Synthesis of 4-Acyl- and 4-Alkenyl-3,5-dimethylisothiazole Derivatives

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4-Acyl- and 4-alkenyl-3,5-dimethylisothiazole derivatives, not available by direct electrophilic substitution [1-5] have been prepared from 3,5-dimethyl-4-isothiazolylcarbonitrile **1** and the corresponding aldehyde **2** in satisfactory yields. Both compounds, **1** and **2**, are readily obtained from 3,5-dimethyl-4-iodoisothiazole, whose preparation we have previously reported [6].

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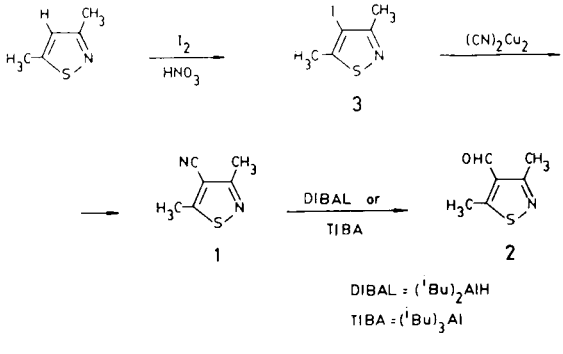
4-Acyl- and 4-alkenylisothiazoles are of remarkable interest in many synthetic pathways [7-13]. Moreover, they are present in many pharmaceutical products [14-17] and have been employed as intermediates in the preparation of diverse natural products with biological and insecticidal activity [17-23]. So far, there is not reported any general procedure for the preparation of 4-acyl- and 4-alkenylisothiazoles, and it is not possible to obtain them by a Friedel-Crafts reaction and related processes [1-5].

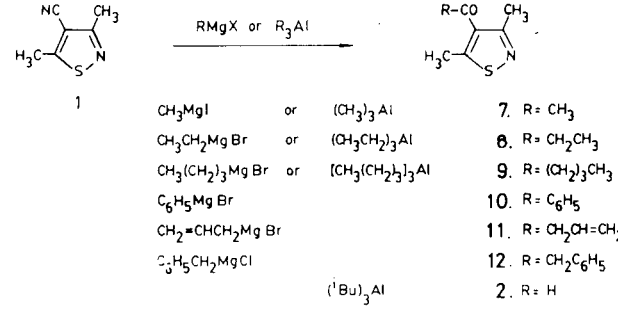
In the course of our investigations on the synthesis of heteropentacycles with potential biological interest [24], we found that 4-acyl- and 4-alkenylisothiazole derivatives have great importance as intermediates in the synthesis of analogues of penicillin and cephalosporin systems, in which the benzene nucleus is substituted by a heteroaromatic compound [12,17,22,23,25]. Also, formylisothiazoles have been employed in the preparation of antihistamine products [21,26,27].

In this paper we report a convenient synthesis of both 4-acyl- and 4-alkenylisothiazole derivatives from 3,5-dimethyl-4-isothiazolylcarbonitrile (**1**) and carboxaldehyde **2**. The previously reported synthesis of nitrile **1** [28], has been also improved in our work. It has been reported [29] that a cyano group attached at C-4 of the 3,5-dimethylisothiazole system is not reduced by diverse lithium aluminum hydrides; consequently, the introduction of a formyl group at C-4 has been carried out by using 4-isothiazolylcarboxilic acid derivatives [26-30]. Now, we have found that 3,5-dimethyl-4-isothiazolylcarbonitrile **1** reacts with both diisobutylaluminum hydride (DIBAL) and triisobutylaluminum (TIBA) affording the corresponding aldehyde **2** in high yields (about 80%) (Scheme 1).



Scheme 1

The nitrile **1** reacts with organometallic compounds, leading to 4-acylisothiazoles (Scheme 2) in yields which depend on the nature and hindrance of the reagent (Table 1). As expected, organoaluminum reagents provide higher yields than the corresponding Grignard ones. In the first case, 4-isothiazolylketones are obtained, except in the reaction with triisbutylaluminum (TIBA), in which 3,5-dimethyl-4-isothiazolylcarboxaldehyde **2** is obtained as the only product *via* hydride transfer, yield 75%. Grignard compounds add to nitrile **1**, leading to 4-acylisothiazoles, although yields in these reactions are less than 40% in all cases.



Scheme 2

According to the above results, **1** seems to be the suitable precursor of 4-acylisothiazoles by reaction with organoaluminum compounds.

The synthesis of 4-alkenylisothiazoles has been carried out by two different ways. 3,5-Dimethyl-4-isothiazolylcarboxaldehyde (**2**), by reaction with organometallic compounds leads to 4α-hydroxyalkyl derivatives (Scheme 3).

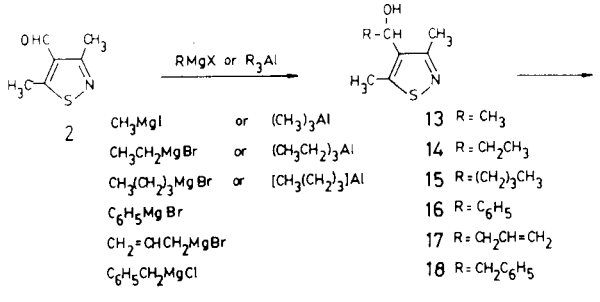
The above 4α-isothiazolylcarbinols (Table 2) are direct precursors of 4-alkenylderivatives by dehydration with *p*-toluenesulfonic acid (*p*-TSA).

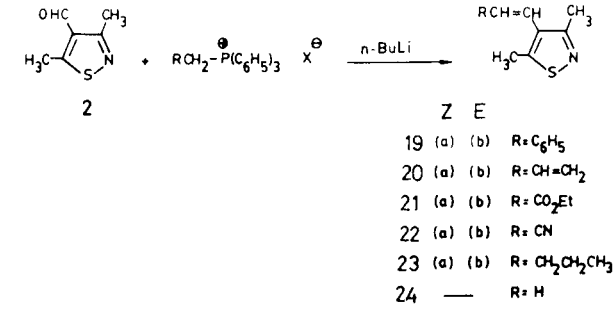
Table 1

Reactions of 3,5-Dimethyl-4-isothiazolylcarbonitrile (**1**) with Organometallic Reagents

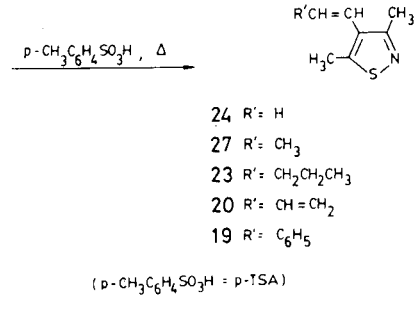
Organometallic reagent	Product (%)	Mp (°C) or Bp (°C)/Torr	Ir ν [cm^{-1}] (film or potassium bromide)	^{1}H NMR δ [ppm] (Deuteriochloroform)
CH_3MgI	**7** [a] (41)	49-50 (benzene)	1670, 1250 (CO), 1510 (ring)	2.45 (s, 3H), 2.55 (s, 3H), 2.65 (s, 3H)
$(CH_3)_3Al$	**7** [a] (67)	"	"	"
CH_3CH_2MgBr	**8** [b] (29)	90-91/1.0	1670, 1210 (CO), 1510 (ring)	1.15 (t, 3H), 2.50 (s, 3H), 2.65 (s, 3H), 2.40-2.60 (q, 2H)
$(CH_3CH_2)_3Al$	**8** [b] (70)	"	"	"
$CH_3(CH_2)_3MgBr$	**9** [c] (32)	100-101/0.6	1670, 1230 (CO), 1530 (ring)	0.90 (t, 3H), 1.30 (m, 4H), 2.30 (s, 3H), 2.40 (s, 3H), 2.70 (m, 2H)
$(CH_3(CH_2)_3)_3Al$	**9** [c] (59)	"	"	"
C_6H_5MgBr	**10** [d] (38)	63-64 (benzene)	1670, 1270 (CO), 1610, 1590, 750, 790 (Ph), 1540 (ring)	2.30 (s, 3H), 2.35 (s, 3H), 7.50-8.00 (m, 5H)
$CH_2=CHCH_2MgBr$	**11** [e,f] (19)	- - -	- - -	- - -
$C_6H_5CH_2MgCl$	**12** [e,g] (23)	- - -	- - -	- - -

[a] 2,4-DNPH, mp 136-137° (ethanol). [b] 2,4-DNPH, mp 124-126° (ethanol). [c] 2,4-DNPH, mp 174-175° (ethanol). [d] 2,4-DNPH, mp 168-169° (ethanol). [e] This compound was only characterized as its 2,4-DNPH derivative. [f] 2,4-DNPH, mp 151-152° (ethanol). [g] 2,4-DNPH, mp 136-137° (ethanol).





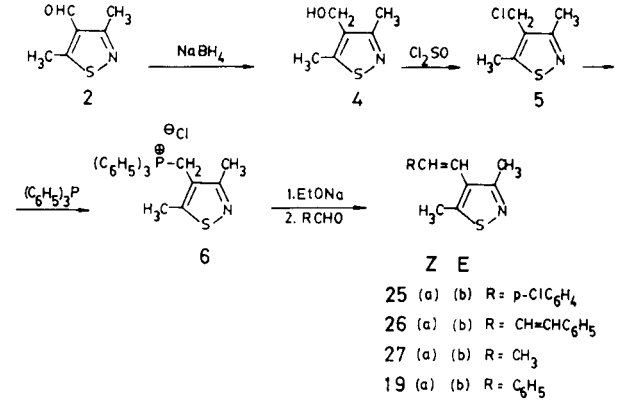
Scheme 4



Scheme 3

On the other hand, the Wittig reaction has been used with success in the synthesis of 4-alkenylisothiazoles. Aldehyde **2** reacts with phosphorus ylids affording the corresponding olefins (Scheme 4) in high yields (Table 3).

In order to complete the study of the scope of the reaction we have synthesized the phosphonium salt derived from 4-chloromethyl-3,5-dimethylisothiazole (**5**). This salt, **6**, was transformed into the corresponding phosphorus ylid with ethanolic sodium ethoxide (Scheme 5). It reacts with aldehydes yielding the olefins **19**, **25**, **26** and **27** (Table 4).



Scheme 5

Table 2

Reactions of 3,5-Dimethyl-4-isothiazolylcarboxaldehyde (**2**) with Organometallic Reagents

Organometallic reagent	Product (%)	Mp (°C) or Bp (°C)/Torr	Ir ν [cm^{-1}] (film or potassium bromide)	^{1}H NMR δ [ppm] (Deuteriochloroform)
CH_3MgI	**13** (34)	70-71/0.5	3600-3000 (OH), 1090 (C-O), 1560 (ring)	1.45 (d, 3H), 2.40 (s, 3H), 2.50 (s, 3H), 3.80 (br s, 1H), 5.00 (q, 1H)
$(CH_3)_3Al$	**13** (69)	"	"	"
CH_3CH_2MgBr	**14** (39)	74-75/0.3	3350 (OH), 1040 (C-O), 1550 (ring)	0.85 (t, 3H), 1.75 (m, 2H), 2.25 (s, 3H), 2.45 (s, 3H), 4.35 (s, 1H), 4.65 (d, 1H)
$(CH_3(CH_2)_3Al$	**14** (73)	"	"	"
$CH_3(CH_2)_3MgBr$	**15** (24)	80-81/0.3	3300 (Oh), 1030 (C-O), 1540 (ring)	0.90 (t, 3H), 1.25 (m, 4H), 2.05 (m, 2H), 2.20 (s, 3H), 2.30 (s, 3H), 3.60 (m, 1H), 5.10 (br s, 1H)
$(CH_3(CH_2)_3)Al$	**15** (65)	"	"	"
C_6H_5MgBr	**16** (27)	82-83 (ether)	3250 (OH), 1040 (C-O), 1600, 1500, 740, 690 (Ph), 1550 (ring)	2.20 (s, 3H), 2.35 (s, 3H), 4.20 (br s, 1H), 6.00 (s, 1H), 7.30 (s, 5H)
$CH_2=CHCH_2MgCl$	**17** [a,b] (22)	- - -	- - -	- - -
$C_6H_5CH_2MgCl$	**18** [a,c] (19)	- - -	- - -	- - -

[a] This compound was only characterized as its phenylsulfenylcarbamate derivative. [b] Phenylsulfenylcarbamate, mp 174-175° (hexane). [c]Phenylsulfenylcarbamate, mp 198-199° (benzene-hexane).

Table 3

Wittig Reactions of 3,5-Dimethyl-4-isothiazolylcarboxaldehyde (**2**) with Phosphorus Ylids

Phosphonium salt	Product (%) [a]	*Z*:*E* ratio
$C_6H_5CH_2P(C_6H_5)_3Cl$	**19** (93)	**19a:19b**/1:2
$CH_2=CHCH_2P(C_6H_5)_3Br$	**20** (87)	**20a:20b**/1:1.5
$C_2H_5O_2CCH_2P(C_6H_5)_3Cl$	**21** (81)	**21a:21b**/1:1.1
$NCCH_2P(C_6H_5)_3Cl$	**22** (70)	**22a:22b**/1:1.2
$CH_3(CH_2)_3P(C_6H_5)_3Br$	**23** (85)	**23a:23b**/2.5:1
$CH_3P(C_6H_5)_3I$	**24** (69)	

[a] Yields referred to the mixture of *Z*-*E* isomers.

Table 4

Wittig Reactions of (3,5-Dimethyl-4-isothiazolyl)-methyl Triphenylphosphonium Chloride (**6**) with Aldehydes

Aldehyde	Product (%) [a]	*Z*:*E* ratio
C_6H_5CHO	**19** (73)	**19a:19b**/1:1.1
p-ClC_6H_4CHO	**25** (79)	**25a:25b**/1:1.2
$C_6H_5CH=CHCHO$	**26** (59)	
CH_3CHO	**27** (62)	**27a:27b**/1:0.8

[a] Yields referred to the mixture of *Z*-*E* isomers.

As was expected, the Wittig reaction leads to a mixture of isomers *Z* and *E*, in a ratio which depends on the stabilization of the phosphorus ylid intermediate. So, we have found that the *Z* isomer is predominant when alkyl halides are used to obtain the phosphonium salt (*Z*:*E*/2.5:1); and the *E* isomer is the major product when benzyl- or allylphosphonium salts are used (*Z*:*E*/1:2). However, 3,5-dimethyl-4-isothiazolylmethyltriphenylphosphonium chloride (**6**) leads to a mixture of olefins in a ratio *Z*:*E*/1:1.2. This ratio is less than expected from the analogous reaction (Table 3) of benzyltriphenylphosphonium chloride and 3,5-dimethyl-4-isothiazolylcarboxaldehyde (**2**), in which the ratio was *Z*:*E*/1:2. It may be that the introduction of a bulky substituent at C-4 as well as the steric hindrance of the methyl groups at C-3 and C-5 results in the non-planarity of the system; this effect would explain the above result. Both isomeric olefins are well separated by flash-chromatography. The stereochemistry of the double bond is not important if the 4-alkenyl-3,5-dimethylisothiazoles are to be used as precursors of 4-alkyl derivatives.

EXPERIMENTAL

Melting points were determined with a Buchi apparatus and are uncorrected, as are the boiling points. The ir spectra were recorded by using a Pye-Unicam Model SP-1100 spectrophotometer, and the ^{1}H nmr spectra were performed on a Varian T-60 A instrument; chemical shifts are expressed in δ relative to TMS as internal standard. Elemental microanalyses were performed on a Perkin-Elmer analyzer.

The synthesis of 3,5-dimethylisothiazole and the corresponding 4-iododerivative **3**, was reported in a previous work [6].

3,5-Dimethyl-4-isothiazolylcarbonitrile (**1**).

3,5-Dimethyl-4-iodoisothiazole (**3**) (3.0 g, 0.020 mole) and cuprous cyanide (2.64 g, 0.029 mole) were homogeneously mixed and heated up to 185°. The temperature then rose suddenly to about 250°, and the reaction was kept up to 200° for 30 minutes by heating. After the mixture was cooled down, the residue was extracted with ether. The nitrile **1** was purified by distillation (yield, 76%), bp 158-160° (lit [28], bp 159-160°)

mp 51-52°; ir (film): 2240, 1540 cm^{-1}; ^1H nmr (carbon tetrachloride): δ 2.60 (s, 3H), 2.75 (s, 3H).

Anal. Calcd. for $C_6H_6N_2S$: C, 52.14; H, 4.37; N, 20.27. Found: C, 52.10; H, 4.33; N, 20.30.

3,5-Dimethyl-4-isothiazolylcarboxaldehyde (**2**).

Method A.

A solution of 5.0 g (0.036 mole) of the above nitrile **1** in toluene was added dropwise to a stirred solution of 0.047 mole of diisobutylaluminum hydride in 120 ml of toluene at -70° and the stirring was continued at that temperature for 8 hours. After the mixture was allowed to warm up to 0°, it was hydrolyzed with dilute hydrochloric acid and the product was extracted with ether. The extract was dried over magnesium sulfate and evaporated. The residue was recrystallized from hexane to give 3.93 g (75% yield) of **2**, mp 71-72°; ir (film): 2870, 2760, 1560 cm^{-1}; ^1H nmr (carbon tetrachloride): δ 2.60 (s, 3H), 2.80 (s, 3H), 10.20 (s, 1H).

Anal. Calcd. for C_6H_7NOS: C, 51.04; H, 4.99; N, 9.92. Found: C, 50.99; H, 5.02; N, 9.89.

Method B.

A solution of 5.0 g (0.0362 mole) of nitrile **1** in benzene was added slowly to a solution of 0.109 mole of triisobutylaluminum in 100 ml of dry benzene. The mixture was kept at reflux for 8 hours, and then quenched with ice/water. In this way, aldehyde **2** was obtained in a yield of 78%.

(3,5-Dimethyl-4-isothiazolyl)methyl Triphenylphosphonium Chloride (**6**).

A mixture of 12.38 g (0.076 mole) of 4-chloromethyl-3,5-dimethylisothiazole (**5**) [24b] and 19.90 g (0.076 mole) of triphenylphosphine was placed in 150 ml of dry xylene and was heated at reflux for 20 hours. After cooling at room temperature, the solid formed was collected by filtration, yield 98%, mp 298-299° (colorless prisms from ethanol).

Reactions of Nitrile **1** with Organoaluminum Compounds.

General Procedure.

A solution of 2.0 g (0.0145 mole) of nitrile **1** in 20 ml of dry benzene was added dropwise, with external cooling, to a solution of 0.0433 mole of trialkylaluminum reagent in 70 ml of the same solvent. The mixture was heated at reflux for 8 hours and then cooled, quenched with ice/water, and acidified with dilute hydrochloric acid. It was extracted with ether, and dried over magnesium sulfate. The solvent was evaporated, and the residue chromatographed over silica gel with methylene chloride:hexane (1:3) as eluent. 4-Acyl-3,5-dimethylisothiazoles **7**, **8** and **9** were purified by distillation or recrystallization and characterized as 2,4-dinitrophenylhydrazones (2,4-DNHP) (Table 1).

Reactions of Nitrile **1** with Grignard Reagent.

General Procedure.

A solution of 1.5 g (0.0108 mole) of nitrile **1** in 10 ml of dry ether was added to 0.0180 mole of the Grignard reagent in 20 ml of the same solvent. The resulting suspension was stirred at reflux for 10 hours. After cooling, the mixture was hydrolyzed with dilute hydrochloric acid, the organic layer dried over magnesium sulfate and the solvent distilled off. The residue was purified by chromatography over silica gel, with methylene chloride: hexane (1:3) as eluent. The 4-isothiazolylketones obtained are listed in Table 1, as are their physical and spectral data.

4-Acetyl-3,5-dimethylisothiazole (**7**).

Pure **7** was obtained by recrystallization from benzene, mp 49-50°.

Anal. Calcd. for C_7H_9NOS: C, 54.16; H, 5.84; N, 9.02. Found: C, 54.09; H, 5.79; N, 9.10.

2,4-Dinitrophenylhydrazone, mp 136-137° (from ethanol).

Anal. Calcd. for $C_{13}H_{13}N_5O_4S$: C, 46.56; H, 3.90; N, 20.88. Found: C, 46.56; H, 3.91; N, 20.85.

Ethyl-(3,5-dimethyl-4-isothiazolyl)ketone (**8**).

Pure **8** was obtained by distillation at reduced pressure as colorless liquid, bp 90-91°/1mm.

Anal. Calcd. for $C_8H_{11}NOS$: C, 56.77; H, 6.55; N, 8.27. Found: C, 56.69; H, 6.61; N, 8.25.

2,4-Dinitrophenylhydrazone, mp 124-125° (from ethanol).

Anal. Calcd. for $C_{14}H_{15}N_5O_4S$: C, 48.13; H, 4.32; N, 20.04. Found: C, 48.12; H, 4.32; N, 20.11.

n-Butyl (3,5-Dimethyl-4-isothiazolyl) Ketone (**9**).

This compound had bp 100-101°/0.6 mm.

Anal. Calcd. for $C_{10}H_{16}NOS$: C, 60.56; H, 8.13; N, 7.06. Found: C, 60.60; H, 8.19; N, 7.04.

2,4-Dinitrophenylhydrazone, mp 174-175° (from ethanol).

Anal. Calcd. for $C_{16}H_{19}N_5O_4S$: C, 50.92; H, 5.07; N, 18.55. Found: C, 50.90; H, 5.10; N, 18.54.

4-Benzoyl-3,5-dimethylisothiazole (**10**).

This compound was obtained as colorless plates, mp 63-64° from benzene.

Anal. Calcd. for $C_{12}H_{11}NOS$: C, 66.33; H, 7.66; N, 7.09. Found: C, 66.31; H, 7.62; N, 7.11.

2,4-Dinitrophenylhydrazone, mp 168-169° (from ethanol).

Anal. Calcd. for $C_{18}H_{15}N_5O_4S$: C, 54.40; H, 3.80; N, 17.62. Found: C, 54.41; H, 3.79; N, 17.62.

1-(3,5-Dimethyl-4-isothiazolyl)-3-buten-1-one (**11**).

This compound was only characterized as its 2,4-dinitrophenylhydrazone, mp 151-152° (from ethanol).

Anal. Calcd. for $C_{15}H_{15}N_5O_4S$: C, 49.85; H, 4.18; N, 19.38. Found: C, 49.83; H, 4.21; N, 19.37.

Benzyl (3,5-Dimethyl-4-isothiazolyl) Ketone (**12**).

This compound was only characterized as its 2,4-dinitrophenylhydrazone, mp 136-137° (from ethanol).

Anal. Calcd. for $C_{19}H_{19}N_5O_4S$: C, 55.19; H, 4.63; N, 16.93. Found: C, 55.18; H, 4.63; N, 16.89.

Reactions of Aldehyde **2** with Organoaluminum Compounds.

General Procedure.

The reactions were carried out as described for nitrile **1**, from 2.10 g (0.0145 mole) of 3,5-dimethyl-4-isothiazolylcarboxaldehyde **2** and 0.043 mole of trialkylaluminum reagent in benzene, during 8 hours at reflux. Compounds **13, 14** and **15** were isolated by chromatography over silica gel with methylene chloride as the eluent, and purified by distillation at reduced pressure. Their physical and spectral data are summarized in Table 2.

Reactions of Aldehyde **2** with Grignard Reagents.

General Procedure.

The reactions were carried out in the usual way, from 1.53 g (0.0108 mole) of aldehyde **2** and 0.036 mole of the corresponding Grignard reagent in ether and during a period of 8 hours at reflux. Compounds **13, 14, 15** and **16** were isolated by chromatography over silica gel with methylene chloride as eluent, and purified by distillation or recrystallization, In the reactions with allyl- and benzylmagnesium halides, carbinols **17** and **18** were identified as phenylsulfenylcarbamates. Physical and spectral data for compounds **13-18** are listed in Table 2.

1-(3,5-Dimethyl-4-isothiazolyl)-1-hydroxyethane (**13**).

This compound had bp 70-71°/0.5 mm.

Anal. Calcd. for $C_7H_{11}NOS$: C, 53.47; H, 7.05; N, 8.91. Found: C, 53.47; H, 7.10; N, 8.89.

1-(3,5-Dimethyl-4-isothiazolyl)-1-hydroxypropane (**14**).

This compound had bp 74-75°/0.3 mm.

Anal. Calcd. for $C_8H_{13}NOS$: C, 56.10; H, 7.65; N, 8.18. Found: C, 56.11; H, 7.63; N, 8.18.

1-(3,5-Dimethyl-4-isothiazolyl)-1-hydroxybutane (**15**).

This compound had bp 80-81°/0.3 mm.

Anal. Calcd. for $C_{10}H_{17}NOS$: C, 60.26; H, 8.59; N, 7.02. Found: C, 60.23; H, 8.60; N, 7.04.

(3,5-Dimethyl-4-isothiazolyl)phenylcarbinol (**16**).

Pure **16** was obtained by recrystallization from benzene, mp 82-83°.

Anal. Calcd. for $C_{12}H_{13}NOS$: C, 65.72; H, 5.97; N, 6.38. Found: C, 65.71; H, 6.00; N, 6.37.

Allyl-(3,5-dimethyl-4-isothiazolyl)carbinol (**17**).

This compound was only characterized as its phenylsulfenylcarbamate, mp 174-175° (from hexane).

Anal. Calcd. for $C_{16}H_{18}N_2O_4S_2$: C, 52.44; H, 4.95; N, 7.64. Found: C, 52.44; H, 4.96; N, 7.64.

1-(3,5-Dimethyl-4-isothiazolyl)-1-hydroxy-2-phenylethane (**18**).

This compound was only characterized as its phenylsulfenylcarbamate, mp 198-199° (from hexane-benzene).

Anal. Calcd. for $C_{20}H_{20}N_2O_4S_2$: C, 57.67; H, 4.84; N, 6.72. Found: C, 57.65; H, 4.89; N, 6.70.

Wittig Reactions.

Procedure A. Reactions of 3,5-Dimethyl-4-isothiazolylcarboxaldehyde (**2**) with Phosphorus ylids.

To a stirred suspension of 0.012 mole of phosphonium salt in 100 ml of anhydrous ether was added 0.01 mole of *n*-butyl lithium *via* a syringe under nitrogen and allowed to stir for 1 hour at room temperature. A solution of 1.4 g (0.01 mole) of aldehyde **2** in 20 ml of ether was then added dropwise and the stirring was continued for 6 hours. The solid triphenylphosphine oxide was removed by filtration and the filtrate was evaporated to give a mixture of *Z* and *E* olefins **19-24** in varying proportions (Table 3). Chromatography of the residue over silica gel with hexane as eluent gave a first fraction of pure *Z* olefin, followed by the *E* isomer. Physical and spectral data for 4-alkenylisothiazoles **19-24** are listed in Table 5.

Procedure B. Reactions of (3,5-Dimethyl-4-isothiazolyl)methyl Triphenylphosphonium Chloride (**6**) with Aldehydes.

The salt **6** (0.008 mole) and the corresponding aldehyde were placed in 50 ml of anhydrous ethanol. A freshly prepared (from 0.196 g of sodium and 25 ml of ethanol) ethanolic sodium ethoxide solution was added slowly with stirring. The mixture was heated at reflux during 4 hours, then hydrolyzed with dilute hydrochloric acid and extracted with methylene chloride. Solvent evaporation gave a mixture of *Z* and *E* olefins **19**, **25**, **26** and **27** in varying proportions (Table 4), which were separated by chromatography over silica gel with hexane as eluent. Physical and spectral data for pure *Z* and *E* isomeric compounds are listed in Table 5.

Z-1-(3,5-Dimethyl-4-isothiazolyl)-2-phenylethylene (**19a**).

This compound had bp 107-108°/2 mm.

Anal. Calcd. for $C_{13}H_{13}NS$: C, 72.51; H, 6.08; N, 6.50. Found: C, 72.49; H, 6.10; N, 6.50.

E-1-(3,5-Dimethyl-4-isothiazolyl)-2-phenylethylene (**19b**).

Pure **19b** was obtained by recrystallization from benzene, mp 70-71°.

Anal. Calcd. for $C_{13}H_{13}NS$: C, 72.51; H, 6.08; N, 6.50. Found: C, 72.50; H, 6.09; N, 6.52.

Table 5

4-Alkenyl-3,5-dimethylisothiazoles

Mp (°C) or Isothiazole	Bp (°C)/Torr	IR ν [cm^{-1}] (film or Potassium bromide)	^1H NMR δ (Deuteriochloroform)
19a	107-108/2	1600, 770 (C=C), 1530 (ring), 1500, 710, 690 (Ph)	2.20 (s, 3H), 2.40 (s, 3H), 6.30 (d, 1H), 6.70 (d, 1H), 6.80-7.40 (m, 5H)
19b	70-71 (benzene)	1620, 930 (C=C), 1520 (ring), 1580, 1480, 720, 690 (Ph)	2.60 (s, 3H, 2.70 (s, 3H), 6.90 (d, 2H), 7.40 (m, 5H)
20a	69-70/0.1	1610, 780 (C=C), 1540 (ring),	2.20 (s, 3H), 2.30 (s, 3H), 5.10-5.30 (m, 2H), 6.00-6.50 (m, 3H)
20b	70-72/0.2	1620, 900 (C=C), 1530 (ring)	2.40 (s, 3H), 2.50 (s, 3H), 5.00-5.50 (m, 2H), 5.80-6.00 (d, 3H)
21a	49-50/1	1690, 1280 (CO_2Et), 1610, 740 (C=C), 1510 (ring)	1.30 (t, 3H), 2.50 (s, 3H), 2.60 (s, 3H), 4.10 (q, 2H), 6.00 (d, 1H), 7.40 (d, 1H)
21b	49-50/1	1690, 1280 (CO_2Et), 1620, 910	1.30 (t, 3H), 2.55 (s, 3H), 2.65 (s, 3H), 4.10 (q, 2H), 6.70 (m, 2H)
22a	75-76/1.5	2230 (CN), 1520 (ring), 1610, 760 (C=C)	2.40 (s, 3H), 2.45 (s, 3H), 6.20 (d, 1H), 7.50 (d, 1H)
22b	79-80/1	2220 (CN), 1530 (ring), 1620, 890 (C=C)	2.45 (s, 3H), 2.50 (s, 3H), 7.00 (m, 2H)
23	65-66/0.4	1630, 960 (C=C), 1540 (ring)	0.90 (t, 3H), 1.40 (m, 2H), 1.80 (m, 2H), 2.30 (s, 3H), 2.40 (s, 3H), 5.90 (m, 1H), 6.30 (d, 1H)
24	70-71/0.5	1610, 985, 900 (C=C), 1540 (ring)	2.50 (s, 3H), 2.60 (s, 3H), 5.40 (dd, 1H), 5.60 (dd, 1H), 6.60 (dd, 1H)
25a	80-81 (benzene-hexane)	1650, 780 (C=C), 1540 (ring)	2.20 (s, 3H), 2.30 (s, 3H), 6.30 (d, 1H), 6.70 (d, 1H), 6.95 (d, 2H), 7.20 (d, 2H)
25b	90-91 (benzene-hexane)	1620, 940 (C=C), 1540 (ring)	2.50 (s, 3H), 2.55 (s, 3H), 6.85 (d, 2H), 7.35 (s, 4H)
26	117-118 (benzene)	1640, 890 (C=C), 1540 (ring)	2.40 (s, 6H), 6.30-6.80 (m, 4H), 7.10-7.50 (m, 5H)
27a	69-70/0.3	1640, 790 (C=C), 1540 (ring)	1.63 (d, 3H), 2.35 (s, 3H), 2.40 (s, 3H), 5.80-6.30 (m, 2H)
27b	72-73/0.5	1670, 940 (C=C), 1530 (ring)	2.00 (d, 3H), 2.45 (s, 3H), 2.55 (s, 3H), 5.70-6.00 (m, 2H)

Z-1-(3,5-Dimethyl-4-isothiazolyl)-1,3-butadiene (**20a**).

This compound had bp 69-70°/0.1 mm.

Anal. Calcd. for $C_9H_{11}NS$: C, 65.41; H, 6.71; N, 8.47. Found: C, 65.41; H, 6.71; N, 8.50.

E-1-(3,5-Dimethyl-4-isothiazolyl)-1,3-butadiene (**20b**).

This compound had bp 70-72°/0.2 mm.

Anal. Calcd. for $C_9H_{11}NS$: C, 65.41; H, 6.71; N, 8.47. Found: C, 65.40; H, 6.69; N, 8.47.

Z-Ethyl 3-(3,5-Dimethyl-4-isothiazolyl)propenoate (**21a**).

This compound had bp 49-50°/1 mm.

Anal. Calcd. for $C_{10}H_{13}NO_2S$: C, 56.84; H, 6.20; N, 6.63. Found: C, 56.83; H, 6.19; N, 6.63.

E-Ethyl 3-(3,5-Dimethyl-4-isothiazolyl)propenoate (**21b**).

This compound had bp 49-50°/1 mm.

Anal. Calcd. for $C_{10}H_{13}NO_2S$: C, 56.84; H, 6.20; N, 6.63. Found: C, 56.84; H, 6.21; N, 6.60.

Z-3-(3,5-Dimethyl-4-isothiazolyl)propenenitrile (**22a**).

This compound had bp 75-76°/1.5 mm.

Anal. Calcd. for $C_8H_8N_2S$: C, 58.51; H, 4.91; N, 8.52. Found: C, 58.50; H, 4.91; N, 8.50.

E-3-(3,5-Dimethyl-4-isothiazolyl)propenenitrile (**22b**).

This compound had bp 79-80°/1 mm.

Anal. Calcd. for $C_8H_8N_2S$: C, 58.51; H, 4.91; N, 8.52. Found: C, 58.48; H, 4.90; N, 8.52.

E-1-(3,5-Dimethyl-4-isothiazolyl)-1-pentene (**23**).

This compound had bp 65-66°/0.4 mm.

Anal. Calcd. for $C_{10}H_{15}NS$: C, 66.25; H, 8.34; N, 7.72. Found: C, 66.26; H, 8.33; N, 7.70.

3,5-Dimethyl-4-vinylisothiazole (**24**).

This compound had bp 70-71°/0.5 mm.

Anal. Calcd. for C_7H_9NS: C, 60.39; H, 6.51; N, 10.06. Found: C, 60.38; H, 6.50; N, 10.10.

Z-1-(3,5-Dimethyl-4-isothiazolyl)-2-*p*-chlorophenylethylene (**25a**).

Pure **25a** was obtained by recrystallization from benzene-hexane, mp 80-81°.

Anal. Calcd. for $C_{13}H_{12}ClNS$: C, 62.51; H, 4.84; N, 5.60. Found: C, 62.51; H, 4.85; N, 5.62.

E-1-(3,5-Dimethyl-4-isothiazolyl)-2-*p*-chlorophenylethylene (**25b**).

Pure **25b** was obtained by recrystallization from benzene-hexane, mp 90-91°.

Anal. Calcd. for $C_{13}H_{12}ClNS$: C, 62.51; H, 4.84; N, 5.60. Found: C, 62.50; H, 4.85; N, 5.61.

E-1-(3,5-Dimethyl-4-isothiazolyl)-4-phenyl-1,3-butadiene (**26**).

Pure **26** was obtained by recrystallization from benzene, bp 117-118°.

Anal. Calcd. for $C_{15}H_{15}NS$: C, 74.64; H, 6.26; N, 5.80. Found: C, 74.62; H, 6.25; N, 5.80.

Z-1-(3,5-Dimethyl-4-isothiazolyl)-1-propene (**27a**).

This compound had bp 69-70°/0.3 mm.

Anal. Calcd. for $C_6H_{11}NS$: C, 62.70; H, 7.23; N, 9.14. Found: C, 62.68; H, 7.23; N, 9.13.

E-1-(3,5-Dimethyl-4-isothiazolyl)-1-propene (**27b**).

This compound had bp 72-73°/0.5 mm.

Anal. Calcd. for $C_6H_{11}NS$: C, 62.70; H, 7.23; N, 9.14. Found: C, 62.71; H, 7.22; N, 9.10.

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