Reduction of 1,3-Diimines. A New and General Method of Synthesis of γ-Diamines, β-Amino Ketones, and Derivatives with Two and Three Chiral Centers

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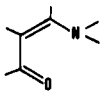
Received July 20, 1982

1,3-Diimines **1** are easily reduced with Na/*i*-PrOH to afford unsymmetrical N-substituted γ-diamines **8** in nearly quantitative yields. Since three chiral centers are generated, compounds **8** are isolated as a mixture of diastereoisomers which are easily separated. Complex metal hydrides $LiAlH_4$ and $NaBH_4$ are suitable reducing agents for the synthesis of different 1,3-difunctionalized derivatives (**3–6** and **8**) from **1**. The nature of the reduction compound depends on the reducing agent chosen and also on the reaction conditions.

Diimines **1** are easily obtained by reaction of Schiff bases and saturated nitriles under $AlCl_3$ catalysis[1] and also from C_α-lithiated Schiff bases and saturated nitriles.[2] These diimines are always isolated in the vinylogous amidine form **1a** or **1b** (Scheme I) and, due to their structure, have been found to be suitable starting materials for the synthesis of a wide variety of five-[3] and six-membered heterocycles.[4]

As part of our continuing study on the reactivity of diimines **1**, we now report our results on the reduction of these systems with various reducing agents such as, for instance, complex metal hydrides ($LiAlH_4$ and $NaBH_4$) and dissolved metals (Na/isopropyl alcohol).

The reduction of these systems has been little studied. Jutz and co-workers[5] described the formation of *N,N'*-disubstituted γ-diamines by reduction of vinylogous formamidines with sodium borohydride. More attention has been paid to the reduction of enaminones **2** which are



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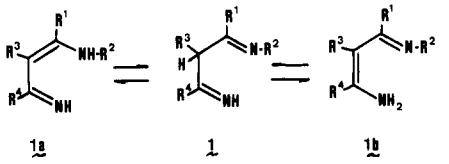
structurally related to diimines **1**. Greenhill[6] pointed out that the reduction of enaminones **2** takes place with difficulty, but these compounds can be reduced to 1,3-amino alcohols by complex metal hydrides[7,8] ($LiAlH_4$ or $NaBH_4$) or catalytic hydrogenation.[7]

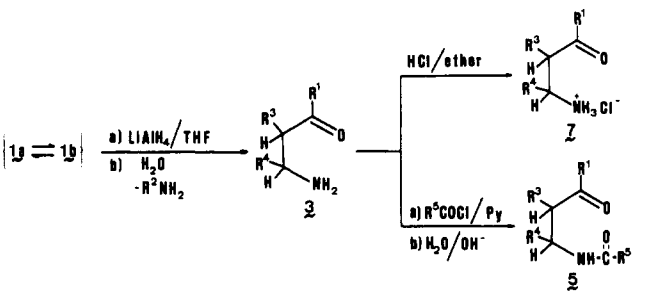
Results and Discussion

(I) Reduction of 1 (1a ⇌ 1b) with Complex Metal Hydrides. The reduction of diimines **1** with an excess of lithium aluminum hydride in refluxing THF for 20 h led after hydrolysis to the β-amino ketones **3** in excellent yields (see Scheme II and Table I). Compounds **3** were isolated

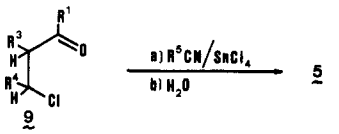
Scheme I



Scheme II



Scheme III



in the form of viscous oils which slowly decompose at room temperature with loss of ammonia, and for this reason they were characterized as the hydrochlorides **7** (see Table I) or *N*-acyl derivatives **5** (Table II). Compounds **5** were easily obtained in yields of 80% or higher with acetyl chloride ($R^5 = CH_3$) in pyridine/THF solution (Table II). The sequence (**1** → **3**) represents a useful preparation method for β-amino ketones, for which only a few methods are available.[9,10]

β-Acylamino ketones **5** have received more attention than their precursors. For instance, Lora-Tamayo and co-workers[11,12] have synthesized these compounds by the reaction of β-chloroketones **9** with a saturated nitrile ($R^5 = CH_3$)–$SnCl_4$ complex (Scheme III). We used this alternative synthesis of β-acylamino ketones **5a,b** (Table II) to corroborate the structure of our products.

(1) H. Hoberg und J. Barluenga, *Synthesis*, 142 (1970).
(2) G. Wittig, S. Fischer, and M. Tanaka, *Justus Liebigs Ann. Chem.* 1075 (1973).
(3) (a) J. Barluenga, J. F. López Ortiz, and V. Gotor, *J. Chem. Soc., Chem. Commun.*, 891 (1979); (b) J. Barluenga, V. Rubio, and V. Gotor, *J. Org. Chem.*, **47**, 1696 (1982).
(4) (a) J. Barluenga, S. Fustero, and V. Gotor, *Synthesis*, 191 (1975); (b) V. Gómez Aranda, J. Barluenga, S. Fustero, and V. Gotor, *ibid.*, 720 (1974); (c) J. Barluenga, J. F. López Ortiz, M. Tomás and V. Gotor, *J. Chem. Soc., Perkin Trans. 1*, 1891 (1981), and references cited therein.
(5) C. Jutz, A. F. Kirschner, and R. M. Wagner, *Chem. Ber.*, **110**, 1259 (1977).
(6) J. V. Greenhill, *Chem. Soc. Rev.*, **6**, 277 (1977).
(7) J. C. Martin, K. R. Barton, P. G. Gott, and R. H. Meen, *J. Org. Chem.*, **31**, 943 (1966).
(8) P. Maroni, L. Cazaux, P. Tisnes, and M. Zambeti, *Bull. Soc. Chim. Fr.*, 179 (1980).
(9) "Organic Syntheses", Collect. Vol. I, Wiley, New York, 1941, p 196.
(10) G. Büchi, J. C. Vederas, *J. Am. Chem. Soc.*, **94**, 9128 (1972), and references cited therein.
(11) M. Lora-Tamayo, R. Madroñero, and H. Leipprand, *Chem. Ber.*, **97**, 2224 (1964).
(12) M. Lora-Tamayo, R. Madroñero, G. Garcia Muñoz, and H. Leipprand, *Chem. Ber.*, **97**, 2234 (1964).

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Table I. β-Amino Ketones 3 from $LiAlH_4$ Reduction of 1

compd[c]	R^4	yield, %	diastereomer ratio,[a] %	3·HCl (7)	mp, °C
3a	C_6H_5	89 (R^2 = p-$CH_3C_6H_4$), 80 (R^2 = C_6H_5)	(S,R/R,S)-3a, 94 (S,S/R,R)-3a, 6[b]	7a b	183-185
3b	p-$CH_3C_6H_4$	82 (R^2 = p-$CH_3C_6H_4$), 72 (R^2 = c-C_6H_{11})	(S,R/R,S)-3b, 96 (S,S/R,R)-3b, 4[b]	7b b	205-207
3c	c-C_6H_{11}	75 (R^2 = p-$CH_3C_6H_4$)	(S,S/R,R)-3c, 100 (S,R/R,S)-3c		

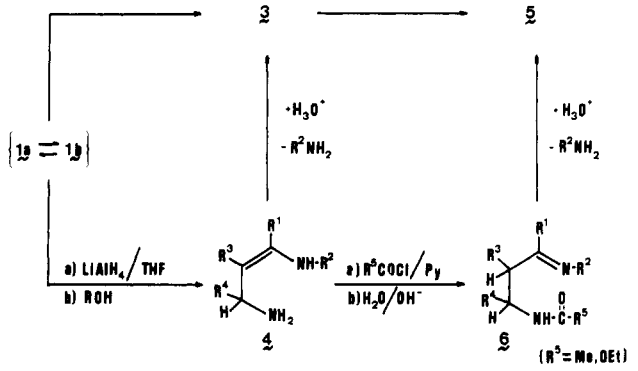
[a] By ^1H NMR from the crude residue (estimated error ≤ ±2). [b] Not isolated. [c] $R^1 = C_6H_5$ and $R^3 = CH_3$ in all cases.

Table II. β-Acylamino Ketones 5 from 3 and Acetyl Chloride

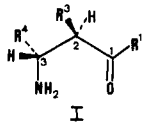
compd[b]	R^4	yield, %	mp, °C
5a	C_6H_5	97 (92)[a]	179-181
5b	p-$CH_3C_6H_4$	90 (70)[a]	169-170
5c	c-C_6H_{11}	82	159-161

[a] From β-chloro ketones by reaction with nitrile/$SnCl_4$ complex. [b] $R^1 = C_6H_5$ and $R^3 = R^5 = CH_3$ in all cases.

Scheme IV



The preparation of β-amino ketones and their derivatives by the sequences 1 → 3 → 7 and 1 → 3 → 5, respectively, involves the formation of two new chiral centers in the target molecule. Spectral data (^1H and ^{13}C NMR) show, in all the cases studied, that the major product is that containing the groups R^3 and R^4 in the anti position. Structures **3a–c** were elucidated on the base of the NMR data for the methyl group at C-2 in the diastereoisomeric mixture. The $J_{H_2H_3}$ coupling constant values measured are clearly consistent with the stereochemistry shown in I.[13]



I

The most characteristic features of the ^1H NMR spectra of **3a** and **3b** are, in both cases, two sets of signals centered at δ 0.90 (d, 3 H, J = 7.0 Hz) and 1.20 (d, 3 H, J = 7.0 Hz) with an ~19:1 relative intensity. These signals are assigned to the methyl substituent in the MeCH grouping and correspond to a mixture of diastereoisomers *S,R/R,S* and *S,S/R,R* (Table I).

The formation of **3** could be explained either by 1,2-reduction of the imine double bond (tautomer **1a**) or by 1,4-reduction[7,14] of the tautomer **1b** followed by elimination of amine (R^2NH_2) from the intermediate β-amino enamine **4** (**1** → **4** → **3**, Scheme IV). The latter mechanism is indicated by the isolation of β-amino enamines **4** (for instance, **4a**, $R^1 = R^2 = R^4 = C_6H_5$ and $R^3 = CH_3$) instead of compounds **3** when the reaction mixtures are solvolyzed with anhydrous protic solvents (i.e., anhydrous methanol). Compounds **4** are relatively stable white solids which decompose slowly at room temperature, but they decompose rapidly in solution when their purification by crystallization is attempted.

Scheme V

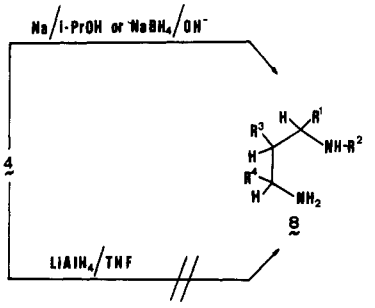
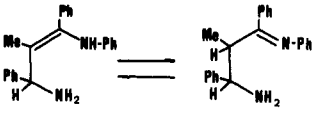


Table III. β-Amino Enamines 4 and Derivatives 6

compd[b]	R^5	yield, %	mp, °C
4a		91	135-138[a]
6a	CH_3	78	146-148
6b	OC_2H_5	75	136-138

[a] Product not recrystallized. [b] $R^1 = R^2 = R^4 = C_6H_5$ and $R^3 = CH_3$ in all cases.

Chemical proofs and spectral data show that compounds **4** are isolated in the tautomer form **4a**.[15] The ^1H NMR spectrum displays two signals centered at δ 1.70 (s, 3 H) and 5.15 (s, 1 H) which are assigned to the groups $CH_3C=$ and >N—CH—C=, respectively. The chemical shifts and multiplicities are not consistent with structure **4a′**.



4a 4a′

Hydrolysis of **4** leads to the corresponding β-amino ketone **3**. It is also noteworthy that **4** cannot be reduced upon treatment with $LiAlH_4$ in THF under reflux, corroborating the enamine structure. Reduction of **4** with $NaBH_4$/OH^-[16,17] or Na/*i*-PrOH leads to the isolation of the cor-

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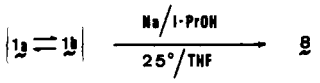
(14) G. N. Walker, *J. Org. Chem.*, 27, 4227 (1962).
(15) H. Finch, E. A. Peterson, and S. A. Ballard, *J. Am. Chem. Soc.*, 74, 2016 (1952).
(16) Lithium aluminum hydride does not generally react with enamines, whereas the reduction often observed when sodium borohydride is used is due to the protonation of the enamine by the solvent (H_2O, ROH) and reduction of the iminium ion thus generated: S. F. Dyke "The Chemistry of Enamines", Cambridge Chemistry Texts, Cambridge, England, 1982, p 52.
(17) Surprisingly, β-amino ketones **3**, instead of the expected γ-diamines **8**, were obtained in less than 15% yields when diimines **1** were reduced with an excess of $NaBH_4$ in EtOH/THF under reflux. The unusual behavior of $NaBH_4$ toward enaminones **2** accounts for this unexpected result. See, for example, references 8 and 18.

Table IV. γ-Diamines 8 from Na/*i*-PrOH Reduction of 1,3-Diimines 1

compd[e]	R^2	R^4	yield, %	diastereomer ratio,[a] %	mp, °C
8a	C_6H_5	C_6H_5	98 (66,[b] 60[c])	(*S,S,R/R,R,S*)-8δ, 40 (42,[b] 10[c])	151-153
				(*R,S,R/S,R,S*)-8γ, 25 (45,[b] 36[c])	110-112
				(*S,S,S/R,R,R*)-8β, 35 (13,[b] 54[c])	90-92
8b	C_6H_5	p-$CH_3C_6H_4$	99	(*S,S,R/R,R,S*)-8δ, 27	172-173
				(*R,S,R/S,R,S*)-8γ, 23	157-158
				(*S,S,S/R,R,R*)-8β, 50	113-115
8c	p-$CH_3C_6H_4$	C_6H_5	90	(*S,S,R/R,R,S*)-8δ, 41	169-170
				(*R,S,R/S,R,S*)-8γ, 27	136-138
				(*S,S,S/R,R,R*)-8β, 32	107-109
8d	p-$CH_3C_6H_4$	p-$CH_3C_6H_4$	90	(*S,S,R/R,R,S*)-8δ, 29	169-171
				(*R,S,R/S,R,S*)-8γ, 22	104-106
				(*S,S,S/R,R,R*)-8β, 49	153-155
8e	p-$CH_3C_6H_4$	c-C_6H_{11}	95	(*S,S,S/R,R,R*)-8δ, 23	140-142
				(*R,S,S/S,R,R*)-8γ, 30	*d*
				(*S,S,R/R,R,S*)-8β, 47	115-117

[a] By ^1H NMR from the crude products (estimated error ≤ ±2). [b] Na/*i*-PrOH reduction of 4. [c] $NaBH_4$ reduction of 4. [d] Not isolated. [e] $R^1 = C_6H_5$ and $R^3 = CH_3$ in all cases.

Scheme VI



responding 1,3-diamines 8, an expected result of the reduction of the enamine double bond[15] (Scheme V).

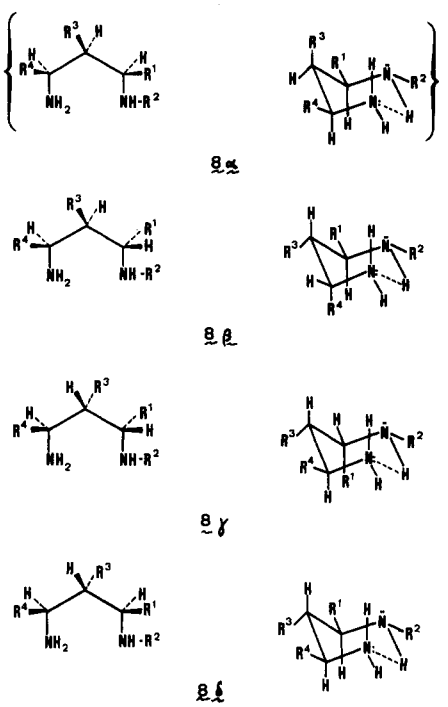
Compounds 4 are best characterized by forming more stable derivatives. The treatment of 4 with acetyl chloride ($R^5 = CH_3$) or ethyl chloroformate ($R^5 = OEt$) in pyridine leads to compounds 6 (in the tautomer form 4a'; see Scheme IV and Table III). Hydrolysis of 6 under mild conditions affords the same β-acylamino ketones 5 ($R^5 = CH_3$) as obtained from 3.

(II) Reduction of 1 with Na/*i*-PrOH. Synthesis of γ-Diamines. The development of the synthesis of γ-diamines 8 in the multistep sequence 1 → 4 → 8 prompted us to attempt the Na/*i*-PrOH reduction of 1 which could afford a more convenient one-step synthesis of 8. The preparation of γ-diamines has been an important synthetic problem since very few methods are known for the preparation of these compounds.[5,19-21] Methods previously reported for the preparation of unsymmetrical γ-diamines 8 are limited to reactions of acrolein[15,22] or acrylonitrile[23,24] with ammonia or amines followed by the reduction of the corresponding addition compound.

Reduction of 1 with sodium and isopropyl alcohol as the proton source in THF at 25 °C yields a diastereoisomeric mixture of γ-diamines 8 in nearly quantitative yields in a few hours (Scheme VI, Table IV)

This mixture was characterized by ^1H and ^{13}C NMR of the crude reduction residue. Only three of the four possible diastereoisomers could be detected and were identified as 8β, 8γ, and 8δ (Chart I),[25] and in no case was the presence of isomer 8α observed, probably because of its sterically crowded structure.

Chart I



For instance, the crude reaction residue 8b ($R^1 = R^2 = C_6H_5$, $R^3 = CH_3$, $R^4 = p$-$CH_3C_6H_4$) displays in the ^1H NMR spectrum three doublets centered at δ 0.50 (3 H), 0.60 (3 H), and 0.90 (3 H) with a 27:23:50 relative intensity ratio (see Table IV). These are assigned to the methyl substituent in the MeCH grouping corresponding to the isomers 8δ, 8γ, and 8β, respectively.

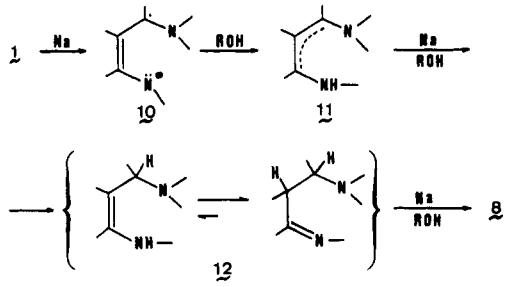
The separation of the diastereoisomers was made based on their different solubility in hexane. Isomer 8δ is nearly insoluble in hot hexane and could be filtered out from the mixture. Isomers 8β and 8γ were separated by successive crystallizations from hexane (see Experimental Section).

The configurational assignment was made from ^1H NMR data corresponding to the CH–R^1 and CH–R^4 groups

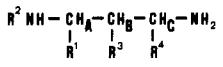
(18) Choji Kashima, *J. Org. Chem.*, **40**, 526 (1975).
(19) M. G. Andrews and J. A. Mosbo, *J. Org. Chem.*, **42**, 650 (1977).
(20) J. Barluenga, F. J. Fañanas, J. Villamaña, and M. Yus, *J. Org. Chem.*, **47**, 1560 (1982).
(21) (a) G. Appleton and J. Robert Hall, *Inorg. Chem.*, **9**, 1807 (1970); (b) H. Piotrowska, T. Urbanski, and W. Bednarska, *Org. Prep. Proc. Int.*, 3 (1), 21 (1971); (c) C. Jutz, Ger. Offen., 2135584; *Chem. Abstr.*, **76**, 98554, (1972).
(22) R. A. Y. Jones, A. R. Katritzky, and M. Snarey, *J. Chem. Soc. B*, 131 (1970).
(23) T. Ueda and K. Ishizaki, *Chem. Pharm. Bull.* **15** (2), 228 (1967).
(24) H. Hoffmann, H. Toussaint, and R. Plass, (Badische Anilin- und Soda-Fabrik A.-G.), Ger. Offen. 2004405; *Chem. Abstr.*, **75**, 88085, (1971).

(25) The pseudochair conformation is assumed as the most likely one on taking into account the possibility of formation of hydrogen bonds (Chart I).

Scheme VII



for each one of the isolated diastereoisomers. For instance, the ^1H NMR spectrum of **8bγ** displays three characteristic doublets centered at δ 0.60 (3 H, J = 7.5 Hz), 3.85 (1 H, J = 7.5 Hz), and 4.75 (1 H, J = 3.0 Hz) corresponding to R^3 (=CH_3) in the R^3–CH_B grouping and to H_C and H_A, respectively (II).



II

The values of δ, the multiplicity of the signals, and the values of the coupling constants corroborate two features of the proposed stereochemistry. On the one hand, the highest field resonances correspond to the C-2 methyl groups in diastereoisomers, with R^3 and R^4 occupying anti possitions (8γ and 8δ). On the other hand from the **8bγ** spectrum can be concluded syn–anti relation for the sequence H_A–H_B–H_C (Chart I and structure II). The same arguments were applied to rationalize the stereochemistry proposed for all diastereoisomers.

The obtention of γ-diamines from 1 implies the reduction of an enamine C=C and an imine double bond. It can be explained by an electron transfer through a conjugate 1,4-addition (Scheme VII), which first leads to the intermediate **10** which is able to abstract a proton from the alcohol to give **11** and afterward **12**. This system is "in situ" reduced to **8**. It is noteworthy that enaminones **2** are not reduced under similar conditions to the corresponding γ-amino alcohols.[10] When the alcohol is substituted by an amine RNH_2 as the proton source, products of a different nature are isolated.[26]

Conclusions

The versatility of 1,3-diamines **1** in organic synthesis is now once more shown by their use as simple precursors for γ-diamines. The possibility of reducing a single double bond in a selective fashion extends the synthetic potential of these systems. In this context, a new and excellent general method for the diastereoselective synthesis of β-amino ketones **3** and derivatives **4–6** by reduction of **1** with $LiAlH_4$ is described.

On the other hand, a diastereoisomeric mixture of N-substituted γ-diamines **8** is obtained through the sequences **1** → **4** → **8** and **1** → **8**. The different diastereoisomers were separated by successive crystallizations and identified by ^1H NMR.

Finally, the sequence **1** → **8** should be, in our opinion, the route of choice for synthesizing γ-diamines **8**.

Experimental Section

General Methods. Melting points are uncorrected. Infrared spectra were recorded in a Nujol suspension on a Pye Unicam SP-1000 spectrophotometer. The ^1H NMR spectra were determined on a Varian FT-80A spectrometer with internal tetramethylsilane as the reference. The ^{13}C NMR spectra were determined on a Varian FT-80A set for performing "off resonance". Mass spectra were taken on a Hewlett-Packard 5930A spectrometer. Microanalyses were performed on a Perkin-Elmer Model 240.

Materials. 1,3-Diimines were prepared according to literature methods.[1] All the other reagents were commercially available (99+%) and were used as received. Tetrahydrofuran was distilled from sodium–benzophenone under argon prior to use.

General Preparative Procedure of β-Amino Ketones 3. A solution of 1,3-diimine (15 mmol) in anhydrous THF was slowly added to a stirred slurry of lithium aluminum hydride (2.0 g, 53 mmol) in anhydrous THF (30 mL) under argon. The temperature was kept at 0–5 °C during the addition. Evolution of hydrogen was observed during the addition. The mixture was refluxed for 15–20 h and then treated with anhydrous MeOH (15 mL) diluted in anhydrous THF (20 mL). When the evolution of gas was complete, the mixture was hydrolized with 2 N H_2SO_4, treated with 3 N KOH until basic, and extracted with ether. The organic layer was dried over sodium sulfate, filtered, and evaporated. The amine (R^2NH_2) was eliminated under vacuum (0.001 torr) to yield β-amino ketones **3a–c** as the residue. The yields are given in Table I.

3-Amino-2-methyl-1,3-diphenylpropan-1-one ((*S*,*R*/*R*,*S*)-3a): IR (film) 3340, 1690, 760, 700 cm^{-1}; ^1H NMR ($DCCl_3$) δ 0.90 (d, 3 H, J = 7.0 Hz), 1.65 (br, NH), 3.70 (m, 1 H), 4.30 (d, 1 H, J = 9.5 Hz), 7.00–8.10 (m, 10 H); ^{13}C NMR (CCl_4/D_2O) δ 193.54, 144.25, 137.23, 132.65, 126.76–129.48, 115.08, 59.17, 49.25, 15.87.

Hydrochloride 7a: mp 183–185 °C (recrystallized from ethanol); IR (Nujol) 2500–3000, 1680, 1600, 760, 700 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 0.85 (d, 3 H), 4.55 (m, 2 H), 7.00–8.30 (m, 10 H) 8.85 (br s, N H); ^{13}C NMR (Me_2SO-d_6) δ 190.73, 135.81, 135.56, 133.71, 128.52–129.50, 55.84, 44.37, 15.14; MS, m/e 275 (M^+) 239, 224, 134, 106, 77, 28. Anal. Calcd for $C_{16}H_{18}NClO$: C, 69.89; H, 6.53; N, 5.08. Found: C, 69.82; H, 6.50; N, 4.87.

Spectral data for compounds **3b,c** and **7b** are included as supplementary material.

General Procedure for N-Acylation of 3. To a solution of **3** (10 mmol) in anhydrous THF (30 mL) and anhydrous pyridine (5 mL) was added acetyl chloride (1.0 g, 13 mmol) with stirring in an ice bath. Stirring was continued for an additional 5 h at room temperature. The mixture was poured onto 3 N KOH and extracted with ether. The extract was dried over sodium sulfate and evaporated under reduced pressure. The residue was purified by recrystallization from *n*-hexane–chloroform (6:1). Yields for compounds **5a–c** and melting points are summarized in Table II.

1-Acetamido-2-methyl-1,3-diphenylpropan-3-one (5a) was obtained from **3a** and acetyl chloride: IR (Nujol) 3320, 1690, 1650, 750, 700 cm^{-1}; ^1H NMR ($DCCl_3$) δ 1.30 (d, 3 H), 2.05 (s, 3 H), 4.10 (m, 1 H), 5.35 (dd, 1 H) 7.00–8.00 (m, 10 H); ^{13}C NMR ($DCCl_3$) δ 197.11, 169.71, 140.90, 136.49, 133.23, 126.07–128.72, 55.75, 44.39, 23.17, 16.35; MS, m/e 281 (M^+) 238, 148, 106, 77, 43. Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.87; H, 6.76; N, 4.98. Found: C, 76.95; H, 6.57; N, 4.80.

Spectral data for compounds **5b** and **5c** are included as supplementary material.

Alternative Procedure for the Preparation of 5b. (A) Preparation of 3-Chloro-2-methyl-1-phenyl-3-*p*-tolylpropan-1-one[13a] (9). Anhydrous hydrogen chloride was bubbled for 30 min with stirring through a solution of propiophenone (150 mmol) and *p*-tolualdehyde (150 mmol) in carbon sulfide (30 mL). The closed flask was left undisturbed at room temperature for 24 h. Petroleum ether (135 mL) was added, and the mixture was cooled at 0 °C to give **9**: 16.6 g (60%); mp 89–92 °C; IR (Nujol) 1680, 800, 760, 700 cm^{-1}; ^1H NMR ($DCCl_3$) δ 0.95 (d, 3 H), 2.35 (s, 3 H), 4.20 (m, 1 H), 5.20 (d, 1 H), 7.00–8.15 (m, 9 H); ^{13}C NMR ($DCCl_3$) δ 201.45, 138.36, 136.53, 136.19, 133.15, 127.50–129.26, 63.55, 48.88, 20.93, 16.78. Anal. Calcd for $C_{17}H_{17}ClO$: C, 74.86; H, 6.24. Found: C, 74.93; H, 6.30.

(B) Preparation of 5b. Compound 5b (3.1 g, 70%) was obtained from 3-chloro-2-methyl-1-phenyl-3-*p*-tolylpropan-1-one (**9**; 4.0 g, 15 mmol) by following the procedure described in the literature by Lora-Tamayo and co-workers.[12]

(26) J. Barluenga, B. Olano, and S. Fustero, work in progress.

2-Methyl-N^1,1,3-triphenylprop-1-ene-1,3-diamine (4a). A solution of 3-imino-2-methyl-*N*,1,3-triphenylprop-1-en-1-amine (5.0 g, 16 mmol) in anhydrous THF was slowly added to a stirred slurry of $LiAlH_4$ (2.0 g, 53 mmol) in anhydrous THF (30 mL) under argon. The temperature was kept at 0–5 °C during the addition, and evolution of hydrogen was observed. The mixture was refluxed for 15–20 h. Anhydrous methanol (15 mL) in anhydrous THF (20 mL) was then added, and the mixture was filtered and evaporated. The residue was stirred with hexane for 0.5 h and filtered. In this way **4a** (4.6 g, 91%) was isolated as a white solid: mp 135–138 °C; IR (Nujol) 3400, 1610, 770, 760, 740, 710, 700 cm^{-1}; ^1H NMR ($DCCl_3$) δ 1.70 (s, 3 H), 3.50 (br, NH), 5.15 (s, 1 H), 6.20–7.70 (m, 15 H).

Treatment of 4a with 2 N Sulfuric Acid. A solution of 2-methyl-N^1,1,3-triphenylprop-1-ene-1,3-diamine (**4a**; 3.2 g, 10 mmol) in THF (50 mL) was stirred with 2 N H_2SO_4 (100 mL) at 25 °C for 0.5 h. The solution was then treated with ice-cooled, concentrated, aqueous KOH until basic, extracted with ether, and evaporated. Aniline (0.8 g) was distilled from the residue under vacuum (0.001 torr) to yield **3a** (2.1 g, 88%).

1-Acetamido-2-methyl-1,3-diphenyl-3-(phenylimino)-propane (6a). Compound **6a** (78%) was obtained by reaction of **4a** with acetyl chloride by following the procedure described for the N-acylation of **3**. The residue was purified by recrystallization from *n*-hexane–chloroform (6:1): mp 146–148 °C; IR (Nujol) 3320, 1650, 1600, 750, 730, 710, 700 cm^{-1}; ^1H NMR ($DCCl_3$) δ 1.40 (d, 3 H), 2.10 (d, 3 H), 3.30 (m, 1 H), 5.30 (dd, 1 H), 6.25–7.45 (m, 15 H), 8.30 (br d, NH); ^{13}C NMR ($DCCl_3$) δ 176.37, 169.72, 149.62, 142.12, 137.72, 126.61–128.52, 124.41, 120.69, 56.79, 48.22, 23.48, 17.98; MS, *m/e* 356 (M^+) 297, 209, 180, 106, 77, 51, 43. Anal. Calcd for $C_{24}H_{24}N_2O$: C, 80.90; H, 6.74; N, 7.87. Found: C, 80.81; H, 6.69; N, 7.97.

Treatment of 6a with 2 N Sulfuric Acid. A solution of 1-acetamido-2-methyl-1,3-diphenyl-3-(phenylimino)propane (**6a**; 3.6 g, 10 mmol) in THF (50 mL) was heated with 2 N H_2SO_4 (100 mL) at 50 °C for 0.5 h. The solution was treated with ice-cooled concentrated KOH until basic, extracted with ether, and evaporated. Aniline (0.7 g) was distilled from the residue to yield **5a** (2.4 g, 85%).

1-(Carbethoxyamino)-2-methyl-1,3-diphenyl-3-(phenylimino)propane (6b). Compound **6b** (75%) was obtained by reaction of **4a** with ethyl chloroformate by following the procedure described for the N-acylation of **3**. The residue was purified by recrystallization from *n*-hexane–THF (6:1): mp 136–138 °C; IR (Nujol) 3320, 1690, 1650, 750, 730, 700 cm^{-1}; ^1H NMR ($DCCl_3$) δ 1.25 (t, 3 H), 1.45 (d, 3 H), 3.40 (m, 1 H), 4.10 (q, 2 H), 5.05 (dd, 1 H), 6.25–7.75 (m, 15 H); ^{13}C NMR ($DCCl_3$) δ 174.19, 156.48, 148.30, 142.48, 137.74, 126.51–128.31, 123.15, 120.60, 60.56, 58.69, 48.47, 17.80, 14.48. Anal. Calcd for $C_{25}H_{26}N_2O_2$: C, 77.72; H, 6.74; N, 7.25. Found: C, 77.62; H, 6.85; N, 7.43.

General Preparative Procedure of γ-Diamines 8. Method A. Reduction of 1 with Na/*i*-PrOH. A solution of **1** (10 mmol) in anhydrous THF (50 mL) and anhydrous *i*-PrOH (16 mL) was added dropwise to a mixture of Na (2.3 g, 100 mmol) and anhydrous THF (20 mL) at room temperature. When the addition was finished, the solution was stirred at room temperature until totally discolored (4 h). The solution was then hydrolyzed with 200 mL of H_2O and extracted with ether; the organic layer was dried over sodium sulfate, filtered, and evaporated under reduced pressure. 1,3-Diamines **8** were obtained as a mixture of diastereoisomers. Reaction yields and diastereoisomer ratios are found in Table IV.

Separation of Diastereoisomers of 8. The crude product containing three isomers was suspended in hexane (30 mL) and slightly heated with stirring. The slurry was filtered while hot. The hot-hexane-insoluble solid, **8δ**, was recrystallized from *n*-hexane–chloroform (6:1). From the filtrate, **8β** and **8γ** were isolated by crystallization. Melting points are given in Table IV.

Method B. Reduction of 4 with Na/*i*-PrOH. A solution of **4** (10 mmol) in anhydrous THF (50 mL) and anhydrous *i*-PrOH (16 mL) was added dropwise to a mixture of Na (2.3 g, 100 mmol) and anhydrous THF (20 mL) at room temperature. When the addition was finished, the solution was stirred at room temperature until totally discolored. The solution was then hydrolyzed with 200 mL of H_2O and extracted with ether; the organic layer was dried over sodium sulfate, filtered, and evaporated under reduced pressure. 1,3-Diamines **8** were obtained as a mixture of diastereoisomers. Reaction yields and diastereoisomer ratios are found in Table IV.

Method C. Reduction of 4 with $NaBH_4$. A solution of $NaBH_4$ (1.0 g, 26 mmol) in MeOH (30 mL) and 3 N NaOH (30 mL) was added dropwise to a solution of **4** (10 mmol) in THF (50 mL) at room temperature. When the addition was finished, the mixture was refluxed for 15–20 h, hydrolyzed with H_2O, and extracted with ether. The organic layer was dried over sodium sulfate, filtered, and evaporated under reduced pressure. 1,3-Diamines **8** were obtained as a mixture of diastereoisomers. Reaction yields and diastereoisomer ratios are found in Table IV.

2-Methyl-N^1,1-diphenyl-3-*p*-tolyl-1,3-propanediamine (8b). Method A. Compound **8b** (3.3 g, 99%) was obtained by reaction of 3-imino-2-methyl-*N*,1-diphenyl-3-*p*-tolylprop-1-en-1-amine (3.3 g, 10 mmol).

***(S,S,R/R,R,S)*-8bδ**: IR (Nujol) 3460, 3340, 1600, 790, 720, 680 cm^{-1}; ^1H NMR ($DCCl_3$) δ 0.50 (d, 3 H, J = 7.5 Hz), 2.15 (m, 1 H), 2.35 (s, 3 H), 2.50–2.70 (br, NH) 3.90 (d, 1 H, J = 7.5 Hz), 4.35 (d, 1 H, J = 7.5 Hz), 6.30–7.40 (m, 14 H); ^{13}C NMR ($DCCl_3$) δ 147.55, 142.40, 142.20, 136.54, 129.00–126.81, 116.99, 113.41, 61.03, 58.40, 46.16, 20.96, 13.98; MS, *m/e* 330 (M^+) 237, 182, 132, 120, 93, 77, 28. Anal. Calcd for $C_{23}H_{26}N_2$: C, 83.64; H, 7.88; N, 8.48. Found: C, 83.42; H, 7.97; N, 8.56.

***(R,S,R/S,R,S)*-8bγ**: IR (Nujol) 3460, 3340, 1600, 790, 730, 690 cm^{-1}; ^1H NMR ($DCCl_3$) δ 0.60 (d, 3 H, J = 7.5 Hz), 2.15 (m, 1 H), 2.30 (s, 3 H), 2.30–2.50 (br, NH), 3.85 (d, 1 H, J = 7.5 Hz), 4.75 (d, 1 H, J = 3.0 Hz), 6.30–7.40 (m, 14 H); ^{13}C NMR ($DCCl_3$) δ 147.56, 142.56, 142.11, 136.56, 129.10–125.69, 116.93, 113.38, 59.06, 57.95, 46.28, 20.91, 12.63; MS, *m/e* 330 (M^+) 237, 182, 132, 120, 93, 77, 28. Anal. Calcd for $C_{23}H_{26}N_2$: C, 83.64; H, 7.88; N, 8.48. Found: C, 83.60; H, 7.61; N, 8.53.

***(S,S,S/R,R,R)*-8bβ**: IR (Nujol) 3440, 3320, 1600, 790, 720, 680 cm^{-1}; ^1H NMR ($DCCl_3$) δ 0.90 (d, 3 H, J = 7.5 Hz), 2.15 (m, 1 H), 2.30 (s, 3 H), 2.00–2.50 (br, NH), 4.05 (d, 1 H, J = 2.0 Hz), 4.30 (d, 1 H, J = 5.0 Hz), 6.30–7.40 (m, 14 H); ^{13}C NMR ($DCCl_3$) δ 148.42, 143.73, 142.90, 136.19, 129.22–125.99, 116.34, 112.98, 62.61, 55.00, 46.11, 21.09, 11.90; MS, *m/e* 330 (M^+) 237, 182, 132, 120, 93, 77, 28. Anal. Calcd for $C_{23}H_{26}N_2$: C, 83.64; H, 7.88; N, 8.48. Found: C, 83.80; H, 7.90; N, 8.46.

Registry No. (±)-**1** (R^1 = R^4 = C_6H_5; R^2 = *p*-$CH_3C_6H_4$; R^3 = CH_3), 85356-23-6; (±)-**1** (R^1 = R^2 = R^4 = C_6H_5; R^3 = CH_3), 85356-24-7; (±)-**1** (R^1 = C_6H_5; R^2 = c-C_6H_{11}; R^3 = CH_3; R^4 = *p*-$CH_3C_6H_4$), 85356-25-8; (±)-**1** (R^1 = C_6H_5; R^2 = R^4 = *p*-$CH_3C_6H_4$; R^3 = CH_3), 85356-26-9; (±)-**1** (R^1 = C_6H_5; R^2 = *p*-$CH_3C_6H_4$; R^3 = CH_3; R^4 = c-C_6H_{11}), 85356-27-0; (±)-**1** (R^1 = R^2 = C_6H_5; R^3 = CH_3; R^4 = *p*-$CH_3C_6H_4$), 85356-28-1; (*S,R/R,S*)-**3a**, 85356-29-2; (*S,S/R,R*)-**3a**, 85356-30-5; (*S,R/R,S*)-**3b**, 85356-31-6; (*S,S/R,R*)-**3b**, 85356-32-7; (*S,R/R,S*)-**3c**, 85356-33-8; (*S,S/R,R*)-**3c**, 85356-34-9; (±)-**4a**, 85356-35-0; (*S,R/R,S*)-**5a**, 85356-36-1; (*S,R/R,S*)-**5b**, 85356-37-2; (*S,S/R,R*)-**5c**, 85356-38-3; (*S,R/R,S*)-**6a**, 85356-39-4; (*S,R/R,S*)-**6b**, 85356-40-7; (*S,R/R,S*)-**7a**, 85356-41-8; (*S,R/R,S*)-**7b**, 85356-42-9; (*S,S,S/R,R,R*)-**8aβ**, 85356-43-0; (*R,S,R/S,R,S*)-**8aγ**, 85405-08-9; (*S,S,R/R,R,S*)-**8aδ**, 85405-09-0; (*S,S,S/R,R,R*)-**8bβ**, 85356-44-1; (*R,S,R/S,R,S*)-**8bγ**, 85405-10-3; (*S,S,R/R,R,S*)-**8bδ**, 85405-11-4; (*S,S,S/R,R,R*)-**8cβ**, 85356-45-2; (*R,S,R/S,R,S*)-**8cγ**, 85405-12-5; (*S,S,R/R,R,S*)-**8cδ**, 85405-13-6; (*S,S,S/R,R,R*)-**8dβ**, 85356-46-3; (*R,S,R/S,R,S*)-**8dγ**, 85405-14-7; (*S,S,R/R,R,S*)-**8dδ**, 85405-15-8; (*S,S,R/R,R,S*)-**8eβ**, 85356-47-4; (*R,S,S/S,R,R*)-**8eγ**, 85405-16-9; (*S,S,S/R,R,R*)-**8eδ**, 85405-17-0; (*S,R/R,S*)-**9**, 85356-48-5; propiophenone, 93-55-0; *p*-tolualdehyde, 104-87-0.

Supplementary Material Available: Spectral data for compounds **3a–c**, **5a–c**, **7a,b**, and **8** (13 pages). Ordering information is given on any current masthead page.