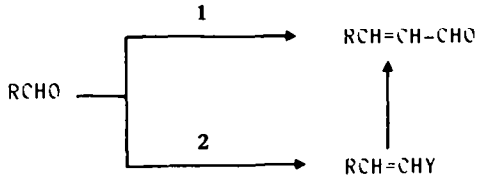
1

a; R = H
b; R = CH_3

$Ph_3\overset{+}{P}-\overset{-}{C}HY$

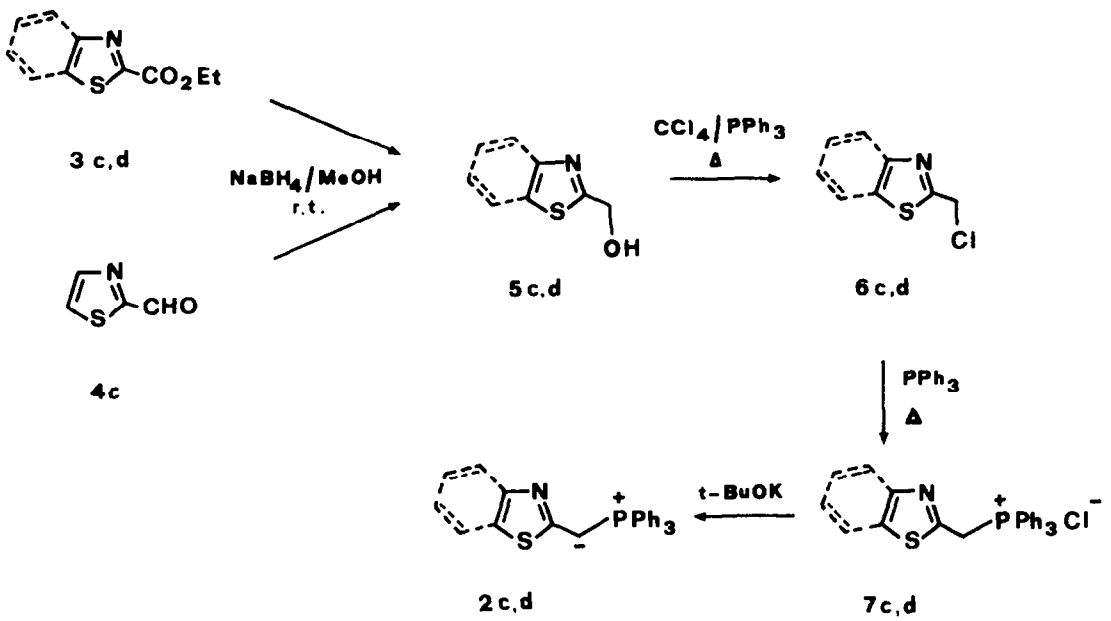
2

a; Y = $CH(OC_2H_5)_2$
b; Y = 4,4-dimethyl-2-oxazinyl
c; Y = 2-thiazolyl
d; Y = 2-benzothiazolyl



prior to their synthetic elaborations. Following our recent work on the stereoselective one-carbon chain-extension of chiral α-hydroxyaldehydes[11] which is centered on the thiazole-formyl equivalence, we have designed the synthesis of thiazolylmethylenetriphenylphosphorane (**2c**) and its use as a Wittig-type reagent with aldehydes to give their protected α,β-unsaturated vinylogues. We report herein some results showing the scope and limitations of this methodology.

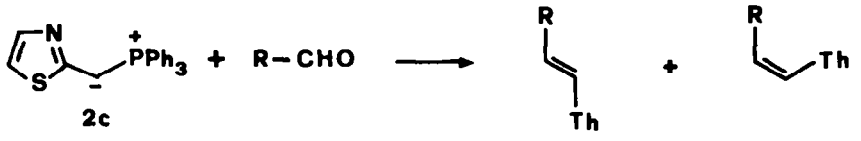
2-Hydroxymethylthiazole[12] (**5c**) and 2-chloromethylthiazole[12a,13] (**6c**), key intermediates to the anticipated phosphorane **2c** (Scheme I) were readily



SCHEME I

available in multigram quantities by new or improved high yield methods. Compound **5c** was in fact conveniently prepared by $NaBH_4$ reduction of the aldehyde **4c**[14] or the ester **3c**[15] and then transformed upon chlorination with the carbon tetrachloride-triphenylphosphine reagent,[16] into the chloromethyl derivative **6c**. The reaction of **6c** with a slight excess of triphenylphosphine in toluene afforded an essentially quantitative yield of the phosphonium salt **7c**. When a

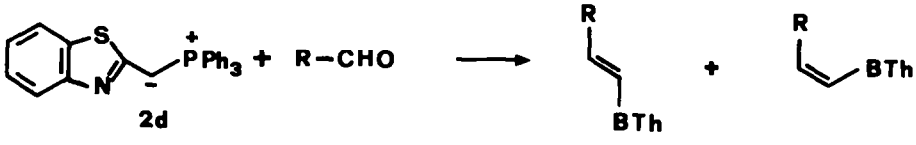
suspension of **7c** in benzene was treated with potassium tert-butoxide and stirred for 2 h at room temperature, a deep yellow solution of the phosphorane **6c** was obtained. Appropriate work-up gave a solid (m.p. 177-180° C) whose nmr spectrum[17] in $CDCl_3$ showed in addition to the signals of thiazole and phenyl rings, a broad signal at δ 3.37 attributable to the methine proton of **2c**. This nmr signal disappeared after 24 h. On the other hand, in the solid state, compound **2c** could be stored for three-five days without precaution still maintaining its reactivity with aldehydes. However, for preparative scale Wittig reactions, **2c** was generated in benzene or tetrahydrofuran and then reacted in situ with the appropriate aldehyde under selected standard conditions (Equation 1). As illustrated in Table I, **2c** exhibited a good degree of reactivity and E-stereoselectivity with various aldehydes affording the corresponding vinylthiazole **8** in very good yield. In some cases however (entries 4, 5, 9 and 11), the Z-isomer formed in comparable amount to E and the overall yield was low. Nevertheless, a quite general olefination methodology of the thiazole ring at C-2 is at hand. This is per se significant in view of the use of vinylthiazoles as sources of polymeric materials whilst their syntheses lie on undisclosed patented procedures.[18]



Eq. 1

Th = 2-Thiazolyl **E-(8)** **Z-(8)**

Encouraged by the above results with **2c**, we prepared the benzo derivative **2d** (Scheme I) although this phosphorane was reported to fail as Wittig reagent.[7] The phosphonium salt **7d** was obtained in very good overall yield through the same sequence as for **7c** starting from 2-(trimethylsilyl)benzothiazole.[19] The phosphorane **2d** generated in situ on treating **7d** with potassium tert-butoxide in benzene proved to react with three selected aldehydes (Equation 2) to give the



Eq. 2

BTh = Benzothiazolyl **E-(9)** **Z-(9)**

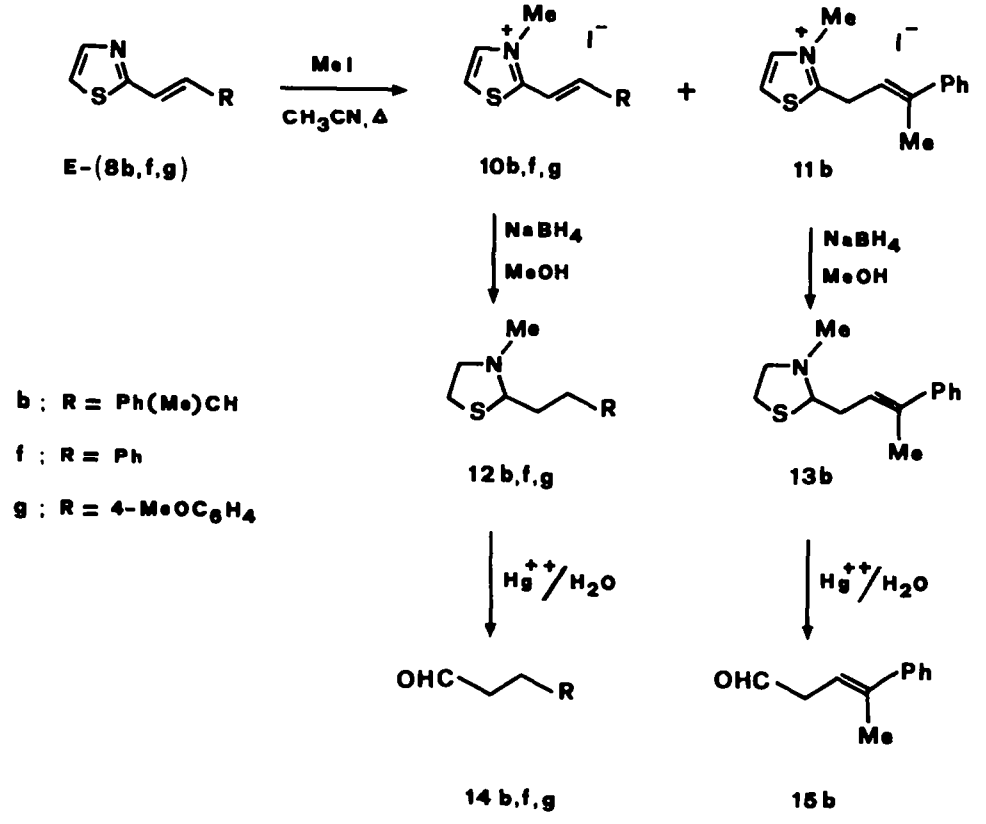
corresponding vinylbenzothiazole **9** in decent yield and dominant E-stereoselectivity (Table I). Hence, although the scope of **2d** as Wittig reagent was not further examined, it is evident that the earlier claim[7] about the inertness of this phosphorane has to be reconsidered.

TABLE I. Vinylthiazoles (**8**) and Vinylbenzothiazoles (**9**) from Wittig Reactions[a] of Phosphoranes **2c** and **2d** with Aldehydes (RCHO).

entry	aldehyde R	phosphorane	time/h	product **8** or **9**	yield[b]	E/Z[c]
1	i-C_3H_7	**2c**	48	**8a**, i-C_3H_7CH=CHTh	86	---
2	PhCHMe	**2c**	48	**8b**, PhCHMeC=CHTh	97	---
3	$CH_3(CH_2)_5$	**2c**	48	**8c**, $CH_3(CH_2)_5$CH=CHTh	25	---
4		**2c**	24	**8d**,  CH=CHTh	43	1.8
5	i-C_3H_7CH=CH	**2c**	48	**8e**, i-C_3H_7CH=CH-CH=CHTh	80	4.3
6	Ph	**2c**	48	**8f**, PhCH=CHTh	80	---
7	4-CH_3O-C_6H_4 (An)	**2c**	48	**8g**, An-CH=CHTh	95	---
8	α-Naphtyl (α-NAP)	**2c**	48	**8h**, α-NAP-CH=CHTh	74	---
9	2-Thiazolyl (Th)	**2c**	24	**8i**, ThCH=CHTh	100	2.3
10	2-Thienyl (Tn)	**2c**	48	**8j**, TnCH=CHTh	78	---
11	2-Furyl (Fu)	**2c**	24	**8k**, FuCH=CHTh	90	9.0
12	i-C_3H_7	**2d**	48	**9a**, i-C_3H_7CH=CHBTh	82	---
13	2-Thiazolyl (Th)	**2d**	24	**9b**, ThCH=CHBTh	56	---
14	2-Furyl (Fu)	**2d**	24	**9c**, FuCH=CHBTh	70	---

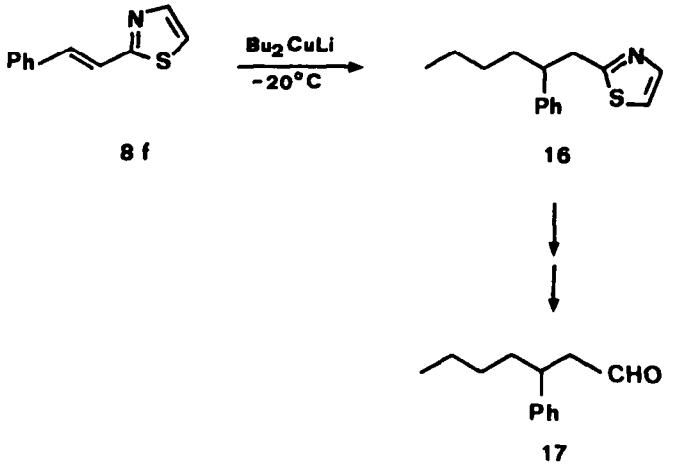
[a] Carried out at r.t. in benzene or THF with 1.5 molar equiv of aldehyde. [b] Weight yield of isolated mixed or separated alkenes. [c] Determined on isolated products after chromatography; omitted values refer to ratio ≥ 95% (nmr).

Since the synthetic utility of vinylbenzothiazoles as protected α,β-unsaturated carbonyl compound has been sufficiently demonstrated,[8] we addressed our attention to vinylthiazoles **8**. The aldehyde release from compounds **8b**, **8f**, and **8g** by our standard procedure[11] (N-methylation, reduction, hydrolysis) afforded the saturated derivatives **14b**, **14f**, and **14g** instead of the corresponding α,β-enals. Each of these arose from the C-2 alkyl substituted thiazolidine **12** which is formed by the reduction of the heterocyclic ring and side-chain carbon-carbon double bond in the corresponding N-methyl quaternary salt **10** (Scheme II). The elaboration of **8b** [R = Ph(Me)CH] gave, in addition to **14b**, the β,γ-unsaturated aldehyde **15b** as main product. This was later proved to be due to the tautomeric equilibrium between the N-methyl quaternary salts **10b** and **11b** (1:1 ratio by nmr) which, upon reduction, gave the thiazolidines **12b** and **13b**, viz. the precursors of the individual aldehydes **14b** and **15b**. Presently, because of the overreduction[20] of the N-methyl thiazolium salt **10** to thiazolidine **12**, vinylthiazoles **8** cannot be considered as actual intermediates for aldehyde vinylogation. However, their value in synthesis as protected α,β-enals can be foreseen from the Michael-type addition of n-butyl lithium



SCHEME II

cuprate to the β-phenyl derivative **8f** to give the alkylthiazole **16** which upon the formyl deblocking afforded 3-phenylheptanal (**17**) (Equation 3). This is noteable since α,β-unsaturated aldehydes tend to react with C-nucleophiles, including cuprates, as carbonyl rather than Michael acceptors.[6]



8f **16** **17**

Eq. 3

In conclusion, it has been proved that the phosphorane **2c** serves, *via* the appropriate protocols, as auxiliary for the two-carbon homologation and/or longer chain-extension of aldehydes to upper saturated terms.

Experimental Section

General Methods. All melting points are uncorrected. ^{1}H NMR spectra were recorded in chloroform-*d* solution, unless otherwise stated, on a 80-MHz Bruker WP-80 spectrometer. Chemical shifts are given in δ downfield from tetramethylsilane. IR spectra were obtained on a Perkin-Elmer Model 297 grating spectrometer. Elemental analyses were performed on a Carlo Erba elemental analyzer Model 1106. All experiments were carried out under N_2 and with freshly distilled and dried solvents. 2-(Carboethoxy)thiazole (**3c**),[15] 2-(carboethoxy)benzothiazole (**3d**),[19] and 2-thiazolecarboxaldehyde (**4c**)[14] were prepared as described.

2-(Hydroxymethyl)thiazole (5c) and its Benzo Derivative 5d. General Procedure. To a stirred solution of the ethyl ester **3** (25 mmol) in methanol (60 mL) was added portionwise (2 h) sodium borohydride (2.15 g, 56 mmol). After 2 h, the reaction mixture was concentrated under vacuum and brine was added (30 mL) to the residue. After neutralization with hydrogen chloride 5%, the mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4, the solvent was evaporated in vacuo and the residue was chromatographed (silica gel, 8:2 petroleum ether-ethyl acetate) to give the hydroxymethyl derivative **5**.

2-(Hydroxymethyl)thiazole (**5c**) (2.5 g, 86%): bp 75-76° C (0.2 mmHg) [lit.[12] bp 70-80° C (0.2 mmHg)]; ^{1}H NMR δ 4.89 (s, 2 H), 5.1 (br, 1 H), 7.21 (d, 1 H, *J* = 3.5 Hz), 7.63 (d, 1 H, *J* = 3.5 Hz).

2-(Hydroxymethyl)benzothiazole (**5d**) (3.4 g, 84%): mp 100-102° C (from diethyl ether-*n*-hexane); (lit.[21] mp 101° C); ^{1}H NMR δ 3.41 (t, 1 H, *J* = 6.0 Hz), 5.04 (d, 2 H, *J* = 6.0 Hz), 7.35 (m, 2 H), 7.85 (m, 2 H).

2-(Hydroxymethyl)thiazole (**5c**) was also obtained by reduction of 2-thiazolecarboxaldehyde (**4c**) (5 g, 44 mmol) with sodium borohydride (2 g, 53 mmol) in methanol (100 mL) at room temperature. Usual work-up gave 4.2 g (85%) of **5c**.

2-(Chloromethyl)thiazole (6c) and its Benzo Derivative 6d. General Procedure. A solution of the alcohol **5** (24 mmol) in carbon tetrachloride (40 mL) and benzene (50 mL) was added to triphenylphosphine (9.68 g, 37 mmol) and the mixture was refluxed with stirring for 2 h. After cooling and filtration through Celite, the solvent was evaporated in vacuo. Chromatography of the residue (silica gel, 9:1 petroleum ether-ethyl acetate) gave the chloromethyl derivative **6**.

2-(Chloromethyl)thiazole (**6c**) (3 g, 95%): bp 63-64° C (5 mmHg) [lit.[12a,13] bp 62° C (5 mmHg)]; ^{1}H NMR δ 4.72 (s, 2 H), 7.19 (d, 1 H, J = 3.5 Hz), 7.55 (d, 1 H, J = 3.5 Hz)).

2-(Chloromethyl)benzothiazole (**6d**) (4 g, 92%): bp 108-110° C (lit.[22] bp 110° C); ^{1}H NMR δ 4.86 (s, 2 H), 7.32 (m, 2 H), 7.82 (m, 2 H).

2-Thiazolylmethyltriphenylphosphonium Chloride (7c) and its Benzo Derivative 7d. General Procedure. The chloromethyl derivative **6** (14 mmol) and triphenylphosphine (4.15 g, 15 mmol) in toluene (6 mL) were refluxed for 18-20 h. The crude phosphonium salt **7** was filtered and washed several times with cold benzene and then with petroleum ether.

2-Thiazolymethyltriphenylphosphonium chloride (**7c**) (5.2 g, 95%): mp 350° C (from ethanol-diethyl ether); ^{1}H NMR (CD_3OD) δ 5.52 (d, 2 H, J = 14.5 Hz), 7.74 (m, 17 H). Anal. Calcd for $C_{22}H_{19}ClNPS$:[3] C, 66.70; H, 4.84; N, 3.54. Found: C, 66.71; H, 4.82; N, 3.53.

2-Benzothiazolylmethyltriphenylphosphonium chloride (**7d**) (5.52 g, 86%): mp 270-272° C (from ethanol-diethyl ether); ^{1}H NMR (CD_3OD) δ 6.22 (d, 2 H, J = 14.0 Hz), 7.3 (m, 2 H), 7.75 (m, 17 H). Anal. Calcd for $C_{26}H_{21}ClNPS$: C, 70.10; H, 4.75; N, 3.14. Found: C, 70.06; H, 4.77; N, 3.16.

2-Thiazolymethylenetriphenylphosphorane (2c) and its Benzo Derivative 2d. General Procedure. To a stirred solution of the phosphonium salt **7** (2.7 mmol) was added potassium tert-butoxide (0.33 g, 2.9 mmol). After 3 h, the yellow orange solution was filtered through Celite and the solvent was evaporated under vacuum to give, after crystallization, the phosphorane **2**.

2-Thiazolylmethylenetriphenylphosphorane (**2c**) (0.87 g, 90%): mp 177-180° C (from benzene-petroleum ether); ^{1}H NMR δ 3.77 (br, 1 H), 6.25 (t, 1 H), 7.0 (d, 1 H), 7.45 (m, 33 H). Anal. Calcd for $C_{22}H_{18}PNS$: C, 73.52; H, 6.86, N, 3.90. Found: C, 73.54; H, 6.84; N, 3.91.

2-Benzothiazolylmethylenetriphenylphosphorane (**2d**) (0.94 g, 85%): mp 164-165° C (from benzene-petroleum ether) (lit.[7] mp 163° C).

Reactions of the Phosphoranes 2c and 2d with Aldehydes. General Procedure. To a stirred suspension of the phosphonium salt **7** (5 mmol) in benzene (50 mL) was added potassium tert-butoxide (0.64 g, 5.5 mmol). After 3 h at room temperature, a solution of the aldehyde (7.5 mmol) in benzene (30 mL) was added dropwise and stirring was continued for the time indicated in Table I. The reaction mixture was filtered through Celite, the solvent was removed under vacuum and the residue was chromatographed (silica gel, 8:2 petroleum ether-ethyl acetate) to give the alkenes **8** or **9**.

3-Methyl-1-(2-thiazolyl)-(1E)-butene E-(**8a**) (0.66 g, 86%): oil; IR (film) 3050, 1680, 1530, 1500 cm^{-1}; ^{1}H NMR δ 1.12 (d, 6 H), 2.52 (m, 1 H), 6.68 (m, 2 H), 7.15 (d, 1 H, J = 3.4 Hz), 7.7 (d, 1 H, J = 3.4 Hz). Anal. Calcd for $C_8H_{11}NS$: C, 62.70; H, 7.24; N, 9.14. Found: C, 62.73; H, 7.20; N, 9.16.

3-Phenyl-1-(2-thiazolyl)-(1E)-butene E-(**8b**) (1.04 g, 97%): oil; IR (film)

2960, 1680, 1630, 1600 cm^{-1}; ^1H NMR δ 1.47 (d, 3 H), 3.67 (m, 1 H), 6.68 (m, 2 H), 7.08 (d, 1 H, J = 3.5 Hz), 7.23 (m, 5 H), 7.66 (d, 1 H, J = 3.5 Hz). Anal. Calcd for $C_{13}H_{13}NS$: C, 72.52; H, 6.09; N, 6.51. Found: C, 72.55; H, 6.07; N, 6.54.

1-(2-Thiazolyl)-(1E)-octene E-(8c) (0.24 g, 25%): oil; IR (film) 2960, 1660 cm^{-1}; ^1H NMR δ 0.9 (m, 3 H), 1.35 (m, 8 H), 2.25 (m, 2 H), 6.65 (m, 2 H), 7.15 (d, 1 H, J = 3.0 Hz), 7.71 (d, 1 H, J = 3.0 Hz). Anal. Calcd for $C_{11}H_{17}NS$: C, 67.64; H, 8.77; N, 7.17. Found: C, 67.66; H, 8.75; N, 7.19.

1-(2-Thiazolyl)-2-[2-(3,4-dihydropyranyl)]-(E)-ethene E-(8d) (0.26 g, 27%): oil; IR (film) 2930, 1660 1500 cm^{-1}; ^1H NMR δ 2.0 (m, 4 H), 4.57 (m, 2 H), 6.40 (d, 1 H, J = 6.0 Hz), 6.65 (d, 1 H, J = 4.0 Hz), 6.85 (d, 1 H, J = 16.0 Hz), 7.18 (d, 1 H, J = 3.5 Hz), 7.71 (d, 1 H, J = 3.5 Hz). Anal. Calcd for $C_{10}H_{11}NOS$: C, 62.15; H, 5.74; N, 7.25. Found: C, 62.18; H, 5.71; N, 7.24.

1-(2-Thiazolyl)-2-[2-(3,4-dihydropyranyl)]-(Z)-ethene Z-(8d) (0.15 g, 16%): oil; IR (film) 2940, 1660, 1500 cm^{-1}; ^1H NMR δ 2.01 (m, 4 H), 4.71 (m, 1 H), 5.4 (m, 1 H), 6.0 (dd, 1 H, J = 12 Hz, J = 7.9 Hz), 6.37 (d, 1 H, J = 6.0 Hz), 6.62 (d, 1 H, J = 12 Hz), 7.27 (d, 1 H, J = 3.5 Hz), 7.77 (d, 1 H, J = 3.5 Hz). Anal. Calcd for $C_{10}H_{11}NOS$: C, 62.15; H, 5.74; N, 7.25. Found: C, 62.14; H, 5.73; N, 7.26.

5-Methyl-1-(2-thiazolyl)-(1E,3E)-exadiene E-(8e) (0.58 g, 65%): oil; IR (film) 2980, 1645 cm^{-1}; ^1H NMR δ 1.05 (d, 6 H), 2.42 (m, 1 H), 5.8-7.1 (m, 4 H), 7.17 (d, 1 H, J = 3.5 Hz), 7.75 (d, 1 H, J = 3.5 Hz). Anal. Calcd for $C_{10}H_{13}NS$: C, 66.99; H, 7.31; N, 7.81. Found: C, 66.97; H, 7.33; N, 7.84.

5-Methyl-1-(2-thiazolyl)-(1Z,3E)-exadiene Z-(8e) (0.13 g, 15%): oil; IR (film) 2975, 1690 cm^{-1}; ^1H NMR δ 1.05 (d, 6 H), 2.45 (m, 1 H), 6.1 (m, 1 H), 6.45 (m, 2 H), 7.25 (m, 2 H), 7.82 (d, 1 H, J = 3.0 Hz). Anal. Calcd for $C_{10}H_{13}NS$: C, 66.99; H, 7.31; N, 7.81. Found: C, 67.01; H, 7.34; N, 7.79.

1-Phenyl-2-(2-thiazolyl)-(E)-ethene E-(8f) (0.75 g, 80%): mp 57-59° C (from diethyl ether-n-hexane); IR ($CHCl_3$) 1625 cm^{-1}; ^1H NMR δ 7.5 (m, 8 H), 7.86 (d, 1 H, J = 3.2 Hz). Anal. Calcd for $C_{11}H_9NS$: C, 70.55; H, 4.84, N, 7.48. Found: C, 70.52; H, 4.81; N, 7.45.

1-(4-Methoxyphenyl)-2-(2-thiazolyl)-(E)-ethene E-(8g) (1.3 g, 95%): mp 64-65° C (from diethyl ether-n-hexane); IR (KBr) 1610 cm^{-1}; ^1H NMR δ 3.85 (s, 3 H), 6.85-7.55 (m, 7 H), 7.77 (d, 1 H, J = 3.0 Hz). Anal. Calcd for $C_{12}H_{11}NOS$: C, 66.33; H, 5.10; N, 6.45. Found: C, 66.30; H, 5.08; N, 6.47.

1-(1-Naphtyl)-2-(2-thiazolyl)-(E)-ethene E-(8h) (0.87 g, 74%): mp 97-99° C (from diethyl ether-n-hexane); IR (KBr) 1600 cm^{-1}; ^1H NMR δ 7.27 (m, 1 H), 7.52 (m, 4 H), 7.82 (m, 4 H), 8.25 (m, 2 H). Anal. Calcd for $C_{15}H_{11}NS$: C, 79.91; H, 4.67; N, 5.90. Found: C, 75.94; H, 4.65; N, 5.92.

1,2-di-(2-Thiazolyl)-(E)-ethene E-(8i) (0.65 g, 70%): oil; IR (CCl_4) 1590 cm^{-1}; ^1H NMR δ 7.33 (d, 2 H, J = 3.5 Hz), 7.61 (s, 2 H), 7.80 (d, 2 H, J = 3.5 Hz). Anal. Calcd for $C_8H_6N_2S_2$: C, 49.46; H, 3.11; N, 14.42. Found: C, 49.43; H, 3.08; N, 14.44.

1,2-di-(2-Thiazolyl)-(Z)-ethene Z-(8i) (0.29 g, 30%)): oil; IR (CCl_4) 1595 cm^{-1}; ^1H NMR δ 7.0 (s, 2 H), 7.4 (d, 2 H, J = 3.5 Hz), 7.90 (d, 2 H, J = 3.5 Hz). Anal. Calcd for $C_8H_6N_2S_2$: C, 49.46; H, 3.11; N, 14.42. Found: C, 49.27; H, 3.14; N, 14.40.

1-(2-Thiazolyl)-2-(2-thienyl)-(E)-ethene E-(8j) (0.75 g, 78%): mp 78-79° C (from diethyl ether-n-hexane); IR (Nujol) 1615 cm^{-1}; ^1H NMR δ 7.2 (m, 5 H), 7.6 (d, 1 H, J = 16 Hz), 7.8 (d, 1 H, J = 3.2 Hz). Anal. Calcd for $C_9H_7NS_2$: C, 55.92; H, 3.65; N, 7.25. Found: C, 55.90; H, 3.66; N, 7.24.

1-(2-Furyl)-2-(2-thiazolyl)-(E)-ethene E-(8k) (0.72 g, 81%): oil; IR ($CHCl_3$) 1630 cm^{-1}; ^1H NMR δ 6.42 (m, 2 H), 7.15 (m, 3 H), 7.37 (s, 1 H), 7.78 (d, 1 H, ^{3}J

= 3.2 Hz). Anal. Calcd for C_9H_7NOS: C, 60.99; H, 3.98; N, 7.90. Found: C, 61.01; H, 3.96; N, 7.93.

1-(2-Furyl)-2-(2-thiazolyl)-(Z)-ethene Z-(**8k**) (0.079 g, 90%): oil; IR ($CHCl_3$) 1620 cm^{-1}; ^1H NMR δ 6.5 (m, 1 H), 6.52 (s, 2 H), 7.28 (d, 1H, J 3.2 Hz), 7.5 (m, 2 H), 7.84 (d, 1 H, J = 3.2 Hz). Anal. Calcd for C_9H_7NOS: C, 60.99; H, 3.98; N, 7.90. Found: C, 60.95; H, 3.94; N, 7.92.

3-Methyl-1-(2-benzothiazolyl)-(1E)-butene E-(**9a**) (0.83 g, 82%): mp 53-55° C (from diethyl ether-n-hexane); IR (CCl_4) 2960, 1640 cm^{-1}; ^1H NMR δ 1.15 (d, 6 H), 2.25 (m, 1 H), 6.7 (m, 2 H), 7.37 (m, 2 H), 7.87 (m, 2 H). Anal. Calcd for $C_{12}H_{13}NS$: C, 70.89; H, 6.45; N, 6.89. Found: C, 70.91; H, 6.43; N, 6.86.

1-(2-Benzothiazolyl)-2-(2-thiazolyl)-(E)-ethene E-(**9b**) (0.68 g, 56%): oil; IR ($CHCl_3$) 1610 cm^{-1}; ^1H NMR δ 7.37 (m, 3 H), 7.65 (s, 2 H), 7.92 (m, 3 H),. Anal. Calcd for $C_{12}H_8N_2S_2$: C, 58.99; H, 3.30; N, 11.47. Found: C, 58.96; H, 3.31; N, 11.45.

1-(2-Benzothiazolyl)-2-(2-furyl)-(E)-ethene E-(**9c**) (0.79 g, 70%): oil; IR ($CHCl_3$) 1640 cm^{-1}; ^1H NMR δ 6.45 (m, 2 H), 7.35 (m, 5 H), 7.85 (m, 2 H). Anal. Calcd for $C_{13}H_9NOS$: C, 68.70; H, 3.99; N, 6.16. Found: C, 68.73; H, 3.96; N, 6.12.

N-Methylation of Vinylthiazoles 8b, 8f, and 8g. General Procedure. A solution of the vinylthiazole **8** (1.6 mmol) and methyl iodide (2.28 g, 16 mmol) in acetonitrile (30 mL) was refluxed for the required time (5-24 h), as determined by t.l.c.. The solvent was removed under vacuum and the crude thiazolium salt **10** was crystallized from ethanol-diethyl ether (yield 92-97%). The reaction of vinylthiazole **8b** gave a mixture (1:1 ratio, nmr) of the salts **10b** and tautomer **11b** which were further elaborated without separation.

10b: ^1H NMR (CD_3OD) (selected): δ 1.57 (d, 3 H, J = 7.0 Hz), 4.15 (s, 3 H).

11b: ^1H NMR (CD_3OD) (selected): δ 2.2 (d, 3 H, J = 1.5 Hz), 4.2 (s, 3 H), 6.07 (qt, 1 H, J = 1.5 Hz, J =7.0 Hz).

10f: ^1H NMR (CD_3OD) δ 4.25 (s, 3 H), 7.42-8.0 (m, 6 H), 8.06 (d, 1 H, J =4.0 Hz), 8.22 (d, 1 H, J = 4.0 Hz).

10g: ^1H NMR (CD_3OD) δ 3.90 (s, 3 H), 4.20 (s, 3 H), 7.07 (d, A_2B_2 system, 2 H), 7.50 (d, 1 H, J = 16.0 Hz), 7.95 (m, 5 H).

Reduction of Vinylthiazolium Salts 10b, 10f, 10g, and 11b. General Procedure. A solution of thiazolium salt (1.4 mmol) in methanol (30 mL) was cooled at -10° C and sodium borohydride (0.05 g, 1.6 mmol) was added portionwise. After 20 min, the reaction mixture was neutralized with hydrogen chloride 5%, the solvent was partially evaporated under vacuum and, after addition of brine (20 mL), the residue was extracted with dichloromethane. The organic layer was dried over anhydrous Na_2SO_4 and the solvent removed in vacuo. The residue was chromatographed (silica gel, 7:3 petroleum ether-diethyl ether) to give the thiazolidine **12** and eventually **13b**.

The mixture of **10b** and **11b** gave the thiazolidines **12b** and **13b** respectively which were were separated by chromatography (see above).

The thiazolidine **12b** (0.12 g, 36%): oil; ^1H NMR δ 1.25 (d, 3 H), 1.62 (m, 4 H), 2.2 (d, 3 H), 2.62 (m, 1 H), 2.92 (m, 4 H), 4.1 (m, 1 H), 7.2 (m, 5 H). Anal. Calcd for $C_{14}H_{21}NS$: C, 71.43; H, 8.99; N, 5.95. Found: C, 71.40; H, 8.95; N, 5.94.

The thiazolidine **13b** (0.23 g, 72%): oil; ^1H NMR δ 2.05 (d, 3 H, J = 3.0 Hz), 2.32 (s, 3 H), 2.58 (m, 2 H), 3.05 (m, 4 H), 4.3 (m, 1 H), 5.77 (qt, 1 H, J = 3.0 Hz, J = 7.0 Hz), 7.2 (m, 5 H). Anal. Calcd for $C_{14}H_{19}NS$: C, 72.05; H, 8.21; N, 6.00. Found: C, 72.07; H, 8.19; N, 6.03.

The thiazolidine **12f** (0.21 g, 75%): oil; ^1H NMR δ 1.97 (m, 2 H), 2.27 (s, 3

H), 2.87 (m, 6 H), 4.17 (m, 1 H), 7.2 (s, 5 H). Anal. Calcd for $C_{12}H_{17}NS$: C, 69.51; H, 8.26; N, 7.76. Found: C, 69.54; H, 8.24; N, 6.78.

The thiazolidine **12g** (0.28 g, 84%): oil; ^1H NMR δ 1.82 (m, 1 H), 2.27 (s, 3 H), 2.67 (m, 1 H), 3.02 (m, 2 H), 3.80 (s, 3 H), 4.15 (m, 1 H), 7.0 (m, A_2B_2 system, 4 H). Anal. Calcd for $C_{13}H_{19}NOS$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.75; H, 8.10; N, 5.94.

Hydrolysis of Thiazolidines 12b, 12f, 12g, and 13b. General Procedure. A solution of the thiazolidine (1 mmol) in 4:1 acetonitrile-water (3 mL) was added to a stirred solution of $HgCl_2$ (0.35 g, 1.2 mmol) in the same solvent (20 mL). After 15 min, the reaction mixture was filtered through Celite, the solvent was partially evaporated and, after addition of brine (20 mL), the mixture was extracted with diethyl ether. The organic layer was dried over anhydrous Na_2SO_4, the solvent was removed in vacuo, and the residue was chromatographed (silica gel, 1:1 petroleum ether-diethyl ether) to give the corresponding aldehydes **14** and eventually **15b**.

4-Phenylpentanal (**14b**) (0.15 g, 96%): oil; IR (film) 1730 cm^{-1}; ^1H NMR δ 1.25 (d, 3 H), 1.96 (m, 2 H), 2.31 (m, 2 H), 2.68 (m, 1 H), 7.2 (m, 5 H), 9.68 (t, 1 H, J = 1.46 Hz). Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.40; H, 8.74.

4-Phenyl-(3*E*)-pentenal (**15b**) (0.06 g, 37%): unstable oil; ^1H NMR δ 2.07 (m, 3 H), 3.34 (m, 2 H), 5.96 (m, 1 H), 7.34 (m, 5 H), 9.76 (t, 1 H, J = 1.8). Anal; Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: 82.40; H, 7.60.

3-Phenylpropanal (**14f**) (0.13 g, 80%); bp 110-112° C (16 mmHg) [lit.[23] bp 104-105° C (13 mmHg)]; IR (CCl_4) 1730 cm^{-1}; ^1H NMR δ 2.87 (m, 4 H), 7.25 (m, 5 H), 9.81 (t, 1 H, J = 1.22 Hz).[4]

3-(4-Methoxyphenyl)-propanal (**14g**) (0.11 g, 70%): oil; IR (film) 1720 cm^{-1}, ^1H NMR δ 2.81 (m, 4 H), 3.78 (s, 3 H), 6.8-7.12 (m, A_2B_2 system, 4 H), 9.79 (t, 1 H, J = 1 Hz). Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 73.17; H, 7.32.

Reaction of 1-Phenyl-2-(2-Thiazolyl)-(*E*)-ethene (8f) with *n*-Butyl Lithium Cuprate. A solution of *n*-BuLi (8 mmol) was added dropwise to a stirred and cooled (0° C) suspension of CuI (0.76 g, 4 mmol) in diethyl ether (30 mL). After 30 min, the reaction mixture was cooled at -20° C and then the alkene **8f** (0.7 g, 3.7 mmol) in diethyl ether (20 mL) was added dropwise. After 2 h stirring, the reaction was washed with saturated $NaHCO_3$, the organic layer was dried over anhydrous Na_2SO_4, filtered and the solvent was removed under vacuum. The residue was chromatographed (silica gel, 9:1 petroleum ether-ethyl acetate) to give 0.3 g (33%) of 2-phenyl-1-(2-thiazolyl)-hexane (**16**): oil; ^1H NMR δ 0.8 (t, 3 H), 1.2 (m, 4 H), 1.7 (m, 2 H), 3.1 (t, 1 H), 3.3 (m, 2 H), 7.08 (d, 1 H, J = 3.2 Hz), 7.2 (m, 5 H), 7.6 (d, 1 H, J = 3.2 Hz); mass spectrum *m/e* (relative intensity) 245 (M^+, 30), 202 (20), 188 (18), 147 (12), 99 (25), 91 (100). Anal. Calcd for $C_{15}H_{19}NS$: C, 73.44; H, 78.81; N, 5.71. Found: C, 73.48; H, 7.86; N, 5.69.

Compound **16** (0.14 g, 0.56 mmol) was subjected to formyl deblocking as described above for vinylthiazoles (*N*-methylation, reduction, hydrolysis) without isolation of the intermediates. The crude aldehyde was chromatographed (silica gel, 8:2 petroleum ether-ethyl acetate) to give 0.035 g (64%) of pure 3-penylheptanal (**17**): oil; IR (film) 1730 cm^{-1}; ^1H NMR δ 0.8 (t, 3 H), 1.23 (m, 4 H), 1.63 (m, 2 H), 2.68 (m, 2 H), 3.10 (m, 1 H), 7.30 (s, 5 H), 9.65 (t, 1 H, J = 2.0 Hz); mass spectrum *m/e* (relative intensity) 190 (M^+, 52), 133 (96), 105 (87), 91 (100). Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.54. Found: C, 82.11; H, 9.58.

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