1,4-ADDITION OF ORGANOLITHIUM COMPOUNDS TO 6-ETHOXY-3-PHENYL-6*H*-1,2-OXAZINE

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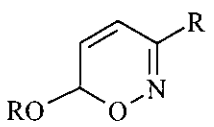
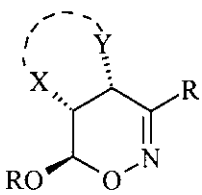
Abstract – Addition of organolithium compounds to 6-ethoxy-3-phenyl-6*H*-1,2-oxazine (**1**) proceeds in conjugate fashion generating 4-lithiated 1,2-oxazines. After trapping with various electrophiles 1,2-oxazines (**2** – **9**) were generally isolated in good yields and with predominant 4,5-*trans*/5,6-*trans*-arrangement of the newly introduced substituents. Scope and limitations of this new route to tetrasubstituted 1,2-oxazines are discussed.

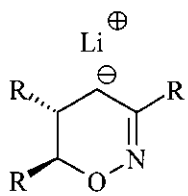
We recently reported an efficient and highly flexible synthesis of various 6-alkoxy-6*H*-1,2-oxazines (**A**).[2] Compounds of this type are of interest since addition of reagents X-Y may lead to 5,6-dihydro-4*H*-1,2-oxazines (**B**) which are excellent precursors for ring transformations and ring cleavage reactions.[3] The additions so far studied are *cis*-dihydroxylation, epoxidation, addition of other oxygen and nitrogen nucleophiles as well as the addition of stabilized carbanions such as nitroalkane and malonic ester anions.[4] Most of these reactions proceed with excellent *trans*-selectivity with respect to the 6-alkoxy group. It was also of high interest whether unstabilized carbanions, e.g. organolithium compounds, can be added and whether the reaction is still stereoselective.



A



B



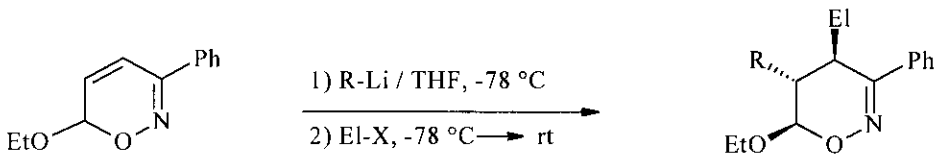
C

Dedicated to Professor Werner Schroth, on the occasion of his 70th birthday.

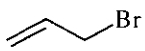
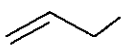
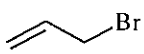
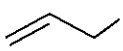
In addition, the 4-lithiated 1,2-oxazine intermediates (**C**)[5] may further react with electrophiles to furnish the desired 5,6-dihydro-4*H*-1,2-oxazines. Again, the stereoselectivity of this second step was a matter of interest. Also, a further point of concern was the question whether attack of these hard nucleophiles to the C=N double bond[6] complicates the anticipated transformation.

RESULTS

As model substrate for this investigation we selected 3-phenyl-substituted 6*H*-1,2-oxazine since no reactions of the organolithium compounds with its substituents are to be taken into account. In general, **1** was given to an excess of the organolithium reagent R-Li at –78 °C over a period of 15 min, then the electrophile was added and the mixture was allowed to warm up to room temperature. This protocol was advantageous compared with addition of R-Li to a solution of **1** where considerable amounts of oligomers could be formed.



1 **2-9**

Entry	R	El-X	Product	El	Yield (%)	*trans* : *cis* [a]
1	*n*-Bu	D_2O	**2**	D	77	94 : 6
2	*n*-Bu	Acetone	**3**	H	76	91 : 9
3	*n*-Bu	Acetone-d_6	**2**	D	83	91 : 9
4	*n*-Bu	MeI	**4**	Me	71	92 : 8
5	*n*-Bu		**5**		76	88 : 12
6	Me	MeI	**6**	Me	15	≥ 97 : 3
7	Ph	D_2O	**7**	D	76	≥ 97 : 3
8	Ph		**8**		75	≥ 97 : 3
9	*sec*-Bu	MeOH	**9**	H	65	≥ 97 : 3 [b]

[a] *Trans:cis* refers to positions 5 and 6 in the heterocycle.- [b] Two diastereomers (52 : 48, determined by ^1H and ^{13}C-NMR) with respect to the acyclic stereogenic centre.

Following this procedure, the reaction of **1** with *n*-butyllithium and subsequent quenching with D_2O provided 1,2-oxazine (**2**) in good yield (Entry 1). According to the NMR spectra a single diastereomer was almost exclusively formed and all the data support 4,5-*trans*/5,6-*trans* configuration as depicted.[7] However, careful inspection of the NMR data and GC-MS analysis revealed the presence of approximately 6% of a second isomer. This diastereomer is most likely a 5,6-*cis*-substituted 1,2-oxazine, since protonation of the intermediate carbanion also gives two diastereomers in a similar ratio (see Entry 2).

When the adduct of *n*-butyllithium and **1** was treated with acetone as electrophile no incorporation of the ketone was observed. Instead, 4-protonated compound (**3**) could be identified as a mixture of 91:9 *trans/cis* isomers (Entry 2). It was not evident whether acetone served as proton source or it did not react at all (protonation during aqueous work up). Therefore, the sequence was repeated with deuterated acetone and in this case deuterium was found in the product (Entry 3). Compound (**2**) was formed again as a mixture of 91:9 *trans/cis* isomers. These experiments demonstrate that the adduct of *n*-butyllithium is rather basic and deprotonates the added carbonyl compound instead of forming a new C-C bond.

However, the reactions of lithiated 1,2-oxazine with S_N2-active alkylating agents such as methyl iodide (Entry 4) and allyl bromide (Entry 5) furnished the expected products (**4**) and (**5**) in good yields and with high diastereoselectivity. Again, two diastereomers were detected in the ratio of approximately 90:10 with 4,5-*trans*/5,6-*trans* configuration for the major diastereomer. The minor isomer should have 4,5-*trans*/5,6-*cis* configuration when the results discussed above are considered.

Methyllithium seems to be too weak as nucleophile under the conditions applied (Entry 6). With methyl iodide as electrophile only 15% of 1,2-oxazine (**6**) could be isolated as diastereomerically pure compound, probably as *trans*/*trans*-diastereomer. Attempts to improve the yield were not successful. Interestingly, the additions of phenyllithium and *sec*-butyllithium were more prominent (Entries 7, 8 and 9). In all cases the expected 1,2-oxazines (**7**), (**8**) and (**9**) were isolated in good yields and as pure *trans*-isomer with respect to the 5,6-configuration.

Our results demonstrate that 1,4-addition of alkyl- and aryllithium compounds to 1,2-oxazines such as **1** is possible and proceeds without detectable interference of competing 1,2-addition to the C=N bond. The 1,4-addition shows high, albeit not always complete *trans*-selectivity with respect to the

6-alkoxy group. Whereas this diastereoselectivity is only in the range of 90:10 for *n*-butyllithium as nucleophile, the attack of electrophiles at C-4 in the lithiated 1,2-oxazine intermediate seems to be highly *trans*-selective. This phenomenon has already been observed with other 4-lithiated 1,2-oxazines generated by deprotonation[5a,5c] and it is mainly due to the 6-substituent which governs electrophiles into a relative *cis*-position. In the examples discussed here the new 5-substituent probably reinforces this effect for steric reasons and thus leads to the observed prefered 4,5-*trans*/5,6-*trans*-configuration of the major isomers. The new 1,2-oxazines synthesized are interesting starting materials for subsequent transformations and we shall report on these studies in due course.

EXPERIMENTAL SECTION

General. ^1H and ^{13}C NMR spectra were recorded on Bruker AC 200 or Bruker AC 300 in $CDCl_3$ solution. The chemical shifts are given in relative to TMS from solvent ($CDCl_3$) signal ($\delta_H = 7.27$, $\delta_C = 77.0$). Missing signals of the minor isomer are hidden by signals of the major isomer or they could not be unambiguously identified due to low intensity. IR spectra were measured with spectrometer Nicolet IR-205. Neutral alumina (activity III, Fa. Merck) was used for column chromatography. Melting points (uncorrected) were measured with an apparatus from Gallenkamp (MPD 350). Determination of the diastereomers were by GC/MS (DB5HT column, l = 15 m, d = 0.32 mm, film thick = 0.1 μm, He, 2 mL/min, 40 → 90 °C [2 min] 90 → 350 °C [13 °C/min], IR detection).

All solvents were dried by standard methods. The experiments were carried out under exclusion of moisture. For the synthesis of starting material (**1**) see ref.[2]

General Procedure for the 1,4-Addition of Organolithium Compounds to 6-Ethoxy-3-phenyl-6*H*-1,2-oxazine.

To a solution of the corresponding organolithium compound (2.2 equivalents) in THF (10 mL/mmol of 1,2-oxazine) was added a solution of 6-ethoxy-3-phenyl-6*H*-1,2-oxazine (**1**) (1 equivalent) in THF (10 mL/mmol of 1,2-oxazine) at –78 °C over a period of 15 min. Then the electrophilic component was added (time is noted in the individual experimental description) before the reaction mixture was allowed to warm up to rt (except in the case of D_2O, the reaction mixture was warmed up immediately). After the addition of sat. ammonium chloride solution (10 mL/mmol of 1,2-oxazine) the mixture was extracted with ether (2x20 mL/mmol of 1,2-oxazine), the combined extracts were dried (Na_2SO_4) and

the solvent removed *in vacuo*. The crude product was purified by column chromatography on alumina (activity III, *n*-hexane/ethyl acetate).

5-Butyl-4-deuterio-6-ethoxy-3-phenyl-5,6-dihydro-4H-1,2-oxazine (2)

According to the general procedure, 0.203 g (1.00 mmol) of **1** treated with 0.88 mL (2.20 mmol, 2.5 M in *n*-hexane) of *n*-BuLi and 0.50 mL of D_2O. Purification by chromatography (*n*-hexane/ethyl acetate, 8:1) provided 0.182 g (77%) of **2** as pale yellow oil. 5,6-*trans* isomer of **2**: ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.76-7.65, 7.44-7.34 (2 m, 2 H, 3 H, Ph), 4.89 (d, J = 3 Hz, 1 H, 6-H), AB part of ABX_3 system (δ_A = 3.91, δ_B = 3.63, $J_{AX} = J_{BX}$ = 7 Hz, J_{AB} = 10 Hz, 2 H, OCH_2), 2.25 (d, J = 2 Hz, 1 H, 4-H), 2.11-1.15 (m, 1 H, 5-H), 1.59-1.12, 0.96-0.81 (2 m, 9 H, 3 H, 3 CH_2, 2 CH_3). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 155.4 (s, C-3), 136.2, 129.4, 128.4, 125.4 (s, 3 d, Ph), 98.8 (d, C-6), 63.6 (t, OCH_2), 32.6 (d, C-5), 30.8, 29.0, 22.7 (3 t, 3 CH_2), 23.1 (m_c, C-4), 15.1, 13.9 (2 q, 2 CH_3). 5,6-*cis* isomer of **2**: ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 125.4 (d, Ph), 98.5 (d, C-6), 63.7 (t, OCH_2). IR (neat): ν 3100-2740 cm^{-1} (C-H), 1590 (C=N). MS (70 eV, EI), major isomer: m/z (%) = 262 (M^+, 7), 218 (11), 201 (30), 161 (100), 145 (11), 131 (7), 104 (33), 85 (7), 77 (Ph^+, 20), 57 ($C_4H_9^+$, 11), 29 ($C_2H_5^+$, 17); minor isomer (5,6-*cis*): m/z (%) = 262 (M^+, 7), 218 (9), 201 (4), 187 (4), 161 (100), 145 (4), 131 (7), 104 (33), 85 (7), 77 (Ph^+, 20), 57 ($C_4H_9^+$, 11), 29 ($C_2H_5^+$, 17). Anal. Calcd for $C_{16}H_{22}DNO_2$: C 73.25, H 9.22, N 5.34. Found C 73.45, H 8.84, N 5.13.

5-Butyl-6-ethoxy-3-phenyl-5,6-dihydro-4H-1,2-oxazine (3)

According to the general procedure, 0.203 g (1.00 mmol) of **1** treated with 0.88 mL (2.20 mmol, 2.5 M in *n*-hexane) of *n*-BuLi and 0.73 mL of acetone (reaction time: 0.5 h). Purification by chromatography (*n*-hexane/ethyl acetate, 15:1) provided 0.198 g (76%) of **3** as pale yellow oil. 5,6-*trans* isomer of **3**: ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.76-7.65, 7.43-7.33 (2 m, 2 H, 3 H, Ph), 4.90 (d, J = 2.5 Hz, 1 H, 6-H), AB part of ABX_3 system (δ_A = 3.92, δ_B = 3.63, $J_{AX} = J_{BX}$ = 7 Hz, J_{AB} = 9.5 Hz, 2 H, OCH_2), 2.82 (dd, J = 7, 18 Hz, 1 H, 4-H_a), 2.28 (dd, J = 2.5, 18 Hz, 1 H, 4-H_e), 2.12-1.85 (m, 1 H, 5-H), 1.63-1.12, 1.02-0.83 (2 m, 6 H, 3 H, 3 CH_2, CH_3). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 155.4 (s, C-3), 136.3, 129.4, 128.4, 125.4 (s, 3 d, Ph), 98.8 (d, C-6), 63.3 (t, OCH_2), 32.7 (d, C-5), 30.9, 29.0, 22.7 (3 t, 3 CH_2), 23.4 (t, C-4), 15.0, 13.9 (2 q, 2 CH_3). 5,6-*cis* isomer of **3**: ^{1}H NMR ($CDCl_3$, 200 MHz): δ 4.80 (d, J = 3 Hz, 1 H, 6-H). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 129.5, 128.5, 125.5 (3 d, Ph), 98.2 (d, C-6), 63.7 (t, OCH_2), 30.8 (t, CH_2). IR (neat): ν 3100-2740 cm^{-1} (C-H), 1590 (C=N). MS (70 eV, EI), major isomer: m/z (%) = 261 (M^+, 13), 217 (7), 214 (5), 200 (27), 172 (7), 160 (100), 145 (9), 144 (13), 130 (9), 117 (9), 104 (27), 91 ($PhCH_2^+$, 9), 77 (Ph^+, 25), 71 (5), 57 ($C_4H_9^+$, 15), 41 (13),

29 ($C_2H_5^+$, 18), 27 (7); minor isomer (5,6-*cis*): m/z (%) = 261 (M^+, 7), 217 (5), 200 (4), 186 (5), 170 (4), 160 (100), 145 (4), 144 (5), 130 (9), 117 (4), 104 (11), 97 (5), 77 (Ph^+, 13), 69 (4), 55 ($C_4H_7^+$, 7), 41 (7), 29 ($C_2H_5^+$, 13), 27 (4). Anal. Calcd for $C_{16}H_{23}NO_2$: C 73.53, H 8.87, N 5.36. Found C 73.52, H 9.04, N 5.62.

*Reaction of **1** with acetone-d_6*

According to the general procedure, 0.101 g (0.50 mmol) of **1** treated with 0.44 mL (1.10 mmol, 2.5 M in *n*-hexane) of *n*-BuLi and 0.37 mL of acetone-d_6 (reaction time: 0.5 h). Purification by chromatography (*n*-hexane/ethyl acetate, 8:1) provided 0.123 g (83%) of **2** as pale yellow oil.

*5-Butyl-6-ethoxy-4-methyl-3-phenyl-5,6-dihydro-4H-1,2-oxazine (**4**)*

According to the general procedure, 0.203 g (1.00 mmol) of **1** treated with 0.88 mL (2.20 mmol, 2.5 M in *n*-hexane) of *n*-BuLi and 0.19 mL (3.00 mmol) of methyl iodide (reaction time: 1.5 h). Purification by chromatography (*n*-hexane/ethyl acetate, 8:1) provided 0.196 g (71%) of **4** as pale yellow oil. 5,6-*trans* isomer of **4**: ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.65-7.53, 7.43-7.33 (2 m, 2 H, 3 H, Ph), 4.92 (d, J = 2.5 Hz, 1 H, 6-H), AB part of ABX_3 system (δ_A = 3.93, δ_B = 3.58, $J_{AX} = J_{BX}$ = 7 Hz, J_{AB} = 10 Hz, 2 H, OCH_2), 2.55 (dq, J = 1.5, 7.5 Hz, 1 H, 4-H), 1.97-1.84 (m, 1 H, 5-H), 1.58-1.15, 1.00-0.87 (2 m, 12 H, 3 H, 3 CH_2, 2 CH_3, 4-CH_3). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 161.1 (s, C-3), 135.7, 129.2, 128.4, 126.5 (s, 3 d, Ph), 99.4 (d, C-6), 63.8 (t, OCH_2), 40.4 (d, C-4), 32.1, 29.2, 22.7 (3 t, 3 CH_2), 30.2 (d, C-5), 19.4 (q, 4-Me), 15.1, 13.9 (2 q, 2 CH_3). 5,6-*cis* isomer of **4**: ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 126.45 (d, Ph), 98.6 (d, C-6), 29.2 (d, C-5), 15.2 (q, CH_3). IR (neat): ν 3150-2750 cm^{-1} (C-H), 1580 (C=N). MS (70 eV, EI), major isomer: m/z (%) = 275 (M^+, 4), 231 (22), 214 (11), 174 (100), 155 (2), 144 (7), 115 (13), 104 (13), 77 (Ph^+, 13), 55 ($C_4H_7^+$, 11), 29 ($C_2H_5^+$, 15); minor isomer (5,6-*cis*): m/z (%) = 275 (M^+, 4), 231 (22), 174 (100), 158 (4), 144 (11), 115 (7), 104 (7), 77 (Ph^+, 3), 55 ($C_4H_7^+$, 4), 29 ($C_2H_5^+$, 9). Anal. Calcd for $C_{17}H_{25}NO_2$: C 74.14, H 9.15, N 5.09. Found C 74.00, H 9.23, N 5.34.

*4-Allyl-5-butyl-6-ethoxy-3-phenyl-5,6-dihydro-4H-1,2-oxazine (**5**)*

According to the general procedure, 0.203 g (1.00 mmol) of **1** treated with 1.00 mL (2.20 mmol, 2.2 M in *n*-hexane) of *n*-BuLi and 0.26 mL (3.00 mmol) of allyl bromide (reaction time: 2 h). Purification by chromatography (*n*-hexane/ethyl acetate, 8:1) provided 0.228 g (76%) of **5** as pale yellow oil. 5,6-*trans* isomer of **5**: ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.65-7.52, 7.44-7.34 (2 m, 2 H, 3 H, Ph), 5.84-5.61 (m, 1 H, C*H*=CH_2), 5.13-4.98 (m, 2 H, CH=CH_2), 4.91 (d, J = 2.5 Hz, 1 H, 6-H), AB

part of ABX_3 system (δ_A = 3.93, δ_B = 3.56, $J_{AX} = J_{BX}$ = 7 Hz, J_{AB} = 9.5 Hz, 2 H, OCH_2),.2.69-2.39 (m, 2 H, $CH_2CH{=}CH_2$), 2.29-2.06 (m, 2 H, 4-H, 5-H), 1.58-1.15, 0.98-0.86 (2 m, 9 H, 3 H, 3 CH_2, 2 CH_3). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 159.9 (s, C-3), 135.72, 135.69 (s, d, *i*-C, $CH{=}CH_2$), 129.3, 128.5, 126.5 (3 d, Ph), 117.5 (t, $CH{=}CH_2$), 99.5 (d, C-6), 63.8 (t, OCH_2), 35.6 (t, $CH_2CH{=}CH_2$), 35.2, 34.8 (2 d, C-4, C-5), 32.0, 29.0, 22.7 (3 t, 3 CH_2), 15.1, 13.9 (2 q, 2 CH_3). 5,6-*cis* isomer of **5**: ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 135.5 (d, $CH{=}CH_2$), 129.4, 128.4 (2 d, Ph), 117.8 (t, $CH{=}CH_2$), 99.4 (d, C-6), 63.4 (t, OCH_2), 22.6 (t, CH_2), 15.0 (q, CH_3). IR (neat): ν 3150-2800 cm^{-1} (C-H), 1630 (C=C), 1580 (C=N). MS (70 eV, EI), major isomer: m/z (%) = 301 (M^+, 3), 260 (7), 240 (41), 216 (100), 200 (48), 160 (19), 156 (7), 128 (22), 105 (22), 77 (Ph^+, 19), 57 ($C_4H_9^+$, 19), 29 ($C_2H_5^+$, 22); minor isomer (5,6-*cis*): m/z (%) = 301 (M^+, 3), 260 (7), 240 (37), 216 (100), 200 (48), 160 (22), 158 (11), 128 (19), 104 (15), 77 (Ph^+, 15), 55 ($C_4H_7^+$, 15), 29 ($C_2H_5^+$, 22). Anal. Calcd for $C_{19}H_{27}NO_2$: C 75.71, H 9.03, N 4.65. Found C 75.79, H 9.19, N 4.97.

6-Ethoxy-4,5-dimethyl-3-phenyl-5,6-dihydro-4H-1,2-oxazine (6)

According to the general procedure, 0.203 g (1.00 mmol) of **1** treated with 1.37 mL (2.20 mmol, 1.6 M in ether) of methyllithium and 0.19 mL (3.00 mmol) of methyl iodide (reaction time: 1.5 h). Purification by chromatography (*n*-hexane/ethyl acetate, 8:1) provided 0.034 g (15%) of **6** as pale yellow oil. 5,6-*trans* isomer of **6**: ^1H NMR ($CDCl_3$, 200 MHz): δ 7.62-7.50, 7.41-7.31 (2 m, 2 H, 3 H, Ph), 4.77 (d, J = 2.5 Hz, 1 H, 6-H), AB part of ABX_3 system (δ_A = 3.94, δ_B = 3.58, $J_{AX} = J_{BX}$ = 7 Hz, J_{AB} = 10 Hz, 2 H, OCH_2), 2.45 (dq, J = 3, 7.5 Hz, 1 H, 4-H), 2.01 (m_c, 1 H, 5-H), 1.21 (t, J = 7 Hz, 3 H, CH_3), 1.19 (d, J = 7.5 Hz, 3 H, 4-Me), 1.08 (d, J = 7 Hz, 3 H, 5-Me). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 160.9 (s, C-3), 135.6, 129.2, 128.4, 126.6 (s, 3 d, Ph), 100.8 (d, C-6), 64.1 (t, OCH_2), 35.6, 32.6 (2 d, C-4, C-5), 18.9, 17.5 (2 q, 4-Me, 5-Me), 15.2 (q, CH_3). Anal. Calcd for $C_{14}H_{19}NO_2$: C 72.07, H 8.21, N 6.00. Found C 73.68, H 9.06, N 5.73. Due to the low amount of **6** no correct analysis could be obtained.

6-Ethoxy-4-deuterio-3,5-diphenyl-5,6-dihydro-4H-1,2-oxazine (7)

According to the general procedure, 0.203 g (1.00 mmol) of **1** treated with 1.40 mL (2.20 mmol, 1.6 M in cyclohexane/ether, 7:3) of phenyllithium and 0.50 mL of D_2O. Purification by chromatography (*n*-hexane/ethyl acetate, 9:1) provided 0.214 g (76%) of **7** as colourless crystals (mp 89-91 °C). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.79-7.73, 7.43-7.39, 7.34-7.22 (3 m, 2 H, 3 H, 5 H, 2 Ph), 5.07 (d, J = 3 Hz, 1 H, 6-H), AB part of ABX_3 system (δ_A = 3.93, δ_B = 3.65, $J_{AX} = J_{BX}$ = 7 Hz, J_{AB} = 10 Hz, 2 H, OCH_2), 3.35 (m_c, 1 H, 5-H), 2.67 (m_c, 1 H, 4-H), 1.21 (t, $J \approx$ 7 Hz, 3 H, CH_3).- ^{13}C NMR ($CDCl_3$,

75.5 MHz): δ 156.6 (s, C-3), 140.5, 135.7, 129.7, 128.7, 128.5, 127.6, 127.2, 125.5 (2 s, 6 d, 2 Ph), 98.8 (d, C-6), 63.8 (t, OCH_2), 39.2 (d, C-5), 24.1 (m, C-4), 15.0 (q, CH_3). IR (neat): ν 3060-2930 cm^{-1} (C-H, =CH), 1600 (C=N).- MS (70 eV, EI): m/z (%) = 282 (M^+, 1), 221 (8), 206 (9), 106 (11), 105 (100), 104 (23), 91 ($PhCH_2^+$, 14), 78 (9), 77 (Ph^+, 15), 32 (30), 29 ($C_2H_5^+$, 23). Anal. Calcd for $C_{18}H_{18}DNO_2$: C 76.57, H 7.14, N 4.96. Found C 76.74, H 6.79, N 4.97.

*4-Allyl-6-ethoxy-5-phenyl-5,6-dihydro-4H-1,2-oxazine (**8**)*

According to the general procedure, 0.511 g (2.51 mmol) of **1** treated with 3.45 mL (5.54 mmol, 1.6 M in cyclohexane/ether, 7:3) of phenyllithium and 0.64 mL (7.53 mmol) of allyl bromide (reaction time: 2 h). Purification by chromatography (*n*-hexane/ethyl acetate, 15:1) provided 0.603 g (75%) of **8** as colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.64-7.14 (m, 10 H, 2 Ph), 5.78-5.65 (m, 1 H, C*H*=CH_2), 5.29-5.05 (m, 2 H, CH=C*H*$_2$), 5.01 (d, J = 3.5 Hz, 1 H, 6-H), AB part of ABX_3 system (δ_A = 3.94, δ_B = 3.63, J_{AX} = J_{BX} = 7 Hz, J_{AB} = 10 Hz, 2 H, OCH_2), 3.39 (m_c, 1 H, 5-H), 2.92-2.87, 2.64-2.53, 2.34-2.26 (3 m, 1 H each, 4-H, CH_2), 1.19 (t, J = 7 Hz, 3 H, CH_3). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 161.1 (s, C-3), 141.3, 135.2, 129.5, 128.8, 128.7, 128.6, 127.6, 127.1, 126.5 (2 s, 7 d, 2 Ph, =CH), 115.4 (t, $=CH_2$), 99.7 (d, C-6), 64.2 (t, OCH_2), 43.2 (d, C-5), 36.8 (d, C-4), 35.9 (t, CH_2), 15.1 (q, CH_3). IR (neat): ν 3140-2900 cm^{-1} (C-H, =CH), 1625 (C=C), 1585 (C=N). Anal. Calcd for $C_{21}H_{23}NO_2$: C 78.47, H 7.21, N 4.36. Found C 78.39, H 7.47, N 4.68.

*5-(2-Butyl)-6-ethoxy-3-phenyl-5,6-dihydro-4H-1,2-oxazine (**9**)*

According to the general procedure, 0.203 g (1.00 mmol) of **1** treated with 1.69 mL (2.20 mmol, 1.3 M in cyclohexane) of *sec*-BuLi and 1.00 mL of methanol (reaction time: 15 min). Purification by chromatography (*n*-hexane/ethyl acetate, 4:1) provided 0.170 g (65%) of **9** as yellow oil. 5,6-*trans* isomer of **9** (two diastereomers): ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.75-7.67, 7.42-7.35 (2 m, 2 H, 3 H, Ph), 5.04, 4.99 (2 d, J = 3.0 and 3.5 Hz, 0.5 H each, 6-H), 4.00-3.89, 3.70-3.59 (2 m, 1 H each, OCH_2), 2.77, 2.72 (2 dd, J = 7, 17.5 Hz each, 0.5 H each, 4-H), 2.42, 2.41 (2 dd, J = 3.5, 17.5 and 4.5, 17.5 Hz, 0.5 H each, 4-H), 1.96-1.81 (m, 1 H, 5-H), 1.68-1.43, 1.32-1.09, 1.21, 1.20 (2 m, 2 t, J = 7 Hz each, 2.5 H, 0.5 H, 1.5 H, 1.5 H, CH, CH_2, CH_3), 0.99, 0.907 (2 d, J = 7 and 6.5 Hz, 1.5 H each, CH_3), 0.914, 0.88 (2 t, J = 7.5 Hz each, 1.5 H each, CH_3). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 157.2, 157.1 (2 s, C-3), 136.0, 135.9, 129.5*, 128.4*, 125.47, 125.46 (2 s, 4 d, Ph), 98.9, 98.1 (2 d, C-6), 63.8, 63.7 (2 t, OCH_2), 37.8, 37.7 (2 t, C-4, CH_2), 16.2, 15.6, 15.1*, 11.1, 10.9 (5 q, CH_3); * double intensity. IR (neat): ν 3100-2880 cm^{-1} (=C-H, C-H), 1600 (C=N). MS (70 eV, EI), 5,6-*trans* isomer: m/z (%) = 261 (M^+, 11), 217 (8), 161 (12), 160 (100), 130 (10), 104 (14), 103 (8), 91

($PhCH_2^+$, 5), 77 (Ph^+, 25), 57 ($C_4H_9^+$, 10), 55 (11), 41 (11). Anal. Calcd for $C_{16}H_{23}NO_2$: C 73.52, H 8.87, N 5.36. Found C 73.83, H 9.07, N 5.69.

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