Vicarious Nucleophilic Substitution of (Chloroalkyl)oxazolines with Nitroarenes: Synthesis of (Nitrobenzyl)oxazolines

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2-Chloroalkyloxazolines **1a** and **1b** react with nitroarenes in the presence of *t*BuOK in DMSO to give, upon acidic quenching, substituted nitroaryloxazolines **2a**, **2b**, **3a**, **9**, **10**, **11a–d**, **12–19**, and **21–22**, probably by vicarious nucleophilic substitution (VNS). The reaction of **1a** is poorly regioselective, while that of **1b** is completely *para* regioselective, thus showing that the coupling is sterically controlled. Trapping of the carbanionic intermediate **B** of the VNS reaction with electrophiles furnished α,α-disubstituted (nitrobenzyl)oxazolines **4–7**. Attempts to trap **B** with PhCHO failed: the [(*p*-nitrophenyl)oxazolinyl]ethanol **8** was obtained.

Introduction

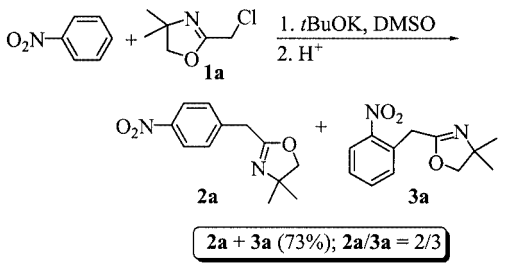
Vicarious nucleophilic substitution (VNS), also known as the Makosza reaction,[1] in which a nucleophile possessing a leaving group at the nucleophilic centre replaces a hydrogen in nitroarenes or some other electron-deficient arenes and heteroarenes, takes place with a variety of nucleophiles, such as carbanions containing halogen, alkoxy, or thioalkoxy leaving groups, alkyl hydroperoxide anions[2] and a number of amination reagents.[3,4] The reaction has proved to be a general method for the introduction of C, O, and N substituents by direct replacement of hydrogen in electron-deficient aromatic rings. Much work to elucidate the essential features of the reaction and to develop applications in synthetic organic chemistry has been carried out in several labs.[5] Some work has also been devoted to improvement of knowledge of the reaction mechanism.[6]

Sodium carbanions of (chloromethyl)phosphane oxides, (chloroethyl)phenyl sulfones, and ethyl-2-chloropropionates with nitrobenzene have been reported to give a series of functionalized phosphane oxides,[7] sulfones,[8] and esters.[9] The VNS reaction followed by alkylation has been successfully applied to the synthesis of biologically active molecules such as Indoprofen.[10]

In previous papers from our laboratories it had been shown that lithiated (chloroalkyl)oxazolines behave as useful Darzens reagents, coupling efficiently with carbonyl compounds and imines to give oxazolinyl oxiranes[11] and aziridines[12] and adding to nitrones to furnish alkenyloxazolines.[13] In this paper we report on the coupling reactions between potassium carbanions of chloroalkyloxazolines and nitroarenes.

Results and Discussion

When a mixture of nitrobenzene (1.1 equiv.) and 2-(chloromethyl)-4,4-dimethyloxazoline **1a** (1 equiv.) was added to a suspension of potassium *tert*-butoxide (*t*BuOK, 3 equiv.) in dimethyl sulfoxide (DMSO), a dark red solution resulted. Quenching of the reaction mixture with sat. aq. ammonium chloride afforded 4-(nitrobenzyl)oxazoline **2a** and 2-(nitrobenzyl)oxazoline **3a** in a poorly regioselective manner (73%, **2a**/**3a** ratio = 2:3; Scheme 1). Such a poor regioselectivity was not unexpected, it having been reported that carbanions derived from a methylene group bearing a good leaving group



Scheme 1

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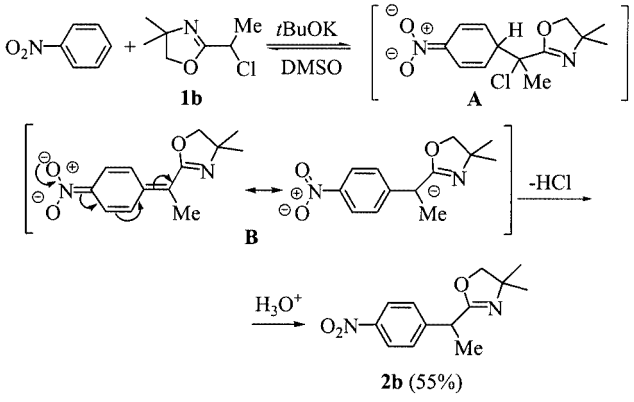
and an electron-withdrawing substituent generally replace hydrogen both *ortho* and *para* to the nitro group.[10a] The use of other bases and solvents such as NaH, NaOH, THF, DMF, and MeCN resulted in much lower yields or in no reaction at all.

In contrast, the reaction between the potassium carbanion of 2-(chloroethyl)oxazoline **1b** and nitrobenzene was completely *para*-regioselective, producing 4-nitrophenylethyloxazoline **2b** (55% yield, Scheme 2). These results can reasonably be accounted for in terms of vicarious nucleophilic substitution (VNS), as illustrated in Scheme 2 for the reaction of **1b**.

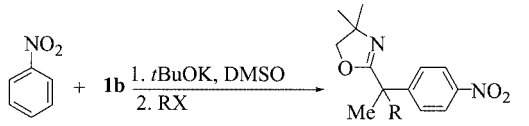


Scheme 2

Accordingly, **1b** anion, generated by deprotonation of **1b**, should rapidly and reversibly add to the nitrobenzene, resulting in the formation of the σ adduct **A**. Base-induced β-elimination would then take place to generate the benzylic carbanion **B** and then compound **2b** upon acidic quenching. The exclusive *para* regioselectivity of the reaction of **1b** anion, in comparison with the very poor regioselectivity of the reaction of **1a** anion, clearly indicates that the process is controlled by steric factors. That tertiary carbanions replace exclusively *para*-hydrogen in VNS reactions is well documented.[8−9]

To establish that the reaction, according to the VNS process, goes through a benzylic carbanion such as **B** (Scheme 2) we attempted its trapping with electrophiles other than ammonium chloride. We found that the benzylic carbanion is indeed formed in the reaction of the potassium anion of 2-(chloroethyl)oxazoline **1b**, as it undergoes methylation, benzylation, allylation and propargylation to give acceptable to good yields of compounds **4**−**7** upon treatment with methyl iodide, benzyl chloride, allyl bromide, and propargyl bromide (Scheme 3). This represents a good route to α-substituted (nitrobenzyl)oxazolines with quaternary centres by a three-component coupling reaction. It might be useful to recall that the VNS reaction normally occurs with yields that are rarely very high whichever the carbanion.[10]

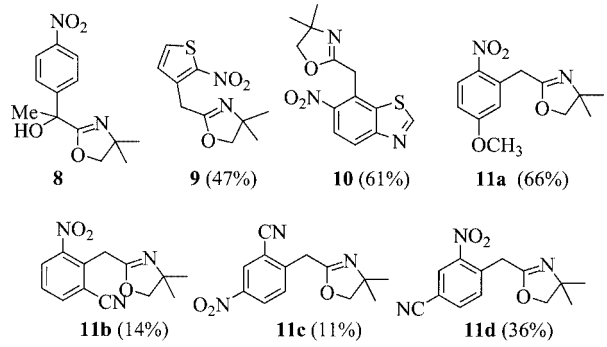
Attempts to trap the carbanion B with benzaldehyde failed, probably because the reaction is reversible and the carbanion is particularly stable. We noted that opening of the reaction flask to the air and warming of the reaction



4 (R = Me): 37%
5 (R = allyl): 42%
6 (R = benzyl): 63%
7 (R = propargyl): 40%

Scheme 3

mixture to 50 °C furnished a compound identifiable as 1-[(*p*-nitrophenyl)-1-oxazolin-2-yl]ethanol (**8**) (Scheme 4). A literature search revealed that the same reaction type had been reported by Lawrence and co-workers when the post-VNS anion originating from the reaction between nitrobenzene and ethyl 2-chloropropanoate was treated with benzaldehyde under an air atmosphere[14] and that a mechanism involving a single-electron transfer process had been proposed. The failure of the reaction of the carbanion **B** of Scheme 1 with aldehydes is common to other carbanions.[10a]

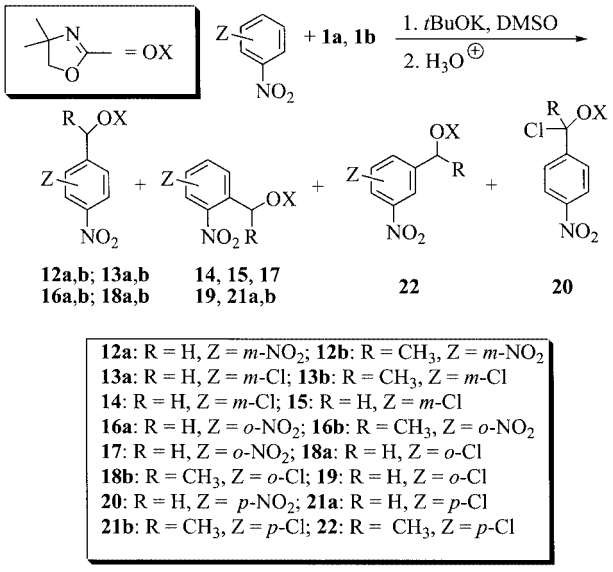


Scheme 4

The success of the above VNS reactions of **1a** anion and **1b** anion is not restricted to nitrobenzene. Indeed, the potassium carbanion of **1a** reacted with 2-nitrothiophene to give **9** (47%) and with 6-nitrobenzothiazole to furnish **10** (61%). The presence of substituents on the ring of nitrobenzene does not significantly affect the VNS reactions of **1a** and **1b** anions. In all cases studied it is the nitro group that pilots the nucleophilic attack. Thus, 4-nitroanisole reacts regioselectively with **1a** anion to give **11a** (66%) while the reaction with 3-nitrobenzonitrile yields a mixture of **11b** (14%), **11c** (11%) and **11d** (36%) (Scheme 4).

As shown in Table 1, treatment of 1,3-dinitrobenzene with potassium anions of heterocycles **1a** and **1b** afforded oxazolines **12a** and **12b** as the sole reaction products. No nitro group displacement was observed. Additionally, the reaction between 3-chloronitrobenzene and the potassium anion of 2-(chloromethyl)oxazoline **1a** afforded mixture of VNS products *ortho* and *para* to the nitro group **13a**, **14** and **15**. The more sterically demanding potassium carbanion of 2-(chloroethyl)oxazoline **1b** exclusively afforded, as would be expected, 4,4-dimethyl-2-[1-(2-chloro-4-nitrophenyl)-

Table 1. Reactions between substituted nitrobenzenes and **1a** or **1b**



12a: R = H, Z = *m*-NO_2; **12b**: R = CH_3, Z = *m*-NO_2
13a: R = H, Z = *m*-Cl; **13b**: R = CH_3, Z = *m*-Cl
14: R = H, Z = *m*-Cl; **15**: R = H, Z = *m*-Cl
16a: R = H, Z = *o*-NO_2; **16b**: R = CH_3, Z = *o*-NO_2
17: R = H, Z = *o*-NO_2; **18a**: R = H, Z = *o*-Cl
18b: R = CH_3, Z = *o*-Cl; **19**: R = H, Z = *o*-Cl
20: R = H, Z = *p*-NO_2; **21a**: R = H, Z = *p*-Cl
21b: R = CH_3, Z = *p*-Cl; **22**: R = CH_3, Z = *p*-Cl

Z	(Chloroalkyl)oxazoline	R	Total yield (%)[a]	Products	Ratio of isomers (%)[b]
m-NO_2	**1a**	H	33	**12a**	–
m-NO_2	**1b**	Me	25	**12b**	–
m-Cl	**1a**	H	63	**13a**, **14**, **15**	**13a/14/15** = 53:25:22
m-Cl	**1b**	Me	25	**13b**	–
o-NO_2	**1a**	H	33	**16a**, **17**	**16a/17** = 66:34
o-NO_2	**1b**	Me	30	**16b**	–
o-Cl	**1a**	H	33	**18a**, **19**	**18a/19** = 64:36
o-Cl	**1b**	Me	62	**18b**	–
p-NO_2	**1a**	H	35	**20**	–
p-NO_2	**1b**	Me	40	**2b**	–
p-Cl	**1a**	H	66	**21a**	–
p-Cl	**1b**	Me	30	**21b**, **22**	**21b/22** = 80:20

[a] Yields of isolated products. [b] Determined by GC and by ^{1}H NMR spectroscopy.

ethyl]-4,5-dihydrooxazole **13b**. In no case involving 1,3-chloronitrobenzene and 1,3-dinitrobenzene did replacement of the chlorine or nitro group by the entering nucleophile take place. This is not surprising in view of the fact that the VNS reaction of hydrogen is usually faster than the SN_{Ar} reaction.[1a–1c]

The behaviour of 1,2-dinitro- and 1,2-chloronitrobenzene towards the anions of oxazolines **1a** and **1b** was then investigated. We found that 1,2-dinitrobenzene couples with the potassium anion of 2-(chloromethyl)oxazoline **1a** with poor regioselectivity, giving a mixture of compounds **16a** and **17**, while the reaction with 2-(chloroethyl)oxazoline **1b** proceeded highly regioselectively, giving the VNS product of 4-hydrogen substitution: compound **16b**. The behaviour of **1a** and **1b** as anions with 1,2-chloronitrobenzene was found to be very similar in terms of regioselectivity to that observed previously, giving compounds **18a**, **19**, and **18b**, respectively.

As was to be expected, when the potassium anions of heterocycles **1a** and **1b** were treated with 1,4-chloronitrobenzene the VNS reaction occurred prevalently *ortho* to the nitro group to give compounds **21a** and **21b**, respectively. Exceptionally, **1b** anion also furnished compound **22**, bearing the oxazolinylethyl group *meta* to the nitro group. This is a quite new and unexpected result that we are unfortunately not able to explain at present.

A completely different pattern was observed when the anions of **1a** and **1b** were treated with 1,4-dinitrobenzene, affording 2-[chloro(4-nitrophenyl)methyl]-4,5-dihydro-4,4-dimethyloxazole **20** and **2b**, respectively. We presume that compound **20** arises from a S_NAr process involving the nucleophilic replacement of one of the two nitro groups by the anion of the used heterocycle. One nitro group probably activates the SN_{Ar} replacement of the other. The formation of compounds such as **20** in a VNS reaction has been reported: chloroacetonitrile and 1,4-dinitrobenzene react under basic conditions to give nitrophenylacetonitrile.[15] The ability of the nitro group to act as a leaving group in a S_NAr process is well known.[16] The fact that an SN_{Ar} process occurs in the reaction of 1,4-dinitrobenzene and not with 1,4-chloronitrobenzene could be accounted for by NO_2 be-

ing a much better leaving group than chlorine in SN_{Ar} reactions.[5c] Compound **2b** might be the result of a reduction reaction of the corresponding SN_{Ar} product by the excess of *t*BuOK.[17]

Conclusion

In conclusion, the work reported in this paper offers the synthetic organic chemist a route to α-substituted (nitrobenzyl)oxazolines, which offer potential for elaboration to a variety of other substances and so are useful in synthetic organic chemistry. Moreover, the potassium carbanions of the chloroalkyloxazolines used in this work broaden the set of activating groups that could be employed in the VNS reactions. The reaction also works well with other oxazolines, chiral ones included, and results will be reported in due course. The unsuccessful reaction of the post-VNS carbanions of (chloroalkyl)oxazolines with carbonyl compounds, which would open a useful route to more functionalized (nitrobenzyl)oxazolines, remains to be studied.

Experimental Section

General: The ^1H and the ^{13}C NMR spectra were recorded with a Bruker Avance 400 apparatus (400.13 MHz and 100.62 MHz, for ^1H and ^{13}C, respectively) and a Bruker AC 200 apparatus (200 MHz and 50.3 MHz, for ^1H and ^{13}C, respectively), with $CDCl_3$ as the solvent and TMS as the internal standard ($\delta_H = 7.24$ for ^1H spectra; $\delta_H = 77.0$ for ^{13}C spectra). The IR spectra were recorded with a Perkin−Elmer spectrometer Model 283. GC-MS analyses were performed with a Shimadzu GC-17A gas chromatograph [5% phenyl(methyl)siloxane capillary column, 30 m, 0.25 mm i.d.], equipped with a Shimadzu GCMS-QP5050A mass-selective detector operating at 70 eV (EI). Melting points were determined on an electrothermal melting point apparatus and were uncorrected. TLC was performed on Merck silica gel plates with F-254 indicator; viewing was by UV light (254 nm). Column chromatography was performed on silica gel (63−200 μm), with petroleum ether/ethyl acetate (EtOAc) mixtures as eluents. All reactions involving air-sensitive reagents were performed under nitrogen in oven-dried glassware by syringe/septum cap techniques. DMSO was distilled and stored on molecular sieves (5Å) prior to use. Starting materials were commercially available or were prepared by known methods.

General Procedure for the Preparation of α-Substituted Nitrobenzyloxazolines: A solution of 2-chloroalkyl-4,4-dimethyl-2-oxazoline[18] (**1a**, **1b**, 1 mmol) and nitroarene (1.1 mmol) in DMSO (2 mL) was added dropwise under N_2 to a vigorously stirred suspension of powdered *t*BuOK (3 mmol) in DMSO (10 mL). The reaction mixture was kept at room temperature for 1 h, quenched with a saturated aqueous NH_4Cl solution (10−20 mL) and extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The crude products were purified by flash column chromatography (silica gel: 63−200 μm; petroleum ether/EtOAc, 1:1) to afford the pure α-substituted (nitrobenzyl)oxazolines; yields: 15−73%. The compounds **4**−**7** were obtained by quenching the mixture with large excesses (5 mmol) of methyl iodide, allyl bromide, benzyl chloride and propargyl bromide, respectively, instead of NH_4Cl solution. Compound **8** was obtained by carrying out the reaction under dry air, with addition of benzaldehyde (5 mmol) after 1 h at room temperature. After 3 h at 50 °C, the mixture was quenched with a saturated aqueous NH_4Cl solution (10−20 mL) and worked up as described above.

4,4-Dimethyl-2-(4-nitrobenzyl)-4,5-dihydrooxazole (2a): Yield: 70 mg (30%), oil. ^1H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.28 (s, 6 H), 3.70 (s, 2 H), 3.94 (s, 2 H), 7.48 (d, *J* = 8.6 Hz, 2 H), 8.17 (d, *J* = 8.6 Hz, 2 H) ppm. ^{13}C NMR (50.3 MHz, ppm): δ = 28.0, 34.5, 67.2, 79.2, 123.7, 129.7, 142.7, 153.0, 162.8. GC-MS (*m*/*z*, %): 234 (44) [M^+], 219 (100), 204 (40), 191 (36), 163 (40), 136 (47). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2969, 1668, 1523, 1348, 1151.

4,4-Dimethyl-2-[1-(4-nitrophenyl)ethyl]-4,5-dihydrooxazole (2b): Yield: 137 mg (55%), oil. ^1H NMR (400.13 MHz, $CDCl_3$, ppm): δ = 1.20 (s, 6 H), 1.56 (d, *J* = 7.2 Hz, 3 H), 3.78(q, *J* = 7.2 Hz, 1 H) 3.90 (s, 2 H), 7.48 (d, *J* = 8.7 Hz, 2 H), 8.17 (d, *J* = 8.7 Hz, 2 H). ^{13}C NMR (100.62 MHz, ppm): δ = 19.1, 28.1, 28.2, 39.3, 67.0, 79.2, 123.8, 128.2, 149.0, 156.0, 166.3. GC-MS (*m*/*z*, %): 248 (100) [M^+], 247 (67), 233 (95), 218 (38), 150 (87). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2972, 1662, 1520, 1349, 1187.

4,4-Dimethyl-2-(2-nitrobenzyl)-4,5-dihydrooxazole (3a): Yield: 100 mg (43%), oil. ^1H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.20 (s, 6 H), 3.90 (s, 2 H), 3.94 (s, 2 H), 7.37−7.59 (m, 3 H), 7.98 (d, *J* = 8.1 Hz, 1 H). ^{13}C NMR (50.3 MHz, ppm): δ = 28.1, 32.8, 67.4, 79.3, 125.2, 128.3, 130.6, 132.4, 133.3, 152.4, 162.7. GC-MS (*m*/*z*, %): 234 (0.4) [M^+], 219 (12), 188 (96), 92 (89), 84 (100). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2969, 1671, 1528, 1354, 1152.

4,4-Dimethyl-2-[1-methyl-1-(4-nitrophenyl)ethyl]-4,5-dihydrooxazole (4): Yield: 98 mg (37%), oil. ^1H NMR (400.13 MHz, $CDCl_3$, ppm): δ = 1.31 (s, 6 H), 1.63 (s, 6 H), 3.89 (s, 2 H), 7.53 (d, *J* = 8.8 Hz, 2 H), 8.17 (d, *J* = 8.8 Hz, 2 H). ^{13}C NMR (100.62 MHz, ppm): δ = 27.0, 28.0, 40.9, 67.0, 79.3, 123.5, 126.5, 146.6, 152.3, 169.3. GC-MS (*m*/*z*, %): 262 (95) [M^+], 261 (82), 247 (100), 232 (12), 217 (13), 216(8), 164 (94). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2960, 1650, 1600, 1510, 1345, 1120, 850, 700.

4,4-Dimethyl-2-[1-methyl-1-(4-nitrophenyl)but-3-enyl]-4,5-dihydrooxazole (5): Yield: 121 mg (42%), oil. ^1H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.31 (s, 6 H), 1.58 (s, 3 H), 2.70 (dd, *J* = 7.1, 13.7 Hz, 1 H) 2.85 (dd, *J* = 7.2, 13.7 Hz, 1 H), 3.88 (s, 2 H), 5.06 (d, *J* = 11.8 Hz, 1 H), 5.07 (d, *J* = 14.7 Hz, 1 H), 5.65 (m, 1 H), 7.50 (d, *J* = 8.8 Hz, 2 H), 8.18 (d, *J* = 8.8 Hz, 2 H). ^{13}C NMR (100.62 MHz, ppm): δ = 23.5, 28.1, 28.3, 43.8, 44.2, 67.2, 79.2, 119.0, 123.5, 127.0, 132.9, 146.7, 151.7, 168.2. GC-MS (*m*/*z*, %): 288 (64) [M^+], 287 (70), 273 (79), 258 (16), 217 (100). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3040, 2920, 1650, 1515, 1350, 1260, 740.

4,4-Dimethyl-2-[1-methyl-1-(4-nitrophenyl)-2-phenylethyl]-4,5-dihydrooxazole (6): Yield: 213 mg (63%), yellow solid, m.p. 87−89 °C (petroleum ether). ^1H NMR (400.13 MHz, $CDCl_3$, ppm): δ = 1.24 (s, 3 H), 1.31 (s, 3 H), 1.54 (s, 3 H), 3.25 (d, *J* = 13.1 Hz, 1 H), 3.43 (d, *J* = 13.1 Hz, 1 H), 3.92 (s, 2 H), 6.89−6.91 (m, 2 H), 7.16−7.18 (m, 3 H), 7.46 (d, *J* = 8.8 Hz, 2 H), 8.16 (d, *J* = 8.8 Hz, 2 H). ^{13}C NMR (100.62 MHz, ppm): δ = 23.2, 28.0, 28.2, 45.2, 45.4, 67.1, 79.0, 123.3, 126.6, 127.2, 127.7, 130.4, 136.2, 146.6, 151.6, 168.0. GC-MS (*m*/*z*, %): 338 (52) [M^+], 323 (43), 261 (10), 217 (12), 216 (11): 91 (100). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2960, 1650, 1595, 1510, 1345, 850, 700.

4,4-Dimethyl-2-[1-methyl-1-(4-nitrophenyl)but-3-ynyl]-4,5-dihydrooxazole (7): Yield = 115 mg (40%), yellow solid, m.p. 127−128 °C (petroleum ether). ^1H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.31 (s,

3 H), 1.32 (s, 3 H), 1.75 (s, 3 H), 1.96 (t, J = 2.4 Hz, 1 H), 2.92 (d, J = 2.4 Hz, 2 H), 3.90 (s, 2 H), 7.53 (d, J = 8.9 Hz, 2 H), 8.18 (d, J = 8.9 Hz, 2 H). ^{13}C NMR (50.3 MHz, ppm): δ = 23.3, 28.0, 28.1, 30.0, 43.9, 67.3, 71.4, 79.5, 79.8, 123.5, 127.1, 147.0, 150.0, 167.5. GC-MS (*m*/*z*, %): 286 (5) [M$^+$], 285 (13), 271 (100), 247 (9), 201 (14), 141 (30), 115 (38). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3300, 2960, 2100, 1650, 1600, 1510, 1345.

1-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-1-(4-nitrophenyl)ethanol (8): Yield: 119 mg (45%), yellow solid, m.p. 97−99 °C (*n*-hexane). ^{1}H NMR (400.13 MHz, $CDCl_3$, ppm): δ = 1.24 (s, 3 H), 1.32 (s, 3 H), 1.79 (s, 3 H), 4.01 (d, J = 8.2 Hz, 1 H), 4.05 (s, 1 H, broad, exchanges with D_2O), 4.10 (d, J = 8.2 Hz, 1 H), 7.77 (d, J = 8.8 Hz, 2 H), 8.19 (d, J = 8.8 Hz, 2 H). ^{13}C NMR (100.62 MHz, ppm): δ = 27.8, 28.0, 67.1, 72.1, 80.9, 123.3, 126.2, 147.3, 151.0, 168.3. GC-MS (*m*/*z*, %): 264 (100) [M$^+$], 249 (58), 219 (60), 150 (34), 69 (99). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 3450, 3040, 2950, 2900, 1650, 1600, 1510, 1350, 1130.

4,4-Dimethyl-2-(2,4-dinitrobenzyl)-4,5-dihydrooxazole (12a): Yield: 92 mg (33%), oil. ^{1}H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.21 (s, 6 H), 3.95 (s, 2 H), 4.07 (s, 2 H), 7.66 (d, J = 8.5 Hz, 1 H), 8.42 (dd, J = 2.4, 8.5 Hz, 1 H), 8.87 (d, J = 2.4 Hz, 1 H). ^{13}C NMR (50.3 MHz, ppm): δ = 27.9, 32.9, 67.5, 79.5, 120.6, 127.3, 133.9, 137.4, 147.2, 149.1, 161.5. GC-MS (*m*/*z*, %): 279 (2) [M$^+$], 278 (2), 264 (100), 233 (26), 181 (10), 84 (98). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2920, 1650, 1605, 1530, 1350, 1160.

4,4-Dimethyl-2-[1-(2,4-dinitrophenyl)ethyl]-4,5-dihydrooxazole (12b): Yield: 73 mg (25%), oil. ^{1}H NMR (400.13 MHz, $CDCl_3$, ppm): δ = 1.28 (s, 3 H), 1.29 (s, 3 H), 1.68 (d, J = 6.9 Hz, 3 H), 3.90 (d, J = 8.1 Hz, 1 H), 3.94 (d, J = 8.1 Hz, 1 H), 4.43 (q, J = 6.9 Hz, 1 H), 7.79 (d, J = 8.6 Hz, 1 H), 8.43 (d, J = 8.6 Hz, 1 H), 8.70 (s, 1 H). ^{13}C NMR (100.62 MHz, ppm): δ = 18.8, 28.1, 28.2, 35.0, 67.5, 79.5, 120.2, 127.1, 130.7, 143.0, 146.7, 149.6, 165.4. GC-MS (*m*/*z*, %): 293 (1) [M$^+$], 278 (21): 247 (24), 149 (43), 100 (42), 84 (100). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2960, 2925, 1660, 1605, 1520, 1350.

2-(2-Chloro-4-nitrobenzyl)-4,5-dihydro-4,4-dimethyloxazole (13a): Yield: 93 mg (33%), oil. ^{1}H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.20 (s, 6 H), 3.72 (s, 2 H), 3.87 (s, 2 H),.7.46 (d, J = 8.5 Hz, 1 H), 8.08 (d, J = 8.5 Hz, 1 H), 8.15 (s, 1 H). ^{13}C NMR (100.62 MHz, ppm): δ = 28.1, 32.4, 67.3, 79.3, 121.7, 124.5, 131.3, 133.2, 140.7, 147.3, 161.7. GC-MS (*m*/*z*, %): 268 (0.2) [M$^+$], 253 (29), 233 (100), 170 (22), 149 (61). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2960, 1660, 1590, 1520, 1450, 1350.

2-[1-(2-Chloro-4-nitrophenyl)ethyl]-4,5-dihydro-4,4-dimethyloxazole (13b): Yield: 70 mg (25%), oil. ^{1}H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.31 (s, 6 H), 1.54 (d, J = 7.1 Hz, 3 H), 3.88−3.96 (m, 2 H), 4.26 (q, J = 7.1 Hz, 1 H), 7.56 (d, J = 8.7 Hz, 1 H), 8.11 (dd, J = 2.3, 8.7 Hz, 1 H), 8.25 (d, J = 2.3 Hz, 1 H). ^{13}C NMR (50.3 MHz, ppm): δ = 19.3, 29.0, 36.5, 67.1, 79.2, 122.0, 123.7, 125.1, 128.7, 135.0, 147.1, 166.0. GC-MS (*m*/*z*, %): 282 (2) [M$^+$], 267 (19), 252 (4), 247 (100), 184 (22). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2960, 1660, 1590, 1515, 1450, 1345.

2-(4-Chloro-2-nitrobenzyl)-4,5-dihydro-4,4-dimethyloxazole (14): Yield: 43 mg (16%), oil. ^{1}H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.17 (s, 6 H), 3.70−3.80 (m, 4 H), 7.50 (d, J = 8.5 Hz, 1 H), 7.80 (d, J = 8.5 Hz, 1 H), 7.95 (s, 1 H). ^{13}C NMR (100.62 MHz, ppm): δ = 28.0, 32.2, 67.2, 79.2, 125.2, 129.0, 133.5, 134.0, 135.2, 149.1, 162.2. GC-MS (*m*/*z*, %): 268 (0.2) [M$^+$], 253 (30), 222 (53), 170 (12), 149 (30), 126 (26), 84 (100). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2960, 1660, 1590, 1520, 1450, 1350.

2-(2-Chloro-6-nitrobenzyl)-4,5-dihydro-4,4-dimethyloxazole (15): Yield: 37 mg (14%), oil. ^{1}H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.18 (s, 6 H), 3.90 (s, 2 H), 4.05 (s, 2 H), 7.33 (t, J = 8.2 Hz, 1 H), 7.62 (d, J = 8.2 Hz, 1 H), 7.81 (d, J = 8.2 Hz, 1 H). ^{13}C NMR (100.62 MHz, ppm): δ = 28.0, 29.0, 67.4, 79.4, 123.5, 128.5, 128.6, 134.1, 137.1, 150.0, 161.6. GC-MS (*m*/*z*, %): 268 (0.3) [M$^+$], 253 (43), 233 (71), 222 (22), 149 (28), 126 (27), 84 (100). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2960, 2925, 1665, 1600, 1525, 1450, 1350.

2-(3,4-Dinitrobenzyl)-4,5-dihydro-4,4-dimethyloxazole (16a): Yield = 61 mg (22%), oil. ^{1}H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.28 (s, 6 H), 3.73 (s, 2 H), 3.96 (s, 2 H), 7.68 (dd, J = 1.7, 8.2 Hz, 1 H), 7.86−7.92 (m, 2 H). ^{13}C NMR (50.3 MHz, ppm): δ = 28.2, 34.2, 65.8, 79.6, 125.6, 130.2, 133.6, 148.1, 149.2, 161.7. GC-MS (*m*/*z*, %): 279 (19) [M$^+$], 264 (100), 249 (34), 208 (20), 191 (10). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2970, 1670, 1544, 1366, 1154.

2-[1-(3,4-Dinitrophenyl)ethyl]-4,5-dihydro-4,4-dimethyloxazole (16b): Yield: 88 mg (30%), oil. ^{1}H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.27 (s, 6 H), 1.58 (d, J = 7.1 Hz, 3 H), 3.85 (q, J = 7.1 Hz, 1 H), 3.92 (s, 2 H), 7.69 (dd, J = 1.8, 8.3 Hz, 1 H), 7.85−7.98 (m, 2 H). ^{13}C NMR (50.3 MHz, ppm): δ = 18.9, 28.2, 28.2, 39.1, 67.3, 79.4, 124.1, 125.4, 130.0, 132.2, 148.1, 148.2, 160.9. GC-MS (*m*/*z*, %): 293 (44) [M$^+$], 278 (100), 263 (17), 195 (20), 84 (17). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2980, 1660, 1605, 1540, 1350.

2-(2,3-Dinitrobenzyl)-4,5-dihydro-4,4-dimethyloxazole (17): Yield: 31 mg (11%), oil. ^{1}H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.26 (s, 6 H), 3.72 (s, 2 H), 3.95 (s, 2 H), 7.63−7.87 (m, 2 H), 8.07 (dd, J = 1.4, 8.1 Hz, 1 H). ^{13}C NMR (50.3 MHz, ppm): δ = 28.0, 30.2, 67.4, 79.5, 124.4, 131.0, 136.7, 142.5, 149.1, 149.2, 160.9. GC-MS (*m*/*z*, %): 279 (1) [M$^+$], 264 (64), 233 (24), 100 (27), 84 (100). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2970, 1670, 1544, 1362, 1154.

2-(3-Chloro-4-nitrobenzyl)-4,5-dihydro-4,4-dimethyloxazole (18a): Yield: 56 mg (21%), oil. ^{1}H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.29 (s, 6 H), 3.64 (s, 2 H), 3.95 (s, 2 H), 7.35 (dd, J = 1.6, 8.3 Hz, 1 H), 7.5 (d, J = 1.6 Hz, 1 H), 7.86 (d, J = 8.3 Hz, 1 H). ^{13}C NMR (100.62 MHz, ppm): δ = 28.2, 34.2, 67.4, 79.5, 125.8, 128.0, 129.4, 132.2, 141.6, 150.7, 162.3. GC-MS (*m*/*z*, %): 268 (40) [M$^+$], 253 (100), 238 (38), 178 (15), 140 (26). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2960, 1655, 1530, 1450, 1350, 1050.

2-[1-(3-Chloro-4-nitrophenyl)ethyl]-4,5-dihydro-4,4-dimethyloxazole (18b): Yield: 175 mg (62%), oil. ^{1}H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.29 (s, 6 H), 1.55 (d, J = 7.2 Hz, 3 H), 3.77 (q, J = 7.2 Hz, 1 H), 3.92 (s, 2 H), 7.38 (dd, J = 1.8, 8.3 Hz, 1 H), 7.52 (d, J = 1.8 Hz, 1 H), 7.86 (d, J = 8.3 Hz, 1 H). ^{13}C NMR (100.62 MHz, ppm): δ = 18.9, 28.0, 28.1, 38.9, 67.0, 79.2, 125.8, 126.5, 127.2, 130.7, 147.9, 165.8. GC-MS (*m*/*z*, %): 282 (99) [M$^+$], 267 (100), 252 (37), 184 (71): 84 (65). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2960, 1595, 1535, 1345, 1050.

2-(3-Chloro-2-nitrobenzyl)-4,5-dihydro-4,4-dimethyloxazole (19): Yield 30 mg (11%), oil. ^{1}H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.26 (s, 6 H), 3.62 (s, 2 H), 3.92 (s, 2 H), 7.30−7.50 (m, 3 H). ^{13}C NMR (100.62 MHz, ppm): δ = 28.5, 31.1, 67.8, 79.9, 126.4, 129.8, 130.0, 130.2, 142.1, 150.6, 162.1. GC-MS (*m*/*z*, %): 268 (1) [M$^+$], 253 (38), 238 (3), 222 (61): 84 (100). IR (film, cm^{-1}), $\tilde{\nu}_{max}$ = 2970, 1650, 1530, 1450, 1355, 1260, 1050.

2-[Chloro(4-nitrophenyl)methyl]-4,5-dihydro-4,4-dimethyloxazole (20): Yield: 94 mg (35%), oil. ^{1}H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.28 (s, 3 H), 1.33 (s, 3 H), 3.99−4.08 (m, 2 H), 5.61 (s, 1 H), 7.73 (d, J = 8.7 Hz, 2 H), 8.24 (d, J = 8.7 Hz, 2 H). ^{13}C NMR (50.3 MHz, ppm): δ = 28.2, 54.2, 68.2, 80.7, 124.3, 129.3, 143.5,

148.6, 162.8. GC-MS (*m*/*z*, %): 268 (2) [M^+], 253 (8), 233 (100), 219 (26), 203 (38), 170 (21). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2975, 1670, 1600, 1515, 1366, 1350, 1165, 1030.

2-(5-Chloro-2-nitrobenzyl)-4,5-dihydro-4,4-dimethyloxazole (21a): Yield: 177 mg (66%), yellow solid, m.p. 76−77 °C (petroleum ether). ^1H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.14 (s, 6 H), 3.84 (s, 2 H), 3.85 (s, 2 H), 7.28−7.34 (m, 2 H), 7.91 (d, *J* = 9.2 Hz, 1 H). ^{13}C NMR (50.3 MHz, ppm): δ = 27.9, 32.7, 67.3, 79.3, 126.5, 128.3, 132.4, 132.5, 139.4, 147.1, 162.1 GC-MS (*m*/*z*, %): 268 (0.2) [M^+], 253 (65), 238 (2), 224 (70), 222 (99), 194 (44), 170 (30), 126 (59), 84 (100). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2960, 1665, 1520, 1340.

2-[1-(5-Chloro-2-nitrophenyl)ethyl]-4,5-dihydro-4,4-dimethyloxazole (21b): Yield: 68 mg (24%), oil. ^1H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.21 (s, 6 H), 1.53 (d, *J* = 7.2 Hz, 3 H), 3.84 (s, 2 H), 4.28 (q, *J* = 7.2 Hz, 1 H), 7.28 (dd, *J* = 1.4, 8.6 Hz, 1 H), 7.43 (d, *J* = 1.4 Hz, 1 H), 7.80 (d, *J* = 8.6 Hz, 1 H). ^{13}C NMR (100.62 MHz, ppm): δ = 19.3, 28.5, 28.6, 35.2, 67.7, 79.7, 123.4, 126.7, 129.7, 130.9, 139.9, 148.3, 166.5. GC-MS (*m*/*z*, %): 282 (0.1) [M^+], 267 (5), 236 (100), 208 (24), 170 (26), 100 (38), 84 (80). IR (film, cm^{-1}): $\tilde{\nu}_{max}$ = 2970, 1660, 1600, 1520, 1460, 1370.

2-[1-(2-Chloro-5-nitrophenyl)ethyl]-4,5-dihydro-4,4-dimethyl**oxazole (22):** Yield: 17 mg (6%), oil. ^1H NMR (200 MHz, $CDCl_3$, ppm): δ = 1.23 (s, 6 H), 1.48 (d, *J* = 7.2 Hz, 3 H), 3.87 (s, 2 H), 4.15 (q, *J* = 7.2 Hz, 1 H), 7.50 (d, *J* = 8.6 Hz, 1 H), 8.00 (dd, *J* = 1.4, 8.6 Hz, 1 H), 8.19 (d, *J* = 1.4 Hz, 1 H). ^{13}C NMR (100.62 MHz, ppm): δ = 18.6, 28.7, 36.6, 67.7, 79.8, 123.8, 125.0, 128.4, 138.7, 141.0, 148.6, 166.5. GC-MS (*m*/*z*, %): 282 (3) [M^+], 267 (31): 252 (6), 247 (100), 184 (33). IR (film, cm^{-1}), $\tilde{\nu}_{max}$ = 2970, 1660, 1600, 1520, 1460, 1370.

Supporting Information Available: Spectroscopic data (proton-decoupled ^{13}C NMR spectra and high-field ^1H NMR spectra) for all compounds. This material is available free of charge on the internet at http://pubs.acs.org.

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