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DIASTEREOSELECTIVE SYNTHESIS OF β-AMINO ALCOHOLS WITH TWO OR THREE CHIRAL CENTERS.

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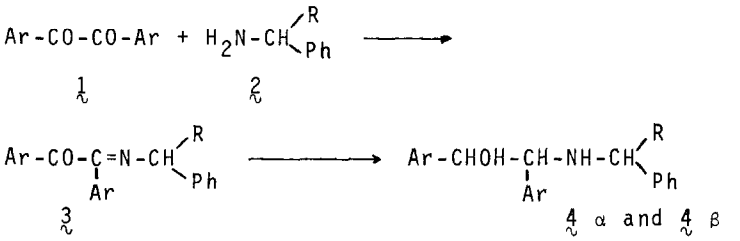
Recently, Jäger and co[1] have reported a method for the stereoselective synthesis of γ-aminoalcohols via reduction of isoxazolines, as a contribution to the general problem of the synthesis of acyclic compounds with multiple chiral centers In this connexion, we report here a simple method for the synthesis of β-aminoalcohols with two or three chiral centers via reduction of monoimines of α-dicarbonyl compounds, according to the following sequence:



The basis of the method is the synthesis of 3, which is easily achieved[3], with high yield by direct condensation of the related benzil, 1, with a primary

Table I

Monoimines of benzil derivatives

Monoimine	R	Ar	Yield[a)]	m.p.
3a	Me	Ph	85	95
b	Et	Ph	90	107-8
c	Pr^i	Ph	80	67-8
d	Bu^t	Ph	76	92-4
e	Ph	Ph	65	130
f	Me	p-MeO-C_6H_4	58	82-3
g	Me	m-Me-C_6H_4	95	94

a) Yields are based in pure products. Microanalysis for C, H, N, correct; maximum error, 0,3%. IR, H^1-NMR and C^{13}NMR spectra in agreement with proposed structures.

amine[4], 2, using the complex salt $ZnCl_2$-amine as catalyst. The synthesis is not perturbed through the formation of diimines, which takes place in more vigorous conditions. Monoimines so prepared are collected in Table I.

Lithium aluminium hydride reduction of monoimines yields, quantitatively, the related β-aminoalcohols in the diastereomeric proportions reported in Table II.

Work on the assignement of configuration to the aminoalcohols is now in - progress.

Table II

Aminoalcohols from monoimines of benzil derivatives

Aminoalcohols	CHOH(NMR)[a]		$J(H_2)$[b]		Stereoselectivity[c]
4a	4,40	-	8,0	-	d
b	4,80	4,43	5,0	9,0	11
c	4,44	4,37	6,5	8,0	1,0
d	4,83	4,78	5,5	9,0	1,6
e	4,65	4,53	6,1	8,5	3,9
f	4,45	-	8,8	-	d
g	4,43	-	8,4	-	d

a) 60 MHz . $CDCl_3$.

b) From crude products. Determined by ^{1}H-NMR integration.

c) Stereoselectivity is expressed in terms of major isomer to minor isomer ratio.

d) Only one product is observed in NMR. Estimated error for the titration 5%. In 4a, the minor isomer could be isolated from the reaction mass, through fractionation from acetone; CHOH = 4,83; J = 5,0 Hz.

References and Notes.

1) V. Jäger, V. Buss and W. Schwab, Tetrahedron Letters 1978, 3133.

2) Aminoalcohols with three quiral centers give, of course, eight diastereomers. However, in the NMR spectrum, differenciation of those having different configurations of carbon 1 and 2 is only possible. So, isomers 4 α and 4 β here considered are in fact, mixtures of diastereomers (1R, 2R, 3R) (1S, 2S, 3S) and (1R, 2R, 3S) (1S, 2S, 3R) on the one hand and (1R, 2S, 3R) - - (1S, 2R, 3S) and (1R, 2S, 3S) (1S, 2R, 3R) on the other. In agreement with this, reduction of imine 4a, prepared from (±)-, (+) and (-)-1-phenylethylamine yielded in every case only two diastereomers which could be distinguished in NMR (See footnote d, Table II).

3) Commercial benzil; p-methoxy and m-methylbenzil prepared by benzoin condensation followed by oxidation of benzoin with ammonium nitrate in glacial acetic acid. See Y. Ogata, and Y. Yamashita; Tetrahedron, 27, 275, (1971).

4) Amines (with exception of 1-phenylethyl-amine, commercial) were prepared by Leukart reaction from the related ketone. See R. Pérez-Ossorio and V. Sánchez del Olmo, An Quim. 56, B 915, - (1966).

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