Tetrahedron Letters,Vol.27,No.39,pp 4727-4730,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

TOTAL SYNTHESES OF (±) AMINOALLOSE DERIVATIVES

Albert DEFOIN, Hans FRITZ, Guillaume GEFFROY and Jacques STREITH
Ecole Nationale Supérieure de Chimie; Université de Haute-Alsace,
F-68093 Mulhouse Cedex, and Physikalische Abteilung CIBA-GEIGY AG CH-4002 Basel

SUMMARY. Acylnitroso derivatives 2, which are obtained by in situ oxidation of the corresponding hydroxamic acids, react with the dimethylacetal of [E,E] hexa-2, 4-dienal 1, leading thereby regio- and stereospecifically to the Diels-Alder adducts 3a-3d. Adduct 3b was transformed stereospecifically and in good yield to the (±)aminoallose derivative 7.

In a preceding paper we described some [4π+2π] cycloaddition reactions of acylnitroso-dienophiles with 1,2-dihydropyridines, followed by cis hydroxylation and hydrogenolysis, whereby diamino-dideoxy lyxopyranose derivatives were obtained (1). The regioselectivity of the Diels-Alder cycloaddition step turned out to be strongly dependent upon the nature of the R group of the acylnitroso R-CO-NO dienophiles.

We describe herein a similar reaction sequence using the dimethylacetal of hexa-2, 4-dienal 1 as the diene partner of the cycloaddition step, which leads in a regio- and stereospecific manner to racemic amino-dideoxyallose derivatives.

The relative reactivity of 1 with various acylnitroso derivatives 2 was as follows (Table 1) : ROCONO > RCONO > ArCONO > R_2NCONO, whereby the best overall yields in cycloadduct formation were obtained with the most reactive dienophiles, i.e. with the carbamate-like derivatives 2a and 2b. All cycloadditions proved to be regiospecific, a result which is obviously due to some steric interaction (2), and not an electronic one, as had been found previously with 1,2-dihydropyridines (1). The starting material 1 being a 80/20 mixture of the [E,E] and of the [E,Z] isomers respectively, it was of no surprise to obtain the corresponding stereoisomeric cycloadducts in the same ratio of which only the major isomer cis 3 is represented here. The two isomers were separated and their configurations were determined by ^{1}H-NMR spectroscopy (2). Cycloadducts 3a and 3b having been obtained in good yields (Table 1), they were used for the synthesis of the corresponding aminoallose derivatives. Cis-hydroxylation was performed with catalytic amounts of OsO_4 in the presence of an excess of N-methyl-morpholine-N-oxide (NMO) (1,3), whereby the corresponding glycols 4a (mp 68-69°C; 100 %) and 4b (mp 92-93°C; 84 %) formed stereospecifically, as we had indeed expected from

previous results (1,3). They were also characterized by their diacetates 5a (mp 85.5-86.5°C) and 5b (resinous compound) whose NMR spectra permitted unambiguous assignment of their dominant conformation and of their relative configuration (4).

Table 1 : Acylnitroso derivatives RCONO 2 and overall yields of cis 3 (and trans) cycloadducts when equimolar amounts of 2 and 3 are used

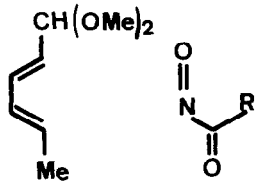
R-group of 2	Overall yields of cycloadducts cis 3 (and trans)* (%)
a MeO	75
b $PhCH_2O$	85
c $PhCH_2$	40
d Ph	23
e Me_2N	< 5

* cis 3/trans ratio = 8/2 in all cases

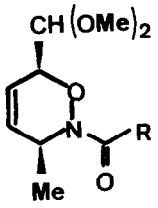
Reductive cleavage of the N-O bond proved to be ineffective when using standard reducing agents like Zn/AcOH, Na/Hg or Al/Hg. Hydrogenolysis of 4a with Raney nickel (40°C; 2d) led to the acyclic acetal 6a (67 %) which was characterized as its triacetate derivative 6b (mp 70-71°C). Catalytic hydrogenation of compound 4b led to a double hydrogenolysis followed by decarboxylation and gave directly the acyclic free amino compound 6c (70 %) which was characterized as its tetraacetyl derivative 6d (mp 110.5-111.5°C). This latter compound was then de-acetalized with 90 % aq. formic acid (2.5 h at 55°C) — whereby cyclization occurred instantaneously — and led stereospecifically to the axial anomer of the tetraacetylated racemic aminoallose 7 (mp 164°C; 81 %) of which one of the two enantiomers is represented below.

Structural and conformational analyses were determined by ^{13}C and ^{1}H-NMR techniques for all cyclic compounds 5; they proved to be of special interest for 5a, 5b and 7. Compound 5a shows in particular a large $H_{5,6}$ coupling constant (Table 2) which clearly indicates that it is present in a chair conformation. From this coupling constant, which is characteristic for two vicinal trans-diaxial hydrogen atoms, all other data follow sequentially and lead unambiguously to the relative configuration as depicted in formula 5a for one of the two enantiomers.

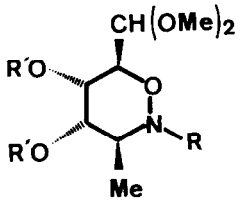
The three-dimensional structure of the final aminoallose 7 could be determined unambiguously by NMR investigations : 7 proved to be a mixture of two rotamers 7A and 7B (N-Ac) which lead to shielding-deshielding effects upon the equatorial H-1 and H-5 hydrogen atoms (Table 3)(5). Furthermore the N-6 nitrogen atom, which is planar, forces both C_1-OH and the C_5-Me substituents to be axial. In the alternative chair conformation both the C_1-OH and C_5-Me would suffer steric repulsion because of severe interaction with the N-Ac group (6,7). This forces compound 7 into the chair conformation in which four axial substituents are to be found. Such cases, in which a double 1,3-diaxial effect leads to a chair conformation bearing four axial substituents are rare, but have already been observed with piperidinoses (8,9). In the more familiar pyranose series the conformational behaviour would have been quite different (10,11). As a matter of fact both rotamers 7A and 7B show identical coupling constants whose magnitudes clearly indicate that none of the vicinal hydrogen atoms are in a trans diaxial configuration. Furthermore $^{4}J_{2,4}$ W-type coupling constants (J = 1.2 Hz) are in good agreement with chair



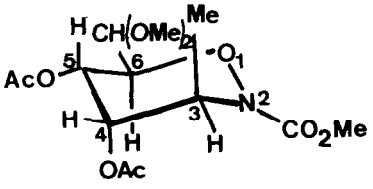
1 2



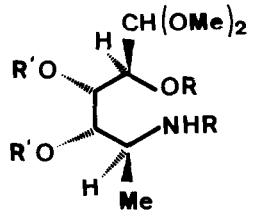
3a R = OMe;
3b R = OCH_2Ph
3c R = CH_2Ph
3d R = Ph
3e R = NMe_2



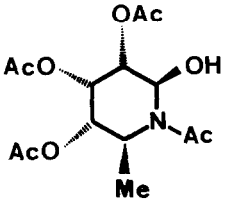
4a R = CO_2Me; R' = H
4b R = CO_2CH_2Ph; R' = H
5a R = CO_2Me; R' = Ac
5b R = CO_2CH_2Ph; R' = Ac
5c R = R' = Ac

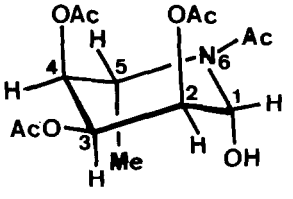


5a



6a R = CO_2Me; R' = H
6b R = CO_2Me; R' = Ac
6c R = R' = H
6d R = R' = Ac





7

conformations, as depicted in formula 7 for one of the enantiomers (the $^4J_{1,5}$ coupling constant, albeit different from 0, could not be determined accurately).

Table 2 ^{1}H-NMR data of compounds 5b and 5a*

	H-3	H-4	H-5	H-6	H-7	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$
5b	4.50	5.05	5.45	4.30	4.46	2.7	3.2	9.3	4.2
5a	4.45	5.07	5.42	4.27	4.45	2.8	3.3	9.3	4.2

* Chemical shifts measured at 20° in $CDCl_3$ for chemical shifts [δ (ppm)] and in C_6D_6 for coupling constants [Hz] (80 MHz).

Table 3 ^{1}H-NMR data of the aminoallose 7 (two rotamers)*

	H-1	H-2	H-3	H-4	H-5	Me	$J_{1,2}$	$J_{1,5}$	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$	$J_{4,5}$
7A	6.12	5.33	5.60	5.23	4.13	1.58	2.6	$\neq 0$	3.6	1.2	3.5	2.2
7B	5.57	5.32	5.60	5.23	4.79	1.41						

* Chemical shifts [δ(ppm)] determined at 400 MHz and coupling constants [Hz] measured at 253 K in $CDCl_3$

ACKNOWLEDGEMENTS. We thank the Centre National de la Recherche Scientifique for its financial support (UA 135)

REFERENCES AND NOTES

1. A. Defoin, Ch. Schmidlin and J. Streith, Tetrahedron Lett., 25, 4515 (1984).
2. G. Kresze and J. Firl, Fortsch. Chem. Forschung, 11, 245 (1969); J. Firl, Chem. Ber., 102, 2177 (1969).
3. G. Augelmann, J. Streith and H. Fritz, Helv. Chim. Acta, 68, 95 (1985).
4. All newly described compounds gave satisfactory elemental and spectral analyses.
5. H. Paulsen and K. Todt, Chem. Ber., 100, 3385 (1967).
6. P. Deslongchamps, Stereoelectronic effects in Organic Chemistry, Pergamon Press, Oxford, 1983.
7. H. Paulsen, K. Todt and H. Ripperger, Chem. Ber., 101, 3365 (1968) and references cited therein.
8. C.V. Holland, D. Horton and J.S. Jewell, J. Org. Chem., 32, 1818 (1967).
9. H. Paulsen, F. Garrido Espinosa, W.P. Trautwein and K. Heyns, Chem. Ber., 101, 179 (1968).
10. S. David, Origin and Consequences of the Anomeric Effect, ACS Symposium Series n° 87 (W.A. Szarek and D. Horton, Editors) p.1, American Chemical Society, Washington D.C. (1979).
11. J. Augé and S. David, Tetrahedron, 40, 2101 (1984).

(Received in France 19 April 1986)