After the mixture was stirred at room temperature for 4 h, the methanol was evaporated and the aqueous solution extracted with fractions of $CHCl_3$ (2 × 15 mL) which were combined and washed with 1 N HCl, dried (Na_2SO_4), and evaporated. The benzyl δ-(methoxycarbonyl)-γ-oxovalerate was isolated by bulb-to-bulb vacuum distillation in 0.20 g (70%) yield as a clear, colorless oil.

Method B. A mixture of 0.26 g (1.50 mmol) of 1-(thiopivaloyl)pyrrolidine and 0.54 g (1.80 mmol) of [(benzyloxy)carbonyl]methyl trifluoromethanesulfonate in 5 mL of CH_2Cl_2 was stirred at room temperature for 15 min under a nitrogen atmosphere. To the solution was added 0.82 g (2.25 mmol) of bis(3-morpholinylpropyl)phenylphosphine, and the sulfur extrusion was allowed to proceed for 0.5 h at room temperature under nitrogen. The mixture was diluted with 15 mL of CH_2Cl_2 and washed several times with 10 mL of 1 N HCl, the solvent was evaporated, and the residue was dissolved in 50 mL of methanol/water (4/1) to which was added 3.0 mL of 1 N HCl. After 1 h, the methanol was evaporated, the aqueous solution was extracted with $CHCl_3$ (3 × 15 mL), and the combined extracts were washed with 20 mL of 1 N HCl and then dried (Na_2SO_4). Evaporation of solvent and bulb-to-bulb vacuum distillation of the residue yielded 0.33 g (94%) of **benzyl γ,γ-dimethyl-β-oxovalerate.**

Method C. A mixture of 0.26 g (1.50 mmol) of 1-(thiopivaloyl)pyrrolidine and 0.42 g (1.80 mmol) of α-cyanoisobutyl trifluoromethanesulfonate was stirred for 0.5 h and allowed to stand 18 h under a nitrogen atmosphere. Sulfur extrusion, hydrolysis, and isolation proceeded as described in method A to yield 0.20 g (80%) of **γ,γ-dimethyl-α-isopropyl-β-oxovaleronitrile.**

Method D. Method C was followed except that after the addition of the bis(3-morpholinyl)propylphenylphosphine, the reaction was refluxed for 15 h under a nitrogen atmosphere. After hydrolysis, the product was separated on a silica gel preparative plate (1/1 ether/hexane).

Registry No. 1 (R = Ph), 15563-45-8; 1 (R = Pr), 66343-95-1; 1 R = *t*-Bu), 77902-87-5; 1 (R = $(CH_2)_2C(O)OMe$), 77902-88-6; 2 (R^1 = H; R^{11} = CH_2Ph; X = SO_3CF_3), 77902-89-7; 2 (R^1 = Me; R^{11} = Et; X = SO_3CF_3), 77902-90-0; 2 (R^1 = *i*-Pr; R^{11} = Me; X = SO_3CF_3, 77902-91-1; 5 (R = Ph; R^1 = H; R^{11} = Me), 614-27-7; 5 (R = Ph; R^1 = Me; R^{11} = Et), 10488-87-6; 5 (R = Pr; R^1 = H; R^{11} = *t*-Bu), 61540-30-5; 5 (R^1 = Pr; R^1 = *i*-Pr; R^{11} = Me), 77924-73-3; 5 (R = Pr; R^1 = H; R^{11} = CH_2Ph), 5006-35-9; 5 (R = *t*-Bu; R^1 = H; R^{11} = CH_2Ph), 77902-92-2; 5 (R = $(CH_2)_2C(O)OMe$; R^1 = H; R^{11} = CH_2Ph), 53314-75-3; α-cyanoisobutyl α-trifluoromethanesulfonate, 77924-74-4; β-oxo-β-phenylpropionitrile, 614-16-4; γ,γ-dimethyl-α-isopropyl-β-oxovaleronitrile, 77902-93-3; bis(3-morpholinylpropyl)phenylphosphine, 77902-94-4; 3-morpholinylpropyl chloride, 7357-67-7; dichlorophenylphosphine, 644-97-3; pyrrolidine, 123-75-1; butyryl chloride, 109-69-3; 1-[β-(methoxycarbonyl)propionyl]pyrrolidine, 77902-95-5; benzyl bromoacetate, 5437-45-6.

Stereochemistry of Imino Group Reduction. 2. Synthesis and Assignment of Configuration of Some *N*-(1-Phenylethyl)-1,2-diaryl-2-aminoethanols

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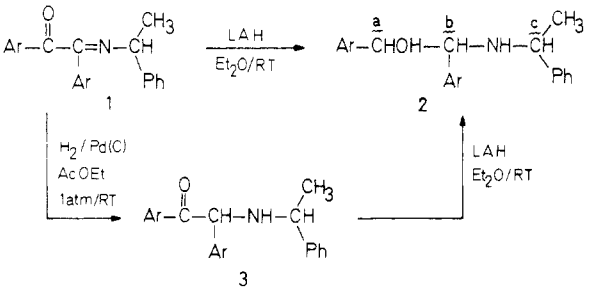
Lithium aluminum hydride reduction of the monoimines prepared by reaction of benzils and 1-phenylethylamine yields a mixture of the related diastereomeric *N*-(1-phenylethyl)-1,2-diaryl-2-aminoethanols. After separation of the diastereomers, assignment of their configuration is made on the basis of their infrared and NMR spectra. Catalytic hydrogenation of the monoimine prepared from benzil yields the amino ketone, which when treated with lithium aluminum hydride yields a mixture of aminoethanols. The composition of this shows that the stereochemical result of this reduction is different from that of the direct reduction. Stereochemical results are analyzed on the basis of models which take into account different initial conformations of the monoimine and the higher probability of attack of hydride at the less hindered side of each conformer.

Previously[1] we reported stereochemical results for the lithium aluminum hydride (LAH) reduction of a series of imines, ArCOCAr=NCHRPh (1).[2] Analysis of the mixture of aminoethanols obtained in this way showed that the reduction process is highly stereoselective for R = Me. With the purpose of obtaining all possible stereoisomers for one imine type, we have further investigated the product of the one-step LAH reduction and also studied the reduction of imine 1 (Ar = C_6H_5) by a two-step process

Scheme I



involving the intermediacy of an amino ketone (Scheme I).

Results

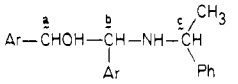
Assignment of Configuration to LAH Reduction Products. The amino alcohols (2) considered in this paper

(1) Part 1 (preliminary communication): R. Haro-Ramos, A. Jimenez-Tebar, R. Pérez-Ossorio, and J. Plumet, *Tetrahedron Lett.*, 1355 (1979).

(2) For the synthesis and structure of this type of compounds, see: (a) J. L. García-Ruano, R. Haro, C. Pascual, R. Pérez-Ossorio, and J. Plumet, *An. Quim.*, **75**, 165 (1979); (b) S. García-Blanco, I. Fonseca, and S. Martínez Carrera, *Acta Crystallogr., Sect. B*, **35**, 2643 (1979); (c) J. L. García-Ruano, M. A. Henao, D. Molina, R. Pérez-Ossorio, and J. Plumet, *Tetrahedron Lett.*, 3123 (1979); (d) J. L. García-Ruano, M. A. Henao, D. Molina, R. Pérez-Ossorio, and J. Plumet, *An. Quim.*, **76C**, 260 (1980).

0022-3263/81/1946-3234$01.25/0

Table I. ^{1}H NMR Spectral Data (δ) of N-(1-Phenylethyl)-1,2-diaryl-2-aminoethanols[a]



Ar	isomer	CH-a	CH-b	$J_{1,2}$	CH-c	CH_3	$J_{CH_3,CH}$
Ph	α	4.40	3.2	8.0	3.4	1.23	6.0
	β	4.40	3.6	8.0	3.5	1.31	6.0
	γ	4.83	3.9	5.0	3.6	1.28	6.0
	δ	4.53	3.5	5.0	3.3	1.15	6.0
p-$CH_3C_6H_4$	α	4.40	3.2	8.0	3.5	1.23	6.0
	β	4.40	3.7	8.0	3.6	1.36	6.0
p-ClC_6H_4	α	4.30	3.2	8.0	3.4	1.26	6.0
	β	4.33	3.6	8.0	3.5	1.33	6.0
m-$CH_3C_6H_4$	α	4.43	3.3	8.4	3.5	1.23	6.0
	β	4.43	3.7	8.4	3.6	1.33	6.0

[a] In $CDCl_3$ at 60 MHz. Coupling constants are in hertz. Magnetic parameters were directly read from conveniently enlarged spectra.

Table II.[a] Absorption Frequencies for Free and Intramolecularly Associated Hydroxy Groups in 1,2-Diarylaminoethanols

Ar	isomer	ν_{OH} (free)	ν_{OH} (associated)	$\Delta\nu$
Ph[b]	α, β	3630	3450	180
	γ, δ	3630	3470	160
p-$CH_3C_6H_4$	α, β	3630	3450	180
p-ClC_6H_4	α, β	3620	3450	170
m-$CH_3C_6H_4$	α, β	3630	3450	180

[a] Measurements were carried out at 10^{-1}, 10^{-2}, and 10^{-3} M concentrations in CCl_4; the latter are shown. The range 3300–4000 cm^{-1} was scanned. Assignment of the bands was based on their change on dilution. For the 10^{-1} and 10^{-2} M solutions a Beckman spectrophotometer, Model 4240, was used. For the 10^{-3} M solutions a Perkin-Elmer 621 spectrophotometer provided with a variable-thickness cell was used. [b] Amino alcohols from reduction of optically active monoimines. The remaining amino alcohols were obtained by reduction of racemic monoimines.

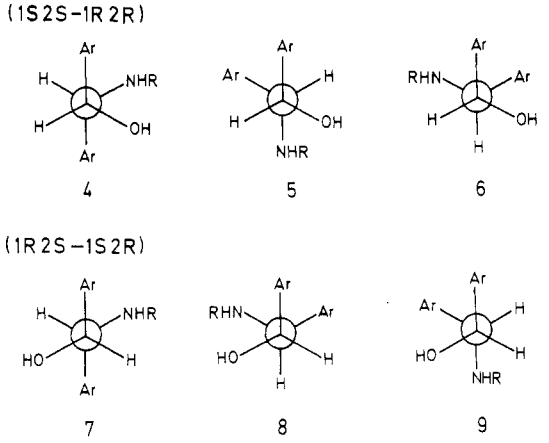
have three chiral centers and therefore can exist as eight stereoisomers, forming four racemates.

After separation of amino alcohols (see Experimental Section), the isomers were differentiated by their ^{1}H NMR spectral properties. We assign α and β labels to the two racemates obtained as major products in all one-step reductions and γ and δ labels to the two racemates obtained as minor products. The γ and δ isomers were the only products formed in the two-step sequence.

Table I summarizes the ^{1}H NMR data for the α and β racemates from the various monoimines and for the γ and δ racemates from monoimine 1 (Ar = Ph). For the assignment of configurations we will consider racemates α and β together on the one hand and racemates γ and δ on the other.[3]

In the 1,2-diphenylaminoethanol systems reported in the literature,[4] particularly those related to ephedrine and their

Scheme II



isomers,[5] a strong intramolecular association between amino and hydroxy groups has been detected by high-dilution infrared spectroscopy. Thus, this technique was applied to the amino alcohols reported in this paper (Table II). Since a high value of $\Delta\nu$ was observed[6] in every case, a high degree of intramolecular association exists to the extent observed in related systems.[4,5] For 1 (Ar = Ph) there is a difference of 20 cm^{-1} between the value of $\Delta\nu$ for isomers α and β on the one hand and γ and δ on the other, which is of the order found for 1,2-diphenylaminoethanol (25 cm^{-1}).[4c]

The conformational equilibrium is influenced by steric interactions and by the formation of intramolecular hydrogen bonds. Thus, in the *RR-SS* (threo) isomer the contribution of conformation **6** (Scheme II) will be minimal. For analogous tertiary amino compounds a conformer like **5** strongly predominates.[4a] However, in our series the RNH group is less sterically demanding than the R_2N group, which increases the proportion of 4 in the conformational equilibrium. The vicinal coupling constant of 8

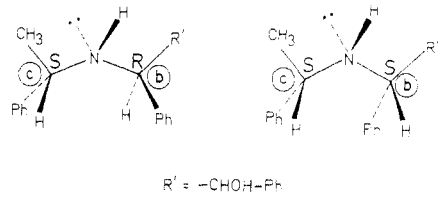
(3) As reported in the Experimental Section, γ and δ racemates obtained as minor products in the one-step reduction process were not isolated in the pure state. But NMR spectra of enriched mixtures allowed the determination of coupling constants ($J_{1,2}$) for all imines: Ar = p-$CH_3C_6H_4$, $J_{1,2}$ = 5.0 Hz; Ar = p-ClC_6H_4, $J_{1,2}$ = 4.0 Hz; Ar = m-$CH_3C_6H_4$, $J_{1,2}$ = 5.4 Hz.

(4) (a) M. E. Munk, M. K. Meilahn, and P. Franklin, *J. Org. Chem.*, **33**, 3481 (1968); (b) G. G. Lyle and M. L. Durand, *ibid.*, **32**, 3295 (1967); (c) G. Drefahl and G. Heubleim, *Chem. Ber.*, **94**, 915, 922 (1961); (d) M. K. Meilahn and M. E. Munk, *J. Org. Chem.*, **34**, 1440 (1969); (e) M. K. Meilahn, Ch. N. Statham, J. L. McManaman, and M. E. Munk, *ibid.*, **40**, 3551 (1975).

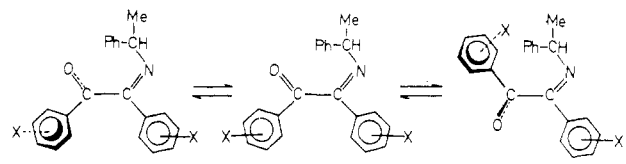
(5) (a) T. Kanzawa, *Bull. Chem. Soc. Jpn.*, **29**, 604 (1956), and references quoted therein; (b) P. S. Portoghese, *J. Med. Chem.*, **10**, 1057 (1967), and references quoted therein.

(6) For the value of $\Delta\nu$ as a measure of the strength of the intramolecular hydrogen bond, see, for instance, A., Chaband, M. Fetizou and M. Golfier, *Bull. Soc. Chim. Fr.*, 252 (1966), and references quoted therein.

Scheme III



Scheme IV



1-A 1-B

X	ΔG* (30°/acetone)
H	23.9 Kcal/mole
m-Me	24.1 "
m-Cl	23.5 "

Hz, rather than 10 Hz,[4a] for the threo isomers reflects on this and corresponds with the coupling of 8 Hz for the pseudoephedrine (threo) isomer.[5b]

In the *RS-SR* (erythro) isomer, conformation **7** will be minor because of the absence of intramolecular association. The vicinal coupling of 5 Hz agrees with the predominance of **8** and **9**.[4a,5b] From the above considerations and ample literature precedent,[4,5] the threo configuration (1*R*2*R*-1*S*2*S*) is assigned to diastereomers α and β and the erythro configuration (1*R*2*S*-1*S*2*R*) to diastereomers γ and δ.

We now consider the assignment of configuration to the three chiral centers in the four racemates from **1** (Ar = Ph). To simplify the problem we have synthesized the amino alcohols from optically active monoimine prepared from (*S*)-1-phenylethylamine. Assignments are based on the chemical shifts of the proton bonded to C-b (Table I). Intramolecular association (OH–NH) determines the preferred conformational arrangement of the compound. Careful examination of molecular models allows one to suggest that these arrangements, as far as the b and c chiral centers are concerned, are as shown in Scheme III.

We see from this that in the *RS* diastereomer the proton of chiral center b is inside the shielding cone of the aromatic group bonded to chiral center c and in the *SS* diastereomer this proton is on the deshielding cone of the phenyl group. From this we conclude that the β and γ diastereomers will have the *SS* configurations of the chiral centers b and c and the α and δ diastereomers the *RS* configuration.

Given the configuration of chiral centers a and b previously discussed and that of centers b and c, the absolute configurations were established as α = *RRS*, β = *SSS*, γ = *RSS*, and δ = *SRS*.

Discussion

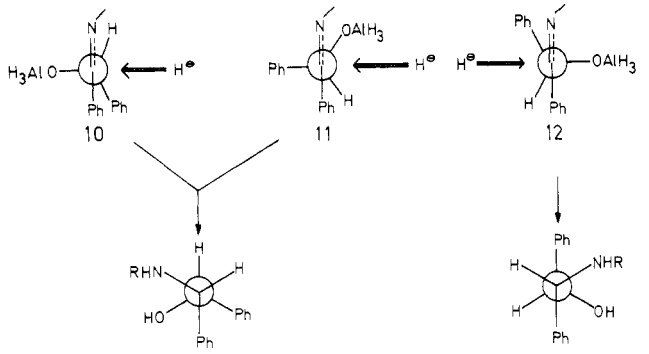
The stereochemistry of reduction of difunctional compounds with the general formula X = CRCR = Y has been studied by Stocker[7] in glyoxal derivatives. Of the various proposed models which could account for the stereochemical course of the reaction those based on the presence of polar groups, as Cornforth's[8] or Cram's[9,10] rigid model, are not valid. Thus, according to Stocker[7] the reduction of α-diketones and α-hydroxy ketones follows the same stereochemical course. The ratio of meso to *dl* glycols is the same whether we start with a particular benzil or with the related benzoin. This result seems to favor a two-step reduction with successive attack of the reagent on each of the carbonyl groups. For monoimines the situation should be roughly the same. Furthermore, in benzils the planes containing both benzoyl groups are nearly orthogonal and in monoimines the phenylimine and benzoyl groups also rest on nearly orthogonal planes.[2a,b] The simultaneous reduction of both functional groups is probably difficult due to the high free energy of activation, ΔG^*, which is needed to place these groups in a coplanar arrangement. This arrangement would allow simultaneous coordination of both groups with a reagent molecule. Through polarimetric measurements using an optically active amine in the phenylamine residue values of ΔG^* for the rotation process **1A** → **1B** (Scheme IV) have been obtained. If the transition state for rotation is planar with the C=O and C=N groups in a syn arrangement, the values of ΔG^* are a measure of the energy barrier for rotation around the O=C—C=N bond.[2c,d] These values are always larger than 83.6 kJ/mol (20 kcal/mol), a value which in turn is much higher than the activation energies found for LAH reductions.[1]

The simultaneous reduction is definitely ruled out for the following reasons. When monoimines derived from benzil and benzhydrylamine[1] and benzil and benzylamine[12] are reduced with LAH, a fairly high stereoselectivity is obtained. Neither rigid nor dipolar models will predict any stereoselectivity in these cases. Two step-by-step reductions come into consideration: (a) a previous reduction of the keto group with intermediate formation of an α-imino alkoxide and (b) a previous reduction of the imino group, yielding an α-amino ketone as intermediate. Independent synthesis of these intermediates followed by their reduction with LAH will allow a choice between both possibilities. Experiments on the synthesis of imino alcohols have up to now failed, but we have successfully prepared the amino ketone by catalytic hydrogenation of the monoimine (Scheme I). The amino ketone is fairly unstable, reverting to the starting monoimine either by standing at room temperature or by silica gel chromatography. However, the hydrochloride could be quantitatively isolated by bubbling anhydrous hydrogen chloride through an ether solution of recently prepared amino ketone. From the stable hydrochloride pure amino ketone was recovered quantitatively by treatment with alkali. When pure amino ketone was reduced by LAH in ether at room temperature, a mixture containing only γ and δ diastereomers (1*R*2*S*-1*S*2*R*) was obtained. This stereochemical result, the opposite to that of the one-step reduction, showed that the imino alcohol is the first product in the direct reduction of monoimine with LAH.

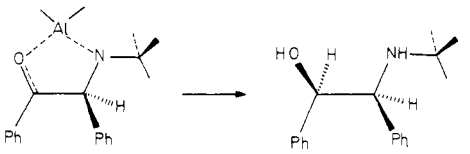
The monoimines of 1,2-dicarbonyl compounds are ambident electrophiles with the carbonyl and imino groups

(7) H. Stocker, *J. Org. Chem.*, **29**, 3593 (1964).
(8) J. W. Cornforth, R. M. Cornforth, and K. K. Mathews, *J. Chem. Soc.*, 112 (1959).
(9) D. J. Cram and K. R. Kopecky, *J. Am. Chem. Soc.*, **81**, 2748 (1959).
(10) For several considerations about these two models, see N. Trong Ahn and O. Eisenstein, *Nouv. J. Chem.* 1, 61 (1977).
(11) H. C. Brown and S. Krishnamurthy, *Tetrahedron*, **35**, 567 (1979), and references quoted therein.
(12) In the lithium aluminum hydride reduction of the monoimine prepared from benzil and benzylamine the observed stereoselectivity was *RR,SS/SR,SR* = 2.0 (unpublished results).
(13) Catalytic hydrogenation of an imino group in the presence of a carbonyl group may be similar to the reported catalytic hydrogenation of oximino ketones to the corresponding amino ketones. (a) W. H. Hartung, *J. Am. Chem. Soc.*, **53**, 2248 (1931); (b) T. Matsumoto, T. Nishida, and H. Shirama, *J. Org. Chem.*, **27**, 79 (1962).

Scheme V



Scheme VI



as two reactive sites. These groups may be considered as isolated electrophilic entities due to the near orthogonality between benzoyl and phenylimino groups. In the LAH reduction hydride is transferred preferentially to the carbonyl group, whereas in the catalytic hydrogenation a hydrogen atom is transferred to the imino group.

Catalytic hydrogenation of the monoimine derived from benzil and 1-phenylethylamine yields a nearly 1:1 mixture of the two diastereomeric amino ketones. Interpretation of this stereochemical result should be postponed until results for other substrates are available.

The stereochemical results of direct reduction with LAH, accepting the previous nonstereoselective reduction of the carbonyl group,[14] may be accounted for by application of Pérez-Ossorio's model.[15] This model, related to that of Karabatsos,[16] which has been applied to the LAH reductions and Grignard condensations of carbonyl compounds,[17] is used here only qualtitatively.

According to Pérez-Ossorio model the transition states to be considered for reaction of an imino alkoxide are those derived from conformations **10**–**12** (Scheme V). Attack at the less hindered sides of **10** and **11** yields the minor diastereomer and at **12** yields the major diastereomer. This result may be explained since conformation **10** will be very unstable due to crowding and **11** will be less stable than **12** due to the large interaction $(OAlH_3—N=)_{1,2}$[e] present in **11**.

The Felkin model[18] may also be used. Since $OAlH_3$ is the bulkiest group in the alkoxide, the transition states to be considered are those related to **10** and **12** that yield (Scheme V), respectively, the minor and major diastereomers. Transition state **12** will be the most stable since according to Karabatsos[19] differences of eclipsing energies (=NPh)–(=NH) are on the order of 700 cal/mol and differences in the eclipsing energies (PhPh)–(PhH) should be much higher. This reasoning should be valid, although wholly eclipsed interactions are not operative.

Finally, the stereochemical results for the reduction of amino ketone with lithium aluminum hydride can be explained, as in many related cases,[14a] by application of Cram's rigid model (Scheme VI). The five-membered-ring conformation yields the most stable transition state by attack by hydride at the least hindered side of the carbonyl group, affording the diastereomer experimentally obtained.

Table III

fraction	wt, mg	amino alcohols, %	major isomers, %
A	100	100	100 (β)
B	300	89[a,b]	75[a] (β)
C	300	84[a,b]	95[a] (α)
D	100	100	100 (α)

[a] Determined by NMR integration. [b] Impurity in amino alcohols was *p*-methylbenzyl alcohol, formed by hydrogenolysis of the benzyl bond. Yield of amino alcohol (isomer mixture) was 720 mg (83%). Estimated ratio of major isomers mixture/minor isomers mixture ≃ 8. Anal. Calcd for $C_{24}H_{27}NO$: C, 83.47; H, 7.82; N, 4.05. Found for fraction A: C, 83.01; H, 7.69; N, 4.12. Found for fraction D: C, 83.36; H, 7.91; N, 4.16.

Table IV

fraction	wt, mg	amino alcohols, %	major isomers, %
A	160	100	82[a] (β)
B	200	72[a,b]	78[a] (β)
C	200	100	100 (α + β)
D	100	100	100 (α + β)
E	160	100	100 (α)

[a] Determined by NMR integration. [b] Impurity in amino alcohol was *m*-methylbenzyl alcohol. Yield of amino alcohol (diastereomer mixture) was 760 mg (89%). Estimated ratio of major isomers mixture/minor isomer mixture ≃ 11.6. Anal. Calcd for $C_{24}H_{27}NO$: C, 83.47; H, 7.82; N, 4.05. Found for fraction A: C, 83.61; H, 8.01; N, 4.00. Found for fraction E: C, 83.66; H, 7.99; N, 4.21.

Experimental Section

Melting points are uncorrected. ^1H NMR spectra were recorded with a Varian T 60-A apparatus. Optical rotations were taken on a Perkin-Elmer Model 141 polarimeter. Monoimines were synthesized from the related benzils and 1-phenylethylamine.[2]

Amino alcohols were prepared by reaction of monoimines with excess LAH at room temperature for 12–17 h in yields of 83–94%. After reaction, the mixture was hydrolyzed, the ether layer decanted, and the aqueous layer extracted with ether. Dried ether extracts were concentrated and the resulting crude reaction mixtures treated as described below.

Separation of Diastereomeric Amino Alcohols. *N*-(1-Phenylethyl)-1,2-diphenyl-2-aminoethanol (2). From 8.98 g of crude reaction product, by repeated crystallizations from *n*-heptane, was isolated 180 mg of the γ isomer: mp 134–135 °C; $[\alpha]^{30}_{476}$ 38.68° (*c* 0.568, $CHCl_3$). Anal. Calcd for $C_{22}H_{23}NO$: C,

(14) The absence of asymmetric induction in this reduction process is expected. It is a 1,4 induction in the presence of one heteroatom in position 3, and it is known that most 1,3 induction processes lack appreciable stereoselectivity. (a) J. D. Morrison and H. S. Mosher, "Asymmetric Organic Reactions", Prentice Hall, New York, 1971; (b) F. Fernández González and R. Pérez-Ossorio, *An. Quim.*, **69**, 101 (1973); (c) C. Alvarez Ibarra, F. Fernández González, and R. Pérez-Ossorio, *ibid.*, **71**, 412 (1975).

(15) F. Fernández González and R. Pérez-Ossorio, *An. Quim.*, **68**, 1411 (1972).

(16) G. J. Karabatsos, *J. Am. Chem. Soc.*, **89**, 1367 (1967).

(17) (a) C. Alvarez Ibarra, F. Fernández González, A. García-Martínez, R. Pérez-Ossorio, and M. L. Quiroga, *Tetrahedron Lett.*, 2715 (1973); (b) F. Fernández González, R. Pérez-Ossorio, and M. L. Quiroga, *An. Quim.*, **70**, 536 (1974); (c) F. Fernandez González, R. Pérez-Ossorio, and J. Plumet, *ibid.*, **71**, 208 (1975); (d) C. Alvarez Ibarra, A. I. Blanch, F. Fernández González, A. García Martínez, R. Pérez-Ossorio, J. Plumet, and M. L. Quiroga, *Rev. R. Acad. Cienc.*, 233 (1975); (e) J. A. Cereceda, R. Pérez-Ossorio, and M. L. Quiroga, *An. Quim.*, **75**, 349 (1979).

(18) M. Cherest, H. Felkin, and N. Prudent, *Tetrahedron Lett.*, 220 (1968).

(19) G. J. Karabatsos and D. J. Fenoglio, *Top. Stereochem.*, **5**, 167 (1970).

Table V

fraction	wt, mg	amino alcohols, %	major isomers, %
A	200	100	100 (β)
B	260	100	86[a] ($\alpha + \beta$)
C	300	70[a,b]	80[a] ($\alpha + \beta$)
D	190	80[a,b]	100 ($\alpha + \beta$)
E	210	100	100 ($\alpha + \beta$)
F	320	100	100 (α)

[a] Determined by NMR integration. [b] Impurity accompanying the amino alcohol was characterized as *p*-chlorobenzyl alcohol. Yield of amino alcohol (diastereomer mixture) was 1350 mg (85%). Estimated ratio of isomers mixture/minor isomers mixture ≃ 12. Anal. Calcd for $C_{22}H_{21}NOCl_2$: C, 68.39; H, 5.44; N, 3.63; Cl, 18.39. Found for fraction A: C, 67.99; H, 5.61; N, 3.71; Cl, 18.54. Found for fraction F: C, 68.19; H, 5.62; N, 3.70; Cl, 18.51.

83.28; H, 7.25; N, 4.41. Found: C, 83.33; H, 7.53; N, 4.68.

Mother liquor (4.11 g) containing the α and β isomers was chromatographed over silica gel (30 g of gel/g of product); benzene–ether mixtures were used as eluant, starting with a 12:1 mixture and ending with a 2.8:1 mixture. The β isomer (720 mg) was first isolated as an oil which could not be crystallized, $[\alpha]^{30}_{476}$ 91.21° (*c* 1.821, $CHCl_3$). Anal. Found: C, 83.41; H, 7.15; N, 4.36. After several intermediate fractions the α isomer (1261 mg) was isolated as an oil, $[\alpha]^{30}_{476}$ 115.1° (*c* 2.137, $CHCl_3$). Anal. Found: C, 83.15; H, 7.46; N, 4.80.

When one started with racemic monoimine, through fractional crystallization from *n*-heptane the mixture of minor isomers (mp 124–125 °C, correct analysis) could be separated from that of major isomers, which in this case was crystalline (mp 116–118°, correct analysis).

***N*-(1-Phenylethyl)-1,2-di-*p*-tolyl-2-aminoethanol (2).** The crude reaction mixture (820 mg) was purified by chromatography over silica gel, using a 9:1 benzene–ether mixture as eluant. The composition of the oily fractions obtained is indicated in Table III.

***N*-(1-Phenylethyl)-1,2-di-*m*-tolyl-2-aminoethanol (2).** The crude reaction mixture (810 mg) was chromatographed over silica gel with a 9:1 benzene–ether mixture as eluant. The composition of the oily fractions obtained is indicated in Table IV.

***N*-(1-Phenylethyl)-1,2-bis(*p*-chlorophenyl)-2-aminoethanol (2).** The crude reaction mixture (1.49 g) was chromatographed over silica gel with a benzene–ether (9:1) mixture as eluant. The fractions shown in Table V were separated as oils.

***N*-(Phenylethyl)-1-phenyl-1-benzoylmethylamine (3).** The monoimine prepared from benzil and (±)-1-phenylethylamine (2.00 g, 6.40 mmol) was catalytically hydrogenated in ethyl acetate (200 mL) with 5% Pd/C (0.3 g). The initial pressure of 27 psi became stabilized at 16 psi in 1 h. Catalyst was filtered off, solvent was evaporated at reduced pressure, and an oil (2.00 g) was left; this was identified as the amino ketone by spectroscopic data: crude yield 100%; IR (oil) 3340 (NH), 1680 (C=O) cm^{-1}; NMR ($CDCl_3$) 1.32 and 1.40 (2 d, J = 6.0 Hz, CH_3CH), 3.06 (s, NH), 3.40 and 3.68 (2 q, J = 6.0 Hz, $CHCH_3$), 5.02 (br s, PhCH(CO)NH), 6.7–7.4 (m, aromatic protons). The product appears to be a mixture of the two diastereomers in a ratio of roughly 1:1 (estimated from the quartets ($CHCH_3$) on an enlarged spectrum).

***N*-(1-Phenylethyl)-1-phenyl-1-benzoylmethylamine Hydrochloride (3·HCl).** Dry hydrogen chloride was bubbled through an ether solution of recently prepared amino ketone (2.00 g, 6.35 mmol); a white precipitate quickly settled. After filtration and washing with ether, the hydrochloride (2.00 g, 5.69 mmol) separated as a white solid which was recrystallized from ethanol: mp 204–207 °C dec; yield 90%; IR (KBr) 2700 (NH_2^+), 1680 (C=O) cm^{-1}; NMR (Me_2SO-d_6) 1.66 (d, CH_3CH), 4.23 (q, $CHCH_3$), 6.13 (br s, CH(CO)Ph), 7.06–8.03 (m, aromatic protons), 10.5 (br, NH_2^+). Anal. Calcd for $C_{22}H_{22}NOCl$: C, 75.11; H, 6.26; N, 3.98; Cl, 10.10. Found: C, 75.02; H, 6.39; N, 4.07; Cl, 9.89.

The hydrochloride (1.00 g, 2.84 mmol) dissolved in methanol was treated with a 1 M solution of sodium hydroxide. After extraction with ether, the ether solution was dried over magnesium sulfate and the solvent evaporated; 0.80 g (2.54 mmol) of amino ketone was isolated (yield 90%). No appreciable increase in a particular diastereomer was observed.

LAH Reduction of 3. To LAH (0.12 g, 3.16 mmol) in anhydrous ether was slowly added an ether solution of amino ketone (0.82 g; 2.60 mmol) with stirring. The reaction mixture, after standing at room temperature of 4 h, was hydrolyzed. After ether extraction, drying of the ether extracts, and elimination of solvent, *N*-(1-phenylethyl)-1,2-diphenyl-2-aminoethanol separated (0.75 g, 2.36 mmol) as a yellow oil (yield 88%).

From the NMR spectrum the presence of two diastereomers roughly in a 1:1 ratio was deduced. They were identified as the γ and δ isomers of the amino alcohol. Separation was carried out by silica gel chromatography, using a 9:1 mixture of benzene–ether as eluant; the γ diastereomer was eluted first. The δ diastereomer separated as a colorless oil which could not be crystallized. Anal. Calcd for $C_{22}H_{23}NO$ (δ diastereomer): C, 83.28; H, 7.25; N, 4.41. Found: C, 83.01; H, 7.24; N, 4.62.

Registry No. (*RRS*)-**2** (Ar = Ph), 77789-90-3; (*SSS*)-**2** (Ar = Ph), 77789-91-4; (*RSS*)-**2** (Ar = Ph), 77789-92-5; (*RRS-SSR*)-**2** (Ar = Ph), 77789-93-6; (*SSS-RRR*)-**2** (Ar = Ph), 77789-94-7; (*RSS-SRR*)-**2** (Ar = Ph), 77789-95-8; (*SRS-RSR*)-**2** (Ar = Ph), 77789-96-9; (*RRS-SSR*)-**2** (Ar = *p*-$CH_3C_6H_4$), 77727-44-7; (*SSS-RRR*)-**2** (Ar = *p*-$CH_3C_6H_4$), 77789-97-0; (*RRS-SSR*)-**2** (Ar = *m*-$CH_3C_6H_4$), 77789-98-1; (*SSS-RRR*)-**2** (Ar = *m*-$CH_3C_6H_4$), 77789-99-2; (*RRS-SSR*)-**2** (Ar = *p*-ClC_6H_4), 77727-45-8; (*SSS-RRR*)-**2** (Ar = *p*-ClC_6H_4), 77790-00-2; (*RR-SS*)-**3** (Ar = Ph), 77727-46-9; (*RS-SR*)-**3** (Ar = Ph), 77727-47-0; (*RR-SS*)-**3**·HCl (Ar = Ph), 77727-48-1; (*RS-SR*)-**3**·HCl (Ar = Ph), 77727-49-2.