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Palladium(0)-Catalyzed Alkylation of Thiols

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Abstract. **Palladium(0)-catalyzed alkylation of various allylic carbonates by aromatic thiols allowed the easy preparation of various allylic aryl sulphides in quite good yields. The reaction was regioselective with substitution at the less hindered side of the π-allyl system whatever the temperature of the reaction, and was diastereoselective with net retention of configuration.**

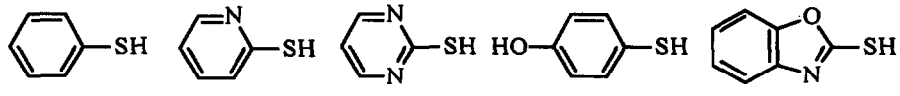
INTRODUCTION

Palladium(0)-catalyzed nucleophilic substitution of allylic compounds is now an usual tool in organic synthesis.[1] The wide application of this methodology in synthetic strategies is mainly due to the facile reaction of the allylic substrates and also the high stereospecificity and the chemoselectivity of the reaction. However, although catalytic alkylation using phosphine-palladium complexes and allylic acetates or carbonates has been carried out with carbon , oxygen and nitrogen nucleophiles, the sulfur nucleophiles are not so popular in such reactions. Effectively under classical alkylation conditions, sulfur nucleophiles could poisoned the catalyst system by precipitating the palladium from the solution, or tying-up the complex in solution in an unreactive form. Bosnich *et al.*[2] used an *O*-allyl *S*-alkyl dithiocarbonate substrate; in the presence of palladium(0), allyl alkyl sulfides are obtained with quite good yields. By reacting silylated thiols with allylic carbonates, Trost *et al.*[3] also obtained the corresponding allyl alkyl sulfides. However the major drawback of these two methodologies is the preparation, for each sulfur nucleophile, of the corresponding *O*-allyl *S*-alkyl dithiocarbonate or silylated thiol. We described in a preliminary communication [4] the clean and quantitative reaction of thiols with allylic carbonates in the presence of a catalytic amount of palladium(0) affording the corresponding allyl alkyl sulfide; similar results were also published by Moreno-Mañas *et al.*[5] More recently, efficient removal of allyloxycarbonyl protecting group by palladium catalyzed reaction was shown to occur in the presence of sulfur nucleophiles.[6] We report in this paper the details of our work in this field and particularly the regio and stereoselectivity of the reaction.

RESULTS AND DISCUSSION

We recently described the alkylation of allylic carbonates by oxygen nucleophiles.[7] We thought that this methodology could also be advantageously used for sulfur nucleophiles; in this case the nucleophile being produced in small concentrations, never higher than those of the π-allyl intermediate, would not interfere with the catalyst by coordination.

We have studied the palladium(0)-catalyzed alkylation of several thiols, i.e. thiophenol **1**, 2-mercaptopyridine **2**, 2-mercaptopyrimidine **3**, 4-hydroxythiophenol **4**, and thiobenzoxazolone **5**; it is to be noticed that compounds **2**, **3**, **4** and **5** are ambident nucleophiles. Our results are collected in Table 1.



1 (R^1SH) **2** (R^2SH) **3** (R^3SH) **4** (R^4SH) **5** (R^5SH)

Scheme 1. Structures of Thiols

Allyl methyl carbonate **6** and cinnamyl methyl carbonate **7** reacted with thiophenol at 50 °C to give the corresponding allylated compounds **15** and **20** with quite good yields (runs 1 and 6); in the case of cinnamyl thiophenyl **20** we only observed the presence of the *E*-isomer characterized by the coupling constant ^3J = 15.7 Hz for the ethylenic proton. Reactions of allylic carbonates **6** and **7** with the ambident nucleophiles **2**, **3** and **5** afford the *S*-allyl and *S*-cinnamyl derivatives (runs 2, 3, 5, 7 and 8), showing preferential attack of the π-allyl intermediate by the sulfur nucleophilic center. This regioselectivity was determined by ^{1}H-NMR and ^{13}C-NMR spectroscopy. The signals for the S-C*H*$_2$ appear as a doublet at approximatively 4 ppm (see Experimental Part), the N-C*H*$_2$ signal appearing at 4.5-5.0 ppm; the signal for the S-*C*H$_2$ appear in ^{13}C-NMR at ~ 33.0 ppm whereas those for N-*C*H$_2$ would appear above 40 ppm. Similar results were obtained by Moreno-Mañas *et al.*[5] Here again we observed for cinnamyl compounds **21** and **22** the presence of a single stereoisomer of *E* configuration as shown by the coupling constant for the ethylenic proton (^3J = 15.7 Hz for **21** and 15.6 Hz for **22**). Hydroxythiophenol **4** gives the product **18** resulting from a *(S)*-allylation as indicated by the chemical shift of the -CH$_2$- at δ = 3.41 ppm in the ^{1}H NMR and 39.3 ppm in the ^{13}C NMR); this is due to the higher acidity of the thiol function *versus* the alcohol function.

A secondary carbonate **8** or a tertiary carbonate **9** (runs 9 and 10) are also alkylated by thiopyridine **2**; in the later case we observed the formation of a single isomeric product **24** by attack of the nucleophile at the less substituted allylic termini of the π-allyl complex. The reaction of the carbonate **10** derived from geraniol with thiopyridine (run 11) is sluggish (only 50 % conversion after 24 h); we noticed the preferential formation of the *E* isomer **25** (*E*/*Z* ratio 76/24) as shown by ^{13}C NMR and this is different from Trost's results [3] who obtained only the *E* isomer using thiophenol as a nucleophile.

Regioisomeric allylic carbonates **11** and **12** (entries 12,13 and 14) gave identical mixtures of regio and stereoisomeric sulfides. The more substituted alkene is predominant (95 % vs 5 %) using thiophenol **1** or thiopyridine **2** as a nucleophile, a mixture of *E* and *Z* isomers (85/15) being obtained as shown by ^{13}C-NMR. The structure of compound **29** was determined by comparison of the ^{1}H and ^{13}C spectra with an authentic sample prepared by a Mitsunobu reaction using thiopyridine and the corresponding branched alcohol. In the case of the linear sulfide **28**, the *E* and *Z* stereochemistry was determined on the basis of the NMR spectra of the mixture. The chemical shifts for the allylic carbons of the major isomer at 32.6 ppm and 34.4 ppm are at higher field than those of the minor isomer (δ = 27.3 and 29.3 ppm) and correspond to the *E* isomer. The signals corresponding to the allylic protons are also shielded in the case of the *E* isomer. This stereochemistry was confirmed by the coupling constant of the ethylenic proton for the major isomer (^3J = 15.2 Hz) characteristic of a *E* stereochemistry.

Table 1. Palladium(0)-Mediated Allyl Sulfide Synthesis.[a]

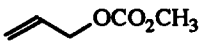
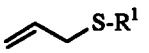
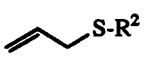
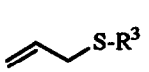
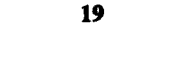
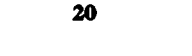
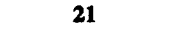
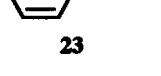
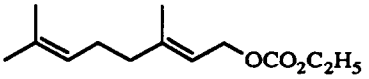
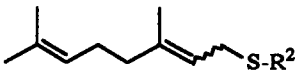
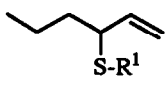
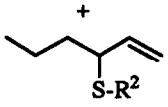
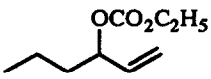
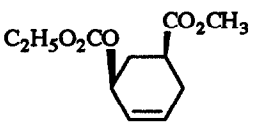
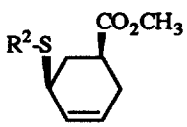
Run	Carbonate	Thiol	Product(s)	Yield (%)[b] (ratio)[c]
1	 **6**	1	 **15**	83
2	**6**	2	 **16**	86
3	**6**	3[d]	 **17**	77
4	**6**	4	 **18**	87
5	**6**	5	 **19**	44
6	**7**	1	 **20**	60
7	**7**	2	 **21**	74
8	**7**	3	 **22**	76
9	**8**	2	 **23**	89
10	 **9**	2	 **24**	51

Table 1 (continued)

11	 **10**	2	 **25** (*E*/*Z* : 76/24)	43 (50)[e]
12	 **11**	1	 **26** (*E*/*Z* : 80/20)[c] +  **27**	82 (95/5)
13	**11**	2	 **28** (*E*/*Z* : 85/15)[c] +  **29**	98 (95/5)
14	 **12**	2	**28** (*E*/*Z* : 85/15) + **29**	96 (98/2)
15	 **13**	2	 **30** (*E*/*Z* : 90/10)[c]	92
16	 **14**	2	 **31**	71

[a] General conditions: [carbonate]:[thiol]:[Pd]:[dppb] = 30:25:1:2; solvent tetrahydrofuran; 50 °C; 12 h; quantitative transformation. [b] Isolated yields and not optimized. [c] Determined by ^1H and ^{13}C NMR and finally gas chromatography. [d] Dimethylformamide was used as the solvent. [e] Only 50 % transformation.

We also undertook a study on the influence of the temperature on the ratio of *n/iso* sulfides in the reaction of thiophenol or thiopyridine with compounds **11** and **12** (Table 2). The ratio *n/iso* was about 90/10 whatever the temperature used, even at - 90 °C or + 60 °C. Treatment of compound **29**, containing a small amount of the linear sulfide **28** (6 %), by a catalytic amount of palladium(0) under the same conditions as those used for the alkylation (THF/ 60 °C) did not give predominantly the linear isomer **28**. This experiment shows that there is no transformation of the *iso* isomer to the linear one under our conditions; the sulfur nucleophile, which could be considered as a large nucleophile, attacks at the less substituted termini of the π-allyl intermediate, the steric effect being predominant.

Table 2. Influence of the Temperature on the *n/iso* Ratio in the Allylation of Thiols **1** and **2** with Carbonates **11** and **12**.[a]

Carbonate	Thiol	T °C	Time	*n/iso* [b]
12	**1**	60	5 mn	86/14
			24 h	87/13
		25	5 mn	84/16
			24 h	86/14
		- 90	60 mn (30 %)	83/17
			24 h	82/18
11	**2**	60	5 mn	83/17
			5 h	91/9
		25	5 mn	84/16
			24 h	88/12
12	**2**	60	5 mn	84/16
			24 h	93/07
		25	5 mn	83/17
			24 h	87/13
		0	15 mn (93 %)	82/18
			22 h	83/17
		- 40	15 mn (82 %)	80/20
			24 h	83/17
		- 90	20 mn (54 %)	84/16
			24 h	83/17

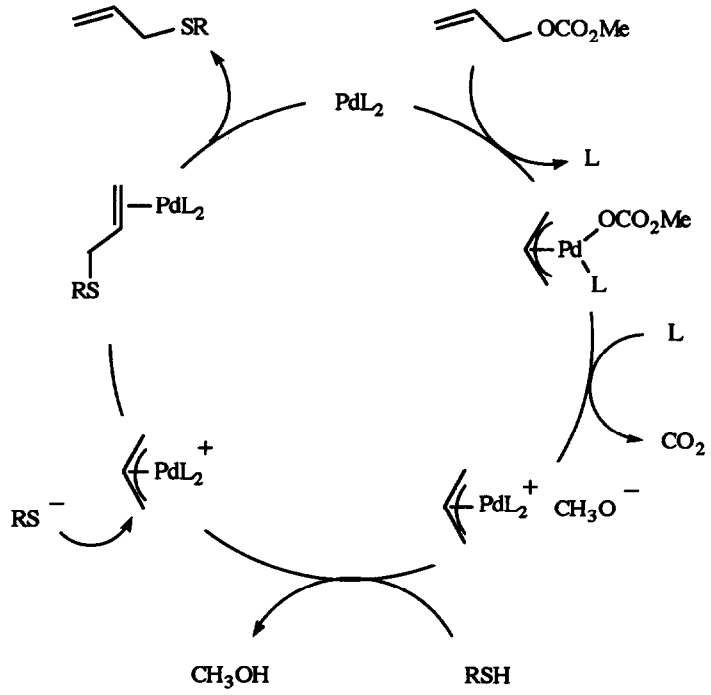
[a] General conditions: [carbonate]:[thiol]:[Pd]:[dppb] = 30:25:1:2; solvent tetrahydrofuran; quantitative transformation except when indicated into brackets, determined by gas chromatography. [b] Determined by gas chromatography.

On reaction with thiopyridine **2**, the *Z* allylic carbonate **13** (run 15) gives a mixture of *E* and *Z* allylic sulfides **30** (90/10). The assignment of the configuration was again mainly based on the ^{13}C NMR data; the signals of C-1 and C-4 corresponding to the major isomer are at lower field (δ = 69.9 ppm and 31.6 ppm respectively) than those corresponding to the minor isomer (δ = 65.6 and 27.1 ppm). The loss of the

stereochemistry of the double bond is due to the $\pi \rightleftharpoons \sigma \rightleftharpoons \pi$ equilibrium usually found in the π-allyl palladium complexes.

Finally entry 16 illustrates the stereoselectivity of the sulfur alkylation. As preceedingly shown, the reaction proceeds with overall retention of geometry. The *cis* isomer **14** gave only the *cis* isomer **31**, at 25 °C or 60 °C. The *cis* stereochemistry of compound **31** was determined from NOE experiments; irradiation of the proton at 4.65 ppm (>C*H*CO_2Me) shows an enhancement of 12 % of the signal at 2.77 ppm (>C*H*-S) and reversily irradiation of the signal at 2.77 ppm shows an enhancement of 13 % for the signal at 4.65 ppm.

The mechanism for the alkylation of allylic carbonate with sulfur nucleophiles in the presence of a catalytic amount of palladium(0) is the following one, analogous to the mechanism proposed by Tsuji for allylic carbonate alkylation with carbonucleophiles[1h] (Scheme 2). The first step is the formation of the π-allyl palladium species with inversion of configuration, leading to the formation of an alkoxide. Exchange with the thiol gives the nucleophile, which attacks the *exo*-face of the coordinated π-allyl giving the allyl alkyl sulfide with an overall retention of configuration.



Scheme 2. Mechanism of palladium(0)-mediated *S*-alkylation

CONCLUSION

Allylsulfides are important as synthetic intermediates and this process provides a very valuable solution to the preparation of such compounds starting from very easily accessible carbonates. The reaction is regioselective with formation of the less substituted alkylated sulfide and stereospecific with overall retention

of configuration. This work is now being extended to the preparation of chiral allyl sulfides and these results will be published in due course.

EXPERIMENTAL

^{1}H-NMR (200 and 300 MHz) and ^{13}C-NMR (50.3 MHz) spectra were recorded on Brüker AM 200 and AM 300 spectrometers, with $CDCl_3$ as the solvent. All chemical shifts are reported in ppm using tetramethylsilane as an internal standard. Chromatography was carried out on silica gel, Merck, grade 60 (230-400 mesh, 60 Å). GLC analyses were recorded with a capillary gas chromatography GIRDEL DELSI 330 equipped with a capillary column OV 101 (25 x 0.32 mm). Elemental analysis were performed at the CNRS, Vernaison. Tetrahydrofuran was distilled from sodium/benzophenone. All reactions using palladium complexes were carried out in Schlenk tubes under a nitrogen atmosphere. The carbonates **6-13** were prepared from the corresponding commercial alcohols by conventionnal procedures. Compound **15** is commercial and compounds **16**,[5a] **17**,[8] **20**,[9] **21** [5a] and **22** [5a] were already described in the literature.

General procedure for palladium(0)-mediated alkylation. To a degazed solution of $Pd_2(dba)_3$ (27.0 mg, 0.03 mmol) and 1,4-bis(diphenylphosphino)butane (51.2 mg, 0.12 mmol) in tetrahydrofuran (3 mL) was added a degazed solution of the carbonate (1.8 mmol) and thiol (1.5 mmol) in 2 mL of tetrahydrofuran. The stirred solution was kept 24 h under nitrogen at the desired temperature. Solvent evaporation followed by column chromatography through silica-gel provided the adduct(s).

4-(Allylthio)phenol 18. Oil; ^{1}H NMR (200 MHz) δ 3.41 (d, J = 6.9 Hz, 2 H, -CH_2S-), 4.95 (dd, J = 16.4 Hz, J = 1.2 Hz, 1 H, =CH_2), 4.99 (bd, J = 10.4 Hz, 1 H, =CH_2), 5.83 (ddt, J = 16.4 Hz, J = 10.4 Hz, J = 6.9 Hz, 1 H, -CH=), 6.77 (d, J = 8.5 Hz, 2 H, C_6H_4), 7.28 (d, J = 8.5 Hz, 2 H, C_6H_4); ^{13}C NMR δ 39.3 (CH_2S), 117.4 (=CH_2), 133.6 (-CH=), 116.0, 125.7, 134.1 and 155.1 (C_6H_4). Anal. Calcd. for $C_9H_{10}OS$: C, 65.03; H, 6.06. Found: C, 65.05; H, 6.10.

2-(Allylthio)benzoxazole 19. Oil; ^{1}H NMR (200 MHz) δ 3.94 (bd, J = 6.9 Hz, 2 H, -CH_2S-), 5.19 (dd, J = 10.0 Hz, J = 1.0 Hz, 1 H, =CH_2), 5.38 (dm, J = 16.9 Hz, 1 H, =CH_2), 6.09 (ddt, J = 16.9 Hz, J = 10.0 Hz, J = 6.9 Hz, 1 H, -CH=), 7.16-7.64 (m, 4 H, C_6H_4); ^{13}C NMR δ 34.8 (CH_2S), 119.2 (=CH_2), 132.1 (-CH=), 109.8, 118.4, 123.8, 124.2, 141.9 and 151.8 (C_6H_4), 164.2 (OC=N). Anal. Calcd. for $C_{10}H_9NOS$: C, 62.80; H, 4.74. Found: C, 62.06; H, 4.78.

3-(Pyridyl-2-thio)-1-cyclohexene 23. Oil; ^{1}H NMR (200 MHz) δ 1.58-2.15 (m, 6 H, -CH_2-), 4.57-4.61 (m, 1 H, H-3), 5.75-5.89 (m, 2 H, H-1 and H-2), 6.96 (dd, J = 7.4 Hz, J = 4.8 Hz, 1 H, H-5'), 7.13 (d, J = 8.0 Hz, 1 H, H-3'), 7.44 (ddd, J = 8.0 Hz, J = 7.4 Hz, J = 1.8 Hz, 1 H, H-4'), 8.41 (dd, J = 4.8 Hz, J = 1.8 Hz, 1 H, H-6'); ^{13}C NMR δ 19.8 (C-5), 24.9 (C-4), 29.3 (C-6), 39.9 (C-3), 126.9 and 130.5 (C-1 and C-2), 119.3, 122.4, 135.8, 149.4 and 159.2 (C_5H_4N). Anal. Calcd. for $C_{11}H_{13}NS$: C, 69.07; H, 6.85. Found: C, 69.13; H, 6.96.

3-Methyl-1(pyridyl-2-thio)-2-butene 24. Oil; ^{1}H NMR (200 MHz) δ 1.72 (bs, 6 H, CH_3), 3.81 (d, J = 7.7 Hz, 2 H, -CH_2S-), 5.36 (tm, J = 7.7 Hz, 1 H, -CH=), 6.95 (ddd, J = 7.3 Hz, J = 4.9 Hz, J = 1.0 Hz, 1 H, H-5'),

7.15 (bd, J = 8.1 Hz, 1 H, H-3'), 7.45 (ddd, J = 8.1 Hz, J = 7.3 Hz, J = 1.9 Hz, 1 H, H-4'), 8.42 (dd, J = 4.9 Hz, J = 1.9 Hz, 1 H, H-6'); ^{13}C NMR δ 13.7 (CH_3), 25.7 (CH_3), 28.5 (C-1), 119.2 (C-2), 138.0 (C-3), 119.2, 122.1, 135.8, 149.4 and 159.6 (C_5H_4N). Anal. Calcd. for $C_{10}H_{13}NS$: C, 67.00; H, 7.31. Found: C, 67.08; H, 7.65.

3,7-Dimethyl-1-(pyridyl-2-thio)-2,6-octadiene 25. Oil; ^{1}H NMR (as a mixture of stereoisomers) (200 MHz) δ 1.27, 1.30 and 1.34 (3 s, 9 H, CH_3), 1.91-2.14 (m, 4 H, H-4, H-5), 3.83 (d, 2 H, J = 7.7 Hz, H-1), 5.0-5.2 (bm, 1 H, -CH=), 5.30-5.41 (bm, 1 H, -CH=), 6.96 (dd, J = 7.0 Hz, J = 4.5 Hz, 1 H, H-5'), 7.16 (d, J = 8.1 Hz, 1 H, H-3'), 7.46 (bdd, J = 8.1 Hz, J = 7.0 Hz, 1 H, H-4'), 8.43 (bd, J = 4.5 Hz, 1 H, H-6'); ^{13}C NMR (as a mixture of streoisomers) δ 16.2 (CH_3 of *E* isomer), 17.7 (CH_3), 23.5 (CH_3 of *Z* isomer), 25.7 (CH_3), 26.5 (C-5 of *E* isomer), 26.7 (C-5 of *E* isomer), 28.1 (C-1 of *Z* isomer), 28.4 (C-1 of *E* isomer), 32.0 (C-4 of *Z* isomer), 39.6 (C-4 of *E* isomer), 119.2 (C-5'), 122.0 (C-3' of *Z* isomer), 122.1 (C-3' of *E* isomer), 124.0 (C-2, C-6), 131.5 (C-7), 135.7 (C-4'), 139.8 (C-3), 149.4 (C-6'), 159.7 (C-2'); *m/z* (E.I.) 247 ($M^{+\cdot}$, 2%), 178 (100), 144 (13), 112 (43), 111 (21), 78 (10).

1-Phenylthio-2-hexene 26 and 3-phenylthio-1-hexene 27. Oil; ^{1}H NMR (as a mixture of **26** and **27**) (200 MHz) δ 0.82 (t, CH_3 of *E*-**26**), 0.89 (t, CH_3 of *Z*-**26**), 0.91 (t, CH_3 of **27**), 1.22-1.40 (m, 2H, H-5), 1.50-1.75 (m, H-4 of **27**), 1.89-2.00 (m, H-4 of **26**), 3.49 (bd, J = 5.6 Hz, H-1 of *E*-**26**), 3.56 (bd, J = 6.1 Hz, H-1 of *Z*-**26**), 4.05-4.20 (m, H-3 of **27**), 4.85 (bd, J = 16.9 Hz, H-1 of **27**), 4.92 (bd, J = 10.1 Hz, H-1 of **27**), 5.49 (dt, J = 15.1 Hz, J = 5.6 Hz, H-3 of *E*-**26**), 5.57 (dt, J = 15.1 Hz, J = 5.6 Hz, H-2 of *E*-**26**), 5.35-5.65 (m, H-2, H-3 of *Z*-**26**), 5.65 (ddd, J = 16.9 Hz, J = 10.1 Hz, J = 8.2 Hz, H-2 of **27**), 7.1-7.4 (m, 5H, C_6H_5); ^{13}C NMR (as a mixture of **26** and **27**) δ 13.5 (C-6 of *E*-**26**), 13.7 (C-6 of *Z*-**26** and **27**), 20.4 (C-5 of **27**), 22.3 (C-5 of *E*-**26**), 22.6 (C-5 of *Z*-**26**), 29.2 (C-4 of *Z*-**26**), 31.3 (C-1 of *Z*-**26**), 34.3 (C-4 of *E*-**26**), 36.3 (C-4 of **27**), 36.6 (C-1 of *E*-**26**), 52.0 (C-3 of **27**), 115.4 (C-1 of **27**), 124.6-138.0 (=CH-, C-2 and C-3 of **26**, C-2 of **27**, C_6H_5). Anal. Calcd. for $C_{12}H_{16}S$: C, 74.94; H, 8.39. Found: C, 74.14; H, 8.97.

1-(Pyridyl-2-thio)-2-hexene 28. Oil; ^{1}H NMR (as a mixture of *E* and *Z* isomers) (200 MHz) *E*-**28** δ 0.85 (t, J = 7.1 Hz, 3 H, CH_3), 1.26-1.45 (m, 2 H, H-5), 1.98 (q, J = 7.1 Hz, 2 H, H-4), 3.79 (d, J = 6.4 Hz, 2 H, H-1), 5.60 (dt, J = 15.2 Hz, J = 7.1 Hz, 1 H, H-3), 5.70 (dt, J = 15.2 Hz, J = 6.4 Hz, 1 H, H-2), 6.94 (dd, J = 7.4 Hz, J = 4.9 Hz, 1 H, H-5'), 7.15 (bd, J = 8.0 Hz, 1 H, H-3'), 7.45 (bdd, J = 8.0 Hz, J = 7.4 Hz, 1 H, H-4'), 8.42 (bd, J = 4.9 Hz, 1 H, H-6'); *Z*-**28** δ 0.92 (t, J = 7.1 Hz, 3 H, CH_3), 1.26-1.45 (m, 2 H, H-5), 2.14 (q, J = 7.1 Hz, 2 H, H-4), 3.85 (d, J = 6.4 Hz, 2 H, H-1), 5.50-5.80 (m, 2 H, H-2, H-3), 6.94 (dd, J = 7.4 Hz, J = 4.9 Hz, 1 H, H-5'), 7.15 (bd, J = 8.0 Hz, 1 H, H-3'), 7.45 (bdd, J = 8.0 Hz, J = 7.4 Hz, 1 H, H-4'), 8.42 (bd, J = 4.9 Hz, 1 H, H-6'); ^{13}C NMR (as a mixture of *E* and *Z* isomers) *E*-**28** δ 13.5 (C-6), 22.3 (C-5), 32.6 (C-4), 34.4 (C-1), 119.3, 122.2, 125.2, 134.2, 135.8, 149.4 and 159.1 (C-2, C-3, C_5H_4N); *Z*-**28** δ 13.8 (C-6), 22.7 (C-5), 27.3 (C-4), 29.3 (C-1), 119.3, 122.2, 124.6, 133.5, 135.8, 149.4 and 159.1 (C-2, C-3, C_5H_4N). Anal. Calcd. for $C_{11}H_{15}NS$: C, 68.35; H, 7.82. Found: C, 68.09; H, 7.93.

3-(Pyridyl-2-thio)-1-hexene 29. A mixture of hex-1-en-3-ol (800 mg, 8 mmol), mercaptopyridine (888 mg, 8 mmol), diethyl azodicarboxylate (1.4 g, 8 mmol) and triphenylphosphine (210 mg, 8 mmol) was stirred in THF (200 mL) during 24 h. After conventional work-up followed by a column chromatography, compound **29** was obtained as an oil (Yield 15 %). ^{1}H NMR (200 MHz) δ 0.94 (t, J = 7.2 Hz, 3 H, CH_3), 1.26-1.57 (m,

2 H, H-5), 1.61-1.80 (m, 2 H, H-4), 4.38 (dt, J = 8.3 Hz, J = 7.6 Hz, 1 H, H-3), 5.01 (bd, J = 10.1 Hz, 1 H, H-1), 5.19 (bd, J = 17.0 Hz, 1 H, H-1), 5.82 (ddd, J = 17.0 Hz, J = 10.1 Hz, J = 8.3 Hz, 1 H, H-2), 6.97 (dd, J = 7.4 Hz, J = 4.9 Hz, 1 H, H-5'), 7.17 (bd, J = 8.0 Hz, 1 H, H-3'), 7.47 (bdd, J = 8.0 Hz, J = 7.4 Hz, 1 H, H-4'), 8.43 (bd, J = 4.9 Hz, 1 H, H-6'); ^{13}C NMR δ 13.9 (C-6), 20.4 (C-5), 36.3 (C-4), 47.4 (C-3), 115.5 (C-1), 138.8 (C-2), 119.7, 123.4, 135.9, 149.5 and158.7 (C_5H_4N).

1-Benzyloxy-4-(pyridyl-2-thio)-2-butene 30. Oil; ^{1}H NMR (as a mixture of *E* and *Z* isomers) (200 MHz) δ 3.84 (m, H-4 of *Z* isomer), 3.85 (bd, J = 5.0 Hz, H-4 of *E* isomer), 3.99 (bd, J = 3.7 Hz, H-1), 4.45 (s, OCH_2Ph of *E* isomer), 4.53 (s, OCH_2Ph of *Z* isomer), 5.7-6.0 (m, , 2H, H-2, H-3), 6.97 (dd, J = 7.5 Hz, J = 5.0 Hz, 1 H, H-5'), 7.16 (bd, J = 8.0 Hz, 1 H, H-3'), 7.30-7.35 (m, 5 H, C_6H_5), 7.45 (bdd, J = 8.0 Hz, J = 7.5 Hz, 1 H, H-4'), 8.42 (bd, J = 5.0 Hz, 1 H, H-6'); ^{13}C NMR (as a mixture of *E* and *Z* isomers) δ 27.1 (C-4 of *Z* isomer), 31.6 (C-4 of *E* isomer), 65.6 (C-1 of *Z* isomer), 69.9 (C-1 of *E* isomer), 71.3 (CH_2Ph of *E* isomer), 72.1 (CH_2Ph of *Z* isomer), 128.3 (C-3 of *Z* isomer), 128.9 (C-3 of *E* isomer), 129.1 (C-2 of *Z* isomer), 129.5 (C-2 of *E* isomer), 119.3, 122.1, 127.4, 127.6, 128.2, 135.8, 138.2, 149.3,and 158.4 (C_6H_5 and C_5H_4N).Anal. Calcd. for $C_{16}H_{17}NOS$: C, 70.82; H, 6.31. Found: C, 71.31; H, 6.28.

***cis*-3-Ethoxycarbonyloxy-5-carbomethoxy-1-cyclohexene 14**. *Cis*-3-hydroxy-5-carbomethoxy-1-cyclohexene[10] (4.0 g, 26 mmol) was treated by ethylchloroformate (5.56 g, 51.3 mmol) in ether (50 mL) in the presence of triethylamine (5.18 g, 51.3 mmol) and dimethylaminopyridine (10 mg). Standard work-up after 24 h gave an oil which was purified by column chromatography on silica to give 5.3 g of compound **14** (yield 90 %). Oil; ^{1}H NMR (300 MHz) δ 1.31 (t, J = 7.0 Hz, 3 H, CH_3), 1.83 (ddd, J = 12.7 Hz, J = 9.3 Hz, J = 9.3 Hz, 1 H, H-4_{ax}), 2.25-2.35 (m, 2 H, H-6), 2.45 (ddd, J = 12.7 Hz, J = 5.6 Hz, J = 2.9 Hz, 1 H, H-4_{eq}), 2.71 (dddd, J = 9.3 Hz, J = 7.4 Hz, J = 4.5 Hz, J = 2.9 Hz, 1 H, H-5), 3.70 (s, 3 H, OCH_3), 4.19 (q, J = 7.0 Hz, 2 H, OCH_2), 5.20-5.30 (m, 1 H, H-3), 5.70 (bd, J = 10.2 Hz, 1 H, H-2), 5.89 (m, 1 H, H-1); ^{13}C NMR δ 14.3 (CH_3CH_2), 27.2 (C-4), 30.5 (C-6), 37.7 (OCH_3), 51.9 (C-5), 63.9 (OCH_2), 72.7 (C-3), 126.2 (C-1), 129.6 (C-2), 154.7 (OCO_2), 174.4 (CO_2). Anal. Calcd. for $C_{11}H_{16}O_5$: C, 57.89; H, 7.07. Found: C, 57.93; H, 7.05.

***cis*-3-(Pyridyl-2-thio)-5-carbomethoxy-1-cyclohexene 31**. Oil; ^{1}H NMR (300 MHz) δ 1.81 (ddd, J = 12.8 Hz, J = 12.2 Hz, J = 10.7 Hz, 1 H, H-4_{ax}), 2.25-2.35 (m, 2 H, H-6), 2.58 (ddd, J = 12.8 Hz, J = 5.8 Hz, J = 2.9 Hz, 1 H, H-4_{eq}), 2.77 (dddd, J = 12.2 Hz, J = 9.5 Hz, J = 5.6 Hz, , J = 2.9 Hz, 1 H, H-5), 3.69 (s, 3 H, OCH_3), 4.60-4.70 (m, 1 H, H-3), 5.77 (bd, J = 10.0 Hz, 1 H, H-2), 5.84 (ddd, J = 10.0 Hz, J = 4.5 Hz, J = 2.5 Hz, 1 H, H-1), 7.00 (ddd, J = 7.4 Hz, J = 5.0 Hz, J = 1.0 Hz, 1 H, H-5'), 7.18 (dd, J = 8.1 Hz, J = 1.0 Hz, 1 H, H-3'), 7.50 (ddd, J = 8.1 Hz, J = 7.4 Hz, J = 1.9 Hz, 1 H, H-4'), 8.44 (dd, J = 5.0 Hz, J = 1.9 Hz, 1 H, H-6'); ^{13}C NMR δ 27.3 (C-4), 32.2 (C-6), 39.7 and 39.9 (C-3 and CH_3), 51.7 (C-5), 127.5 and 128.3 (C-1 and C-2), 119.6, 122.7, 135.9, 149.5 and 158.3 (C_5H_4N), 175.1 (CO). Anal. Calcd. for $C_{13}H_{15}NO_2S$: C, 62.63; H, 6.06. Found: C, 62.19; H, 6.12.

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