Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Synthesis of N-Benzyl Nitrones

A. Dondoni [a], S. Franco [b], F. Junquera [b], F. L. Merchán [b], P. Merino [b] & T. Tejero [b]

[a] Laboratorio di Chimica Organica, Dipartimento di Chimica, Università, I-44100, Ferrara, Italy

[b] Departamento de Química Orgánica, ICMA. Universidad de Zaragoza, E-50009, Zaragoza, Spain

Available online: 23 Sep 2006

To cite this article: A. Dondoni, S. Franco, F. Junquera, F. L. Merchán, P. Merino & T. Tejero (1994): Synthesis of N-Benzyl Nitrones, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 24:18, 2537-2550

To link to this article: http://dx.doi.org/10.1080/00397919408010565

SYNTHETIC COMMUNICATIONS, 24(18), 2537-2550 (1994)

SYNTHESIS OF N-BENZYL NITRONES

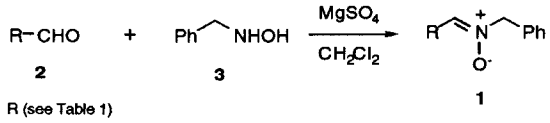
A. Dondoni*,
Laboratorio di Chimica Organica. Dipartimento di Chimica. Università.
I-44100 Ferrara. Italy.

S. Franco, F. Junquera, F. Merchán, P. Merino* and T. Tejero
Departamento de Química Orgánica. ICMA. Universidad de Zaragoza
E-50009 Zaragoza. Spain.

Abstract: A general procedure for the synthesis of twenty-seven chiral and achiral N-benzyl nitrones **1** is described.

The utility of nitrones as useful synthetic intermediates has been extensively demonstrated[1] and several methods for synthesizing nitrones have been described.[1,2] However, in spite of that well-documented utility there have not been described any method for the general preparation of chiral nitrones, and only a few of such compounds bearing a chiral substituent either at nitrogen or at carbon atom are described in the literature.[3] In the course of our studies on the synthesis of α-aminoaldehydes through nucleophilic additions to organic compounds bearing a nitrogen atom as potential amino group,[4] an efficient synthesis of pure N-benzyl nitrones **1** has been required. N-benzyl nitrones **1** are particularly interesting as synthetic intermediates, since the possibility of further removal of the benzyl group from the nitrogen atom makes that such N-benzyl group acts as a protecting one, thus achieving the installation of a primary amino function in the molecule. We have

* To whom correspondence should be addressed.



Scheme 1

recently applied succesfully this argumentation to the synthesis of several natural products.[4a,5]

To our best knowledge there has been no reports concerning the synthesis of chiral N-benzyl nitrones **1** with the only exception of some particular case.[3b,d,e] Thomas and co-workers,[3c] reported the synthesis of various N-benzyl nitrones but no homochiral compounds were prepared. We report herein a general procedure for the preparation of the title compounds by condensation of the corresponding aldehyde **2** with N-benzylhydroxylamine[6] **3** in an organic solvent and in the presence of an heterogeneous drying agent. The best results were obtained when dichloromethane was used as a solvent and anhydrous magnesium sulfate as a desiccant.[7] The use of other solvents like diethyl ether or chloroform gave similar results for small-scale reactions (up to 2.0 g). For larger scale the use of such solvents presents some limitations due to the partial solubility of some nitrones which produces loss of the product during the work-up. When sodium sulfate or calcium dichloride were used instead of magnesium sulfate a larger amount of desiccant and longer times of reaction were needed for rising similar values of chemical yields.

Using this widely applicable method we have synthesized twenty-seven N-benzyl nitrones derived from aryl, alkyl, hetaryl, α-amino- and α-alcoxyaldehydes (Table 1). A single isomer was obtained in all cases and the expected Z configuration was confirmed by nuclear Overhauser effect difference spectroscopy which showed an enhancement of N-CH_2-Ph signal upon irradiation of the azomethine hydrogen as well as an enhancement of the azomethine proton signal upon irradiation of the methylene group in the N-benzyl moiety.

In conclusion, a general procedure for the synthesis of N-benzyl nitrones in good yields is described, starting from the readily accessible N-benzylhydroxylamine[6] and the corresponding aldehydes easily available by the procedures described in the literature. The use of the prepared compounds as key

Table 1. Physical properties of N-benzyl nitrones **1**.[a]

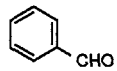
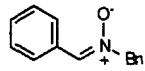
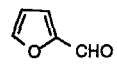
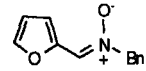
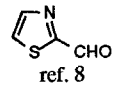
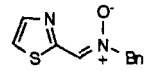
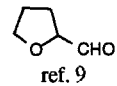
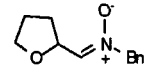
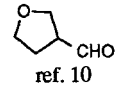
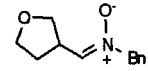
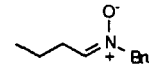
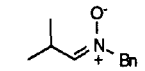
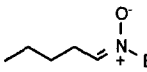
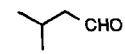
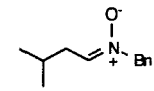
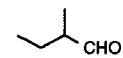
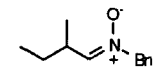
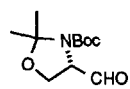
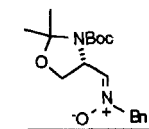
entry	aldehyde[b]	nitrone[b]	yield (%)[c]	mp (°C)[d]	$[\alpha]_D$ (c)[e]
a			62	83[f]	-----
b			72	88	-----
c	 ref. 8		59	122	-----
d	 ref. 9		77	68	-----
e	 ref. 10		70	54	-----
f			89	76	-----
g			83	70[g]	-----
h			87	73	-----
i			84	51	-----
j			90	42	-----
k	 ref. 11		75	57	-46.6 (1.8)

table continues ..

Table 1. (continuation)

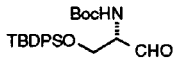
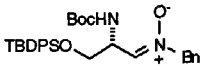
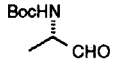
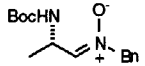
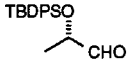
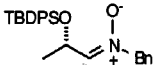
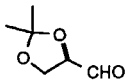
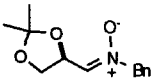
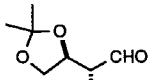
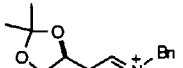
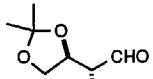
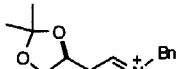
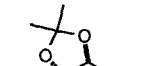
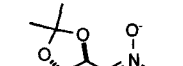
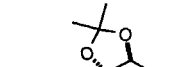
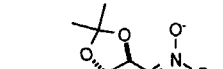
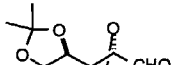
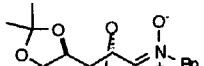
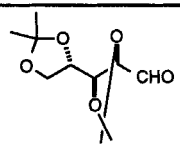
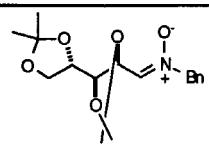
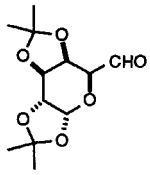
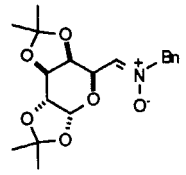
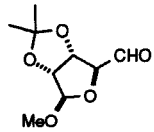
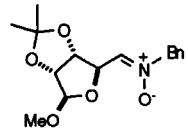
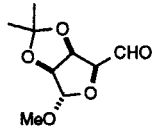
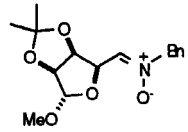
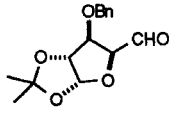
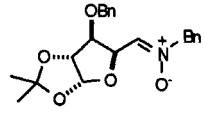
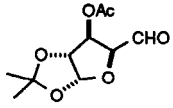
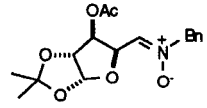
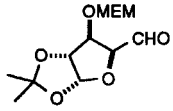
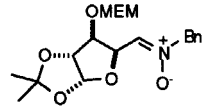
entry	aldehyde[b]	nitrone[b]	yield (%)[c]	mp (°C)[d]	$[\alpha]_D$ (c)[e]
l	 ref. 12		80	110	+2.5 (1.7)
m	 ref. 13		83	94	+3.9 (1.2)
n	 ref. 14		83	73	+15.4 (0.8)
o	 ref. 15		86	88[h]	+96.7 (0.5)
p	 ref. 16		75	34	+3.7 (1.0)
q	 ref. 17		83	oil	-19.2 (0.4)
r	 ref.18		85	68	+20.3 (0.4)
s	 ref. 19		80	oil	+28.6 (0.7)
t	 ref. 20		72	90	-17.9 (1.3)

table continues ...

Table 1. (continuation)

entry	aldehyde[b]	nitrone[b]	yield (%)[c]	mp (°C)[d]	$[\alpha]_D$ (c)[e]
u	 ref. 21		73	90	+18.3 (1.1)
v	 ref. 22		80	106	-120.5 (1.0)
w	 ref. 23		76	54	-85.7 (0.9)
x	 ref. 24		78	74	-65.8 (0.8)
y	 ref. 25		86	96	-135.7 (0.4)
z	 ref. 26		80	138	-102.0 (0.9)
aa	 ref. 27		71	52	-93.4 (0.6)

[a] Spectroscopic properties are given in the experimental part. All products gave satisfactory microanalysis. [b] Bn=benzyl; Boc=*tert*-butoxycarbonyl; TBDMS=*tert*-butyldimethylsilyl; TBDPS=*tert*-butyldiphenylsilyl; Ac=acetyl; MEM=methoxyethoxymethyl. [c] Isolated yield. [d] Melting points are uncorrected. [e] Solvent: $CHCl_3$. [f] Lit. (ref. 28) no data reported. [g] Lit. (ref. 3b) mp 69.5-70°C. [h] Lit. (ref. 3b) mp 88-89 °C.

intermediates in the synthesis of natural products and related compounds is undergoing in our laboratories and will be reported in due course.

Experimental

General: Melting points were determined on a Büchi 510 apparatus and are uncorrected. Optical rotations were measured using a Perkin Elmer Model 214 polarimeter. IR spectra were recorded on a Perkin Elmer FT1600 spectrophotometer. ^{1}H and ^{13}C NMR were recorded on a Varian 300 Unity instrument. NMR spectra were taken in $CDCl_3$, and chemical shifts are expressed in ppm (δ) relative to TMS.

Materials: Column chromatography was carried out on SiO_2 (silica gel 60, 40-63 μm). Dichloromethane was freshly distilled from calcium hydride. Magnesium sulfate was used in commercial grade (Aldrich) without further purification. Benzaldehyde, furfural, butyraldehyde, isobutyraldehyde, valeraldehyde, isovaleraldehyde, and 2-methylbutyraldehyde was purchased from Aldrich and distilled before use. Non-commercially available aldehydes were prepared according the literature procedures (see Table 1). N-benzylhydroxylamine **3** was prepared as described.[6]

Synthesis of N-benzyl nitrones. General Procedure: To a well-stirred solution of the aldehyde (20 mmol) in dichloromethane (150 ml), N-benzylhydroxylamine[6] (2.46 g, 20 mmol) and anhydrous magnesium sulfate (2.41 g, 20 mmol) were added dropwise and the stirring was maintained at room temperature for 4 h. The mixture was filtered and the filtrate evaporated to yield the crude product which was chromatographed on silica gel to afford the pure nitrones **1** (eluent is given in brackets for each compound).

(Z)-N-Benzylidenebenzylamine N-oxide (1a). (Hexano : diethyl ether, 1:4); IR($\nu_{C=N}$) 1581 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.03 (s, 2H), 8.37-8.54 (m, 9H), 8.20 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 71.17, 128.37, 128.52, 128.88, 129.13, 130.36, 133.19, 134.15.

(Z)-N-(2-Furyl)methylenebenzylamine N-oxide (1b). (Hexano : diethyl ether, 1:4); IR($\nu_{C=N}$) 1582 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.97 (s, 2H), 6.51 (dd, 1H, J = 6.9, 3.5 Hz), 7.32-7.44 (m, 6H), 7.50 (s, 1H), 7.75 (d, 1H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 69.50, 112.22, 115.28, 125.10, 128.97, 129.00, 129.32, 132.73, 143.58, 146.74.

(Z)-N-(2-Thiazolyl)methylenebenzylamine N-oxide (1c). (Diethyl ether : methanol, 20:1); IR($\nu_{C=N}$) 1568 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.14 (s, 2H), 7.39-7.45 (m, 6H), 7.99 (d, J = 3.1 Hz), 8.12 (d, 1H, J = 3.1 Hz); ^{13}C NMR ($CDCl_3$) δ 69.44, 120.67, 129.21, 129.47, 129.69, 130.58, 131.76, 143.93, 156.46.

(Z)-N-(Oxolan-2-yl)methylenebenzylamine N-oxide (1d). (Diethyl ether : methanol, 20:1); IR($\nu_{C=N}$) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.62-1.92 (m, 3H), 2.35 (ddt, 1H, J = 12.4, 7.5, 6.0 Hz), 3.75 (m, 2H), 4.80 (s, 2H), 4.88 (pseudo q, 1H, J = 7.0 Hz), 6.74 (d, 1H, J = 5.2 Hz), 7.27 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 25.58, 29.57, 68.41, 68.95, 74.32, 128.81, 128.86, 129.22, 132.32, 140.87.

(Z)-N-(Oxolan-3-yl)methylenebenzylamine N-oxide (1e). (Diethyl ether : methanol, 20:1); IR($\nu_{C=N}$) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.72 (td, 1H, J = 12.9, 7.6 Hz), 2.16-2.28 (m, 2H), 3.53-3.64 (m, 2H), 3.66-3.74 (m, 1H), 3.81 (td, 1H, J = 8.5, 5.6 Hz), 3.88-3.94 (m, 1H), 4.82 (s, 2H), 6.64 (d, 1H, J = 6.3 Hz), 7.33 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 30.18, 36.69, 67.78, 69.09, 70.68, 128.84, 128.88, 129.10, 132.55, 140.23.

(Z)-N-Butylidenebenzylamine N-oxide (1f). (Diethyl ether : methanol, 20:1); IR($\nu_{C=N}$) 1595 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3H, J = 7.3 Hz), 1.49 (m, 2H), 2.42 (bq, 2H, J = 7.1 Hz), 4.83 (s, 2H), 6.61 (t, 1H, J = 5.9 Hz), 7.36 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 13.82, 18.28, 28.48, 69.01, 128.73, 128.76, 129.10, 132.86, 139.36.

(Z)-N-(2-Methylpropylidene)benzylamine N-oxide (1g). (Diethyl ether : methanol, 20:1); IR($\nu_{C=N}$) 1582 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01 (d, 6H, J = 6.7 Hz), 3.12 (dh, J = 7.6, 6.7 Hz), 4.79 (s, 2H), 6.43 (d, 1H, J = 7.6 Hz), 7.36 (s, 5H); ^{13}C NMR ($CDCl_3$) δ 18.68, 25.81, 69.13, 128.61, 128.72, 128.90, 133.00, 144.42.

(Z)-N-Pentylidenebenzylamine N-oxide (1h). (Diethyl ether : methanol, 20:1); IR($\nu_{C=N}$) 1596 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (t, 3H, J = 7.1 Hz); 1.3 (m, 2H), 1.42 (m, 2H), 2.44 (bq, 2H, J = 7.1 Hz), 4.82 (s, 2H), 6.60 (t, 1H, J = 5.9 Hz), 7.33 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 13.61, 22.45, 26.33, 27.47, 69.00, 128.72, 128.77, 129.12, 132.88, 139.43.

(Z)-N-(3-Methylbutylidene)benzylamine N-oxide (1i). (Diethyl ether : methanol, 20:1); IR($\nu_{C=N}$) 1594 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (d, 6H, J = 6.7 Hz), 1.84 (m, 1H), 2.37 (dd, 2H, J = 5.9, 6.8 Hz), 4.85 (s, 2H), 6.63 (t, 1H, J = 5.9 Hz), 7.39 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 22.45, 25.84, 35.31, 69.15, 128.74, 128.78, 129.10, 132.92, 138.54.

(Z)-N-(2-Methylbutylidene)benzylamine N-oxide (1j). (Diethyl ether : methanol, 20:1); IR($\nu_{C=N}$) 1592 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (t, 3H, J = 7.3 Hz), 1.02 (d, 3H, J = 6.8 Hz), 1.43 (m, 2H), 3.01 (m, 1H), 4.86 (s, 2H), 6.45 (d, 1H, J = 7.6 Hz), 7.37 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 11.51, 16.04, 26.82, 32.44, 69.38, 128.81, 128.90, 129.10, 133.2, 144.19.

(Z)-N-[(4R)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-1,3-oxazolidin-4-yl]benzylamine N-oxide (1k). (Hexane : diethyl ether, 19:1); IR($\nu_{C=N}$) 1599 cm^{-1}; ^1H NMR ($CDCl_3$, 55 °C) δ 1.38 (s, 9H), 1.42 (s, 3H), 1.51 (s, 3H), 4.01 (dd, 1H, J = 2.5, 9.5 Hz), 4.18 (dd, 1H, J = 6.6, 9.5 Hz), 4.81 (s, 2H), 4.92 (ddd, 1H, J = 2.5, 4.7, 6.6 Hz), 6.88 (d, 1H, J = 4.7 Hz), 7.28 (m, 5H); ^{13}C NMR ($CDCl_3$, 55 °C) δ 23.08, 26.40, 28.27, 54.97, 66.44, 69.01, 80.37, 94.43, 128.94, 129.10, 129.22, 132.41, 140.19, 151.50.

(Z)-N-[(2R)-2-(*tert*-Butoxycarbonylamino)-3-(*tert*-butyldiphenylsilyloxy)-propylidene]benzylamine N-oxide (1l). (Hexane : diethyl ether, 1:4); IR($\nu_{C=N}$) 1603 cm^{-1}; ^1H NMR ($CDCl_3$, 55 °C) δ 1.02 (s, 9H), 1.39 (s, 9H), 3.93 (dd, 1H, J = 9.9, 5.4 Hz), 4.00 (dd, 1H, J = 9.9, 4.7 Hz), 4.72 (dddd, 1H, J = 8.0, 5.8, 5.4, 4.7 Hz), 4.82 (s, 2H), 5.61 (bs, 1H), 6.74 (d, 1H, J = 5.8 Hz), 7.32 (m, 11H), 7.57 (m, 4H); ^{13}C NMR ($CDCl_3$, 55 °C) δ 19.30, 26.93, 28.37, 50.68, 62.77, 69.76, 79.72, 127.83 (x2), 128.97 (x2), 129.38, 129.85, 132.71, 133.22, 133.32, 135.52 (x2), 135.59, 136.76, 155.30.

(Z)-N-[(2S)-2-(*tert*-Butoxycarbonylamino)propylidene]benzylamine N-oxide (1m). (Ethyl acetate); IR($\nu_{C=N}$) 1605 cm^{-1}; ^1H NMR ($CDCl_3$, 55 °C) δ 1.37 (d, 3H, J = 7.3 Hz), 1.39 (s, 9H), 4.50 (m, 1H), 4.84 (s, 2H), 5.75 (bs, 1H), 6.77 (d, 1H, J = 5.7 Hz), 7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 55 °C) δ 16.19, 28.30, 44.24, 69.48, 79.60, 128.95, 128.99, 129.18, 132.57, 139.11, 155.22.

(Z)-N-[(2S)-2-(*tert*-Butyldiphenylsilyloxy)propylidene]benzylamine N-oxide (1n). (Hexane : diethyl ether, 2:3); IR($\nu_{C=N}$) 1595 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01, (s, 9H), 1.35 (d, 1H, J = 6.4 Hz), 4.62 (d, 1H, J = 14.0 Hz), 4.68 (d, 1H, J = 14.0 Hz), 5.02 (dq, 1H, J = 6.4, 5.6 Hz), 6.63 (d, 1H, J = 5.6 Hz), 7.20 (m, 2H), 7.30-7.40 (m, 9H), 7.52-7.61 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 19.01, 19.55, 26.80, 65.76, 68.99, 127.60 (x2), 127.63, 128.82, 129.22, 129.71, 129.74, 132.18, 133.24, 133.86, 135.50, 135.55, 142.73.

(Z)-N-(1-Deoxy-2,3-O-isopropylidene-D-glycero-1-yliden)benzylamine N-oxide (1o). (Hexane : ethyl acetate, 1:8); IR($\nu_{C=N}$) 1599 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.37 (s, 3H), 3.82 (dd, 1H, J = 8.7, 5.9 Hz), 4.35

(dd, 1H, J = 8.7, 7.1 Hz), 4.80 (s, 2H), 5.08 (ddd, 1H, J = 7.1, 5.9, 4.6 Hz), 6.78 (d, 1H, J = 4.6 Hz), 7.37 (m, 5H) ; ^{13}C NMR ($CDCl_3$) δ 24.86, 26.19, 67.84, 66.99, 72.01, 109.84, 129.06, 129.22, 129.42, 132.10, 139.11.

(Z)-N-[2-O-(*tert*-Butyldimethylsilyl)-1-deoxy-3,4-O-isopropylidene-D-erythro-1-yliden]benzylamine N-oxide (1p). (Hexane : diethyl ether, 1:9); IR($\nu_{C=N}$) 1530 cm^{-1}; ^1H NMR ($CDCl_3$) δ -0.06 (s, 3H), 0.20 (s, 3H), 0.89 (s, 9H), 1.28 (s, 3H), 1.32 (s, 3H), 3.81 (dd, 1H, J = 8.3, 6.3 Hz), 3.90 (dd, 1H, J = 8.3, 6.4 Hz), 4.19 (ddd, 1H, J = 6.4, 6.3, 4.9 Hz), 4.91 (s, 2H), 5.01 (dd, 1H, J = 6.8, 4.9 Hz), 6.59 (d, 1H, J = 6.8 Hz), 7.35 (s, 5H); ^{13}C NMR ($CDCl_3$) δ -5.23, -5.06, 17.96, 25.22, 25.66, 26.32, 65.28, 66.99, 69.98, 77.21, 109.39, 128.86, 129.05, 129.32, 132.39, 137.74.

(Z)-N-[2-O-(*tert*-Butyldiphenylsilyl)-1-deoxy-3,4-O-isopropylidene-D-erythro-1-yliden]benzylamine N-oxide (1q). (Hexane : diethyl ether, 2:3); IR($\nu_{C=N}$) 1530 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02 (s, 9H), 1.29 (s, 3H), 1.32 (s, 3H), 3.82 (d, 1H, J = 6.3 Hz), 4.28 (ddd, 1H, J = 6.3, 6.3, 3.4 Hz), 4.45 (d, 1H, J = 13.6 Hz), 4.53 (d, 1H, J = 13.6 Hz), 5.24 (dd, 1H, J = 6.6, 3.4 Hz), 6.36 (d, 1H, J = 6.6 Hz), 7.07-7.66 (m, 15 H) ; ^{13}C NMR ($CDCl_3$) δ 19.23, 25.21, 26.20, 26.87 (x3), 64.95, 68.10, 69.48, 77.10, 109.37, 127.65, 127.71, 128.83, 128.93, 129.36, 129.84, 129.88, 132.16, 132.90, 133.76, 135.67, 135.77, 137.44

(Z)-N-(4-O-Benzyl-1-deoxy-2,3-O-isopropylidene-L-threo-1-yliden)-benzylamine N-oxide (1r). (Hexane : diethyl ether, 1:4); IR($\nu_{C=N}$) 1580 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.43 (s, 3H), 3.72 (dd, 1H, J = 10.5, 6.6 Hz), 3.89 (dd, 1H, J = 10.5, 2.8 Hz), 4.15 (ddd, 1H, J = 7.3, 6.6, 2.8 Hz), 4.57 (s, 2H), 4.85 (s, 2H), 4.99 (dd, 1H, J = 7.3, 5.6 Hz), 6.78 (d, 1H, J = 5.6 Hz), 7.21-7.40 (m, 10H) ; ^{13}C NMR ($CDCl_3$) δ 26.29, 26.83, 69.50, 71.49, 73.15, 73.56, 79.77, 110.70, 127.41, 127.70, 128.24, 129.03, 129.17, 129.27, 132.20, 137.21, 138.16.

(Z)-N-[4-O-(*tert*-Butyldimethylsilyl)-1-deoxy-2,3-O-isopropylidene-L-threo-1-yliden]benzylamine N-oxide (1s). (Hexane : diethyl ether, 2:3); IR($\nu_{C=N}$) 1597 cm^{-1}; ^1H NMR ($CDCl_3$) δ -0.05 (s, 3H), -0.04 (s, 3H), 1.02 (s, 9H), 1.24 (s, 3H), 1.33 (s, 3H), 3.79 (dd, 1H, J = 11.0, 4.9 Hz), 3.86 (dd, 1H, J = 11.0, 2.9 Hz), 3.94 (ddd, 1H, J = 6.8, 4.9, 2.9 Hz), 4.75 (s, 2H), 4.95 (dd, 1H, J = 6.8, 5.4 Hz), 6.74 (d, 1H, J = 5.4 Hz), 7.26 (m, 5H); ^{13}C NMR ($CDCl_3$) δ -5.72, -5.63, 18.00, 25.58, 26.04, 26.45, 63.98, 68.97, 72.38, 81.06, 110.03, 128.61, 128.71, 128.85, 132.08, 137.43.

(Z)-N-(1-Deoxy-2,3:4,5-di-O-isopropylidene-D-arabino-1-yliden)-benzylamine N-oxide (1t). (Hexane : diethyl ether, 1:15); IR($\nu_{C=N}$) 1584 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (s, 3H), 1.31 (s, 3H), 1.33 (s, 3H), 1.40 (s, 3H), 3.92 (dd, 1H, J = 8.3, 6.0 Hz), 3.96 (dd, 1H, J = 7.3, 5.4 Hz), 4.08 (dd, 1H, J = 8.3, 6.3 Hz), 4.30 (ddd, 1H, J = 6.3, 6.0, 5.4 Hz), 4.86 (s, 2H), 4.94 (dd, 1H, J = 7.3, 6.1 Hz), 6.72 (d, 1H, J = 6.1 Hz), 7.34 (s, 5H) ; ^{13}C NMR ($CDCl_3$) δ 25.14, 26.31, 26.51, 26.67, 65.52, 69.71, 73.15, 75.86, 79.62, 109.40, 110.67, 128.94, 129.10, 129.24, 132.14, 135.79.

(Z)-N-(1-Deoxy-2,3:4,5-di-O-isopropylidene-L-arabino-1-yliden)-benzylamine N-oxide (1u). (Hexane : diethyl ether, 1:15); IR($\nu_{C=N}$) 1584 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (s, 3H), 1.31 (s, 3H), 1.33 (s, 3H), 1.41 (s, 3H), 3.92 (dd, 1H, J = 8.2, 6.2 Hz), 3.96 (dd, 1H, J = 7.3, 5.4 Hz), 4.08 (dd, 1H, J = 8.2, 6.6 Hz), 4.30 (ddd, 1H, J = 6.6, 6.2, 5.4 Hz), 4.86 (s, 2H), 4.94 (dd, 1H, J = 7.3, 6.1 Hz), 6.73 (d, 1H, J = 6.1 Hz), 7.36 (s, 5H) ; ^{13}C NMR ($CDCl_3$) δ 25.15, 26.29, 26.54, 26.68, 65.55, 69.72, 73.13, 75.88, 79.64, 109.35, 110.69, 128.92, 129.08, 129.22, 132.12, 135.77.

(Z)-N-(6-Deoxy-1,2:3,4-di-O-isopropylidene-α-D-galacto-1,5-pyranose-6-yliden)benzylamine N-oxide (1v). (Ethyl acetate); IR($\nu_{C=N}$) 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (s, 3H), 1.30 (s, 3H), 1.39 (s, 3H), 1.53 (s, 3H), 4.30 (dd, 1H, J = 5.0, 2.6 Hz), 4.60 (dd, 1H, J = 7.9, 2.5 Hz), 4.73 (dd, 1H, J = 7.9, 2.0 Hz), 4.88 (s, 2H), 5.0 (dd, 1H, J = 5.1, 2.0 Hz), 5.49 (d, 1H, J = 5.0 Hz), 6.72 (d, 1H, J = 5.1 Hz), 7.38 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 24.26, 24.87, 25.93, 26.09, 65.53, 69.27, 69.81, 70.35, 70.40, 96.07, 109.09, 109.33, 128.88, 128.99, 129.47, 132.30, 136.61.

(Z)-N-(5-Deoxy-2,3-O-isopropylidene-1-O-methyl-β-D-ribo-1,4-furanose-5-ylidene)benzylamine N-oxide (1w). (Diethyl ether); IR($\nu_{C=N}$) 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (s, 3H), 1.41 (s, 3H), 3.14 (s, 3H), 4.43 (d, 1H, J = 5.9 Hz), 4.74 (d, 1H, 5.9 Hz), 4.84 (s, 2H), 4.91 (s, 1H), 5.18 (d, 1H, J = 5.3 Hz), 6.56 (d, 1H, 5.3 Hz), 7.34 (s, 5H). ; ^{13}C NMR ($CDCl_3$) δ 24.77, 26.17, 54.68, 68.97, 82.16, 82.25, 84.10, 109.78, 112.50, 128.85, 129.02, 129.47, 132.11, 137.74.

(Z)-N-(5-Deoxy-2,3-O-isopropylidene-1-O-methyl-α-D-lyxo-1,4-furanose-5-ylidene)benzylamine N-oxide (1x). (Diethyl ether); IR($\nu_{C=N}$) 1599 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (s, 3H), 1.34 (s, 3H), 3.24 (s, 3H), 4.54 (d, 1H, J = 5.7 Hz), 4.89 (s, 1H), 4.92 (s, 2H), 5.02 (bt, 1H, J = 4.3 Hz), 5.10 (dd,

1H, J = 5.7, 4.0 Hz), 6.78 (d, 1H, J = 4.5 Hz), 7.39 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 24.56, 26.02, 54.41, 68.90, 79.83, 80.01, 84.10, 106.22, 112.14, 128.42, 128.50, 129.10, 132.10, 136.23.

(Z)-N-(3-O-Benzyl-5-deoxy-1,2-O-isopropylidene-α-D-xylo-1,4-furanose-5-yliden)benzylamine N-oxide (1y). (Hexane : diethyl ether, 1:4); IR($\nu_{C=N}$) 1595 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.24 (s, 3H), 1.43 (s, 3H), 4.38 (d, 1H, J = 11.7 Hz), 4.46 (d, 1H, J = 11.7 Hz), 4.52 (d, 1H, J = 3.20 Hz), 4.57 (d, 1H, J = 3.7 Hz), 4.80 (d, 1H, J = 13.5 Hz), 4.86 (d, 1H, J = 13.5 Hz), 5.25 (pseudo t, 1H, J = 3.8 Hz), 5.92 (d, 1H, J = 3.7 Hz), 6.82 (d, 1H, J = 4.5 Hz), 7.30 (m, 10H) ; ^{13}C NMR ($CDCl_3$) δ 26.24, 26.84, 69.11, 72.53, 77.85, 82.25, 82.76, 104.82, 112.11, 127.31, 127.72, 128.31, 128.86, 129.05, 129.47, 132.07, 135.91, 137.48.

(Z)-N-(3-O-Acetyl-5-deoxy-1,2-O-isopropylidene-α-D-xylo-1,4-furanose-5-yliden)benzylamine N-oxide (1z). (Diethyl ether : methanol, 25:1); IR($\nu_{C=N}$) 1601 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (s, 3H), 1.48 (s, 3H), 1.83 (s, 3H), 4.51 (d, 1H, J = 3.7 Hz), 4.83 (d, 1H, J = 13.7 Hz), 4.88 (d, 1H, J = 13.7 Hz), 5.34 (pseudo t, 1H, J = 3.9 Hz), 5.54 (d, 1H, J = 3.2 Hz), 5.86 (d, 1H, J = 3.7 Hz), 6.71 (d, 1H, J = 4.7 Hz), 7.35 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 20.39, 26.19, 26.70, 69.37, 75.77, 76.30, 83.12, 104.52, 112.60, 128.99, 129.19, 129.37, 132.32, 133.61, 169.09.

(Z)-N-(5-Deoxy-1,2-O-isopropylidene-3-methoxyethoxymethyl-α-D-xylo-1,4-furanose-5-yliden)benzylamine N-oxide (1aa). (Diethyl ether); IR($\nu_{C=N}$) 1605 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.24 (s, 3H), 1.41 (s, 3H), 3.29 (s, 3H), 3.34-3.52 (m, 5H), 4.49 (d, 1H, J = 7.1 Hz), 4.52 (d, 1H, J = 7.1 Hz), 4.61 (dd, 1H, J = 3.7, 8.3 Hz), 4.77 (d, 1H, J = 13.4 Hz), 4.82 (d, 1H, J = 13.4 Hz), 5.17 (pseudo t, 1H, J = 3.9 Hz), 5.85 (d, 1H, J = 3.7 Hz), 6.80 (d, 1H, J = 4.4 Hz), 7.35 (m, 5H) ; ^{13}C NMR ($CDCl_3$) δ 26.08, 26.71, 58.85, 67.12, 69.03, 71.44, 77.49, 80.27, 82.97, 95.21, 104.62, 111.98, 128.72, 128.96, 129.32, 132.29, 135.51.

Acknowledgements: We thank the Ministerio de Educación y Ciencia (Madrid, Spain. Project PM92-0253) and CNR (Rome, Italy) for financial support. We are also indebted to the Diputación General de Aragón for a fellowship to S.F. and the MTM Foundation for a fellowship to F.J.

References and Notes

1. (a) Tufariello, J.J., in *1,3-Dipolar Cycloaddition Chemistry*, Padwa, A., Ed.; Wiley-Interscience; New York, 1984; vol. 2; chapter 9; pp. 83-168. (b) Confalone, P.N. and Huie, E.M. *Organic Reactions*, **1988**, *36*, 1. (c) Torssell, K.G.B., *Nitrile Oxides, Nitrones, and Nitronates in Organic Synthesis*. VCH, 1988; chapter 3; pp. 75-93.
2. (a) Hamer, J. and Macaluso, A., *Chem. Rev.*, **1964**, *64*, 473. (b) Delpierre, G.R. and Lamchen, M., *Quart. Rev.*, **1965**, *19*, 329. (c) Rundel, W. in *Houben-Weyl: Methoden der Organischen Chemie*, 1968, 10:4, 309; Muller, E., Ed.; G. Thieme Verlag, Stuttgart. (d) Torssell, K. and Zeuthen, O., *Acta Chem. Scand. Ser. B*, **1978**, *32*, 118. (e) Cummins, C.H. and Coates, R.M., *J. Org. Chem.*, **1983**, *48*, 2070. (f) Christensen, D. and Jorgensen, K.A., *J. Org. Chem.*, **1989**, *54*, 126. (g) Murahashi, S.-I.; Mitsui, H.; Shiota, T.; Tsuda, T. and Watanabe, S., *J. Org. Chem.*, **1990**, *55*, 1736. (h) Murray, R.W. and Singh, M., *J. Org. Chem.*, **1990**, *55*, 2954. (i) Hinton, R.D. and Janzan, E.G., *J. Org. Chem.*, **1992**, *57*, 2646.
3. (a) Vasella, A. and Voeffray, R., *Helv. Chim. Acta*, **1982**, *65*, 1134. (b) DeShong, P.; Dicken, C.M.; Leginus, J.M. and Whittle, R.R., *J. Am. Chem. Soc.*, **1984**, *106*, 5598. (c) Fray, M.J.; Jones, R.H. and Thomas, E.J., *J. Chem. Soc. Perkin Trans. I*, **1985**, 2753. (d) Ito, Y.; Kimura, Y. and Terashima, S., *Bull. Chem. Soc. Jpn.*, **1987**, *60*, 3337. (e) Kita, Y.; Itoh, F.; Tamura, O.; Ke, Y.Y. and Tamura, Y., *Tetrahedron Lett.*, **1987**, *28*, 1431. (f) DeShong, P.; Li, W.; Kennington Jr., J.W.; Ammon, H.L. and Leginus, J.M., *J. Org. Chem.*, **1991**, *56*, 1364. (g) Fisera, L.; Al-Timari, U.A.R.; Ertl, P., *ACS Symposium Series*, **1992**, *494*, 158.
4. (a) Dondoni, A.; Junquera, F.; Merchán, F.L.; Merino, P. and Tejero, T., *Tetrahedron Lett.*, **1992**, *33*, 4221. (b) Dondoni, A.; Franco, S.; Merchán, F.L.; Merino, P. and Tejero, T., *Tetrahedron Lett.*, **1993**, *34*, 5475.
5. (a) Dondoni, A.; Franco, S.; Merchán, F.L.; Merino, P. and Tejero, T., *Tetrahedron Lett.*, **1993**, *34*, 5479. (b) Dondoni, A.; Franco, S.; Merchán, F.L.; Merino, P. and Tejero, T., *Synlett*, **1993**, 78.
6. Borch, R.F.; Berstein, M.D. and Durst, H.D., *J. Am. Chem. Soc.*, **1971**, *93*, 2897.
7. These conditions have been used by DeShong and co-workers (see ref. 3f) in the preparation of a chiral N-methyl nitrone intermediate in the total synthesis of Nogalomycin.

8. Dondoni, A.; Fantin, G.; Fogagnolo, M.; Medici, A. and Pedrini P., *Synthesis*, **1987**, 998.
9. The aldehyde was prepared from 2-tetrahydrofurfuryl alcohol (Aldrich) by a Swern[29] oxidation.
10. The aldehyde was prepared from 3-tetrahydrofurfuryl alcohol (Aldrich) by a Swern[29] oxidation.
11. Garner, P. and Park, J.M., *Org. Synth.*, **1991**, *70*, 18. This procedure has been recently improved by McKillop and co-workers (see: McKillop, A.; Taylor, R.J.K.; Watson, R.J. and Lewis, N., *Synthesis*, **1994**, 31).
12. The aldehyde was prepared as described (see: Sugano, H. and Myoshi, M., *J. Org. Chem.*, **1976**, *41*, 2352) using *tert*-butyldiphenylsilyl chloride instead benzyl bromide, as protecting group.
13. Fehrentz, J.-A. and Castro, B., *Synthesis*, **1983**, 676.
14. Massad, A.K.; Hawkins, L.D. and Baker, D.C., *J. Org. Chem.*, **1983**, *43*, 5180.
15. Schmid, C.R.; Bryan, J.D.; Dowlatzedah, M.; Phillips, J.E.; Prather, D.E.; Schantz, R.D.; Sean, N.L. and Vianco, C.S., *J. Org. Chem.*, **1991**, *56*, 4056.
16. Dondoni, A.; Merino, P. and Orduna, J., *Synthesis*, **1992**, 201.
17. The same procedure to that described in the ref. 16 was used, employing *tert*-butyldiphenylsilyl chloride as protecting group.
18. Mukaiyama, T.; Suzuki, K.; Yamada, T. and Tabusa, F., *Tetrahedron*, **1990**, *46*, 265.
19. Iida, H.; Yamazaki, N. and Kibayashi, C., *J. Org. Chem.*, **1987**, *52*, 3337.
20. Zinner, H.; Wittenburg, E. and Rembara, G.. *Chem. Ber.*, **1959**, *92*, 1614.
21. The same procedure to that described in the ref. 20 was applied to the L-arabinose.
22. Butterworth, R.F. and Hanessian, S., *Synthesis*, **1971**, 70.
23. Sepulchre, A.M.; Vass, G. and Gero, S.D., *Tetrahedron Lett.*, **1973**, 3619.
24. The aldehyde was prepared from methyl 2,3-O-isopropylidene-α-D-lyxo-1,4-furanose by a Swern[29] oxidation.
25. Wolfram, M.L. and Hanessian, S., *J. Org. Chem.*, **1962**, *27*, 1800.
26. The same procedure to that described in the ref. 25 was used, employing acetic anhydride in pyridine as protecting group.
27. The same procedure to that described in the ref. 25 was used, employing methoxyethoxymethyl chloride as protecting group. The introduction of the

MEM group was carried out as described (see: Corey, E.J.; Gras, J.L. and Ulrich, P.,*Tetrahedron Lett.,* **1976**, *11*, 809).

28. Mancini, F.; Pazza, M.G. and Trombini, C., *J. Org. Chem.*, **1991**, *56*, 4246.
29. Mancuso, A.J. and Swern, *Synthesis*, **1981**, 165.

(Received in the UK 01 March 1994)