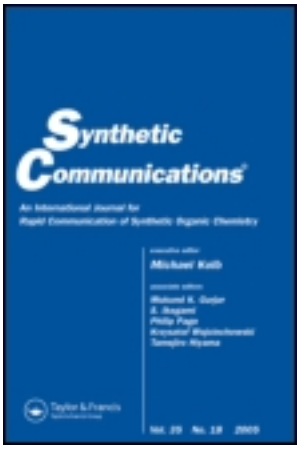

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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Version of record first published: 13 Nov 2012.

To cite this article: Guido Galliani , Bruno Rindone , Ricardo Suarez-Bertoa , Francesco Saliu & Alberto Terraneo (2013): Stereoselective Addition of Grignard Reagents and Lithium Alkyls onto 3,5-Disubstituted-1,3-oxazolidine-2,4-diones, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 43:5, 749-757

To link to this article: http://dx.doi.org/10.1080/00397911.2011.609301

Synthetic Communications®, 43: 749–757, 2013

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397911.2011.609301

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STEREOSELECTIVE ADDITION OF GRIGNARD REAGENTS AND LITHIUM ALKYLS ONTO 3,5-DISUBSTITUTED-1,3-OXAZOLIDINE-2,4-DIONES

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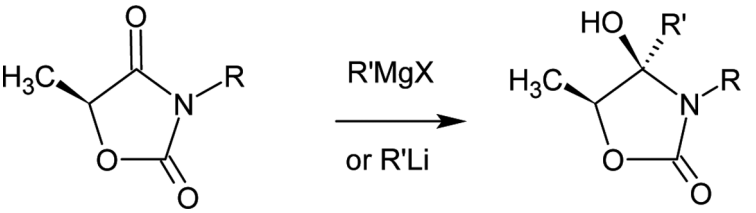
GRAPHICAL ABSTRACT



Abstract *3-Benzyl-5-methyl-1,3-oxazolidine-3,4-diones react with Grignard reactants and with lithium alkyls to yield 4-substituted 3-benzyl-4-hydroxy-5-methyl-1,3-oxazolidine-2-ones. The reaction is stereoselective and follows Cram's rule.*

Keywords Grignard; lithium alkyls; oxazolidinedione; stereoselectivity

INTRODUCTION

1,3-oxazolidine-2,4-diones are useful intermediates for the preparation of biologically active compounds.[1–7] These compounds are hydrolyzed in alkaline conditions by attack of the three available bonds, namely the amide C-N bond and the two carbamate C-O and C-N bonds, depending on substrate and reaction conditions. Scarce data on their reactivity with nucleophiles are available. Recently, we found that 3,5-dialkyl-1,3-oxazolidine-2,4-diones (**1**) react with primary aliphatic amines to give N-lactylureas (**4**) (Scheme 1, path a). Reactions are performed in solventless conditions and require a temperature of 80–90 °C to proceed, with rates being enhanced by microwaves.[8,9] The carbamate carbonyl is attacked by primary

Received April 29, 2011.
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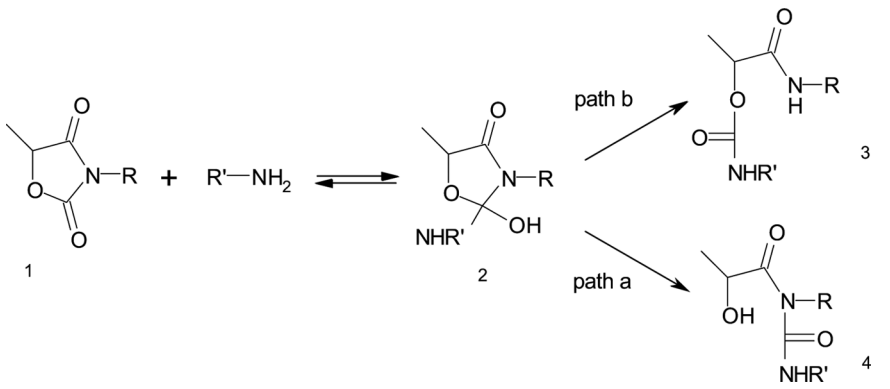


Scheme 1. Reaction scheme of 3-substituted 5-methyl-1,3-oxazolidine-2,4-diones with primary aliphatic amines. Only N-lactylureas (path a) are formed.

aliphatic amines and the bond broken during the reaction is the C-O bond. No substantial amounts of the products from path b were found.

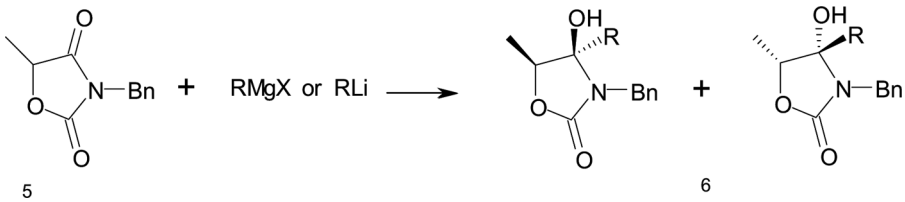
RESULTS AND DISCUSSION

In the search for additional data on the reactivity of 3,5-dialkyl-1,3-oxazolidine-2,4-diones with nucleophiles, 3-benzyl-5-methyl-1,3-oxazolidine-2,4-dione (**5**) (Scheme 2) was reacted with several carbon-centered nucleophiles. The starting material was prepared by condensation of urea and ethyl lactate with sodium ethoxide in ethanol, followed by N-alkylation (86% yield).[10]

With Grignard reagents and with lithium alkyls, the reaction product obtained at low temperatures (−30 °C) was identified as the cyclic adduct (**6**) (Scheme 2), namely a 4-substituted 3-benzyl-4-hydroxy-5-methyl-1,3-oxazolidin-2-one, as a couple of enantiomers. The formation of the adduct at low temperature is an example of stereoselective additions to carbonyls. The stereochemistry of the adducts is in line with Cram's rule,[11] the incoming group attacking carbonyl from the side of the small group, hydrogen in this case, more preferably than on the side of the large group, namely methyl in the present case.

Proofs of the structure are given by the following pieces of evidence:

1. Liquid chromatography–mass spectrometry (LC-MS) data of the purified products, typical for adducts.



Scheme 2. Reaction of 3-benzyl-5-methyl-1,3-oxazolidine-3,4-diones with alkyl Grignard reactants and with lithium alkyls at −30 °C in THF.

2. A hydrogen atom on a heteroatom is present (1 H in the ^{1}H NMR spectrum in the range of 4–5 ppm, disappearing upon treatment with D_2O).
3. The amide carbonyl of the starting product, giving a signal at 172 ppm in the ^{13}C NMR, disappears, whereas the carbamate carbonyl (at 158 ppm) is retained during the reaction, unlike in the reaction with primary amines.
4. APT (attached proton test) ^{13}C NMR spectrum shows that a quaternary sp^3 carbon is formed, with a signal close to 82, according to the group attached during the reaction.
5. The C-H carbon bearing the 5 methyl group is shifted in the ^{13}C NMR spectrum to a value close to 90 ppm, instead of 76 ppm of the starting material, as predicted by ^{13}C NMR simulation (ChemOffice 2005). Addition of the R group of the metallorganic reagent onto the carbamate would not affect the signal. Figure 1 shows both simulated signals and those actually found for the adduct of 3-benzyl-5-methyl-1,3-oxazolidine-2,4-dione with methyl magnesium bromide (compound **9a** of Table 1).
6. Correlation spectroscopy / nuclear overhauser effect spectroscopy (COSY/NOESY) experiments on compound **9a** (Table 1) indicate a long-range interaction between the hydrogen atom at 4.35 ppm and the methyl group entered by the addition of the Grignard reagent, resonating at 1.29 ppm. The interaction is consistent with *cis* configuration of these groups (Fig. 2).
7. Compound **9a** structure was confirmed by an independent synthesis on the analogy of similar compounds obtained by reaction of 2-hydroxybutanone and isocyanates.[12,13] Moreover, stereochemistry was confirmed as well, COSY/NOESY experiments showing the same pattern described in these papers.

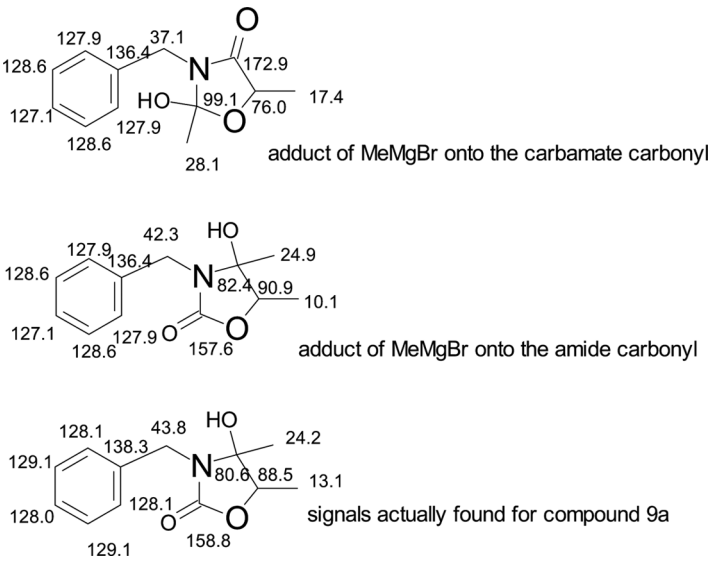
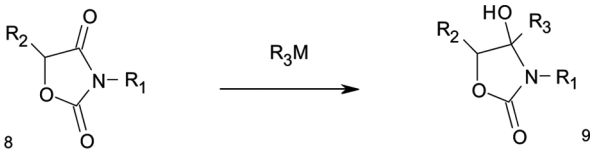
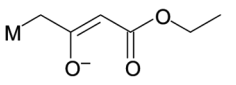


Figure 1. ^{13}C NMR simulated spectra for the two possible adducts of MeMgBr onto carbonyl groups of 3-benzyl-5-methyl-1,3-oxazolidine-2,4-dione. A comparison with the spectrum actually found shows that the Grignard reagent attacks the amide carbonyl.

Table 1. Reaction of 1,3-oxazolidine-2,4-diones (**8**) with either Grignard reagents or lithium alkyls to give adducts (**9**)





(10)

Entry	R_1	R_2	R_3	M	Yield (%)
a	Benzyl	Methyl	Methyl	MgBr	76
b	Benzyl	Methyl	Ethyl	MgBr	80
c	Benzyl	Methyl	n-Butyl	MgBr	58
c′	Benzyl	Methyl	n-Butyl	Li	47
d	Benzyl	Methyl	Propynyl	MgCl	64
e	Benzyl	Methyl	Allyl	MgBr	64
f	Benzyl	Methyl	4-Ethoxy-2,4-dioxobut-1-yl (as a reaction product) Structure **10** (as a reactant)	Li	57
g	Benzyl	Methyl	2-Methyl-1,3-dithian-2-yl	Li	44
h	Benzyl	n-Butyl	Methyl	MgBr	62
i	n-Pentyl	Methyl	Ethyl	MgBr	83
j	n-Hexyl	Methyl	Allyl	MgBr	75

Table 1 (entries a–g) reports the yields obtained after flash chromatography of the crude reaction mixture, which contained only reaction product and starting material. Yields are not optimized. Reaction products were identified by infrared (IR), LC-MS, and ^{1}H and ^{13}C NMR. The reaction seems to be of general application, because compounds with different substitutions both in positions 3 and 5 give analogous reaction products, as shown in Table 1, entries h, i, and j.

Reactions of 3-benzyl-5-methyl-1,3-oxazolidine-2,4-dione (**5**) with the same carbon centered nucleophiles in refluxing tetrahydrofuran (THF) retained chemoselectivity. In these conditions, however, stereoselectivity was lost. As a matter of fact,

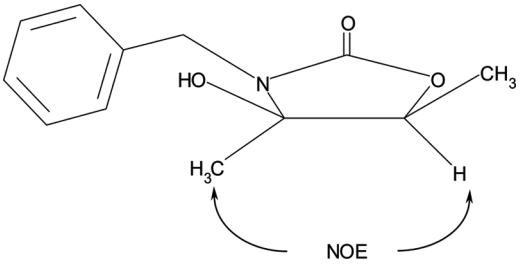
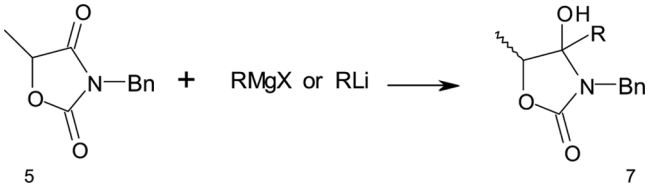


Figure 2. NOESY shows a long-range interaction between the hydrogen atom and the methyl group in the enantiopure couple obtained at −30 °C.



5 7

Scheme 3. Reaction of 3-benzyl-5-methyl-1,3-oxazolidine-3,4-diones with alkyl Grignard reactants and with lithium alkyls at reflux in THF.

both diastereoisomers on position 4 were found (Scheme 3). Similar diastereoisomers were described as well in the reaction of 2-hydroxybutanone with isocyanates.[12] Moreover, both products converged to a single product in dehydrating condition already described in the same paper, to give a 4-oxazolin-2-one.

The reaction of Grignard reagents and lithium alkyls with 3,5-disubstituted-1,3-oxazolidine-2,4-diones at $-30\,^{\circ}C$ is a new entry to 3,4-substituted 4-hydroxy-1,3-oxazolidin-2-ones, as an alternative method to published procedures.[13] Advantages of this new method are a good control of stereochemistry and the possibility of introducing different groups onto position 4.

EXPERIMENTAL

All chemicals were purchased from Aldrich or Fluka chemical companies. ^{1}H and ^{13}C were recorded on a Varian Mercury 400 instrument in $CDCl_3$. Chemical shifts were reported in parts per million (δ) relative to the internal standard of tetramethylsilane (TMS). Melting points were determined in open capillaries using an Electrothermal melting-point apparatus and are uncorrected. All products where analyzed by LC/MS (column Gemini C18, 5 micron, 4.6×150 mm, 80% ammonium acetate 0.01 M pH 3.5, 20% acetonitrile, $30\,^{\circ}C$). Infrared spectra (IR) spectra in solution were recorded on a Nicolet Avatar 360 Fourier transform (FT-IR) spectrometer, using calcium fluoride cells previously purged with nitrogen. Elemental analyses were carried out on a Perkin-Elmer series II 2400 instrument. All reactions were monitored by thin-layer chromatography (TLC). Flash chromatography was performed on silica gel (100–200 mesh).

Typical Procedure for Addition of Either Grignard Reagents or Lithium Alkyks

4-Benzyl-5-methyl-1,3-oxazolidine-2,4-dione (2 g, 9.75 mmol) was dissolved in 40 mL of anhydrous THF. The solution was cooled at $-40\,^{\circ}C$ under nitrogen. Methyl magnesium chloride 3 M (3.25 ml) in THF (9.75 mmol) was dropped into the solution, keeping temperature below $-30\,^{\circ}C$. Temperature was then raised from $-30\,^{\circ}C$ to $5\,^{\circ}C$ in 5 h, this final temperature being maintained for an additional hour. After quenching with 200 mL of a saturated aqueous solution of ammonium chloride, the mixture was extracted with methylene chloride (2×200 mL). The combined organic phases were washed with brine (100 mL), dried over anhydrous sodium

sulfate, filtered, and evaporated under reduced pressure. The residue was purified by flash chromatography, eluting with n-hexane/ethyl acetate 4:1.

Reaction with the Lithium Derivative of the Sodium Enolate of Methyl Acetoacetate (Table 1, Entry f)

Methylacetoacetate (1.8 mL, 17 mmol) was added dropwise in a suspension of 0.41 g of sodium hydride (17 mmol) in 200 mL of dry THF at −15 °C under a nitrogen atmosphere. The mixture was stirred for 40 min, and then 6.8 mL of 2.5 M butyl lithium in THF (17 mmol) were added dropwise at the same temperature. A solution of 2.0 g of 4-benzyl-5-methyl-1,3-oxazolidine-2,4-dione in 30 mL of dry THF was added at −15 °C. The mixture was allowed to reach 0 °C during 2 h, and then it was worked up as in the general procedure.

Reaction with the Lithium Derivative of 2-Methyl-1,3-dithiane (Table 2, Entry g)

0.93 mL of 2.5 M butyl lithium in THF (10 mmol) were added dropwise into a solution of 2-ethyl-1,3-dithiane (1.5 mL, 12.5 mmol) in 100 mL of dry THF at −20 °C under an argon atmosphere. After stirring for 30 min at the same temperature, a solution of 2.0 g of 4-benzyl-5-methyl-1,3-oxazolidine-2,4-dione in 30 mL of dry THF was added dropwise at −20 °C. The mixture was allowed to reach 20 °C. Workup was done as in the general procedure.

Spectroscopic Data for Reaction Products (Table 1)

Compound 9a. Mp: 65 °C. IR (KBr): 3275, 1718, 1702, 1640 cm^{-1}. MS: 222 ($M^+ + 1$).^{1}H NMR: δ = 7.33 (t, J = 2.4 Hz, 4H), 7.26 (d, J = 2.8 Hz, 1H), 4.50 (AB, J = 16.0, 1H), 4.47 (AB, J = 16.0 Hz, 1H), 4.35 (q, J = 8.0 Hz, 1H), 4.08 (s, 1H), 1.41 (d, J = 8.0 Hz, 3H), 1.29 (s, 3H). ^{13}C NMR: δ = 158.8 (C=O), 138.3 (C), 129.1 (CH), 128.1 (CH), 128.0 (CH), 88.5 (CH), 80.6 (C), 43.8 (CH_2), 24.2 (CH_3), 13.1 (CH_3). Anal. calcd. for $C_{12}H_{15}NO_3$: C, 65.13%; H, 6.85%; N, 6.33%. Found: C, 64.97%; H, 6.80%, N, 6.27%.

Compound 9b. Mp: 57 °C IR: 3280, 1720, 1702, 1645 cm^{-1}. MS: 236 ($M^+ + 1$).^{1}H NMR: δ = 7.28–7.18 (m, 5H), 4.39 (AB, J = 16.0 Hz, 1H), 4.35 (AB, J = 16.0 Hz, 1H), 4.41 (s, 1H), 4.37 (q, J = 6.8 Hz, 1H), 1.65 (ddd, J = 7.6, 14.4, 22.0 Hz, 1H), 1.48 (ddd, J = 7.6, 12.0, 22.0 Hz, 1H), 1.35 (d, J = 6.8 Hz, 3H), 0.63 (t, J = 7.6 Hz, 3H). ^{13}C NMR: δ = 159.1 (C=O), 138.4 (C), 128.8 (CH), 127.9 (CH), 127.6 (CH), 90.7 (CH), 78.5 (C), 43.9 (CH_2), 30.7 (CH_2), 14.6 (CH_3), 8.0 (CH_3). Anal. calcd. for $C_{13}H_{17}NO_3$: C, 66.35%; H, 7.30%; N, 5.95%. Found: C, 66.46%; H, 7.41%; N, 5.91%.

Compound 9c. Mp: 51 °C. IR (KBr): 3260, 1722, 1695, 1650 cm^{-1}. MS: 264 ($M^+ + 1$).^{1}H NMR: δ = 7.36–7.25 (m, 5H), 4.46 (AB, J = 16.0 Hz, 1H), 4.42 (AB, J = 16.0 Hz, 1H), 4.44 (q, J = 6.4 Hz, 1H), 4.39 (s, 1H), 1.72–1.44 (overlapping, 2H), 1.41 (d, J = 6.4 Hz, 3H), 1.29–1.04 (m, 2H), 1.00–0.87 (m, 2H), 0.70 (t, J = 7.2 Hz, 3H). ^{13}C NMR: δ = 159.1 (C=O), 138.3 (C), 128.7 (CH), 128.2 (CH),

127.6 (CH), 90.6 (CH), 78.6 (C), 43.9 (CH_2), 37.2 (CH_2), 25.8 (CH_2), 22.8 (CH_2), 14.4 (CH_3), 13.9 (CH_3). Anal. calcd. for $C_{15}H_{21}NO_3$: C, 68.40%; H, 8.05%; N, 5.32%. Found: C, 68.23%; H, 8.20%; N, 5.21%.

Compound 9d. Mp: 61 °C. IR (KBr): 2295, 2231, 1730, 1715 cm^{-1}. MS: 246 ($M^+ + 1$).^{1}H NMR: $\delta = 7.36$–7.25 (m, 5H), 4.46 (AB, $J = 16.0$ Hz, 1H), 4.42 (AB, $J = 16.0$ Hz, 1H), 4.44 (q, $J = 6.4$ Hz, 1H), 4.39 (s, 1H), 1.72–1.44 (overlapping, 2H), 1.41 (d, $J = 6.4$ Hz, 3H), 1.29–1.04 (m, 2H), 1.00–0.87 (m, 2H), 0.70 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR: $\delta = 157.3$ (C=O), 137.6 (C=O), 128.8 (CH), 128.4 (CH), 127.8 (CH), 84.9 (C), 83.6 (C), 81.0 (CH), 75.1 (C), 45.1 (CH_2), 12.9 (CH_3), 3.6 (CH_3). Anal. calcd. for $C_{14}H_{15}NO_3$: C, 68.54%; H, 6.18%; N, 5.71%. Found: C, 68.67%; H, 6.10%; N, 5.78%.

Compound 9e. Oil. IR (KBr): 3250, 1731, 1697, 1644 cm^{-1}. MS: 248 ($M^+ + 1$).^{1}H NMR: $\delta = 7.37$–7.25 (m, 5H), 5.47 (dd, $J = 7.2$, 17.2 Hz, 1H), 5.04–4.96 (overlapping, 2H), 4.50 (AB, $J = 16.0$ Hz, 1H), 4.46 (AB, $J = 16.0$ Hz, 1H), 4.61 (s, 1H), 4.46 (q, $J = 6.0$ Hz, 1H), 2.50–2.21 (overlapping, 2H), 1.39 (d, $J = 6.0$ Hz, 3H). ^{13}C NMR: $\delta = 157.3$ (C=O), 137.6 (C), 131.5 (CH), 128.8 (CH), 128.4 (CH), 127.8 (CH), 120.0 (CH_2), 89.7 (CH), 78.8 (C), 44.0 (CH_2), 42.6 (CH_2), 14.1 (CH_3). Anal. calcd. for $C_{14}H_{17}NO_3$: C, 68.03%; H, 6.88%; N, 5.67%. Found: C, 67.89%; H, 7.01%; N, 5.52%.

Compound 9f. Mp: 69 °C. IR (KBr): 3875, 1746,1713, 1695, 1660 cm^{-1}. MS: 336 ($M^+ + 1$).^{1}H NMR: $\delta = 7.38$–7.28 (m, 5H), 5.11 (s, 1H), 4.54 (AB, $J = 16.0$ Hz, 1H), 4.49 (AB, $J = 16.0$ Hz, 1H), 4.53 (q, $J = 6.5$ Hz, 1H), 3.70 (t, j = 6.5 Hz, 2H), 3.05 (q, $J = 6.5$ Hz, 3H), 2.80 (AB, $J = 16.9$ Hz, 1H), 2.77 (AB, $J = 16.9$ Hz, 1H), 1.42 (d, $J = 6.5$ Hz, 3H). ^{13}C NMR: $\delta = 202.5$ (C=O, ketone), 167.2 (C=O, ester), 158.0 (C=O, carbamate), 137.8 (C), 129.3 (CH), 129.2 (CH), 128.2 (CH), 88 (CH), 79.7 (C), 52.9 (CH_2), 49.8 (CH_2), 49.3 (CH_2), 44.2 (CH_2), 14.3 (2 CH_3). Anal. calcd. for $C_{17}H_{21}NO_6$: C, 60.88%; H, 6.32%; N, 4.18%. Found: C, 60.78%; H, 6.39%; N, 4.31%.

Compound 9g. Oil. IR (KBr): 3280, 1712, 1688, 1640 cm^{-1}. MS: 326 ($M^+ + 1$).^{1}H NMR: $\delta = 7.46$ (d, $J = 7.3$ Hz, 2H), 7.33 (dd, $J = 7.1$, 7.7 Hz, 2H), 7.28(d, $J = 7.3$ Hz, 1H), 4.93 (AB, $J = 15.7$, 1H), 4.91 (AB, $J = 15.7$,1H), 4.83 (q, $J = 6.4$ Hz, 1H), 3.77 (s, 1H), 3.42 (ddd, $J = 7.4$, 10.4, 13.6 Hz, 1H), 3.18 (ddd, $J = 7.6$, 10.8, 13.8 Hz, 1H), 2.71 (ddd, $J = 3.4$, 6.7, 8.3 Hz, 1H), 2.63 (ddd, $J = 3.2$, 5.3, 8.9 Hz, 1H), 1.47 (d, $J = 6.4$ Hz, 3H), 1.42 (s, 3H);^{13}C NMR: $\delta = 158.5$ (<u>C</u>=O), 138.9 (C), 128.8 (CH), 128.2 (CH), 97.5 (C), 78.2 (CH), 46.1 (C), 29.3 (CH_2), 28.9 (CH_2), 25.6(CH_3), 24.8 (CH_2), 16.7(CH_3). Anal. calcd. for $C_{15}H_{19}NO_3S_2$: C, 55.35%; H, 5.90%; N, 4.30%; S, 19.71%. Found: C, 55.19%; H, 5.73%; N, 4.21%; S, 19.56%.

Compound 9h. Mp: 47 °C IR (KBr): 3264, 1720, 1695. MS: 264 ($M^+ + 1$).^{1}H NMR: $\delta = 7.35$ (d, $J = 4.0$ Hz, 2H), 7.32–7.27 (m, 3H), 4.52 (AB, $J = 16.0$, 1H), 4.48 (AB, $J = 16.0$, 1H), 4.19 (q, $J = 4.0$ Hz, 1H), 4.03 (s, 1H), 1.87–1.83 (m, 1H), 1.73–1.70 (m, 1H), 1.47–1.44 (m, 1H), 1.42–1.38 (overlapping, 3H), 1.32 (s, 3H), 0.93 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR: $\delta = 158.9$ (C=O), 138.5 (C), 129.0 (CH), 128.0 (CH), 127.8 (CH), 88.6 (CH), 84.7 (C), 43.9 (CH_2), 28.4 (CH_2), 28.1 (CH_2), 24.8

(CH_3), 22.9 (CH_2), 14.3 (CH_3). Anal. calcd. for $C_{15}H_{21}NO_3$: C, 68.40%; H, 8.05%; N, 5.32%. Found: C, 68.54%; H, 7.84%; N, 5.42%.

Compound 9i. Oil. IR (KBr): 3260, 1732, 1710, 1650 cm^{-1}. MS: 216 ($M^+ + 1$).^{1}H NMR: $\delta = 4.61$ (s, 1H), 4.60 (q, $J = 6.8$ Hz, 1H), 3.34 (t, $J = 7.6$ Hz, 2H), 1.75–1.69 (m, 2H), 1.58 (5, $J = 6.8$ Hz, 3H), 1.48–0.91 (overlapping, 6H), 0.89–0.87 (overlapping, 6H); ^{13}C NMR: $\delta = 157.5$ (C=O), 83.7 (CH), 80.9 (C), 42.1 (CH_2), 31.8 (CH_2), 29.0 (CH_2), 27.0 (CH_2), 18.2 (CH_2), 14.4 (CH_3), 13.0 (CH_3), 13.0 (CH_3). Anal. calcd. for $C_{11}H_{21}NO_3$: C, 61.35%; H, 9.85%; N, 6.51%. Found: C, 61.50%; H, 10.01%; N, 6.65%.

Compound 9j. Oil. IR (KBr): 3306, 1727, 1705, 1642 cm^{-1}. MS: 242 ($M^+ + 1$).^{1}H NMR: $\delta = 5.76$ (ddt, $J = 7.2$, 9.6, 16.1 Hz, 1H), 5.20–5.16 (overlapping, 2H), 4.39 (s, 1H), 4.39 (q, $J = 6.5$ Hz, 1H), 3.20 (t, $J = 7.5$ Hz, 2H), 2.63–2.57 (ABX, $j_{AB} = 14.3$ Hz, 1H), 2.46–2.40 (ABX, $j_{AB} = 14.3$ Hz, 1H), 2.01–1.98 (m, 1H), 1.68–1.58 (m, 1H), 1.38–1.30 (overlapping, 9H), 0.91 (t, $J = 6.7$ Hz, 3H);^{13}C NMR: $\delta = 158.5$ (C=O), 131.9 (CH), 120.1 (CH_2), 89.6 (CH), 78.5 (C), 42.3 (CH_2), 40.9 (CH_2), 29.7 (CH_2), 29.5 (CH_2), 22.7 (CH_2), 14.4 (CH_3), 14.2 (CH_3). Anal. calcd. for $C_{13}H_{23}NO_3$: C, 64.68%; H, 9.62%; N, 5.80%. Found: C, 64.61%; H, 9.45%; N, 5.91%.

Typical Example of Reaction at Reflux

3-Benzyl-5-methyl-1,3-oxazolidine-2,4-dione (2.0 g, 9.75 mmol) were dissolved in 40 mL of anhydrous THF, and 3.25 mL of methyl magnesium chloride 3 M in THF (9.75 mmol) were dropped into the solution blanketed with nitrogen, keeping temperature below 10 °C. Temperature was then raised to reflux and maintained at such temperature for 3 h. After quenching with 200 mL of a saturated aqueous solution of ammonium chloride, the mixture was extracted with methylene chloride (2×200 mL). The combined organic phases were washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The residue was purified by flash chromatography, eluting with n-hexane / ethyl acetate 4:1. In addition to 0.9 g of the product obtained at −30 °C, 1.1 g of its isomer were recovered, showing the following spectroscopic data: mp: 59 °C, IR: 3380 (broad), 1723, 1655, 1620 cm^{-1}; MS: 222 ($M^+ + 1$); ^{1}H NMR: $\delta = 7.36$–7.25 (m, 5H), 4.56 (AB, $J = 15.6$ Hz, 1H), 4.40 (AB, $J = 15.6$ Hz, 1H), 4.49 (q, $J = 6.6$ Hz, 1H), 3.71 (broad, 1H), 1.31 (d, $J = 6.6$ Hz, 2H), 1.27 (s, 3H); ^{13}C NMR: d = 166.5 (C=O), 138.0 (C=O), 128.7 (CH), 127.5 (CH), 89.4 (C), 82.2 (CH), 43.4 (CH_2), 20.9 (CH_3), 16.8 (CH_3). Anal. calcd. for $C_{12}H_{15}NO_3$: C, 65.13%; H, 6.85%; N, 6.33%. Found: C, 65.03%; H, 6.69% N, 6.42%.

Typical Dehydration Procedure

The crude mixture obtained from 3-benzyl-5-methyl-1,3-oxazolidine-2,4-dione and methyl magnesium chloride in refluxing THF was heated in dimethylsulfoxide at 80 °C for 12 h to give a single product, corresponding to the dehydrated product, namely 3-benzyl-4,5-dimethyl-4-oxazolin-2-one. Yield (after workup): 77%. Oil, MS: 203 (M^+); ^{1}H NMR: 1.82 (s, 3H), 2.02 (s, 3H), 4.72 (s, 2H), 7.36–7.24 (m,

5H). Anal. calcd. for $C_{12}H_{13}NO_2$: C, 70.90%; H, 6.46%; N, 6.89%. Found: C, 70.77%; H, 6.52% N, 7.02%.

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