Reaction of *o*-Oxazolinylphenyllithium with Carbon Monoxide. Carbonylative Cyclization via an Aroyllithium Intermediate

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The carbonylation of a phenyllithium containing an oxazoline group at the ortho position, followed by quenching with water, afforded a tricyclic compound, 3,3-dimethyl-2,3-dihydrooxazolo[2,3-*a*]-isoindol-5(9b*H*)-one, in 91% yield. This reaction proceeded via an intramolecular cyclization of the aroyllithium species, to give the tricyclic dienolate. Treatment of the tricyclic dienolate with electrophiles, such as alkyl halides, aldehydes, ketones, and epoxides gave the substituted oxazolo-[2,3-*a*]isoindolinones in good yield.

Introduction

It is well-known that carbonyllithium species (aroyllithium **1**, acyllithium **2**, and carbamoyllithium **3**, Figure 1) are easily generated via the reaction of organolithium compounds with carbon monoxide as the intermediate.[1] These species are not only strong nucleophiles but are also electrophiles, since they contain a carbonyl function that is susceptible to nucleophilic attack. Because of this, the carbonylation of organolithium compounds generally results in a complex mixture of products.

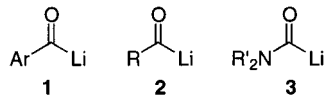

Figure 1. Carbonyllithium species: aroyllithium **1**, acyllithium **2**, carbamoyllithium **3** (R = alkyl; R′ = alkyl or Ar).

Reactions of aryllithium derivatives with carbon monoxide generally tends to give products which arise from two (or more) molecules of the aryllithium. To our knowledge, the first report on carbonyllithium appeared in 1940, when Wittig described, in a footnote in a paper on reactions of phenyllithium, that the reaction of phenyllithium with carbon monoxide at a low temperature gave α,α-diphenylacetophenone.[2] This reaction was later examined in detail by Ryang and Tsutsumi,[3] Jutzi,[4] Whitesides,[5] and Nudelman,[6,7] who independently showed that aroyllithium **1** was the initial intermediate. Ryang and Tsutsumi reported that aryllithiums reacted with carbon monoxide to afford symmetrical diaryl ketones, after treatment with water.[8] The highly selective formation of α,α-diphenylacetophenone was reported by Nudelman as the result of a reaction of phenyllithium with carbon monoxide in the absence of solvent.[9] α-Hydroxy ketones and symmetrical α-diketones were obtained in good yields, in the case of a bulky aryllithium.[10]

Although most of these reactions proceeded with low selectivity, there are a few examples in which aryllithium compounds were efficiently carbonylated with carbon monoxide. Seyferth has shown that the in situ reaction of aroyllithiums with electrophiles such as aldehydes, ketones, and esters to produce α-hydroxy ketones and α-diketones proceeds in a highly selective manner under specifically defined reaction conditions.[11] Kambe showed that benzoyllithiums were efficiently generated from the reaction of telluroesters with BuLi by means of tellurium−lithium exchange[12] and reacted with electrophiles in situ to afford α-hydroxy ketones in good yields.[13] Intramolecular reactions were reported by Smith, who found that aroyllithium derivatives could be trapped intramolecularly with an amide carbonyl group.[14]

In this laboratory, we previously reported on the intramolecular conversion of acyllithium **2** and carbamoyllithium **3** into more stable species, such as enolates and an ynolate.[15] Our goal is to realize a clean reaction via aroyllithium species **1** by means of an intramolecular conversion reaction. We now report that the reaction of phenyllithium having an oxazoline group at the ortho

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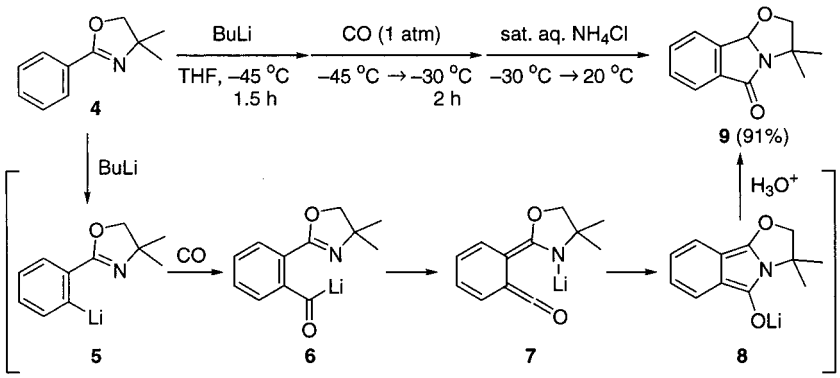
Scheme 1



position with carbon monoxide proceeds in a highly selective manner via an intramolecular conversion to give oxazolo[2,3-*a*]isoindolinone derivatives in good yields.

Results and Discussion

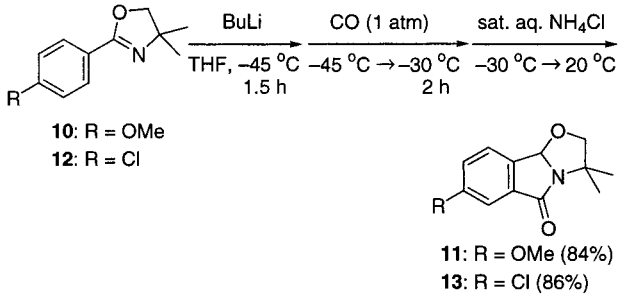
In our previous papers,[15b,c,f] we reported that the reaction of vinyllithium and azadienyllithium with carbon monoxide involved a selective intramolecular cyclization with the participation of the π-electron systems and led to more stable enolates. A similar intramolecular cyclization would be expected in the case of an aroyllithium derivative which contained a C = X (X = heteroatom) substituent on the aryl ring. For this purpose, we chose an oxazoline group, which contains an unsaturated C=N linkage as the substituent. In addition, the oxazoline group is relatively stable toward anionic systems.[16] The generation of a phenyllithium, containing an oxazoline group is readily achieved, since the ortho lithiation of phenyloxazoline **4** with BuLi, as independently reported by Geswend[17] and Meyers,[18] has been extensively studied.

The reaction was carried out as follows. To a THF solution of phenyloxazoline **4** was added a hexane solution of BuLi at −45 °C, and the reaction mixture was stirred for 1.5 h. The mixture was then exposed to carbon monoxide at atmospheric pressure and gradually warmed to −30 °C over a 2 h period. On treatment with saturated aqueous NH_4Cl, a tricyclic compound, 3,3-dimethyl-2,3-dihydrooxazolo[2,3-*a*]isoindol-5(9b*H*)-one (**9**), was isolated as the sole product in 91% yield after column chromatography on silica gel.

The reaction sequence envisaged is shown in Scheme 1. An aroyllithium derivative **6** is generated from the reaction of lithium phenyloxazoline **5** with carbon monoxide, and the intramolecular reaction of aroyllithium **6** then gives the cyclic dienolate **8**, via the ketene intermediate **7**. The C=N linkage of the oxazoline moiety, which is conjugated with the benzene ring, would facilitate generation of ketene intermediate **7**, which, after the subsequent intramolecular addition of lithium amide to the ketene, gives the cyclic dienolate **8**. It was found that the presence of two methyl groups on an oxazoline is not essential for the reaction to proceed, but is required for efficient ortho lithiation. In fact, lithium phenyloxazoline, which contains no methyl groups on the oxazoline group and which was prepared from the reaction of 2-(2-bromophenyl)-2-oxazoline with 2 equiv of *t*-BuLi by means of halogen−lithium exchange, was smoothly carbonylated to give the corresponding oxazolo[2,3-*a*]isoindolinone derivative in 83% yield. However, the corresponding aryllithium could not be generated by ortho lithiation.

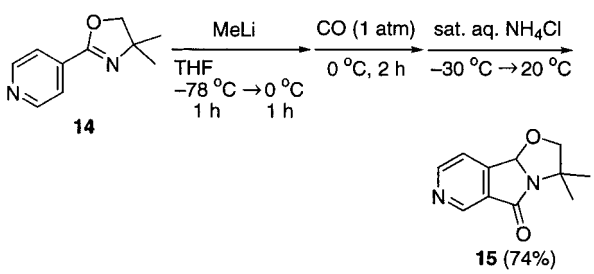
The carbonylation of phenyllithium derivatives with either a methoxy and a chloro substituent on the aromatic ring also led to a clean cyclization reaction to afford the corresponding products **11** and **13**, respectively (Scheme 2).

Scheme 2



The present method provides a new route to a new and novel ring-system. The reaction of pyridinyloxazoline **14** gaves the heterocyclic compound **15** in 74% yield (Scheme 3).

Scheme 3



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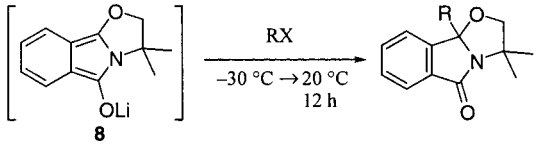
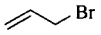
In these cases, formal [4 + 1] cyclocoupling reactions of π-conjugation systems with carbon monoxide appear to have occurred.[15b,c] That highly selective reactions can be attained via aroyllithium is rather exceptional. The key to the present success is the utilization of the intramolecular reaction.

As shown in Scheme 1, the intramolecular conversion of aroyllithium derivative **6** gave the cyclic dienolate **8**, which should be still reactive and useful as the synthetic intermediate. The cyclic dienolate **8** was subsequently reacted with various electrophiles. The reaction of **8** with methyl iodide resulted in *C*-alkylation to give the methylated tricyclic γ-lactam **16** (entry 1 in Table 1). No *O*-alkylation product was formed. The alkylation with benzyl-, allyl-, and butyl bromide also afforded the corresponding products (entry 2−4). In all cases, the alkylation of the cyclic dienolate **8** occurred at the γ-carbon, accompanied by aromatization to a ring in **8**.

Table 1. Reactions of the Cyclic Dienolate 8 with Alkyl Halides

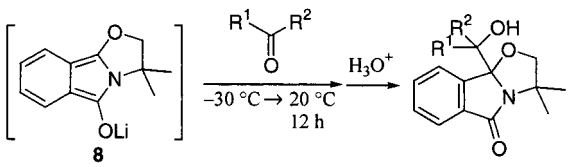


entry	RX	product	yield (%)[a]
1	MeI	**16**	84
2	BnBr	**17**	90
3		**18**	86
4	BuBr	**19**	82

[a] Isolated yields (based on phenyloxazoline **4** used as the starting material).

The use of carbonyl compounds, such as aldehyde and ketone as electrophiles, also led to similar types of transformations (Table 2). In the reaction with benzaldehyde, the adduct **20** was obtained as a mixture of diastereomers in a total yield of 81% (entry 1). Trapping with pivalaldehyde was successful and gave the isoindolinone **21** as the single diastereomer[19] in 83% yield (entry 2). In the reaction with an enolizable carbonyl compound, such as cyclohexanone (entry 3), the expected product **22** was isolated in 70% yield, along with 12% of **9**. The formation of **9** would be caused by the abstraction of an α-hydrogen from cyclohexanone by **8**.

Table 2. Trapping of the Cyclic Dienolate 8 with Aldehydes and a Ketone

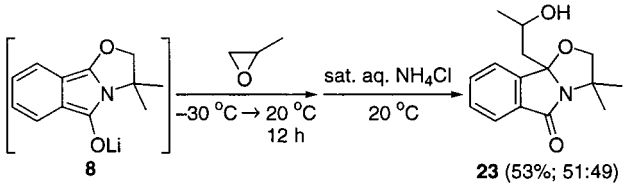


entry	R^1	R^2	product	yield (%)[a]
1	Ph	H	**20**	81 (74:26)[b]
2	*t*-Bu	H	**21**	83 (100)[b]
3	$-(CH_2)_5-$		**22**	70[c]

[a] Isolated yields (based on phenyloxazoline **4**). The ratios in parentheses are diastereomeric ratios. [b] The stereochemistry of the diastereomer was not established yet. [c] The protonated product **9** was obtained in 12% yield.

Propylene oxide could also be used as the electrophile. The reaction of **8** with propylene oxide resulted in regioselective ring opening to afford the secondary alcohol **23** in 53% yield as a 1:1 mixture of diastereomers after treatment with saturated aqueous NH_4Cl (Scheme 4).

Scheme 4



In all cases described above, carbon electrophiles were introduced into the γ-carbon, but not the dienolate oxygen atom. All efforts to trap electrophiles at the oxygen site in **8** were in vain. With silylating reagents such as TMSCl, TESOTf, and TBDMSOTf, the reaction gave only a complicated mixture. The use of pivaloyl chloride did not lead to *O*-acylation, but, rather, the introduction of the pivaloyl group into the γ-carbon (Figure 2). This unusually high *C*-selectivity (γ-selectivity) suggests that the driving force for the alkylation arises from the energetically favorable aromatization.

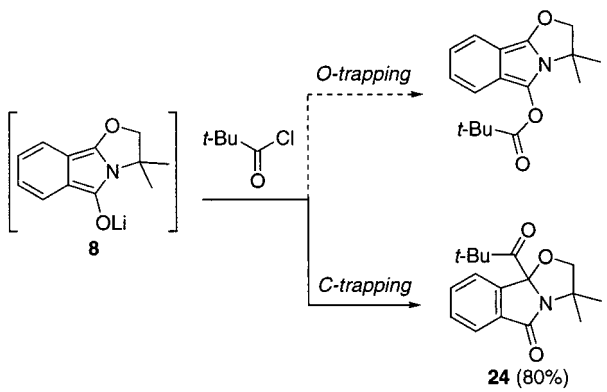


Figure 2. The reaction with pivaloyl chloride proceeded via *C*-trapping.

Conclusion

In summary, we demonstrate here that the reaction of a phenyllithium derivative, which contains an oxazoline group at the ortho position, with carbon monoxide proceeds selectively via the cyclization of the generated aryllithium derivative **6**. The presence of a C=N linkage conjugated with the benzene ring is critical for a selective reaction. The cyclic dienolate **8** was trapped with various

(19) Although the formation of a single diastereomer was confirmed by ^{1}H NMR analysis of the crude mixture, the stereochemistry of **21** could not be confirmed.

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carbon electrophiles to provide substituted oxazolo[2,3-*a*]isoindolinones in high yields. Oxazolo[2,3-*a*]isoindolinones have been prepared by several methods.[20−26] However, there are only two methods for the preparation of oxazolo[2,3-*a*]isoindolinones, which contain a carbon-substituent at the N,O-acetal position. One involves the condensation of 2-aroyl- or 2-acylbenzoic acids with a *β*-amino alcohol,[20] while the other involves the nucleophilic addition of oraganolithium and magnesium compounds, to *N*-(2-haloethyl)phthalimide, followed by intramolecular cyclization.[21] The preparation of substituted oxazolo[2,3-*a*]isoindolinones **20**−**24** by known methods appears to be difficult. This carbonylation of lithium phenyloxazolines represents a possible alternative for the preparation of this type of heterocycles. We are examining further applications of intramolecular reactions of carbonyllithium species at present.

Experimental Section

Materials. THF was distilled from sodium benzophenone ketyl immediately prior to use. A hexane solution of BuLi and an ether solution of MeLi were purchased from Nakalai Tesque, Inc. and Kanto Chemical Co., Inc., respectively. 4,4-Dimethyl-2-phenyl-2-oxazoline (**4**) was purchased from Aldrich Chemical Co. and substituted phenyloxazoline **10**,[16,27] **12**,[16,27] and pyridinyloxazoline **14**[28] were prepared according to literature procedure. All reagents were used after distillation or recrystallization.

General Procedure for the Preparation of Oxazolo-[2,3-*a*]isoindolinones 9, 11 and 13. A 30 mL round-bottomed flask equipped with a magnetic stirring bar, a three-way stopcock, and a nitrogen line was flame-dried under a stream of nitrogen. In the reaction flask were placed 10 mL of dry THF and 2.0 mmol of phenyloxazoline, and the solution was then cooled to −45 °C. To the stirred solution was added 1.6 mL of a hexane solution of BuLi (1.5 M, 2.4 mmol) via a syringe. After stirring for 1.5 h, the reaction mixture was stirred under an atmospheric pressure of carbon monoxide for 2 h. To the mixture was added 2 mL of saturated aqueous NH_4-Cl, and the resulting mixture was allowed to cool to room temperature. After aqueous workup, the solvents were removed under reduced pressure to give a green oil, which was subjected to column chromatography on silica gel to give an analytically pure sample of the oxazolo[2,3-*a*]isoindolinone derivative.

3,3-Dimethyl-2,3-dihydrooxazolo[2,3-*a*]isoindol-5(9b*H*)-one (9). 91% yield, colorless oil, R_f = 0.14 (hexane/EtOAc = 5/1): ^{1}H NMR ($CDCl_3$) δ 1.53 (s, 3H), 1.64 (s, 3H), 4.06 (d, J = 8.4 Hz, 1H), 4.15 (d, J = 8.4 Hz, 1H), 5.92 (s, 1H), 7.53−7.59 (c, 3H), 7.77 (d, J = 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 23.0, 26.4, 58.9, 84.4, 91.7, 123.3, 123.6, 130.0, 132.0, 134.8, 141.0, 169.4; IR (neat) 1713 s; MS, *m*/*z* (relative intensity, %) 203 (M^+, 4.0), 173 (100). Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.65; H, 6.46; N, 6.90.

7-Methoxy-3,3-dimethyl-2,3-dihydrooxazolo[2,3-*a*]isoindol-5(9b*H*)-one (11). 84% yield, colorless solid, mp 98−99 °C, R_f = 0.17 (hexane/EtOAc = 3/1): ^{1}H NMR ($CDCl_3$) δ 1.52 (s, 3H), 1.63 (s, 3H), 3.86 (s, 3H), 4.03 (d, J = 8.4 Hz, 1H), 4.15 (d, J = 8.4 Hz, 1H), 5.86 (s, 1H), 7.10 (dd, J = 8.3 Hz, J = 2.3 Hz, 1H), 7.23 (d, J = 2.3 Hz, 1H) 7.46 (d, J = 8.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 23.1, 26.4, 55.4, 58.9, 84.5, 91.5, 106.7, 119.8, 124.2, 133.3, 136.6, 161.4, 169.4; IR (KBr) 1690 s; MS, *m*/*z* (relative intensity, %) 233 (M^+, 25), 203 (100). Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.01. Found: C, 66.76; H, 6.55; N, 6.04.

7-Chloro-3,3-dimethyl-2,3-dihydrooxazolo[2,3-*a*]isoindol-5(9b*H*)-one (13). 86% yield, colorless solid, mp 84−85 °C, R_f = 0.20 (hexane/EtOAc = 4/1): ^{1}H NMR ($CDCl_3$) δ 1.51 (s, 3H), 1.63 (s, 3H), 4.03 (d, J = 8.6 Hz, 1H), 4.14 (d, J = 8.6 Hz, 1H), 5.88 (s, 1H), 7.48−7.55 (c, 2H), 7.70−7.75 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 23.2, 26.4, 59.3, 84.6, 91.3, 123.9, 124.7, 132.2, 136.5, 136.8, 139.3, 167.9; IR (KBr) 1696 s; MS, *m*/*z* (relative intensity, %) 237 (M^+, 6), 207 (100). Anal. Calcd for $C_{12}H_{12}NO_2Cl$: C, 60.64; H, 5.09; N, 5.89. Found: C, 60.35; H, 5.05; N, 5.86.

3,3-Dimethyl-2,3-dihydrooxazolo[3′,2′:1,5]pyrrolo[3,4-c]pyridin-5(9b*H*)-one (15). In a manner similar to that described for **9**, ortho lithiation was carried out under a following condition.:[28] To a THF solution of pyridinyloxazoline **14** was added at −78 °C 2.2 mL of a pentane solution of MeLi (1.1 M; 2.4 mmol), and the reaction mixture was stirred at the same temperature for 1 h and allowed to warm to 0 °C for 1 h. Under an atmospheric pressure of CO, the mixture was stirred at 0 °C for 2 h.; 74% yield, colorless solid, mp 102−103 °C, R_f = 0.26 (hexane/EtOAc = 1/3): ^{1}H NMR ($CDCl_3$) δ 1.52 (s, 3H), 1.63 (s, 3H), 4.03 (d, J = 8.6 Hz, 1H), 4.13 (d, J = 8.6 Hz, 1H), 5.91 (s, 1H), 7.52 (d, J = 5.0 Hz, 1H), 8.81 (d, J = 5.0 Hz, 1H), 9.01 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 22.9, 26.2, 59.3, 84.4, 91.0, 118.2, 130.2, 145.7, 148.9, 152.3, 167.3; IR (KBr) 1712 s; MS, *m*/*z* (relative intensity, %) 204 (M^+, 25), 57 (100). Anal. Calcd for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.66; H, 5.97; N, 13.66.

General Procedure for the Reaction of the Cyclic Dienolate 8 with Carbon Electrophiles. To a THF solution of the cyclic dienolate **8** was added 2.2 mmol of the carbon electrophile at −30 °C, and the reaction mixture was stirred at 20 °C for 12 h. After aqueous workup, the oxazolo[2,3-*a*]-isoindolinone was isolated by column chromatography on silica gel. Yields described below are based on phenyloxazoline **4**.

3,3,9b-Trimethyl-2,3-dihydrooxazolo[2,3-*a*]isoindol-5(9b*H*)-one (16). In this reaction, 20 mmol of methyl iodide was added. 84% yield, colorless solid, mp 102−103 °C, R_f = 0.20 (hexane/EtOAc = 5/1): ^{1}H NMR ($CDCl_3$) δ 1.57 (s, 3H), 1.59 (s, 3H), 1.74 (s, 3H), 4.12 (d, J = 8.9 Hz, 1H), 4.28 (d, J = 8.9 Hz, 1H), 7.49−7.57 (c, 3H), 7.73 (d, J = 6.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 23.5, 24.2, 27.8, 59.3, 83.2, 99.9, 121.5, 123.8, 129.7, 132.5, 133.2, 147.0, 170.3; IR (KBr) 1701 s; MS, *m*/*z* (relative intensity, %) 217 (M^+, 2), 61 (100). Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45. Found: C, 71.65; H, 7.00; N, 6.44.

9b-Benzyl-3,3-dimethyl-2,3-dihydrooxazolo[2,3-*a*]isoindol-5(9b*H*)-one (17). 90% yield, colorless oil, R_f = 0.20 (hexane/EtOAc = 4/1): ^{1}H NMR ($CDCl_3$) δ 1.60 (s, 3H), 1.69 (s, 3H), 3.19 (d, J = 13.5 Hz, 1H), 3.49 (d, J = 13.5 Hz, 1H), 4.21 (d, J = 8.6 Hz, 1H), 4.44 (d, J = 8.6 Hz, 1H), 6.95−7.05 (c, 2H), 7.05−7.20 (c, 4H), 7.33−7.47 (c, 2H), 7.53−7.58 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 24.2, 27.4, 42.1, 59.6, 83.0, 102.1, 122.4, 123.3, 126.5, 127.6, 130.2, 131.7, 133.9, 134.5, 145.3, 170.4; IR (neat) 1709 s; MS, *m*/*z* (relative intensity, %) 293 (M^+, 0.06), 202 (100). Anal. Calcd for $C_{19}H_{18}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 77.50; H, 6.57; N, 4.71.

9b-Allyl-3,3-dimethyl-2,3-dihydrooxazolo[2,3-*a*]isoindol-5(9b*H*)-one (18). 86% yield, colorless oil, R_f = 0.20 (hexane/EtOAc = 5/1): ^{1}H NMR ($CDCl_3$) δ 1.58 (s, 3H), 1.60 (s, 3H), 2.80 (dd, J = 13.5 Hz, J = 7.4 Hz, 1H), 2.91 (dd, J = 13.5 Hz, J = 7.4 Hz, 1H), 4.15 (d, J = 8.6 Hz, 1H), 4.31 (d, J = 8.6 Hz, 1H), 4.91−5.00 (c, 2H), 5.36−5.54 (m, 1H), 7.44−7.59 (c, 3H), 7.69−7.74 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 24.3, 27.5, 40.2, 59.2, 83.3, 101.4, 119.4, 122.0, 123.5, 129.6, 130.8, 132.2, 134.0, 145.3, 170.3; IR (neat) 1714 s; MS, *m*/*z* (relative intensity, %) 229 (M^+, 0.2), 202 (100). Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.65; H, 7.15; N, 5.94.

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9b-Butyl-3,3-dimethyl-2,3-dihydrooxazolo[2,3-*a*]isoindol-5(9b*H*)-one (19). 82% yield, colorless oil, R_f = 0.23 (hexane/EtOAc = 3/1): ^{1}H NMR ($CDCl_3$) δ 0.68−0.82 (m, 1H), 0.80 (t, J = 7.1 Hz, 3H), 1.10−1.35 (c, 3H), 1.55 (s, 3H), 1.60 (s, 3H), 2.05−2.20 (c, 2H), 4.12 (d, J = 8.6 Hz, 1H), 4.28 (d, J = 8.6 Hz, 1H), 7.45−7.60 (c, 3H), 7.73 (d, J = 7.59 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.7, 22.5, 24.4, 25.7, 27.5, 35.2, 59.3, 83.4, 102.6, 121.6, 123.7, 129.7, 132.4, 134.2, 145.7, 170.6; IR (neat) 1714 s; MS, *m*/*z* (relative intensity, %) 259 (M^+, 1.1), 202 (100). Anal. Calcd for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 73.83; H, 8.14; N, 5.54.

9b-(Hydroxyphenylmethyl)-3,3-dimethyl-2,3-dihydrooxazolo[2,3-*a*]isoindol-5(9b*H*)-one (20). 81% yield (74:26), each diastereomer was separated by column chromatography on silica gel. A major isomer, colorless solid, mp 158−159 °C, R_f = 0.26 (CH_2Cl_2/EtOAc = 10/1): ^{1}H NMR ($CDCl_3$) δ 1.59 (s, 3H), 1.74 (s, 3H), 3.01 (d, J = 1.7 Hz, 1H), 4.23 (d, J = 8.6 Hz, 1H), 4.46 (d, J = 8.6 Hz, 1H), 5.39 (d, J = 1.7 Hz, 1H), 6.95−7.10 (c, 5H), 7.30−7.43 (c, 2H), 7.46−7.52 (m, 1H), 7.80 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 24.2, 27.4, 60.0, 74.1, 83.0, 103.2, 123.1, 124.0, 126.8, 127.1, 127.3, 129.6, 131.7, 134.4, 136.5, 143.0, 171.1; IR (KBr) 1681 s; MS, *m*/*z* (relative intensity, %) 309 (M^+, 0.07), 199 (100). Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.16; N, 4.53. Found: C, 73.79; H, 6.31; N, 4.53. A minor isomer, colorless solid, mp 212−213 °C, R_f = 0.14 (CH_2Cl_2/EtOAc = 10/1): ^{1}H NMR ($CDCl_3$) δ 1.59 (s, 3H, CH_3), 1.70 (s, 3H, CH_3), 2.66 (d, J = 2.6 Hz, 1H, OH), 4.21 (d, J = 8.6 Hz, 1H), 4.56 (d, J = 8.6 Hz, 1H), 5.31 (d, J = 2.6 Hz, 1H), 6.47 (d, J = 7.3 Hz, 1H), 7.25−7.44 (c, 7H), 7.64 (d, J = 7.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 24.5, 27.8, 60.6, 73.7, 84.4, 104.2, 123.5, 123.8, 127.4, 127.7, 127.9, 129.9, 131.7, 135.0, 137.8, 143.5, 172.1; IR (KBr) 1687 s; MS, *m*/*z* (relative intensity, %) 309 (M^+, 0.08), 199 (100). Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.16; N, 4.53. Found: C, 73.63; H, 6.24; N, 4.57.

9b-(1-Hydroxy-2,2-Dimethylpropyl)-3,3-dimethyl-2,3-dihydrooxazolo[2,3-*a*]isoindol-5(9b*H*)-one (21). This product was purified by recrystallization from hexane/EtOAc; 83% yield, colorless solid, mp 169−171 °C: ^{1}H NMR ($CDCl_3$) δ 0.64 (s, 9H), 1.59 (s, 6H), 2.83 (d, J = 1.8 Hz, 1H), 4.05 (d, J = 1.8 Hz, 1H), 4.13 (d, J = 8.9 Hz, 1H), 4.32 (d, J = 8.9 Hz, 1H), 7.45−7.55 (c, 2H), 7.70−7.80 (c, 2H); ^{13}C NMR ($CDCl_3$) δ 24.8, 27.7, 27.8, 34.1, 60.2, 77.8, 82.4, 103.0, 123.6, 125.5, 130.1, 131.9, 133.9, 144.8, 171.4; IR (KBr) 1686 s; MS, *m*/*z* (relative intensity, %) 289 (M^+, 0.04), 202 (100). Anal. Calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01; N, 4.84. Found: C, 70.34; H, 8.09; N, 4.80.

9b-(1-Hydroxycyclohexyl)-3,3-dimethyl-2,3-dihydrooxazolo[2,3-*a*]isoindol-5(9b*H*)-one (22). 70% yield, colorless solid, mp 180−182 °C, R_f = 013 (hexane/EtOAc = 4/1): ^{1}H NMR ($CDCl_3$) δ 0.69−0.79 (m, 1H), 0.80−1.05 (m, 1H), 1.30−1.80 (c, 9H), 1.45 (s, 3H), 1.60 (s, 3H), 4.05 (d, J = 7.9 Hz, 1H), 4.55 (d, J = 7.9 Hz, 1H), 7.44−7.70 (c, 3H), 7.73 (d, J = 6.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.9, 21.2, 24.7, 25.3, 26.4, 30.3, 33.6, 61.4, 77.6, 85.0, 107.0, 123.0, 123.8, 129.5, 132.3, 134.5, 147.8, 174.4; IR (KBr) 1699 s; MS, *m*/*z* (relative intensity, %) 301 (M^+, 0.16), 148 (100). Anal. Calcd for $C_{18}H_{23}NO_3$: C, 71.73; H, 7.69; N, 4.65. Found: C, 71.67; H, 7.71; N, 4.58.

9b-(2-Hydroxypropyl)-3,3-dimethyl-2,3-dihydrooxazolo[2,3-*a*]isoindol-5(9b*H*)-one (23). 53% yield (51:49), colorless solid, mp 126−129 °C, R_f = 0.10 (hexane/EtOAc = 1/1); The spectra data was obtained as a 51:49 mixture of diastereomers.: ^{1}H NMR ($CDCl_3$) δ 1.05 (d, J = 6.3 Hz, 3H), 1.18 (d, J = 6.3 Hz, 3H), 1.59 (s, 6H), 1.62 (s, 6H), 1.87 (dd, J = 2.3 Hz, J = 14.5 Hz, 1H), 2.22 (dd, J = 2.0 Hz, J = 14.5 Hz, 1H), 2.42 (dd, J = 8.9 Hz, J = 12.2 Hz, 1H), 2.47 (dd, J = 9.6 Hz, J = 12.2 Hz, 1H), 2.52 (s, 1H), 2.79 (s, 1H), 3.20−3.35 (m, 1H), 4.05−4.20 (c, 3H), 4.27 (d, J = 8.6 Hz, 1H), 4.35 (d, J = 8.6 Hz, 1H), 7.47−7.66 (c, 6H), 7.77 (d, J = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 23.5, 23.8, 24.2, 24.2, 27.3, 27.5, 43.8, 44.1, 59.3, 60.2, 63.7, 64.0, 82.8, 82.9, 101.4, 101.4, 122.1, 122.4, 123.8, 129.8, 130.0, 132.3, 132.9, 133.2, 133.4, 145.5, 145.6, 170.2, 171.5; IR (KBr) 1706 s; MS, *m*/*z* (relative intensity, %) 261 (M^+, 0.42), 202 (100). Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.98; H, 7.23; N, 5.37.

9b-(2,2-Dimethylpropionyl)-3,3-dimethyl-2,3-dihydrooxazolo[2,3-*a*]isoindol-5(9b*H*)-one (24). 80% yield, colorless oil, R_f = 0.24 (hexane/EtOAc = 4/1): ^{1}H NMR ($CDCl_3$) δ 1.00 (s, 9H), 1.47 (s, 3H), 1.60 (s, 3H), 3.99 (d, J = 8.6 Hz, 1H), 4.11 (d, J = 8.6 Hz, 1H), 7.40−7.42 (m, 1H), 7.56−7.62 (c, 2H), 7.77−7.85 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 23.9, 26.4, 28.1, 44.3, 60.6, 83.7, 102.6, 123.0, 124.1, 130.9, 132.6, 134.6, 141.9, 171.9, 209.3; IR (neat) 1723 s, 1707 s; MS, *m*/*z* (relative intensity, %) 287 (M^+, 0.04), 202 (100). Anal. Calcd for $C_{17}H_{21}NO_3$: C, 71.06; H, 7.37; N, 4.87. Found: C, 70.89; H, 7.47; N, 4.99.

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Supporting Information Available: Characterization data for the compounds **9**, **11**, **13**, **15**−**24**. This material is available free of charge via the Internet at http://pubs.acs.org.

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