Stereochemistry of Imino-group Reduction. Part 6.[1] Stereochemistry of Reduction of 1,2-Imino Ketones having a Pre-existing Chiral Centre. Synthesis of Amino Alcohols with Three Chiral Centres

Benito Alcaide, Gema Dominguez, Carmen López-Mardomingo, Rafael Pérez-Ossorio,* and Joaquín Plumet
Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Complutense, 28040 Madrid, Spain

Stereochemical results of the lithium aluminium hydride and sodium borohydride reduction of 1,2-imino ketones, PhCOCPh=NCHRPh (R = Me, Et, Pr, Bu, Bu^i, Pr^i, Bu^t), are reported. The stereoselectivity is accounted for by competition between two possible reactions: that proceeding through previous reduction of the carbonyl group and that involving previous reduction of the imino group. The relative involvement of both reaction routes depends upon the nature of the reagent and the relative hard–soft character of both functional groups in the imino ketones. The influence of steric effects of the R groups is discussed.

We have previously reported the lithium aluminium hydride (LAH) reduction of 1,2-imino ketones, ArCOCAr=NR, affording 1,2-amino alcohols, ArCHOHCHArNHR. Our previous papers include a preliminary account of the results obtained when R is a chiral α-phenylalkyl group,[2] a stereochemical study of the reduction of *N*-(1-phenethyl)-substituted imino ketones, ArCOCAr–NCHMePh,[3] and an extension of this study to achiral benzil monoimines, PhCOCPh=NR.[4] In the latter case we have also considered the reduction with sodium borohydride.

We now report the streochemical result of the reduction with both LAH and $NaBH_4$ of benzyl monoimines, PhCOCPh=NCHRPh. The stereochemical influence of the *N*-alkyl group in the reduction process is thus analysed. The amino alcohols obtained [(**1**)–(**7**)] have three chiral centres and can exist as

$$\overset{1}{\text{Ph}}\text{–}\overset{2}{\text{CHOH}}\text{–}\overset{3}{\text{CHPh}}\text{–NH–CHRPh}$$

(**1**) R = Me (**4**) R = Bu (**6**) R = Pr^i
(**2**) R = Et (**5**) R = Bu^i (**7**) R = Bu^t
(**3**) R = Pr

eight stereoisomers forming four racemates. Configurational assignment of these stereoisomers has been accomplished by analysis of spectral data and is reported elsewhere.[5]

LAH Reduction of Benzil Monoimines.—The proportions of isomers obtained in the reduction processes are shown in Table 1.

The observed changes in stereoselectivity seem to depend on the relative operation of the reaction routes 1 and 2 (Scheme 1)[3,4] involving, respectively, previous reduction of the carbonyl group (with formation of the related imino alkoxide) and previous reduction of the imino group (with formation of amino ketone).

When the stereoisomeric amino ketones obtained by reduction of the imino ketones are in turn reduced with LAH a 1:1 mixture of the amino alcohols (1*S*,2*R*,3*R*/1*R*,2*S*,3*S*) and (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) results. These isomers are the minor products in the direct LAH reduction of imino ketones. On the other hand, in this direct reduction, whatever the nature of the R group, the major products have the configuration (*RR*/*SS*) in the chiral centres 1 and 2 created in the reduction process. A small proportion, lower than 10%, of isomers having the (*RS*/*SR*) configuration in positions 1 and 2 is obtained. From all this it may be concluded that route 2 would yield exclusively the isomers (1*S*,2*R*,3*R*/1*R*,2*S*,3*S*) and (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*).

In this latter case, Cram's cyclic model can account for the stereochemistry of the reduction of amino ketones to the related amino alcohols (Scheme 1). The carbonyl group will be attacked at the less hindered side in (**III**) and (**IV**). This will be decided by the stereochemistry of C-2 since the chiral centre C-3 is too far away to have any particular influence on the attack. On the other hand, considerations based upon the orbital control of this type of reduction,[4,7] as well as experimental data,[6] seem to indicate that reduction of the carbonyl group precedes that of the imino group when LAH in ether is used as reducing agent. This means that route 1 is favoured over 2, leading to the intermediate species (**I**) and (**II**). The stereochemical course of the reduction of these imino alkoxides can be predicted by application of Pérez-Ossorio and Felkin models as already reported.[3,4] Reagent attack would take place at the less hindered side, that opposed to the alkoxide residue. Apart from the influence of C-1, some additional influence of C-3 cannot be disregarded. Attack on (**I**) and (**II**) in the opposite direction to the one indicated in Scheme 1 would lead to amino alcohols with (1*R*,2*S*/1*S*,2*R*) configurations, *i.e.* to the isomers obtained as minor products in the reduction processes.

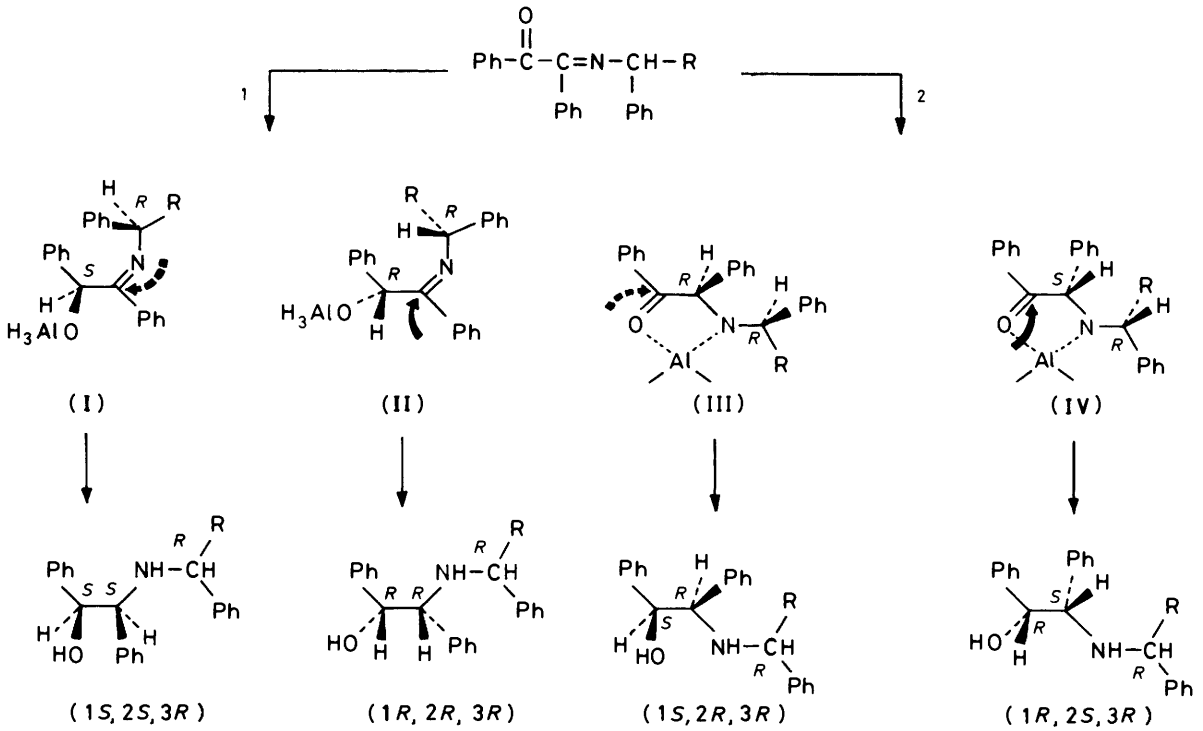
The difference in the percentage of major amino alcohols

Table 1. Isomer proportions[a] in the LAH reduction of benzil monoimines, PhCOCPh=NCHRPh

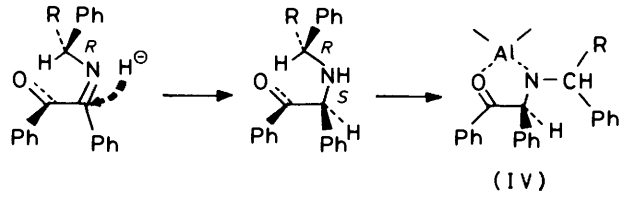
Compound	(1*R*,2*R*,3*R*/1*S*,2*S*,3*S*)	(1*R*,2*R*,3*S*/1*S*,2*S*,3*R*)	(1*R*,2*S*,3*S*/1*S*,2*R*,3*R*)	(1*R*,2*S*,3*R*/1*S*,2*R*,3*S*)
(**1**)	25	65	7	3
(**2**)	36	55	5	4
(**3**)	51	40	9	0
(**4**)	20	72	8	0
(**5**)	30	67	3	0
(**6**)	47	45	8	0
(**7**)	58	42	0	0

[a] Reaction products were separated by chromatography and ^{1}H n.m.r. spectra of the fractions were taken. Integration allowed us to deduce the percentage of the various isomers. The estimated error so introduced is of 5—8%. Attempted complete chromatographic separation (g.l.c. and t.l.c.) failed.

† Reduction of α-imino ketones with H_2–Pd–C, LAH–Pyridine, or $LiAl(OBu^t)_3H$–THF yields the related amino ketones.[6]



Scheme 1.



Scheme 2.

seems to be due neither to the formation of one of them through route 2 nor to the reduction of intermediate alkoxides (I) or (II) at the more hindered side (Scheme 1) as already mentioned.

Some influence of the chiral centre C-3 in the reduction of the carbonyl group, leading to unequal percentages of (I) and (II), seems more probable. Due to the *anti*-phenyl configuration of the *N*-alkyl group, C-3 lies not far from the carbonyl group. In any case, differences in the percentages of (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) and (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) isomers are difficult to rationalize. However, it is observed that the ratio (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*):(1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) decreases on the whole on increase in the size of the alkyl group in the series (**1**), (**2**), (**6**), and (**7**).

The data in Table 1 show that the amino alcohol (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) is formed in very small proportion, if at all. This may have its origin in the reduction of imino group through route 2. From the structure of these imino ketones[8] it may be inferred that the most favourable conformational arrangement of the groups attacked to C-3 is that shown in Scheme 2, with the smallest group close to the benzoyl group. Then attack at the side shown would be made more difficult by a bulky group R. It is this attack that yields the intermediate (**IV**) which in turn affords the (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) isomer. This isomer is only obtained, and in very small amounts, when R is Me or Et.

Table 2. Comparison of stereochemical results[a] for reduction of benzil monoimines, PhCOCPh=NCHRPh, with LAH and $NaBH_4$

	$NaBH_4$–EtOH		LAH–Et_2O	
Compd.	(1*R*,2*R*/1*S*,2*S*)	(1*R*,2*S*/1*S*,2*R*)	(1*R*,2*R*/1*S*,2*S*)	(1*R*,2*S*/1*S*,2*R*)
(**1**)	50	50	90	10
(**2**)	43	57	91	9
(**3**)	26	74	91	9
(**4**)	28	72	92	8
(**5**)	31	69	97	3
(**6**)	21	79	92	8
(**7**)	8	92	100	0

[a] Results are given in percentages and refer to chiral centres C-1 and C-2. Thus the percentage of (1*R*,2*R*/1*S*,2*S*) isomers includes the (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) and (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) isomers and that of (1*R*,2*S*/1*S*,2*R*) the (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) and (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) isomers.

In summary, it is proposed that the major isomers, which are formed in proportions of from 90 to 100% (Table 1), result only from the previous reduction of the carbonyl group (route 1).

Although the relative hard–soft character of the carbonyl and imino groups is considered to be the major factor in deciding the regioselectivity of the reduction process,[6] the steric effect introduced by the R group may have an additional influence by retarding the reduction of the imino group. Thus, increasing the bulk of R would decrease the possibility of reduction of the imino group and increase the regioselectivity of the process in favour of the imino alkoxides (**I**) and (**II**).

$NaBH_4$ *Reduction of Benzil Monoimines.*—Stereochemical results are collected in Table 2 in which a summary of those gathered in Table 1 is included for comparison.

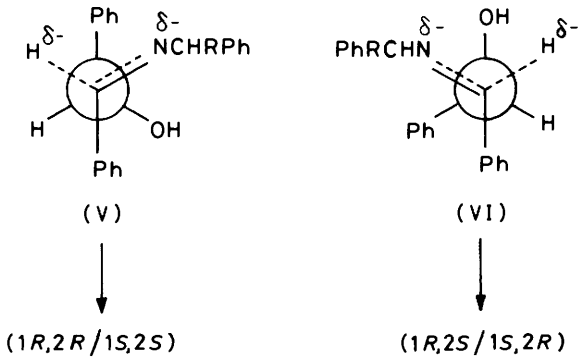
The data in Table 2 show that the regioselectivity of reduction is lower when $NaBH_4$ is used as the reagent. The relative hardness–softness of both reagents can account for these results;

$NaBH_4$ is less selective in its attacks on the carbonyl and imino groups.

It has been observed qualitatively that with $NaBH_4$ the reduction rate is very sensitive to the steric effects originating in the R group. The amount of the imino ketone reduced decreases on increasing the bulk of R (see Experimental section). On the other hand, when reduction is slow enough, samples isolated at various reaction times show the presence of amino ketone together with other products produced by hydrogenolysis. This shows that the amino ketone is an intermediate in the reduction process.[6] It has been reported[9] that $NaBH_4$ reductions of previously isolated amino ketones yield exclusively amino alcohols of (1*R*,2*S*/1*S*,2*R*) configuration. The two possible isomers are obtained in equimolecular amounts. Thus, it seems that (1*R*,2*R*/1*S*,2*S*) alcohols are formed exclusively, by reduction of the carbonyl group.

It can also be seen that on increasing the bulk of R, the ratio (1*R*,2*S*/1*S*,2*R*):(1*R*,2*R*/1*S*,2*S*) increases. This rather unexpected result cannot be explained by increased attack on the imino group, since in that case the opposite result would be obtained. Thus, a course of reaction similar to 1 (Scheme 1) should be responsible for the increasing proportion of the (1*R*,2*S*/1*S*,2*R*) isomers on increasing the bulk of R. This requires a transition state for the $NaBH_4$ reduction of imino alcohols which differs from that accepted for the LAH reduction.

As already reported,[4] we propose that amino alcohols are the final products, and that the transition states are product-like, in the $NaBH_4$ reduction.[10] Competition between intramolecularly associated intermediates (**V**) and (**VI**) (Scheme 3) would be responsible for the observed results. It may tentatively be supposed that, the NCHRPh group being more hindered in (**V**) than in (**VI**), an increase in the bulk of R would favour the latter, increasing the amount of the (1*R*,2*S*/1*S*,2*R*) isomers. Route 2 might also contribute to the observed results.



Scheme 3.

Experimental

M.p.s are not corrected. I.r. and ^1H n.m.r. spectra were obtained under the conditions already reported.[5]

Benzil Monoimines.—The synthesis and physical and spectroscopic characteristics of imino ketones (**1**), (**2**), (**6**), and (**7**) have already been reported.[8b] The remaining imino ketones were synthesized by the same general procedure. Equimolecular amounts of benzil and the appropriate amine were refluxed in toluene in the presence of a small amount of $ZnCl_2$–1-phenethylamine complex as catalyst; a Dean–Stark device was used to separate the water formed. 1-Phenethylamine was commercial; the remaining amines were prepared by the Leuckart reaction. Experimental conditions and analytical data are shown in Table 3.

N-(1-*Phenylalkyl*)-*substituted* 1,2-*Diphenyl*-2-*aminoethanols.*—The synthesis and isomer separation of amino alcohols when R = Me have already been reported.[3] In the remaining cases isomer isolation was carried out either from the reaction product of the LAH reduction of imino ketones or through the two-step sequence: catalytic hydrogenation of imino ketone to amino ketone[11] followed by reduction of the latter either with LAH or $NaBH_4$.[9]

LAH Reduction of Benzil Monoimines: General Procedure.—A 0.02M solution of imino ketone in ether was added slowly to a suspension of LAH in ether (molar ratio LAH:imino ketone 2:1) at 0 °C with stirring. Reduction occurred instantaneously. After hydrolysis with the minimum amount of water, aluminium salts were filtered off and the ether solution was dried ($MgSO_4$). The usual work-up yielded an oily mixture of diastereoisomeric amino alcohols. From this, isomers (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) and (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) were separated by the method reported below. I.r. and ^1H n.m.r. data have been reported elsewhere.[5]

The following compounds were obtained in this way:

N-(1-*Phenylpropyl*)-1,2-*diphenyl*-2-*aminoethanol* (**2**). The product (1 740 mg) was chromatographed on silica gel, using benzene as eluant. Analysis of the various fractions gave: (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) isomer, 529 mg; (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) isomer, 73 mg; (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) isomer, 59 mg; (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) isomer, 809 mg. Isomers are quoted in order of elution; the former and latter of them were isolated as pure products. (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) Isomer (Found: C, 83.4, H, 7.5; N, 4.3%). (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) Isomer (Found: C, 83.4; H, 7.5; N, 4.3. $C_{23}H_{25}NO$ requires C, 83.4; H, 7.55; N, 4.2%).

Table 3. Preparation and characterization of benzil monoimines, PhCOCPh=NCHRPh

R	Benzil (mmol)	Amine (mmol)	Toluene (ml)	*t* (h)	Yield[a] (%)	m.p.[b]/°C	$\nu_{max.}$[c] C=O	$\nu_{max.}$[c] C=N		Analysis (%) Calc.	Analysis (%) Found
Pr	40.0	40.0	100	21	69	64—65	1 662	1 625	C	84.5	84.4
									H	6.7	6.7
									N	4.1	4.1
Bu	28.0	28.0	60	18	63	68—70	1 665	1 625	C	84.5	84.45
									H	7.0	7.1
									N	3.9	4.0
Bu[i]	26.0	26.0	60	22	61	*d*	1 672	1 625	C	84.5	84.6
									H	7.0	7.1
									N	3.9	4.1

[a] Of pure product with correct analysis. [b] Crystallization from methanol or ethanol. [c] In KBr. [d] This imine failed to crystallize; it was purified by silica gel chromatography using benzene as eluant.

N-(1-*Phenylbutyl*)-1,2-*diphenyl*-2-*aminoethanol* (**3**). The product was treated as before (760 mg). Isomer (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) was eluted first as pure product (388 mg). Isomers (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) (72 mg) and (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) (288 mg) could not be completely separated from each other. (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) Isomer (Found: C, 83.6; H, 8.05; N, 3.9%). For (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) (containing 1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) (Found: C, 83.6; H, 8.1; N, 4.0. $C_{24}H_{27}NO$ requires C, 83.4; H, 7.8; N, 4.1%).

N-(1-*Phenylpentyl*)-1,2-*diphenyl*-2-*aminoethanol* (**4**). Separation of isomers was carried out as before from 1 320 mg of reaction product. Isomer (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) was eluted first as pure product (250 mg). Analysis of the remaining fractions gave (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) isomer (100 mg) and (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) isomer (900 mg). The latter was also obtained in pure conditon from the later elution fractions. (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) Isomer (Found: C, 83.6; H, 8.1; N, 3.95%). (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) Isomer (Found: C, 83.5; H, 8.1; N, 4.0. $C_{25}H_{29}NO$ requires C, 83.6; H, 8.1; N, 3.9%).

N-(1-*Phenyl*-3-*methylbutyl*)-1,2-*diphenyl*-2-*aminoethanol* (**5**). The product (1 830 mg) was worked up as in the remaining cases. Analysis of the various isomers gave (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) isomer (549 mg); (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) isomer (55 mg); (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) isomer (1 226 mg). Isomers are quoted in order of elution; the first and last were obtained in pure condition. (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) Isomer (Found: C, 83.5; H, 8.1; N, 3.9%). (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) Isomer (Found: 83.6; H, 8.0; N, 3.95. $C_{25}H_{29}NO$ requires C, 83.6; H, 8.1; N, 3.9%).

N-(1-*Phenyl*-2-*methylpropyl*)-1,2-*diphenyl*-2-*aminoethanol* (**6**). The product (655 mg) was worked up as before. The order of elution and isomer composition were (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) (308 mg); (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) (52 mg); (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) (295 mg). Analysis of the isolated isomers as pure products: (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) Isomer (Found: C, 83.5; H, 7.9: N, 4.0%). (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) Isomer (Found: C, 83.4; H, 7.7; N, 4.1. $C_{24}H_{27}NO$ requires C, 83.5; H, 7.8; N, 4.1%).

N-(1-*Phenyl*-2,2-*dimethylpropyl*)-1,2-*diphenyl*-2-*aminoethanol* (**7**). From the reaction product (700 mg) only the isomers (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) (42%) and (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) (58%) were isolated, the latter being eluted first. (1*R*,2*R*,3*S*/1*S*,2*S*,3*R*) Isomer (Found: C, 83.6; H, 8.1; N, 3.9%). (1*R*,2*R*,3*R*/1*S*,2*S*,3*S*) Isomer (Found: C, 83.5; H, 8.2; N, 3.9. $C_{25}H_{29}NO$ requires C, 83.6; H, 8.1; N, 3.9%).

Catalytic Hydrogenation of Imino Ketones.—The reported procedure[11] was used. Experimental data are given in Table 4 and physical and spectroscopic data for the related newly reported amino ketones (**3**)—(**5**) are gathered in Table 5.

LAH Reduction of α-Amino Ketones.—A 0.02M solution of the amino ketone in anhydrous ether was added slowly to a suspension of LAH in ether (molar ratio LAH:amino ketone 1:1) at 0 °C with stirring. Reduction occurred instantaneously. The product was worked up as in the case of imino ketones and an oil was isolated. It was characterized as a mixture of (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) and (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) isomers.

LAH Reduction of N-(1-*Phenylpropyl*)-2-*aminodeoxybenzoin.*—The product (710 mg) was crystallized from hexane. A crystalline mixture of (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) and (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) isomers in proportions close to 1:1 was obtained. Isomer separation was performed by column chromatography of the crystalline mixture (460 mg) over silica gel (35 g) using benzene–ether (98:2) as eluant. The (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) isomer was eluted first. The amino alcohols were crystallized from hexane. (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) Isomer: needles, m.p. 97—98 °C (Found: C, 83.3; H, 7.5; N, 4.3. $C_{23}H_{25}NO$ requires C, 83.4; H, 7.55; N, 4.2%). (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) Isomer: cubic crystals, m.p. 118—119 °C (Found: C, 83.3; H, 7.5; N, 4.2%).

LAH Reduction of N-(1-*Phenylbutyl*)-2-*aminodeoxybenzoin.*—The (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) isomer was directly isolated by crystallization of the product in hexane: m.p. 112—114 °C. The (1*S*,2*R*,3*S*/1*R*,2*S*,3*R*) isomer remained in the mother liquor. Chromatography of this through silica gel using benzene as eluant yielded it as an oil which could not be crystallized. (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) Isomer (Found: C, 83.6; H, 8.1; N, 3.8%). (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) Isomer (Found: C, 83.5; H, 8.0; N, 4.0. $C_{24}H_{27}NO$ requires C, 83.5; H, 7.8; N, 4.1%).

LAH Reduction of N-(1-*Phenylpentyl*)-2-*aminodeoxybenzoin.*—Isolation of isomers was performed by silica gel chromatography of the reaction product (860 mg) using benzene as eluant. The (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) isomer was crystallized from hexane, m.p. 102—104 °C. (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) Isomer (Found: C, 83.5; H, 8.1; N, 3.9%). (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) Isomer (Found: C, 83.5; H, 8.1; N, 3.95. $C_{25}H_{29}NO$ requires C, 83.6; H, 8.1; N, 3.9%).

LAH Reduction of N-(1-*Phenyl*-3-*methylbutyl*)-2-*aminodeoxybenzoin.*—From the product (1 500 mg) by fractional crystallization from hexane, the (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) isomer was isolated (756 mg), m.p. 126—128 °C. The isomer (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) was obtained (615 mg) from the mother liquor by silica gel chromatography using benzene as eluant. (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) Isomer (Found: C, 83.7; H, 8.0; N, 3.9%). (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) Isomer (Found: C, 83.6; H, 8.0; N, 3.9. $C_{25}H_{29}NO$ required C, 83.6; H, 8.1; N, 3.9%).

Table 4. Experimental conditions for catalytic hydrogenation of imino ketones, PhCOCPh=NCHRPh

R	Imine (mmol)	Pd–C 5% (mg)	AcOEt (ml)	Pressure (lb in^{-2}) initial	final	*t* (h)	Yield (%)
Pr	1.47	50	60	35	29	5	82
Bu	1.42	50	60	36	29	5	83
Bu^i	4.42	240	100	40	30	15	78

Table 5. Physical and spectroscopic data of amino ketones, Ph–CO–CHPh–NH–CHRPh.

Compd.	I.r. (cm^{-1})[a] CO	NH	^{1}H N.m.r.[b] (p.p.m.)	Analysis[c]	Calc.	Found
(**3**)	1 680	3 340	3.27 (s, NH);	C	75.99	76.1
			3.37 (t, CHPr);	H	6.86	6.7
			5.16 (s, CHCO);	N	3.69	3.6
			6.8—7.8 (m, ArH)	Cl	9.23	9.0
(**4**)	1 680	3 330	3.30 (s, NH);	C	76.34	76.4
			3.37 (t, CHBu);	H	7.12	7.3
			5.15 (s, CHCO);	N	3.56	3.4
			6.8—7.8 (m, ArH)	Cl	8.19	7.9
(**5**)	1 685	3 340	3.35 (s, NH);	C	76.34	76.5
			3.28 (t, CHBu^i);	H	7.12	7.1
			5.09 (s, CHCO);	N	3.56	3.6
			6.8—7.8 (m, ArH)	Cl	8.19	8.2

[a] Liquid film between KBr crystals. [b] 60 MHz; $CDCl_3$ solution. [c] Of related hydrochlorides prepared by bubbling dry hydrogen chloride through an ether solution of the amino ketone. Hydrochlorides were crystallized from ethanol.

Table 6. $NaBH_4$ Reduction of benzil monoimines, Ph–CO–CPh=NCHRPh

Compd.	Imine (mmol)	$NaBH_4$ (mmol)	Ethanol (ml)	*t* (h)	Yield (%)
(**1**)[a]	4.79	9.58	50	3	100
(**2**)	0.61	1.24	5	3	95
(**3**)	0.58	1.17	6	18	84
(**4**)	0.56	1.12	6	18	88
(**5**)	0.84	1.68	9	23	82
(**6**)[b]	0.58	4.47	20	31	80
(**7**)[b]	0.56	7.11	20	48	80

[a] Analysis was carried out by ^1H n.m.r. integration of the fractions obtained in the isomer separation. On addition of ethanol to the reaction product (1.5 g) the (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) isomer crystallized out (580 mg). The remaining mixture was chromatographed on a silica gel column, using benzene–ether (9:1) as eluant. [b] ^1H N.m.r. spectra of samples isolated at various reaction times showed the presence of amino ketone.

LAH Reduction of N-(1-*Phenyl*-2-*methylpropyl*)-2-*amino-deoxybenzoin.*—From the product (389 mg) both isomers were isolated by silica gel chromatography using benzene–ether (95:5) as eluant. No intermediate fractions were isolated. The (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) isomer was eluted first; 182 mg were obtained of each isomer (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) Isomer (Found: C, 83.6; H, 7.85; N, 4.2%). (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) Isomer (Found: C, 83.4; H, 7.7; N, 4.1. $C_{24}H_{27}NO$ requires C, 83.5; H, 7.8; N, 4.1%).

LAH Reduction of N-(1-*Phenyl*-2,2-*dimethylpropyl*)-2-*amino-deoxybenzoin.*—From the product (760 mg) isomers separation proceeded as before. 190 mg were obtained of each isomer as pure products together with 390 mg of a mixture of both. (1*R*,2*S*,3*S*/1*S*,2*R*,3*R*) Isomer (Found: C, 83.6; H, 8.1; N, 3.8%). (1*R*,2*S*,3*R*/1*S*,2*R*,3*S*) (Found: C, 83.5; H, 8.0; N, 4.0. $C_{25}H_{29}NO$ requires C, 83.6; H, 8.1; N, 3.9%).

$NaBH_4$ Reduction of α-Imino Ketones: General Procedure.—2:1 mixture (except when indicated) of $NaBH_4$ and imino-ketone was refluxed in absolute ethanol until disappearance of the imino ketone. The mixture was cooled, poured onto ice, and extracted with ether. The dried ether extracts were worked up as usual. The mixture of isomeric amino alcohols so obtained was analysed by ^1H n.m.r. Integration of the proton attached to the hydroxylated carbon atom was employed. Reaction conditions are summarized in Table 6. Results are collected in Table 2 (see above).

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