RING-OPENING OF ISOXAZOLIDINE NUCLEUS BY TRIMETHYL POSPHATE TREATMENT: FORMATION OF TERTIARY ALLYLIC ALCOHOLS VIA INTERMEDIATE 1,3-OXAZINIUM SALTS

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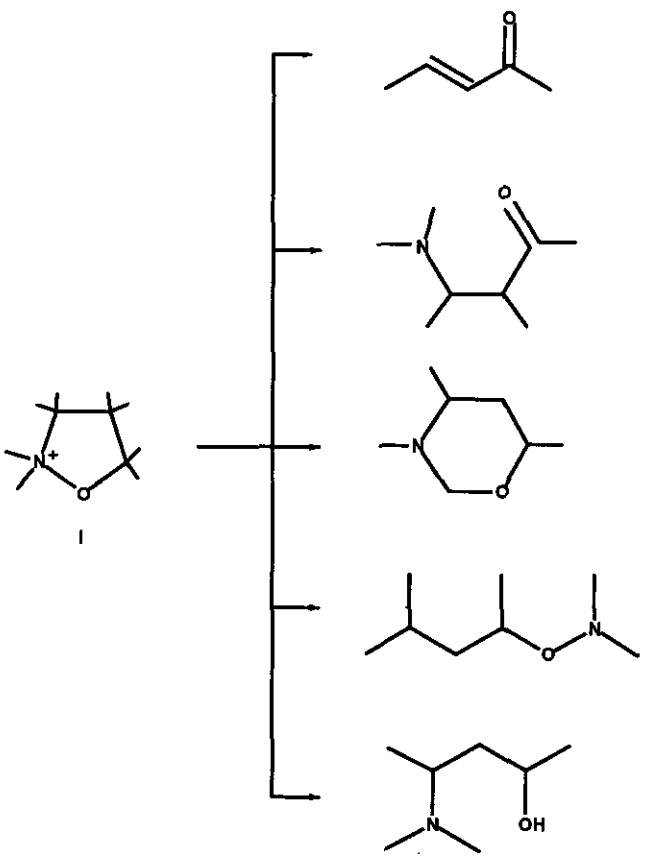
Abstract — 5,5-Disubstituted isoxazolidines undergo ring opening reaction, leading to tertiary allylic alcohols, by sequential treatment with trimethyl phosphate (TMP) and NaH. The reaction proceeds through sequence steps which involve an initial alkylation to isoxazolidinium intermediate, followed by ring expansion to tetrahydro-1,3-oxazine, further alkylation and a Hofmann-like elimination towards the final products promoted by NaH.

1,3-Dipolar cycloaddition of nitrones to alkenes leading to isoxazolidine derivatives[1-5] has recently found wide application in organic synthesis as a versatile tool towards target heterocycles, fruitfully convertible into a variety of complex molecules having synthetic and biological interest.

The exploitation of this approach to carbon-carbon bond formation depends on the subsequent chemical modification of the N-O bond in the five-memberd ring, which opens up new methods for transforming the N,O-heterocyclic nucleus into suitably functionalized open-chain molecules.

Novel reaction paths have been discovered based on the cationization of isoxazolidine nucleus by its conversion into quaternary ammonium cations.[6-18] The isoxazolidinium salts (I), formed by independent procedures, can undergo chemical modifications which involve overall processes leading to the five-membered ring-opening, as

Scheme 1



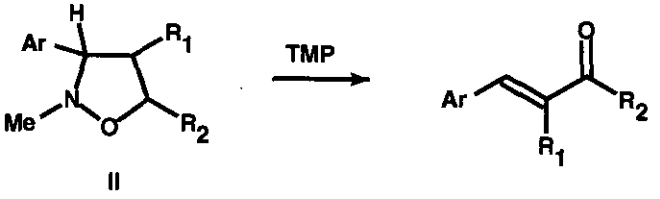
I

shown in Scheme 1.

A reaction channel widely explored corresponds to the base-catalyzed conversion of *N,N*-dimethyl isoxazolidinium salts into chalcones, driven by a N-O bond dissociation followed by a Hofmann-like degradation.

In this context, the treatment of 5-monosubstituted isoxazolidines (II) with trimethyl phosphate (TMP) has shown

Scheme 2



II

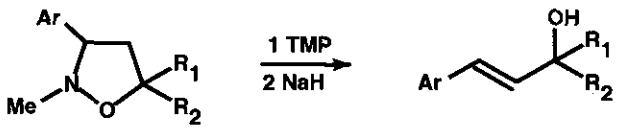
to be a one-flask conversion of isoxazolidine nucleus into α,ß-enones (Scheme 2) with high efficiency.[19]

The process takes place *via* a primary alkylating reaction of TMP on the isoxazolidine substrate, followed by a

Hofmann-like elimination promoted by the attack of the dimethyl phosphate anion onto the H-5. The alternative elimination pathway, leading to substituted hydroxylamines by basic attack at the C-4 hydrogen atoms, has been shown to be thermodinamically less favored.

In this paper we have examined the analogous reaction performed on isoxazolidines (III), lacking hydrogen atoms at C-5. A different rearrangement channel of initial N,O-cycloadducts has been populated; the N,O-heterocycles, modified by treatment with TMP and subsequent reaction with NaH, permit the in situ formation of tertiary allylic

Scheme 3



III IV

alcohols (IV), according to Scheme 3, via the corresponding intermediate 1,3-oxazinium salts.

Other reaction products could, however also be isolated, depending on the experimental adopted conditions.

RESULTS AND DISCUSSION

Isoxazolidines (**9-21**) have been prepared by 1,3-dipolar cycloaddition of *N*-methylnitrones (**1-3**) to alkenes (**4-8**). Pure epimers have been isolated after the conventional work-up and purified by short column chromatography under slight pressure (Table 1).

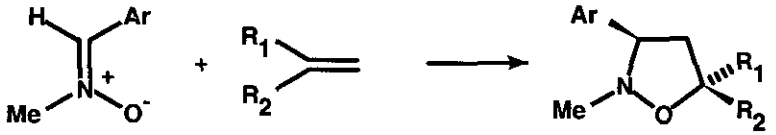
The structures of cycloadducts (**9-21**) have been ascertained by analytical and spectroscopic methods. Configurational assignments to epimeric isoxazolidines (**14-15**, **16-17** and **18-19**) were achieved by correlation of their ^{1}H nmr chemical shifts with those of compounds (**12**) and (**13**), already reported in literature, and by NOE experiments.[20,21] In particular, owing to the deshielding effect exercised by phenyl substituents, in cis isomers (**12**, **14**, **16** and **18**), where phenyl groups at C-3 and C-5 are on the same side of the pentatomic ring, two methylene protons at C-4 show well distinct chemical shifts ($\Delta\delta = 0.3$) with respect to trans isomers ($\Delta\delta = 0.1$).

Reaction of 5,5-disubstituted isoxazolidines (**9-21**) with TMP, in the absence of solvent, as described in the experimental section, gave the oxazinium salts (**22-34**) in high yields (Table 2).

The molecular structure of the reaction products was well established by chemical and physical evidences.

The mass spectra of compound (**22**), taken as model system, is highly diagnostic of the original structure. The base peak at *m/z* 58, corresponding to dimethyliminium ion, arises from an intermediate formed by C_4-N bond cleavage;

Table 1. Reaction of nitrones (**1-3**) with alkenes.



1-3 **4-8** **9-21**

	Ar	R_1	R_2	Yield (%)
1, 4, 9	Ph	Ph	Ph	90
2, 4, 10	*p*-Me-C_6H_4	Ph	Ph	90
3, 4, 11	*p*-MeO-C_6H_4	Ph	Ph	80
1, 5, 12	Ph	Me	Ph	40
1, 5, 13	Ph	Ph	Me	45
2, 5, 14	*p*-Me-C_6H_4	Me	Ph	40[a]
2, 5, 15	*p*-Me-C_6H_4	Ph	Me	45[a]
3, 5, 16	*p*-MeO-C_6H_4	Me	Ph	45
3, 5, 17	*p*-MeO-C_6H_4	Ph	Me	40
1, 6, 18	Ph	Me	*n*-Pr	50
1, 6, 19	Ph	*n*-Pr	Me	35
1, 7, 20	Ph	-$CH_2(CH_2)_3CH_2$-		90
1, 8, 21	Ph	-$CH_2(CH_2)_2CH_2$-		85

[a]Ratio of cis/trans epimers estimated from the integrals of the ^{1}H nmr resonances in the crude reaction mixture was 1:1.

Scheme 4

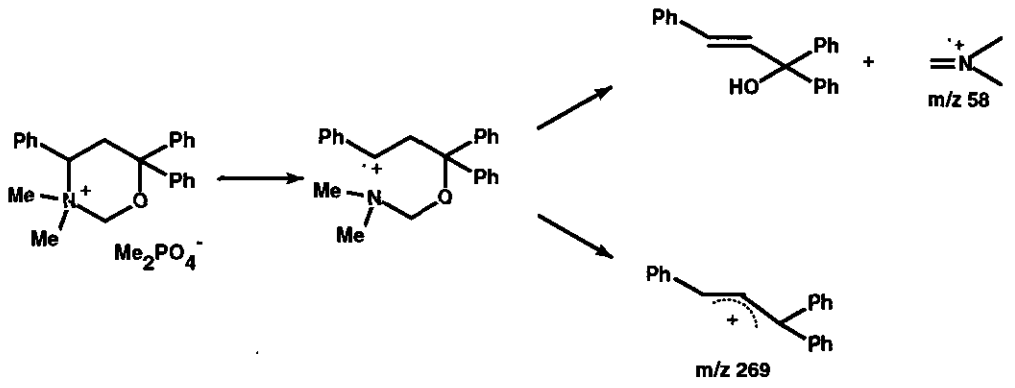
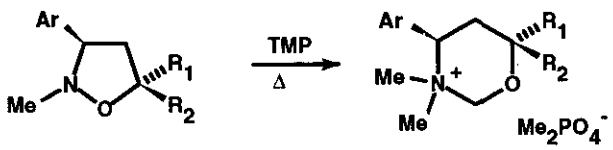


Table 2. Preparation of substituted 1,3-oxazinium salts (**22-34**).



9-21 22-34

Isoxazolidine	Ar	R_1	R_2	Oxazolidinium salts	Yield %
9	Ph	Ph	Ph	**22**	95
10	*p*-Me-C_6H_4	Ph	Ph	**23**	97
11	*p*-MeO-C_6H_4	Ph	Ph	**24**	96
12	Ph	Me	Ph	**25**	95
13	Ph	Ph	Me	**26**	93
14	*p*-Me-C_6H_4	Me	Ph	**27**	not separable
15	*p*-Me-C_6H_4	Ph	Me	**28**	mixture
16	*p*-MeO-C_6H_4	Me	Ph	**29**	95
17	*p*-MeO-C_6H_4	Ph	Me	**30**	97
18	Ph	Me	*n*-Pr	**31**	98
19	Ph	*n*-Pr	Me	**32**	93
20	Ph	$-CH_2(CH_2)_3CH_2-$		**33**	95
21	Ph	$-CH_2(CH_2)_2CH_2-$		**34**	98

the same intermediate is also the precursor of the diagnostic fragment at m/z 269 (Scheme 4).

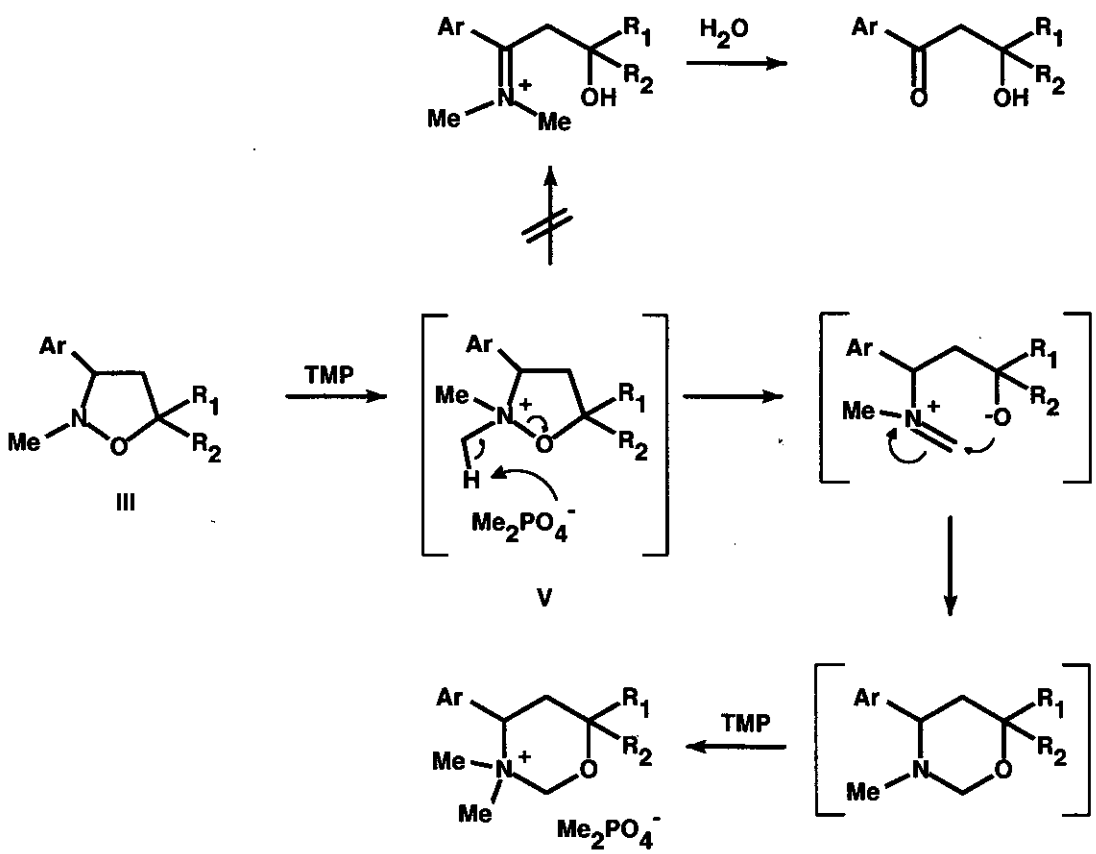
The ^{1}H nmr spectrum of **22** showed for methylene protons at C-2 two doublets, centered at δ 4.81 and 5.81, while methylene protons at C-5 gave rise to two multiplets centered at δ 2.95 and 3.75. Furthermore, the nmr spectrum shows the methyl groups of the dimethyl phosphate ion at δ 3.55 and 3.57 respectively, while the *N*-methyl groups resonate at δ 3.07 and 3.28.

The stereochemistry of the isoxazolidine precursors is maintained in the obtained oxazinium salts. Configurational assignments to epimeric oxazinium salts have been achieved by NOEDS spectroscopy. In compounds (**25**, **29**, and **31**) the positive NOE observed for a R_1 groups at C-6 on irradiating the C-4 proton is clearly indicative of their cis *relationship*.

Formation of oxazinium salts can develop through a sequence of steps where the ring opening of the reacting

system is envisaged as an attack of the dimethyl phosphate ion at *N*-methyl hydrogens on the quaternary ammonium

Scheme 5



intermediate (V) proposed in Scheme 5.

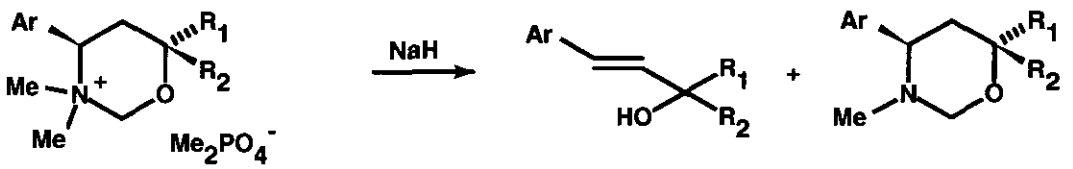
The so formed β-hydroxy iminium derivative undergoes a rapid cyclization with ring expansion to 1,3-oxazine which is alkylated by the excess of TMP. The mechanistic path thus proposed should be similar to that already verified in different reacting media.[8,22] In fact, an independent chemical evidence of the suggested mechanism could be found by an additional mechanistic check. The isoxazolidinium salt intermediate with Ar = R_1 = R_2= Ph has been alternatively obtained, with the counter ion being the iodide, by treatment of the corresponding isoxazolidine with MeI. The obtained methiodide was reacted with NaH to give the expected 1,3-oxazine,[22] which by treatment with TMP gave the oxazinium salt (**22**).

Abstraction of the more acidic H-3 in V could be an alternative reaction channel, giving rise to the corresponding β-hydroxy ketone, which has not been detected in the reaction mixture. The orientation effect experienced in the

ring opening process of oxazinium salts should be determined entirely by steric factors which greatly favor the formation of 1,3-oxazinium salts. Furthermore, the attack by the bulky dimethyl phosphate ion to N-Me group appears to be favored from a purely statistical basis.

The obtained oxazinium derivatives have been further reacted with NaH; the reaction afforded the tertiary allylic alcohols (**35-43**), whose structure was ascertained by spectroscopic methods (see experimental), together with

Table 3. Reaction of 1,3-oxazinium dimethyl phosphate (**22-34**) with NaH.



22-34 **35-43** **44-56**

Oxazolidinium salts	Ar	R_1	R_2	Alcohol (Yield %)	Oxazine (Yield %)
22	Ph	Ph	Ph	**35** (83)	**44** (9)
23	*p*-Me-C_6H_4	Ph	Ph	**36** (75)	**45** (10)
24	*p*-MeO-C_6H_4	Ph	Ph	**37** (72)	**46** (12)
25	Ph	Me	Ph	**38** (64)	**47** (10)
26	Ph	Ph	Me	**38** (82)	**48** (8)
27	*p*-Me-C_6H_4	Me	Ph	**39** (68)	**49** (15)
28	*p*-Me-C_6H_4	Ph	Me		**50**
29	*p*-MeO-C_6H_4	Me	Ph	**40** (70)	**51** (10)
30	*p*-MeO-C_6H_4	Ph	Me	**40** (82)	**52** (10)
31	Ph	Me	*n*-Pr	**41** (68)	**53** (20)
32	Ph	*n*-Pr	Me	**41** (78)	**54** (10)
33	Ph	-$CH_2(CH_2)_3CH_2$-		**42** (70)	**55** (20)
34	Ph	-$CH_2(CH_2)_2CH_2$-		**43** (70)	**56** (20)

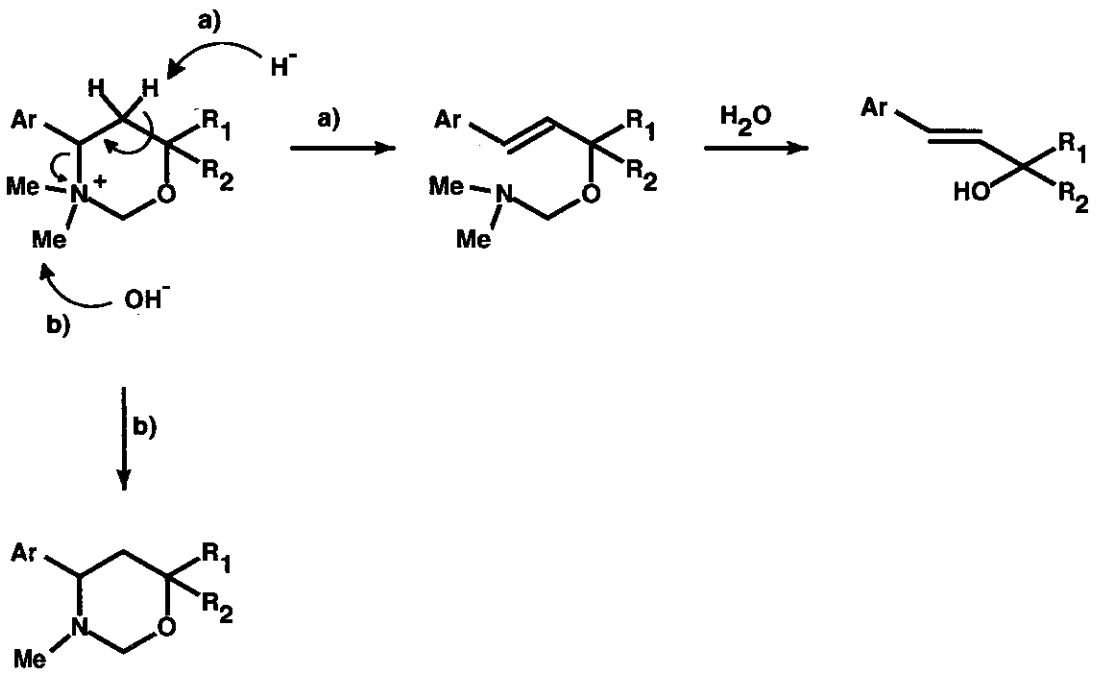
[a]Not separable mixture.

variable yields of 1,3-oxazines (Table 3).

The process takes place *via* an Hofmann-like elimination of the oxazinium salt promoted by the attack of the hydride ion onto H-5. The aminoacetal intermediate evolves towards the formation of the allylic alcohol with

removal of the nitrogen moiety as dimethylamine, detected in the reaction medium (Scheme 6, path a). The formation of tetrahydro-1,3-oxazines, as by-products of the reaction, is imputable to a competitive reaction pathway starting from the tetrahydro-1,3-oxazinium salts. In fact, the high hygroscopicity of these compounds induces, because of the presence of the hydride ion, the formation of the hydroxide ion, which promotes a nucleophilic S_N2

Scheme 6



attack to the methyl group linked to the nitrogen atom (Scheme 6, path b).

In order to provide an additional support to this hypothesis, we have treated at reflux temperature the 1,3-oxazinium salt (**33**) with an aqueous 10% sodium hydroxide solution. Isolation of the 1,3-oxazine (**55**), as the only product of the reaction, confirms that dealkylation process of compounds (**22-34**) is determined by the presence of water in the reaction mixture.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Elemental analyses were performed with a Perkin-Elmer elemental analyzer. Infrared spectra were recorded on a Perkin-Elmer 225 spectrophotometer and ^1H and ^{13}C nmr spectra on Bruker WP 200 SY instrument; chemical shifts are reported in

ppm from internal Me_4Si and refer to $CDCl_3$ solutions. NOE measurements were performed by the FT difference method on carefully degassed $CDCl_3$ solutions: the data were obtained by the PAPS sequence. Mass spectra were determined on a Varian MAT CH-5 DF and GC-MS HP 5890 A instruments. Reaction mixtures were analyzed by tlc on silica gel GF 254 (Merck) and the spots were detected under UV light (254nm). Flash chromatography was carried out with Kieselgel 60 (Merck). Fisical properties of allylic alcohols are in agreement with these reported in literature.

Reaction of Nitrones (1-3) with Alkenes (4-8).

General procedure. A solution of nitrone (1.48 mmol) and alkene (35 mmol) in the presence of 11 mg (0.1 mmol) of cathecol in anhydrous toluene (10 ml) was heated at 120 °C, under stirring, until tlc showed the disappearance of the starting nitrone (5-10 days). The solvent was removed at room temperature with rotary evaporator and the residue subjected to flash chromatography on silica gel column with hexane-ether 95:5 as eluent. Compound (**9**) and epimeric mixture of **12** and **13** have been reported in literature.[23]

Reaction of C-p-tolyl-N-methylnitrone (**2**) with 1,1-diphenylethene (**4**). Reaction time 6 days. First fractions gave 438 mg of 2-methyl-3-*p*-tolyl-5,5-diphenylisoxazolidine (**10**), 90% yield; light pale oil; ν_{max} 3000-2800, 1600, 1510, 1450, 1300, 1260, 1210, 1180, 1110, 1050, 990, 910, 860, 820, 750, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 2.15 (s, 3H, CH_3), 2.80 (3H, s, CH_3-N), 3.30 (2H, m, H_4), 3.83 (1H, m, H_3), 7.12-7.65 (14H, m, aromatic protons). Anal. Calcd for $C_{23}H_{23}NO$: C, 83.90; H, 7.04; N, 4.12. Found: C, 83.96; H, 7.16; N, 4.12.

Reaction of C-p-methoxyphenyl-N-methylnitrone (**3**) with 1,1-diphenylethene (**4**). Reaction time 5 days. Column chromatography gave 408 mg of 2-methyl-3-*p*-methoxyphenyl-5,5-diphenylisoxazolidine (**11**), 80% yield; pale yellow oil; ν_{max} 3100-2780, 1660, 1660, 1480, 1450, 1400, 1080, 900, 800, 750, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 2.73 (3H, s, N-CH_3), 3.35 (2H, m, H_2), 3.83 (3H, s, O-CH_3), 3.87 (1H, m, H_3), 6.81-7.90 (14H, m, aromatic protons). Anal. Calcd for $C_{23}H_{23}NO_2$: C, 79.97; H, 6.71; N, 4.05. Found: C, 79.89; H, 6.61; N, 4.15.

Reaction of C-phenyl-N-methylnitrone (**1**) with 1-methylstyrene (**5**). Reaction time 8 days. First eluted product was (3R*, 5S*)-2,5-dimethyl-3,5-diphenylisoxazolidine (**12**), 40% yield (111mg) ; pale yellow oil; ν_{max} 3040-2830, 1600, 1500, 1450, 1400, 1360, 1300, 1220, 1160, 1130, 1090, 1070, 1030, 920, 900, 850, 760, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.75 (3H, s, CH_3), 2.52 (1H, dd, J= 10.0 and 12.5 Hz, H_4), 2.65 (3H, s, N-CH_3), 2.81 (1H, dd, J= 7.5 and 12.5 Hz, H_4), 3.51 (1H, dd, J= 7.5 and 10.0 Hz, H_3), 7.18-7.25 (10H, m, aromatic protons). Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 79.99; H, 7.60; N, 5.57. Further fractions gave 114 mg of (3R*, 5R*)-2,5-dimethyl-3,5-diphenylisoxazolidine (**13**), 45% yield; white solid, mp 62-64 °C (from

hexane-benzene); ν_{max} 3040-2830, 1600, 1500, 1450, 1390, 1360, 1300, 1250, 1230, 1200, 1180, 1150, 1080, 1070, 1030, 960, 890, 830, 770, 700, 550 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.62 (3H, s, CH_3), 2.34-2.54 (2H, m, H_4), 2.68 (3H, s, N-CH_3), 3.79 (1H, dd, J= 9.0 and 10.0 Hz, H_3), 7.24-7.68 (10H, m, aromatic protons). Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.00; H, 7.53; N, 5.60.

Reaction of C-p-tolyl-N-methylnitrone (**2**) with 1-methyl-styrene (**5**). Reaction time 8 days. Flash chromatography gave 336 mg of an inseparable mixture 1:1 ratio of epimeric cis- and trans- 2,5-dimethyl-3-*p*-tolyl-5-phenyl-isoxazolidine (**14**) and (**15**) respectively, 85% yield; pale yellow solid; ν_{max} 3100-2970, 1950, 1800, 1660, 1510, 1490, 1360, 1310, 1030, 900, 820, 750, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.72 (3H, s, CH_3), 1.78 (3H, s, CH_3), 2.25 (3H, s, CH_3), 2.30 (3H, s, CH_3), 2.57 (3H, s, CH_3-N), 2.59 (3H, s, CH_3-N), 2.80-3.30 (4H, m, H_4), 3.83 (2H, m, H_3), 7.12-7.65 (18H, m, aromatic protons); ms: m/z 267 (M^+). Anal. Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.73; H, 7.90; N, 5.32.

Reaction of C-p-methoxyphenyl-N-methylnitrone (**3**) with 1-methyl-styrene (**5**). Reaction time 6 days. First fractions gave 188 mg of (3R*, 5S*)-2,5-dimethyl-3-*p*-methoxyphenyl-5-phenylisoxazolidine (**16**), 45% yield; oil; ν_{max} 3080-2940, 2840, 2740, 1690, 1600, 1530, 1450, 1370, 1310, 1250, 1160, 1030, 890, 835, 765, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.80 (3H, s, CH_3), 2.55 (1H, dd, J= 7.5 and 10.0 Hz, H_4), 2.70 (3H, s, N-CH_3), 2.90 (1H, dd, J= 5.0 and 10.0 Hz, H_4), 3.60 (1H, dd, J= 5.0 and 7.5 Hz, H_3), 3.80 (3H, s, O-CH_3), 6.85-7.80 (9H, m, aromatic protons). Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 77.00; H, 7.52; N, 4.70. Second fractions gave 167 mg of (3R*, 5R*)-2,5-dimethyl-3-*p*-methoxyphenyl-5-phenylisoxazolidine (**17**), 40% yield; oil; ν_{max} 3100-2850, 2780, 1685, 1615, 1515, 1450, 1370, 1249, 1175, 1030, 950, 835, 765, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.55 (3H, s, CH_3), 2.60 (3H, s, N-CH_3), 2.72 (1H, dd, J= 6.0 and 10.0 Hz, H_4), 2.80 (1H, dd, J= 5.0 and 10.0 Hz, H_4), 3.70 (1H, dd, J= 5.0 and 6.0 Hz, H3), 3.84 (3H, s, O-CH_3), 6.75-7.6 (9H, m, aromatic protons). Anal. Calcd for $C_{18}H_{21}NO_2$: C,76.29; H,7.47; N,4.94. Found: C, 76.80; H, 7.55; N, 4.87.

Reaction of C-phenyl-N-methylnitrone (**1**) with 2-methyl-1-pentene (**6**). Reaction time 10 days. First eluted product was (3R*, 5S*)-2,5-dimethyl-3-phenyl-5-propylisoxazolidine (**18**), 50% yield (162 mg); pale yellow oil; ν_{max} 3100-2780, 1605, 1450, 1380, 1310, 1205, 1165, 1070, 1030, 980, 750 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.09 (3H, t, J= 6.7 Hz, CH_3), 1.25 (3H, s, CH_3), 1.45 (2H, m, CH_2), 1.80 (2H, m, CH_2), 2.20 (1H, dd, J= 7.5 and 10.0 Hz, H_4), 2.30 (1H, dd, J= 5.0 and 10.0 Hz, H_4), 2.50 (3H, s, N-CH_3), 3.50 (1H, dd, J= 5.0 and 7.5 Hz, H_3), 7.20-7.40 (5H, m, aromatic protons). Anal. Calcd for $C_{14}H_{21}NO$: C,76.67; H,9.65; N,6.39. Found: C, 76.90; H, 9.45; N, 6.42. Further eluted product was (3R*, 5S*)-2,5-dimethyl-3-phenyl-5-propylisoxazolidine (**19**), 35% yield (113 mg); pale yellow oil; ν_{max} 3100-2780, 1610, 1500, 1460, 1400, 1365, 1160, 1075, 1010, 880, 750 700 cm^{-1}; ^1H nmr: δ

($CDCl_3$) 1.09 (3H, t, J= 7.0 Hz, CH_3), 1.25 (3H, s, CH_3), 1.45 (2H, m, CH_2), 1.80 (2H, m, CH_2), 2.20 (1H, dd, J= 7.5 and 10.0 Hz, H_4), 2.30 (1H, dd, J= 5.0 and 10.0 Hz, H_4), 2.52 (3H, s, N-CH_3), 3.50 (1H, dd, J= 5.0 and 7.5 Hz, H_3) 7.20-7.40 (5H, m, aromatic protons). Anal. Calcd for $C_{14}H_{21}NO$: C, 76.67; H, 9.65; N, 6.39. Found: C, 76.36; H, 9.58; N, 6.48.

Reaction of C-phenyl-N-methylnitrone (**1**) with methylenecyclohexane (**7**). Reaction time 9 days. Column chromatography gave 308 mg of 2-methyl-3-phenyl-5-spirocyclohexylisoxazolidine (**20**), 90% yield; pale yellow oil; ν_{max} 3080-2750, 1950, 1600, 1490, 1450, 1350, 1300, 1150, 1100, 1050, 1025, 950, 875, 750, 700, 650 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.25-1.95 (10H, m, CH_2), 2.10-2.40 (2H, m, H_4), 2.48 (3H, s, N-CH_3), 3.50 (1H, dd, J= 5.0 and 8.0 Hz, H_3), 7.15-7.40 (5H, m, aromatic protons). Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.91. Found: C, 77.53; H, 9.35; N, 6.98.

Reaction of C-phenyl-N-methylnitrone (**1**) with methylenecyclopentane (**8**). Reaction time 9 days. Column chromatography gave 273 mg of 2-methyl-3-phenyl-5-spirocyclopentylisoxazolidine (**21**), 85% yield; pale yellow oil; ν_{max} 3075-2750, 1600, 1490, 1450, 1300, 1250, 1150, 1050, 950, 750, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.45-1.95 (8H, m, CH_2), 2.28 (1H, dd, J= 7.0 and 12.5 Hz, H_4), 2.55 (3H, s, N-CH_3), 2.60 (1H, dd, J= 5.0 and 12.5 Hz, H_4), 3.50 (1H, dd, J= 5.0 and 7.0 Hz, H_3), 7.15-7.45 (5H, m, aromatic protons). Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.44. Found: C, 77.36; H, 8.78; N, 6.39.

Preparation of Substituted 1,3-Oxazolidinium Salts (22-34).

General procedure. A stirred solution of isoxazolidine (3.17 mmol) in 2 ml of trimethyl phosphate was heated at 160 °C under nitrogen atmosphere for 30 min. The reaction mixture was then treated with a saturated solution of sodium bicarbonate and extracted with chloroform. The organic layer was dried over magnesium sulfate and the solvent was concentrated under reduced pressure to give 90-100% yields of the expected 1,3-oxazolidinium salts as oil.

Reaction of isoxazolidine (**9**) with trimethyl phosphate gave 1.41 g of 3,3-dimethyl-4,6,6-triphenyltetrahydro-1,3-oxazinium dimethyl phosphate (**22**), 95% yield; colorless oil; ν_{max} 3450, 3100-2960, 1650, 1450, 1210, 1140, 1040, 830, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 2.95 (1H, m, H_5), 3.07 (3H, s, N-CH_3), 3.28 (3H, s, N-CH_3), 3.55 (3H, s, P-CH_3), 3.57 (3H, s, P-CH_3), 3.75 (1H, m, H_5), 4.56 (1H, dd, J= 5.0 and 12.0 Hz, H_4), 4.81 (1H, d, J= 10.0 Hz, H_2), 5.81 (1H, d, J= 10.0 Hz, H_2), 7.21-7.60 (15H, m, aromatic protons); ms: m/z 344 (M^+-125, 20), 269(15), 248(17), 191(25), 181(34), 167(39), 131(18), 127(37), 115(22), 105(37), 91(100), 87(16), 77(25), 58(86), 46(49), 45(60), 44(90), 46(47). Anal. Calcd for $C_{26}H_{32}NO_5P$: C, 66.51; H, 6.87; N, 2.98. Found: C, 66.44; H, 6.83; N, 2.93.

Reaction of isoxazolidine (**10**) with trimethyl phosphate gave 1.38 g of 3,3-dimethyl-4-*p*-tolyl-6,6-diphenyltetrahydro-1,3- oxazinium dimethyl phosphate (**23**), 97% yield; colorless oil; ν_{max} 3450, 3100-2860, 1640, 1450, 1230, 1140, 1045, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 2.43 (3H, s, CH_3), 3.05 (1H, m, H_5), 3.09 (3H, s, N-CH_3), 3.25 (3H, s, N-CH_3), 3.60 (3H, s, P-CH_3),3.71 (3H, s, P-CH_3), 3.75 (1H, m, H_5), 4.66 (1H, dd, J= 5.0 and 12.0 Hz, H_4), 4.90 (1H, d, J= 11.0 Hz, H_2), 5.71 (1H, d, J= 11.0 Hz, H_2), 7.40-7.78 (14H, m, aromatic protons); ms: m/z 358 (M^+-125, 36), 269(10), 167(40), 163(20), 149(90), 127(37), 105(40), 91(100), 58(85), 44(90). Anal. Calcd for $C_{27}H_{34}NO_5P$: C, 67.06; H, 7.08; N, 2.89. Found: C, 66.99; H, 7.04; N, 2.85.

Reaction of isoxazolidine (**11**) with trimethyl phosphate gave 1.52 g of 3,3-dimethyl-4-*p*-methoxyphenyl-6,6-diphenyltetrahydro-1,3-oxazinium dimethyl phosphate (**24**), 96% yield; colorless oil; ν_{max} 3455, 3100-2950, 1650, 1455, 1210, 1140, 1045, 830, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 3.07 (3H, s, N-CH_3), 3.28 (3H, s, N-CH_3), 3.55 (3H, s, P-CH_3), 3.57 (3H, s, P-CH_3), 3.75 (1H, m, H_5), 3.8 (3H, s, O-CH_3), 4.56 (1H, dd, J= 5.0 and 12.0 Hz, H_4), 4.80 (1H, d, J= 10.0 Hz, H_2), 5.81 (1H, d, J= 10.0 Hz, H_2), 7.21-7.60 (14H, m, aromatic protons); ms: m/z 374 (M^+ -125,38), 269(15), 248(18), 191(27), 167(38), 127(38), 105(37), 91(100), 77(27), 58(85), 44(90). Anal. Calcd for $C_{27}H_{34}NO_6P$: C, 64.92; H, 6.86; N, 2.80. Found: C, 65.00; H, 6.83; N, 2.85.

Reaction of isoxazolidine (**12**) with trimethyl phosphate gave 1.26 g of (4R*, 6R*)-3,3,6-trimethyl-4,6-diphenyltetrahydro-1,3-oxazinium dimethyl phosphate (**25**), 95% yield; colorless oil; ν_{max} 3400, 3060-2940, 1840, 1640, 1450, 1250, 1140, 1185, 1140, 830, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.60 (3H, s, CH_3), 2.70 (1H, m, H_5), 3.0 (3H, s, N-CH_3), 3.26 (3H, s, N-CH_3), 3.28 (1H, m, H_5), 3.58 (3H, s, P-CH_3), 3.65 (3H, s, P-CH_3), 5.23 (1H, dd, J= 5.0 Hz and 12.0 Hz, H_4), 5.60 (1H, d, J= 10.0 Hz, H_2), 5.87 (1H, d, J= 10.0 Hz, H_2), 7.20-7.60 (10H, m, aromatic protons); ms: m/z 282 (M^+ -125,36), 135(24), 134(52), 121(22), 105(34), 91(42), 77(20), 58(100), 56(56), 52(63), 43(66), 41(69). Anal. Calcd for $C_{21}H_{30}NO_5P$: C, 61.90; H, 7.42; N, 3.44. Found: C, 61.85; H, 7.50; N, 3.48

Reaction of isoxazolidine (**13**) with trimethyl phosphate gave 1.20 g of (4R*, 6R*)-3,3,6-trimethyl-4,6-diphenyltetrahydro-1,3-oxazinium dimethyl phosphate (**26**), 93% yield; colorless oil; ν_{max} 3400, 3060-2940, 1840, 1640, 1450, 1250, 1185, 1140, 1040, 830, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.65 (3H, s, CH_3), 2.28 (1H, m, H_5), 2.68 (1H, m, H_5), 3.00 (3H, s, N-CH_3), 3.25 (3H, s, N-CH_3), 3.53 (3H, s, P-CH_3), 3.65 (3H, s, P-CH_3), 4.32 (1H, dd, J= 5.0 and 12.0 Hz, H_4), 4.60 (1H, d, J= 10.0 Hz, H_2), 5.75 (1H, d, J= 10.0 Hz, H_2), 7.30-7.60 (10H, m, aromatic protons); ms: m/z 282 (M^+-125,36), 135(24), 134(52), 121(22), 105(34), 91(42), 77(20), 58(100), 56(56), 52(63), 43(66), 41(69). Anal. Calcd for $C_{21}H_{30}NO_5P$: C, 61.90; H, 7.42; N, 3.44. Found: C, 61.80; H, 7.53; N, 3.42

Reaction of isoxazolidine (**14**) and (**15**) with trimethyl phosphate gave after usual work up 1.24 g of an inseparable mixture, 1:1 ratio, of epimeric cis- and trans-3,3,6-trimethyl-4-*p*-tolyl-6-phenyltetrahydro-1,3-oxazinium dimethyl

phosphate (**27**) and (**28**) respectively, 93% yield; pale yellow oil; ν_{max} 3400, 3080-2970, 2860, 1650, 1500-1450, 1420, 1395, 1230, 1140, 1045, 910, 800-750, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.70 (3H, s, CH_3), 2.37 (3H, s, CH_3), 2.90-3.15 (1H, m, H_5), 3.20 (3H, s, N-CH_3), 3.60 (3H, s, P-CH_3), 3.70 (3H, s, P-CH_3), 3.80 (1H, m, H_2), 3.90 (3H, s, N-CH_3) 4.28 (1H, dd, J= 3.0 and 13.0 Hz, H_4), 4.60 (1H, d, J= 9.0 Hz, H_2), 5.45 (1H, d, J= 9.0 Hz, H_2), 7.25-7.70 (9H, m, aromatic protons); ms: m/z 296 (M^+ -125,35), 148(53), 121(20), 105(35), 91(43), 77(22), 58(100), 43(68),41(70). Anal. Calcd for $C_{22}H_{32}NO_5P$: C, 62.69; H, 7.65; N, 3.32. Found: C, 62.58; H, 7.68; N, 3.38.

Reaction of isoxazolidine (**16**) with trimethyl phosphate gave 1.32 g of (4R*, 6S*)-3,3,6-trimethyl-4-*p*-methoxyphenyl-6-phenyltetrahydro-1,3-oxazinium dimethyl phosphate (**29**), 95% yield; colorless oil; ν_{max} 3500, 3060-2920, 2850, 1610, 1510, 1380, 1040 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.90 (3H, s, CH_3), 2.27 (1H, m, H_5), 2.65 (1H, m, H_5), 2.90 (3H, s, N-CH_3), 3.13 (3H, s, N-CH_3), 3.64 (3H, s, P-CH_3), 3.71 (3H, s ,P-CH_3), 3.85 (3H, s, O-CH_3), 5.20 (1H, d, J= 10.0 Hz, H_2), 5.40 (1H, dd, J= 5.0 and 12.0 Hz, H_4), 5.60 (1H, d, J= 10.0 Hz, H_2), 7.00-7.59 (9H, m, aromatic protons); ms: m/z 312 (M^+-125, 19), 127(19), 120(11), 74(10), 58(100), 46(16), 44(19). Anal. Calcd for $C_{22}H_{32}NO_6P$: C, 60.40; H, 7.37; N, 3.20. Found: C, 60.48; H, 7.36; N, 3.23.

Reaction of isoxazolidine (**17**) with trimethyl phosphate gave 1.34 g of (4R*, 6R*)-3,3,6-trimethyl-4-*p*-methoxyphenyl-6-phenyltetrahydro-1,3-oxazinium dimethyl phosphate (**30**), 97% yield; colorless oil; ν_{max} 3500, 3060-2920, 2350, 1610, 1510, 1380, 1040 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.65 (3H, s, CH_3), 2.87 (3H, s, N-CH_3), 2.95 (1H, m, H_5), 3.11 (3H, s, N-CH_3), 3.60 (3H, s, P-CH_3), 3.67 (3H, s, P-CH_3), 3.90 (3H, s, O-CH3), 4.37 (1H, dd, J= 5.0 and 12.0 Hz, H_4), 4.65 (1H, d, J= 10.0 Hz, H_2), 5.26 (1H, d, J= 10.0 Hz, H_2), 7.00-7.59 (9H, m, aromatic protons); ms: m/z 312 (M^+-125, 19), 127(19), 120(11), 74(10), 58(100), 46(16), 44(19). Anal. Calcd for $C_{22}H_{32}NO_6P$: C, 60.40; H, 7.37; N, 3.20. Found: C, 60.47; H, 7.33; N, 3.25.

Reaction of isoxazolidine (**18**) with trimethyl phosphate gave 1.16 g of (4R*, 6S*)-3,3,6-trimethyl-4-phenyl-6-propyltetrahydro-1,3-oxazinium dimethyl phosphate (**31**), 98% yield; colorless oil; ν_{max} 3400, 3090-2825, 1650, 1460, 1390, 1240, 1130, 1050, 920, 780, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.00 (3H, t, J= 7.0 Hz, CH_3), 1.60 (3H, s, CH_3), 1.65 (4H, m, CH_2), 2.50 (1H, m, H_5), 2.80 (1H, m, H_5), 2.90 (3H, s, N-CH_3), 3.14 (3H, s, N-CH_3), 3.55 (3H, s, P-CH_3), 3.60 (3H, s, P-CH_3), 4.92 (1H, d, J= 10.0 Hz, H_2), 5.40 (1H, dd, J= 5.0 and 12.0 Hz, H_4), 5.60 (1H, d, J= 10.0 Hz, H_2), 7.30-7.67 (5H, m, aromatic protons); ms: m/z 248 (M^+-125, 62), 173(12), 131(16), 107(11), 91(18), 58(100). Anal. Calcd for $C_{18}H_{32}NO_5P$: C, 57.89; H, 8.63; N, 3.75. Found: C, 57.77; H, 8.52; N, 3.65.

Reaction of isoxazolidine (**19**) with trimethyl phosphate gave 1.10 g of (4R*, 6R*)-3,3,6-trimethyl-4-phenyl-6-propyltetrahydro-1,3-oxazinium dimethyl phosphate (**32**), 93% yield; colorless oil; ν_{max} 3400, 3090-2830, 1650,

1460, 1390, 1240, 1130, 1050, 920, 780, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 0.90 (3H, t, J= 7.2 Hz, CH_3), 1.60 (4H, m, CH_2), 1.63 (3H, s, CH_3), 2.52 (1H, m, H_5), 2.89 (3H, s, N-CH_3), 3.09 (3H, s, N-CH_3), 3.32 (1H, m, H_5) 3.44 (3H, s, P-CH_3), 3.51 (3H, s, P-CH_3), 4.90 (1H, d, J= 10.0 Hz, H_2), 5.25 (1H, dd, J= 5.0 and 12.0 Hz, H_4), 5.40 (1H, d, J= 10.0 Hz, H_2), 7.25-7.70 (5H, m, aromatic protons); ms: m/z 248 (M^+-125, 62), 143(12), 131(16), 107(11), 58(100). Anal. Calcd for $C_{18}H_{32}NO_5P$: C, 57.89; H, 8.63; N, 3.75. Found: C, 57.80; H, 8.59; N, 3.72.

Reaction of isoxazolidine (**20**) with trimethyl phosphate gave 1.16 g of 3,3-dimethyl-4-phenyl-6-spirocyclohexyl-tetrahydro-1,3-oxazinium dimethyl phosphate (**33**), 95% yield; colorless oil; ν_{max} 3500, 3090-2860, 2480, 1650, 1350, 1140, 1060, 970, 920, 780, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.35-2.16 (10H, m, CH_2), 2.42 (1H, m, H_5), 2.95 (3H, s, N-CH_3), 3.10 (3H, s, N-CH_3), 3.33 (1H, s, H_5) 3.50 (3H, s, P-CH_3), 3.54 (3H, s, P-CH_3), 5.00 (1H, d, J= 10.0 Hz, H_2), 5.25 (1H, dd, J= 5.0 and 12.0 Hz, H_4), 5.90 (1H, d, J= 10.0 Hz, H_2), 7.40-7.55 (5H, m, aromatic protons); ms: m/z 260 (M^+-125, 32), 246(12), 185(12), 134(19), 117(22), 105(14),99(12), 91(42), 58(100), 54(19), 44(28). Anal. Calcd for $C_{19}H_{32}NO_5P$: C, 59.21; H, 8.37; N, 3.63. Found: C, 59.28; H, 8.39; N, 3.52.

Reaction of isoxazolidine (**21**) with trimethyl phosphate gave 1.15 g of 3,3-dimethyl-4-phenyl-6-spirocyclo-pentyltetrahydro-1,3-oxazinium dimethyl phosphate (**34**), 98% yield; colorless oil; ν_{max} 3450, 3090-2820, 2500, 1650, 1280, 1180, 1140, 1040, 915, 750, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.35-2.15 (8H, m, CH_2), 2.41 (1H, m, H_5), 2.91 (3H, s, N-CH_3), 3.15 (3H, s, N-CH_3), 3.27 (1H, m, H_5) 3.50 (3H, s, P-CH_3), 3.55 (3H, s , P-CH_3), 4.95 (1H, d, J= 10.0 Hz, H_2), 5.27 (1H, dd, J= 5.0 and 12.0 Hz, H_4), 7.40-7.60 (5H, m, aromatic protons); ms: m/z 246 (M^+-125, 36), 134(16), 105(13), 91(28), 85(23), 67(15), 58(100), 44(25). Anal. Calcd for $C_{18}H_{30}NO_5P$: C, 58.21; H, 8.14; N, 3.77. Found: C, 58.28; H, 8.21; N, 3.62.

Reaction of 1,3-Oxazinium Dimethyl Phosphate (22-34) with NaH.

General procedure. To a stirred solution of 1,3-oxazinium salt (2 mmol) in 50 ml of anhydrous tetrahydrofuran at 25 °C under nitrogen atmosphere was added 62.5 mg (2.60 mmol) of sodium hydride. The mixture was then brought to 65 °C and stirred for 7-10 h, according to the substituents. The solution was cooled, washed with wather, and extracted with 3 x 30 ml of chloroform. The combined organic layer was dried over sodium sulfate, and the solvent was removed under reduced pressure to give a residue which was subjected to silica gel chromatography using a ether-hexane 1:9 mixture as eluent.

Reaction of **22** with NaH. Reaction time 7 h. First fraction gave 59 mg of 3-methyl-4,6,6-triphenyltetra-hydro-1,3-oxazine (**44**), yield 9%, oil; ν_{max} 3100-2750, 1670, 1605, 1450, 1310, 1230, 1105, 990, 740, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.35 (1H, m, H_5), 1.85 (1H, m, H_5), 2.05 (3H, s, N-CH_3), 3. 90 (1H, dd, J= 5.0 and 12.0 Hz,

H_4), 4.20 (1H, d, J= 15.0 Hz, H_2), 4.50 (1H, d, J= 15.0 Hz, H_2), 7.20-7.60 (15H, m, aromatic protons) . Anal. Calcd for $C_{23}H_{23}NO$: C, 83.85; H, 7.04; N, 4.25. Found: C, 83.75; H, 7.09; N, 4.22. Further elution gave 475 mg of 1,1,3-triphenylpropen-1-ol (**35**), yield 83%, white solid , mp 110 °C (from ethanol); ν_{max} 3525, 3080-3020, 1590, 1485, 1265, 1165, 1125, 1065, 980, 895, 760, 700, 630, 560 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 6.63 (1H, d, J= 16.0 Hz, H_2), 6.83 (1H, d, J= 16.0 Hz, H_3), 7.20-7.70 (15H, m, aromatic protons). Anal. Calcd for $C_{21}H_{18}O$: C, 88.08; H, 6.33. Found: C, 88.12; H, 6.35.

Reaction of **23** with NaH. Reaction time 8 h. First fraction gave 68.6 mg of 3-methyl-4-*p*-tolyl-6,6-diphenyltetrahydro-1,3-oxazine (**45**), yield 10%; oil; ν_{max} 3100-2760, 1670, 1605, 1455, 1320, 1180, 1105, 990, 745, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.40 (1H, m, H_5), 1.70 (3H, s, CH_3), 2.00 (1H, m, H_5), 2.35 (3H, s, N-CH_3), 3.55 (1H, dd, J= 5.0 and 12.0 Hz, H_4), 4.35 (1H, d, J= 10.0 Hz, H_2) , 4.60 (1H, d, J= 10.0 Hz, H_2), 7.20-7.60 (14H, m, aromatic protons) . Anal. Calcd for $C_{24}H_{25}NO$: C, 83.93; H, 7.34; N, 4.08. Found: C, 83.97; H, 7.29; N, 4.02. Second fraction gave 450 mg of 1,1-diphenyl-3-*p*-tolylpropen-1-ol (**36**), yield 75%, white solid, mp 98 °C (from ethanol); ν_{max} 3580, 3100-2975, 1600, 1515, 1490, 1450, 1330, 1295, 1156, 1060, 980, 845, 760, 700, 510 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 2.30 (3H, s, CH_3), 6.65 (1H, d, J= 15.8 Hz, H_2), 6.83 (1H, d, J= 15.8 Hz, H_3), 7.15-7.70 (14H, m, aromatic protons). *Anal. Calcd for $C_{22}H_{20}O$: C, 87.96; H, 6.71. Found: C, 87.92; H, 6.75.*

Reaction of **24** with NaH. Reaction time 9 h. First fraction gave 86 mg of 3-methyl-4-*p*-methoxyphenyl-6,6-diphenyltetrahydro-1,3-oxazine (**46**), yield 12%; oil; ν_{max} 3100-2760, 1670, 1605, 1455, 1320, 1180, 1105, 990, 745, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.36 (1H, m, H_5), 1.98 (1H, m, H_5), 2.57 (3H, s, N-CH_3), 3.56 (1H, dd, J= 5.0 and 12.0 Hz, H_4), 3.80 (3H, s, O-CH_3), 4.36 (1H, d, J= 10.0 Hz, H_2), 4.58 (1H, d, J= 10 Hz, H_2), 7.20-7.60 (14H, m, aromatic protons) . Anal. Calcd for $C_{24}H_{25}NO_2$: C, 80.19; H, 7.01; N, 3.90. Found: C, 80.15; H, 7.07; N, 3.94. Second fraction gave 455 mg of 1,1-diphenyl-3-*p*-methoxyphenyl-propen-1-ol (**37**), yield 72%, white solid, mp 92 °C (from ethanol) ; ν_{max} 3490, 3080-2900, 1620, 1520, 1445, 1250, 1180, 1035, 905, 760, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 3.83 (3H, s, O-CH_3), 6.70 (1H, d, J= 16.0 Hz, H_2), 6.90 (1H, d, J= 16.0 Hz, H_3), 7.20-7.70 (14H, m, aromatic protons). Anal. Calcd for $C_{22}H_{20}O_2$: C, 83.51; H, 6.37. Found: C, 83.44; H, 6.33.

Reaction of **25** with NaH. Reaction time 7 h. First eluted product was (4R*, 6S*)-3,6-dimethyl-4,6-diphenyltetrahydro-1,3-oxazine (**47**), 10% yield (53.4 mg), oil; ν_{max} 3100-2740, 1455, 1320, 1230, 1105, 1080, 745, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.31 (3H, s, CH_3), 1.98 (1H, dd, J= 5.0 and 12.0 Hz, H_5), 2.10 (3H, s, N-CH_3) 2.28 (1H, dd, J= 12.0 and 12.2 Hz, H_5), 3.58 (1H, dd, J= 5.0 and 12.2 Hz, H_4), 4.35 (1H, d, J= 9.5 Hz, H_2), 4.58 (1H, d, J= 9.5 Hz, H_2), 7.20-7.70 (10H, m, aromatic protons). Anal. Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.87; H, 7.95; N, 5.20. Further elution gave 287 mg of 2,4-diphenyl-3-buten- 2-ol (**38**), yield

64% , white solid , mp 62 °C (from ethanol); ν_{max} 3450, 3100-2810, 1605, 1500, 1445, 1180, 1070,1035, 975, 890, 760, 695 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.75 (3H, s, CH_3), 6.50 (1H, d, J= 16.0 Hz, H_2), 6.60 (1H, d, J= 16.0 Hz, H_3), 7.15-7.58 (10H, m, aromatic protons). Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 85.62; H, 7.14.

Reaction of **26** with NaH. Reaction time 9 h. First fraction gave 43 mg of (4R*, 6R*)-3,6-dimethyl-4,6-diphenyltetrahydro-1,3-oxazine (**48**), 8% yield, oil; ν_{max} 3090-2720, 1460, 1320, 1230, 1105, 1060, 990, 750, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.45 (3H, s, CH_3), 1.95 (3H, s, N-CH_3), 2.20 (1H, dd, J= 11.6 and 12.0 Hz, H_5), 2.49 (1H, dd, J= 4.2 and 12.0 Hz, H_5), 3.26 (1H, dd, J= 4.2 and 11.6 Hz, H_4), 3.92 (1H, d, J= 10.0 Hz, H_2), 4.38 (1H, d, H_2, J= 10.0 Hz), 7.25-7.70 (10H, m, aromatic protons). Anal. Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.80; H, 7.89; N, 5.19. Second fraction gave 367 mg of 2,4-diphenyl-3-buten- 2-ol (**38**), yield 82%.

Reaction of **27** and **28** with NaH. Reaction time 7 h. First eluted product was an inseparable mixture of 3,6-dimethyl-4-*p*-tolyl-6-phenyltetrahydro-1,3-oxazine (**49**) and (**50**), 15% (84.3 mg), oil; ^1H nmr: δ ($CDCl_3$) 1.40 (2H, m, H_5), 1.70 (3H, s, CH_3), 1.72 (3H, s, CH_3), 2.00 (2H, m, H_5), 2.35 (3H, s, N-CH_3), 2.38 (3H, s, N-CH_3), 3.60 (2H, m, H_4), 4.35 (2H, m, H_2), 4.60 (2H, m, H_2), 7.05-7.70 (10H, m, aromatic protons). Anal. Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.15; H, 8.29; N, 4.94. Further elution gave 324 mg of 2-phenyl-4-*p*-tolyl-3-buten-2-ol (**39**), yield 68%, white solid , mp 92 °C (from ethanol); ν_{max} 3450, 3100-2880, 2800, 1605, 1515, 1450, 1110, 1070, 1030, 975, 850, 805, 765, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.73 (3H, s, CH_3), 2.31 (3H, s, CH_3), 6.44 (1H, d, J= 16.0 Hz, H_2), 6.61 (1H, d, J= 16.0 Hz, H_3), 7.02-7.67 (9H, m, aromatic protons). Anal. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.69; H, 7.63.

Reaction of **29** with NaH. Reaction time 8 h. First eluted product was (4R*, 6S*)-3,6-dimethyl-4-*p*-methoxyphenyl-6-phenyltetrahydro-1,3-oxazine (**51**), 10% (59.4 mg), oil; ν_{max} 3100-2840, 1450, 1370, 1255, 1170, 1050, 835, 765, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.58 (3H, s, CH_3), 2.00 (1H, dd, J= 4.8 and 12.0 Hz, H_5), 2.15 (3H, s, N-CH_3), 2.70 (1H, dd, J= 11.6 and 12.0 Hz, H_5), 3.70 (1H, dd, J= 4.8 and 11.6 Hz, H_4), 3.82 (3H, s, O-CH_3), 4.38 (1H, d, J= 9.6 Hz, H_2), 4.58 (1H, d, J= 9.6 Hz, H_2), 7.25-7.60 (9H, m, aromatic protons). Anal. Calcd for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.79; N, 4.71. Found: C, 76.75; H, 7.77; N, 4.74. Further elution gave 356 mg of 2-phenyl-4-*p*-methoxyphenyl-3-buten-2-ol (**40**), yield 70%, colorless oil; ν_{max} 3500, 3100-2810, 1620, 1500, 1455, 1375, 1100, 1070, 1035, 975, 760, 695 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.63 (3H, s, CH_3), 3.85 (3H, s, O-CH_3), 6.85 (1H, d, J= 16.0 Hz, H_2), 7.01 (1H, d, J= 16.0 Hz, H_3), 7.15-7.56 (9H, m, aromatic protons). Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.22; H, 7.15.

Reaction of **30** with NaH. Reaction time 7 h. First fraction gave 59 mg of (4R*, 6R*)-3,6-dimethyl-4-*p*-methoxyphenyl-6-phenyltetrahydro-1,3-oxazine (**52**), 10%, oil; ν_{max} 3080-2835, 1510, 1450, 1350, 1170, 1060, 840, 770,

700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.38 (3H, s, CH_3), 2.10 (3H, s, N-CH_3), 2.18 (1H, dd, J= 11.4 and 12.0 Hz, H_5), 2.45 (1H, dd, J= 4.4 and 12.0 Hz, H_5), 3.53 (1H, dd, J= 4.4 and 11.4 Hz, H_4), 3.85 (3H, s, O-CH_3), 4.02 (1H, d, J= 10.0 Hz, H_2), 4.23 (1H, d, J= 10.0 Hz, H_2), 7.30-7.65 (9H, m, aromatic protons). Anal. Calcd for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.79; N, 4.71. Found: C, 76.77; H, 7.78; N, 4.74. Second fraction gave 356 mg of 2-phenyl-4-*p*-methoxyphenyl-3-buten-2-ol (**40**), 82% yield.

Reaction of **31** with NaH. Reaction time 8 h. First eluted product was (4R*, 6S*)-3,6-dimethyl-4-phenyl-6-propyl-tetrahydro-1,3-oxazine (**53**), 20% (93 mg), oil; ν_{max} 3100-2740, 1455, 1390, 1370, 1230, 1105, 995, 745, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.00 (3H, t, J= 7.2 Hz, CH_3), 1.32 (3H, s, CH_3), 1.33-1.58 (5H, m, $(CH_2)_2$ + H_5), 1.93 (1H, m, H_5), 2.12 (3H, s, N-CH_3) 3.40 (1H, dd, J= 4.0 and 10.0 Hz, H_4), 4.18 (1H, d, J= 9.0 Hz, H_2), 4.37 (1H, d, J= 9 Hz, H_2), 7.25-7.65 (5H, m, aromatic protons) . Anal. Calcd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93; N, 6.00. Found: C, 77.18; H, 9.98; N, 5.97. Further elution gave 258 mg of 1-phenyl-3-methyl-1-hexen-3-ol (**41**), yield 68%, colorless oil; ν_{max} 3460, 3100-2880, 1500, 1450, 1370, 975, 765, 695 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 0.90 (3H, t, J= 7.0 Hz, CH_3), 1.35 (3H, s, CH_3), 6.28 (1H, d, J= 15.0 Hz, H_2), 6.56 (1H, d, J= 15.0 Hz, H_3), 7.15-7.42 (5H, m, aromatic protons). Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 82.02; H, 9.49.

Reaction of **32** with NaH. Reaction time 7 h. First fraction gave 47 mg of (4R*, 6R*)-3,6-dimethyl-4-phenyl-6-propyltetrahydro-1,3-oxazine (**54**), 10% oil; ν_{max} 3090-2760, 1455, 1390, 1380, 1365, 1230, 1100, 990, 745, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 0.90 (3H, t, J= 7.2 Hz, CH_3), 1.28 (3H, s, CH_3), 1.30-1.78 (6H, m, $(CH_2)_2$ +2 H_5), 1.95 (3H, s, N-CH_3), 3.46 (1H, dd, J= 5.0 and 10.0 Hz, H_4), 4.05 (1H, d, J= 10.0 Hz, H_2), 4.40 (1H, d, J= 10.0 Hz, H_2), 7.15-7.40 (5H, m, aromatic protons). Anal. Calcd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93; N, 6.00. Found: C, 77.26; H, 9.91; N, 6.02. Second fraction gave 296 mg of 1-phenyl-3-methyl-1-hexen-3-ol, (**41**), yield 78%.

Reaction of **33** with NaH. Reaction time 8 h. First eluted products was 3-methyl-4-phenyl-6-spirocyclohexyl-tetrahydro-1,3-oxazine (**55**), yield 20% (98 mg), oil; ν_{max} 3100-2715, 1450, 1400, 1260, 1100, 1070, 910, 780, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.38 (10H, m, $(CH_2)_5$), 1.66 (2H, m, H_5), 2.00 (3H, s, N-CH_3), 3.37 (1H, dd, J= 4.5 and 11.0 Hz, H_4), 4.13 (1H, d, J= 10.5 Hz, H_2), 4.35 (1H, d, J= 10.5 Hz, H_2), 7.24-7.39 (5H, m, aromatic protons). Anal. Calcd for $C_{16}H_{23}NO$: C, 78.32; H, 9.45; N, 5.71. Found: C, 78.35; H, 9.39; N, 5.68. Further eluted products was 1-styryl-cyclohexan-1-ol (**42**), yield 70%, colorless oil (283 mg); ν_{max} 3450, 3100-2880, 1500, 1450, 1380, 975, 765, 695 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.20-1.75 (10H, m, CH_2), 6.33 (1H, d, J= 16.0 Hz, H_2), 6.63 (1H, d, J= 16.0 Hz, H_3), 7.15-7.45 (5H, m, aromatic protons). Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.18; H, 8.95.

Reaction of **34** with NaH. Reaction time 9 h. First fraction gave 94 mg of 3-methyl-4-phenyl-6-spirociclopenthyl-

tetrahydro-1,3-oxazine (**56**), 20% yield, oil; ν_{max} 3080-2705, 1450, 1395, 1250, 1120, 1060, 900, 760, 700 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.78 (2H, m, H_5), 2.02 (3H, s, N-CH_3), 3.30 (1H, dd, J= 4.0 and 11.4 Hz, H_4), 4.04 (1H, d, J= 10.5 Hz, H_2), 4.39 (1H, d, J= 10.5 Hz, H_2), 7.18-7.42 (5H, m, aromatic protons). Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.79; H, 9.09; N, 6.09. Second fraction gave 246 mg of 1-styryl-cyclopentan-1-ol (**43**), yield 70%, white oil; ν_{max} 3450, 3100-2870, 1515, 1445, 1382, 970, 765, 695 cm^{-1}; ^1H nmr: δ ($CDCl_3$) 1.20-1.75 (8H, m, CH_2), 6.29 (1H, d, J= 16.0 Hz, H_2) 6.64 (1H, d, J= 16.0 Hz, H_3). Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.88; H, 8.55.

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