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Short Report

An Easy and Efficient Method to Produce γ-Amino Alcohols by Reduction of β-Enamino Ketones

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A redução de β-enamino cetonas **2** com $NaBH_4$ em ácido acético glacial produziu γ-amino álcoois **1** em 70% a 98% de rendimento, com excessos diastereoméricos, preferencialmente o produto *syn*, de 44% a 90%. A estereoquímica desses compostos foi confirmada pela análise de seus derivados tetraidro-1,3-oxazinas **3**.

Reduction of β-enamino ketones **2** with $NaBH_4$ in glacial acetic acid gave γ-amino alcohols **1** in 70% to 98% yield with diastereomeric excesses, preferentially the *syn* product, from 44% to 90%. The stereochemistry of these compounds was confirmed by analysis of their tetrahydro-1,3-oxazine derivatives **3**.

Keywords: amino alcohols, enamino ketones, oxazines, stereoselective reduction

Introduction

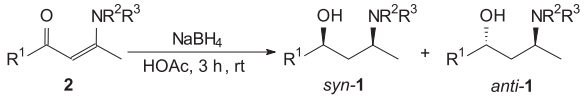
The synthesis of γ-amino alcohols **1** is of great interest due to the pharmacology of these compounds and their derivatives. This functionality is found in several antibiotics and other biologically active natural products.[1] Several synthetic methods have been described for the synthesis of γ-amino alcohols **1** from diols,[2] hydroxazols,[3] lactams[4] and lactones,[5] but the more important methods are those where one can obtain γ-amino alcohols **1** by reduction of 1,3-difunctionalized unsaturated compounds containing nitrogen and oxygen, such as β-hydroxy oximes,[6] β-enamino ketones **2**,[7-11] and, more frequently, by the reduction of β-amino ketones.[1,12-15]

γ-Amino alcohols **1**, mainly *syn*, can be synthesized by reduction of β-enamino ketones **2** with Na in Pr^iOH/tetrahydrofuran or with $CeCl_3$/ $LiBH_4$/tetrahydrofuran.[9] On the other hand, the combination of $NaBH_4$ in a carboxylic acid media has yielded an efficient reducing reagent.[16]

We wish to report herein a simple and efficient method to produce γ-amino alcohols **1** through the reduction of β-enamino ketones **2** with $NaBH_4$ in glacial acetic acid, which has been sucessfully used in our laboratory.[17]

Results and Discussion

Difficulties in reduction of β-enamino ketones **2** have been reported.[10] The use of $NaBH_4$ in a carboxylic acid medium is well known,[16] but its use in the reduction of β-enamino ketones **2** has not been explored. Our results show that the reaction of β-enamino ketones **2** with $NaBH_4$ in glacial acetic acid (3 hours at room temperature, Scheme 1), produces a mixture of *syn*/*anti* γ-amino alcohols **1**, the *syn* isomer being the major product (Table 1).[18]



Scheme 1.

Table 1. Diastereomeric ratios of γ-amino alcohols **1** in the reduction of β-enamino ketones **2**

2	R^1	R^3	R^2	% **1**[c]	*syn*/*anti*[a]
a	Me	H	Ph	98	87/13
b	Me	H	Bn	90	80/20
c	Me	H	^{i}Pr	98	72/28
d	Ph	H	^{i}Pr	85	90/10
f	^{t}Bu	H	Bn	70	> 95/5[b]
e	Me	- (CH_2)$_4$ -		93	75/25

[a] Diastereomeric ratio determined in the mixtures of the tetrahydro-1,3-oxazine derivatives **3** using ^{13}C NMR (75,1 MHz), and confirmed by CG/MS; [b] **1f** was not isolated; it was transformed immediately into **3f**; [c] isolated yield.

When the reaction is carried out without temperature control, the reaction produces the α,β-unsaturated ketone **6** while at 0 °C (hexane/HOAc, CH_2Cl_2/HOAc or HOAc as

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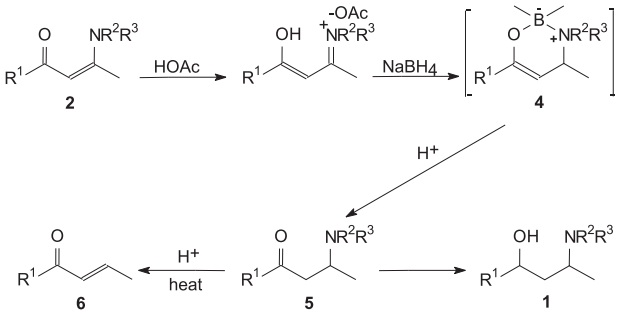
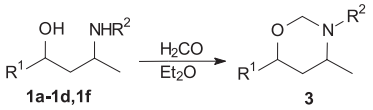
solvent) the product is a mixture of reactant **2**, γ-amino alcohol **1** and the corresponding Mannich base **5**. Another important observation is that, by this methodology, it is impossible to reduce 3-(N-benzylamino)-2-cyclohexen-1-one.

A mechanism is suggested where chelated intermediate **4** is reduced to produce β-amino ketone **5** and γ-amino alcohol **1** (Scheme 2).

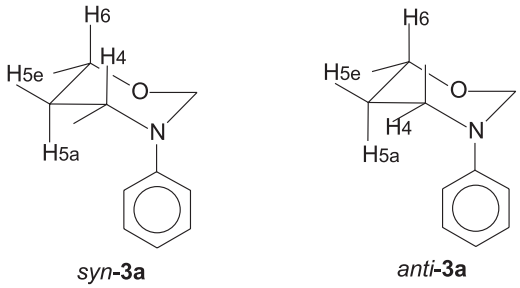


Scheme 2.

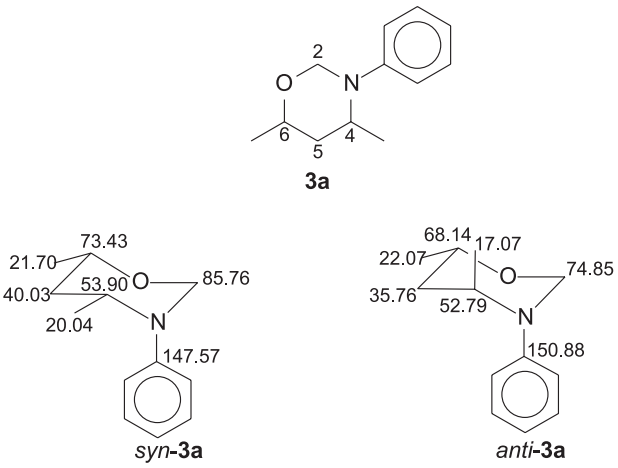
Quantitative conversion of γ-amino alcohols **1** to the corresponding tetrahydro-1,3-oxazine derivatives **3** (formol in diethyl ether, Scheme 3),[19] allow us to assign the *syn* stereochemistry to the major γ-amino alcohol **1** after inspection of their ^{1}H and ^{13}C NMR spectra. Using the *syn*-**3a** compound as an example (Scheme 4), we can see the hydrogen atoms H_4 and H_6 as a double quartet of doublets at 3.27 ppm (J 3.3, 6.3, 11.1 Hz) and 3.68 ppm (J 2.7, 6.3, 12.3 Hz) respectively. These hydrogen atoms and H_{5e} are in a axial-equatorial situation ($\theta \cong 60°$), with coupling constants 2.7 Hz ($J_{H4\text{-}H5e}$) and 3.3 Hz ($J_{H6\text{-}H5e}$). The ^{1}H NMR spectrum shows the axial-axial ($\theta \cong 180°$) relation between H_{5a} and hydrogen atoms H_6 and H_4 ($J_{H4\text{-}H5a}$ 11.1 Hz; $J_{H6\text{-}H5a}$ 12.5 Hz). Furthermore we can see H_{5e} and H_{5a} as a double triplet at 1.57 ppm (J 2.7, 13.5 Hz) and 1.42 ppm (J 11.1, 13.0 Hz), respectively. The analysis of the ^{13}C NMR spectrum (Scheme 5) allows the assignement of the secondary carbons at 40.03 ppm and 85.76 ppm (C_5 and C_2 respectively), and the tertiary carbons at 53.90 ppm and 73.43 ppm (C_4 and C_6 respectively). The chemical shifts of the methyl groups were assigned mainly based on the protective anisotropic effect of the phenyl group at C_4. The chemical shift of the carbon C_6 in the *syn*-**3a** isomer and in the *anti*-**3a** isomer are 73.43 and 68.14 ppm respectively. This upfield shift (*ca.* 5 ppm) is compatible with a γ-gauche exocyclic interaction, showing the axial methyl group at C_4.



Scheme 3.



Scheme 4.



Scheme 5.

In conclusion, the reduction of β-enamino ketones **2** with $NaBH_4$ in acetic acid is a very simple and fast method to obtain γ-amino alcohols **1** (with preferential *syn* configuration) in good chemical yields.

Experimental

General

^{1}H NMR and ^{13}C NMR spectra were recorded on a GEMINI-300 MHz instrument, using $CDCl_3$ as a solvent and TMS as internal reference. The IR spectra were recorded on a Perkin Elmer 1600-FTIR (film in NaCl cell) instrument. Elemental analyses were performed on a Perkin Elmer 2400 instrument. The mass spectra were recorded on a HP 5988^A instrument. The gas chromatographic analysis were performed on a Shimadzu GC/MS Class 5000 chromatograph equipped with a Simplicity-1 (SUPELCO) column. The products were purified by flash chromatography or PLC using SiO_2 as a stationary phase.

*General procedure to obtain γ-amino alcohol, (**1**).* To a solution of β-enamino ketone (**2**, 1 mmol) in glacial acetic acid (6 mL), was slowly added $NaBH_4$ (4 mmol). The reaction was kept at 18-20 °C. The reaction was stirred for 3 hours, and then neutralized with an aqueous solution of

30% NaOH (approximatelly 12 mL) in an ice bath. The reaction mixture was extracted with CH_2Cl_2, the organic phases were combined, dried over $MgSO_4$, and concentrated.

*4-(N-Phenylamino)-pentan-2-ol, (**1a**).* IR (neat) ν_{max}/cm^{-1}: 3350, 3050, 3025, 2970, 2925, 1600, 1500, 1320, 1250, 1130, 750, 690. MS *m/z* (%): 179(37), 164(15), 120(100), 104(7.6), 93(24), 77(22), 45(24). ^{1}H NMR *syn*-**1a** δ: 1.14(d, *J* 6.2 Hz, 3H), 1.18(d, *J* 6.2 Hz, 3H), 1.57(AA'XY, 2H), 3.41(s, large, 2H), 3.66(sext, *J* 6.5 Hz, 1H), 4.01(sext, *J* 6.0 Hz, 1H), 6.57-6.79(m, 3H), 7.12-7.24(m, 2H). ^{13}C NMR *syn*-**1a** δ: 147.13, 129.46, 118.98, 115.29, 67.97, 49.89, 45.76, 23.98, 21.46. ^{1}H NMR *anti*-**1a** δ: 1.17(2 d, 6H), 1.43-1.70(m, 2H), 3.20(s, large, 2H), 3.76(m, 1H), 3.91(m, 1H), 6.49-6.67(m, 3H), 7.00-7.10(m, 2H). ^{13}C NMR *anti*-**1a** δ: 147.73, 129.37, 117.61, 113.73, 67.25, 46.05, 45.70, 24.04, 21.32. Anal. Calc. for $C_{11}H_{17}NO$: C, 73.70; H, 9.56; N, 7.82%. Found: C, 73.91; H, 9.56; N, 7.62%.

*4-(N-Benzylamino)-pentan-2-ol, (**1b**).* IR (neat) ν_{max}/cm^{-1}: 3346, 3286, 3076, 2964, 2925, 1452, 1374, 1165, 1129, 1088, 742, 698. MS *m/z* (%): 193(5), 178(15), 134(83), 106(28), 91(100). ^{1}H NMR *syn*-**1b** δ: 1.12(d, *J* 6.3 Hz, 3H), 1.17(d, *J* 8.1 Hz, 3H), 1.20-1.55(m, 2H), 2.92(dqd, *J* 2.7, 6.3, 10.6 Hz, 1H), 3.71(d, *J* 13.0 Hz, 1H), 3.90(s, large, 1H), 3.93(d, *J* 13.0 Hz, 1H), 3.94(dqd, *J* 2.3, 5.8, 17.0 Hz, 1H), 7.20-7.36(m, 5H). ^{13}C NMR *syn*-**1b** δ: 139.24, 128.72, 128.49, 127.48, 68.94, 54.08, 50.64, 44.91, 23.87, 20.82. ^{1}H NMR *anti*-**1b** δ: 1.15(d, *J* 8.1 Hz, 3H), 1.21(d, *J* 6.6 Hz, 3H), 1.43(ddd, *J* 2.7, 5.1, 14.4 Hz, 1H), 1.70(ddd, *J* 3.3, 9.0, 14.4 Hz, 1H), 3.12(dqd, *J* 3.2, 3.9, 6.6 Hz, 1H), 3.50(s, large, 2H), 3.74(d, *J* 12.6 Hz, 1H), 3.86(d, *J* 12.6 Hz, 1H), 4.15(dqd, *J* 3.0, 6.2, 9.0 Hz, 1H), 7.20-7.37(m, 5H). ^{13}C NMR *anti*-**1b** δ: 139.51, 128.73, 128.43, 127.45, 65.03, 51.48, 51.97, 45.06, 23.56, 19.76. Anal. Calc. for $C_{12}H_{19}NO$: C, 74.55; H, 9.91; N, 7.25%. Found: C, 74.48; H, 10.17; N, 7.31%.

*4-(N-isopropylamino)-pentan-2-ol, (**1c**).* IR (neat) ν_{max}/cm^{-1}: 3340, 3274, 2965, 2927, 1560, 1461, 1382, 1163, 1133, 1084. MS *m/z* (%): 145(0.2), 130(15), 86(65), 45(25). ^{1}H NMR *syn*-**1c** δ: 1.08(d, *J* 6.0 Hz, 3H), 1.10(d, *J* 5.6 Hz, 3H), 1.11(d, *J* 6.2 Hz, 3H), 1.14(d, *J* 6.2 Hz, 3H), 1.20-1.40(m, 1H), 1.53(ddd, *J* 2.2, 2.8, 14.0 Hz, 1H), 3.00(hept, *J* 6.4 Hz, 1H), 3.05(m, 1H), 3.97(dqd, *J* 1.8, 6.2, 10.7 Hz, 1H), 4.30(s, large, 2H). ^{13}C NMR *syn*-**1c** δ: 69.07, 51.68, 45.35, 45.03, 24.23, 24.01, 21.72, 21.13. ^{1}H NMR *anti*-**1c** δ: 1.10(d, *J* 6.2 Hz, 3H), 1.13(d, *J* 6.3 Hz, 3H), 1.18(d, *J* 6.3 Hz, 3H), 1.20(d, *J* 6.6 Hz, 3H), 1.20-1.40(m, 1H), 1.65(ddd, *J* 3.3, 8.1, 13.0 Hz, 1H), 3.00(hept, *J* 6.4 Hz, 1H), 3.26(dqd, *J* 3.8, 6.3, 6.7 Hz, 1H), 4.16(dqd, *J* 3.2, 5.9, 8.4 Hz, 1H), 4.30(s, large, 2H). ^{13}C NMR *anti*-**1c** δ: 65.03, 48.25, 45.77, 41.23, 23.51, 22.70, 22.05, 19.51.

*1-Phenyl-3-(N-isopropylamino)-butan-1-ol, (**1d**).* IR (neat) ν_{max}/cm^{-1}: 3270, 3200, 3040, 3020, 2980, 2880, 1470, 1380, 1330, 1100, 1070, 750, 700. MS *m/z* (%): 207(4.6), 192(2), 107(4.6), 105(6.9), 86(100), 77(20), 70(37). ^{1}H NMR *syn*-**1d** δ: 1.30-1.35(3d, 9H), 1.67(td, *J* 10.7, 14.5 Hz, 1H), 1.92(td, *J* 2.5, 14.5 Hz, 1H), 3.21(hept, *J* 6.2 Hz, 1H), 3.18-3.35(dqd, *J* 2.6, 5.8, 7.0 Hz, 1H), 4.47(s, large, 2H), 5.07(dd, *J* 1.5, 10.6 Hz, 1H), 7.37-7.60(m, 5H). ^{13}C NMR *syn*-**1d** δ: 145.55, 128.11, 126.79, 125.53, 75.08, 51.63, 46.38, 45.30, 24.39, 21.93, 21.83. ^{1}H NMR *anti*-**1d** δ: 1.00(d, *J* 6.3 Hz, 3H), 1.03(d, *J* 6.3 Hz, 3H), 1.07(d, *J* 6.3 Hz, 3H), 1.65(ABMX, *J* 3.9, 7.0, 14.0 Hz, 1H), 1.74(ABMX, *J* 3.6, 6.0, 15.0 Hz, 1H), 2.82(hept, *J* 6.3 Hz, 1H), 2.90(m, 1H), 3.82(s, large, 2H), 4.88(dd, *J* 3.7, 6.7 Hz, 1H), 7.06-7.30(m, 5H). ^{13}C NMR *anti*-**1d** δ: 150.09, 131.91, 130.34, 129.71, 75.19, 51.93, 49.63, 47.58, 27.83, 26.82, 24.70. Anal. Calc. for $C_{13}H_{21}NO$: C, 75.32; H, 10.21; N, 6.75%. Found: C, 75.10; H, 10.22; N, 6.26%.

*4-(N-Pyrrolidinyl)-pentan-2-ol, (**1e**).* IR (neat) ν_{max}/cm^{-1}: 3400, 2980, 2940, 2880, 2830, 1455, 1160, 1150. MS *m/z* (%): 157(4.2), 142(9), 96(100), 70(24), 56(20), 45(24). ^{1}H NMR *syn*-**1e** δ: 0.97(d, *J* 6.6 Hz, 3H), 1.13(d, *J* 6.2 Hz, 3H), 1.34(ddd, *J* 1.8, 3.6, 14.5 Hz, 1H), 1.52(td, *J* 10.9, 14.0 Hz, 1H), 1.70-1.80(AA'B_2, 4H), 2.57-2.80(AA'B_2, 4H), 3.17(dqd, *J* 3.3, 6.9, 10.5 Hz, 1H), 3.96(dqd, *J* 2.0, 6.2, 10.3 Hz, 1H), 6.24(s, large, 1H). ^{13}C NMR *syn*-**1e** δ: 69.08, 55.56, 46.70, 41.94, 23.67, 23.23, 12.43. ^{1}H NMR *anti*-**1e** δ: 1.21(d, *J* 6.2 Hz, 3H), 1.25(d, *J* 6.6 Hz, 3H), 1.55(ddd, *J* 2.6, 7.0, 14.0 Hz, 1H), 1.83(ddd, *J* 6.1, 10.6, 14.0 Hz, 1H), 1.94-2.20(m, 4H), 3.09(t, *J* 6.5 Hz, 4H), 3.50(sext, *J* 6.6 Hz, 1H), 3.90(dqd, *J* 1.8, 5.6, 11.0 Hz, 1H), 5.20(s, large, 1H). ^{13}C NMR *anti*-**1e** δ: 64.43, 57.62, 51.48, 41.05, 23.52, 23.28, 17.28.

*General procedure to obtain tetrahydro-1,3-oxazines, (**3**).* To a solution of γ-amino alcohol (**1**, 1mmol) in diethyl ether (1 mL), was added a solution of 40% formaldehyde (0.1 mL). The reaction was stirred for 16-20 hours at room temperature. After this time, diethyl ether (approximatelly 5 mL) was added, and the solution was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The yield was quantitative.

*3-Phenyl-4,6-dimethyl-tetrahydro-1,3-oxazine, (**3a**).* IR (neat) ν_{max}/cm^{-1}: 2960, 2920, 1600, 1485, 1370, 1250, 1240, 1175, 1100, 1000, 700. MS *m/z* (%): 192(7), 191(50), 190(11), 176(58), 132(83), 120(50), 119(83), 118(22), 106(33), 105(83), 104(91), 91(14), 77(100). ^{1}H NMR *syn*-**3a** δ: 1.02(d, *J* 6.3 Hz, 3H), 1.26(d, *J* 6.3 Hz, 3H), 1.42(dt, *J* 11.1, 13.0 Hz, 1H), 1.57(dt, *J* 2.7, 13.5 Hz, 1H), 3.73(ddq, *J* 3.3, 6.3, 11.1 Hz, 1H), 3.68(ddq, *J* 2.7, 6.3, 12.3 Hz, 1H), 4.39(d, *J* 9.3 Hz, 1H), 4.73(d, *J* 9.3 Hz, 1H), 7.06-7.33(m, 5H). ^{13}C NMR *syn*-**3a** δ: 147.57, 129.02, 126.32, 124.83,

85.76, 73.43, 53.90, 40.03, 21.70, 20.04. ^{1}H NMR *anti*-**3a** δ: 1.16(d, *J* 6.3 Hz, 3H), 1.25(dt, *J* 2.0, 13.0 Hz, 1H), 1.41(d, *J* 6.9 Hz, 3H), 1.75(ddd, *J* 5.4, 12.0, 13.8 Hz, 1H), 3.95(m, 2H), 4.83(d, *J* 11.1 Hz, 1H), 4.98(d, *J* 11.4 Hz, 1H), 6.85(t, *J* 8.4 Hz, 1H), 7.03(d, *J* 7.8 Hz, 2H), 7.22(dd, *J* 7.2, 8.7 Hz, 2H). ^{13}C NMR *anti*-**3a** δ: 150.88, 129.35, 120.65, 119.08, 74.85, 68.14, 52.79, 35.76, 22.07, 17.07. Anal. Calc. for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32%. Found: C, 74.80; H, 8.80; N, 7.37%.

*3-Benzyl-4,6-dimethyl-tetrahydro-1,3-oxazine, (**3b**).* IR (neat) ν_{max}/cm^{-1}: 2980, 2940, 1450, 1370, 1200, 1050, 740, 700. MS *m/z* (%): 206(3), 205(17), 204(8), 190(38), 146(14), 92(42), 91(100). ^{1}H NMR *syn*-**3b** δ: 1.13(d, *J* 6.0 Hz, 6H), 1.20-1.40(m, 2H), 2.95(m, 1H), 3.47(d, *J* 13.5 Hz, 1H), 3.47(m, 1H), 3.79(d, *J* 13.5 Hz, 1H), 3.92(d, *J* 10.2 Hz, 1H), 4.21(d, *J* 10.2 Hz, 1H), 7.20-7.40(AA'BBC, 5H). ^{13}C NMR *syn*-**3b** δ: 139.43, 128.39, 127.74, 126.32, 83.00, 72.79, 55.29, 48.92, 37.29, 21.74, 20.16. ^{1}H NMR *anti*-**3b** δ: 1.17(d, *J* 6.0 Hz, 3H), 1.25(d, *J* 6.0 Hz, 3H), 1.10-1.20(AXYZ, 1H), 1.88(AXYZ, 1H), 2.98(q, *J* 6.0 Hz, 1H), 3.81(dqd, 1H), 3.96(AA', 2H), 4.25(d, *J* 11.0 Hz, 1H), 4.65(d, *J* 11.0 Hz, 1H), 7.40-7.20(m, 5H). ^{13}C NMR *anti*-**3b** δ: 139.67, 128.50, 128.23, 126.89, 78.47, 67.80, 56.92, 49.28, 32.58, 22.20, 18.10. Anal. Calc. for $C_{13}H_{19}NO$: C, 76.06; H, 9.33; N, 6.82%. Found: C, 76.58; H, 9.23; N, 6.60%.

*3-Isopropyl-4,6-dimethyl-tetrahydro-1,3-oxazine, (**3c**).* MS *m/z* (%): 157(20), 142(100), 114(9), 100(14), 98(45), 56(81). ^{1}H NMR *syn*-**3c** δ: 0.92(d, *J* 6.6 Hz, 3H), 1.09(d, *J* 6.6 Hz, 6H), 1.15(d, *J* 6.9 Hz, 3H), 1.03-1.24(m, 2H), 2.75(dqd, *J* 3.0, 12.0 Hz, 1H), 3.22(hept, *J* 6.0 Hz, 1H), 3.39(dqd, *J* 3.0, 6.0, 12.0 Hz, 1H), 3.82(d, *J* 8.7 Hz, 1H), 4.49(d, *J* 9.0 Hz, 1H). ^{13}C NMR *syn*-**3c** δ: 78.47, 72.65, 52.55, 45.03, 41.38, 21.98, 21.68, 19.63, 17.18. ^{1}H NMR *anti*-**3c** δ: 1.02-1.24(m, 1H), 1.09(d, *J* 6.6 Hz, 6H), 1.27(d, *J* 6.3 Hz, 3H), 1.99(d, *J* 7.2 Hz, 3H), 1.62(m, 1H), 3.03(hept, *J* 6.0 Hz, 1H), 3.15(quint, *J* 6.0 Hz, 1H), 3.65(dqd, *J* 3.0, 6.0, 10.5 Hz, 1H), 4.36(AA', 2H). ^{13}C NMR *anti*-**3c** δ: 75.72, 67.20, 51.07, 46.92, 34.72, 22.81, 22.33, 21.82, 18.87.

*6-Phenyl-3-isopropyl-4-methyl-tetrahydro-1,3-oxazine, (**3d**).* IR (neat) ν_{max}/cm^{-1}: 2967, 2922, 2871, 1604, 1495, 1452, 1383, 1210, 1079. MS *m/z* (%): 220(4.3), 219(26.5), 205(10.6), 204(67.4), 174(5.6), 140(5.2). ^{1}H NMR *syn*-**3d** δ: 1.02(d, *J* 6.4 Hz, 3H), 1.20(d, *J* 6.5 Hz, 3H), 1.26(d, *J* 6.7 Hz, 3H), 1.69(AA'Y, 2H), 2.99(dqd, *J* 3.2, 6.4, 10.7 Hz, 1H), 3.36(hept, *J* 6.6 Hz, 1H), 4.45(dd, *J* 3.7, 10.6 Hz, 1H), 4.65(d, *J* 8.9 Hz, 1H), 4.84(d, *J* 8.9 Hz, 1H), 7.21-7.45(m, 5H). ^{13}C NMR *syn*-**3d** δ: 142.63, 128.42, 127.51, 125.96, 79.76, 79.68, 53.13, 45.67, 41.89, 21.96, 19.72, 16.93. ^{1}H NMR *anti*-**3d** δ: 1.14(d, *J* 6.4 Hz, 3H), 1.18(d, *J* 6.5 Hz, 3H), 1.34(d, *J* 7.2 Hz, 3H), 1.60(m, 1H), 1.93(ddd, *J* 6.0, 11.8, 13.4 Hz, 1H), 3.15(quint, *J* 6.6 Hz, 1H), 3.25(m, *J* 6.3 Hz, 1H), 4.59(AA', 2H), 4.60(dd, *J* 3.2, 9.7 Hz, 1H), 7.20(m, 5H). ^{13}C NMR *anti*-**3d** δ: 143.57, 127.91, 126.78, 125.38, 76.33, 73.57, 51.68, 47.31, 35.55, 22.86, 21.95, 18.80. Anal. Calc. for $C_{14}H_{21}NO$: C, 76.06; H, 9.33; N, 6.82%. Found: C, 76.58; H, 9.23; N, 6.60%.

*3-Benzyl-4-methyl-6-terc-butyl-tetrahydro-1,3-oxazine, (**3f**).* IR (neat) ν_{max}/cm^{-1}: 2956, 2869, 1188, 1105, 1027, 734, 698. MS *m/z* (%): 232(9), 190(12), 146(15), 118(4), 91(100). ^{1}H NMR *syn*-**3f** δ: 0.71(s, 9H), 1.02(d, *J* 6.6 Hz, 3H), 1.12(dt, *J* 2.8, 11.3 Hz, 1H), 1.29(AXYZ, 1H), 2.79(dqd, *J* 3.0, 6.6, 11.3 Hz, 1H), 2.87(dd, *J* 11.3, 2.6 Hz, 1H), 3.35(d, *J* 13.5 Hz, 1H), 3.65(d, *J* 13.5 Hz, 1H), 3.83(dd, *J* 0.9, 9.8 Hz, 1H), 4.20(d, *J* 9.8 Hz, 1H), 6.93-7.21(m, 5H). ^{13}C NMR *syn*-**3f** δ: 139.34, 128.74, 127.95, 126.56, 84.55, 83.34, 55.07, 48.26, 34.01, 29.41, 25.64, 20.44.

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