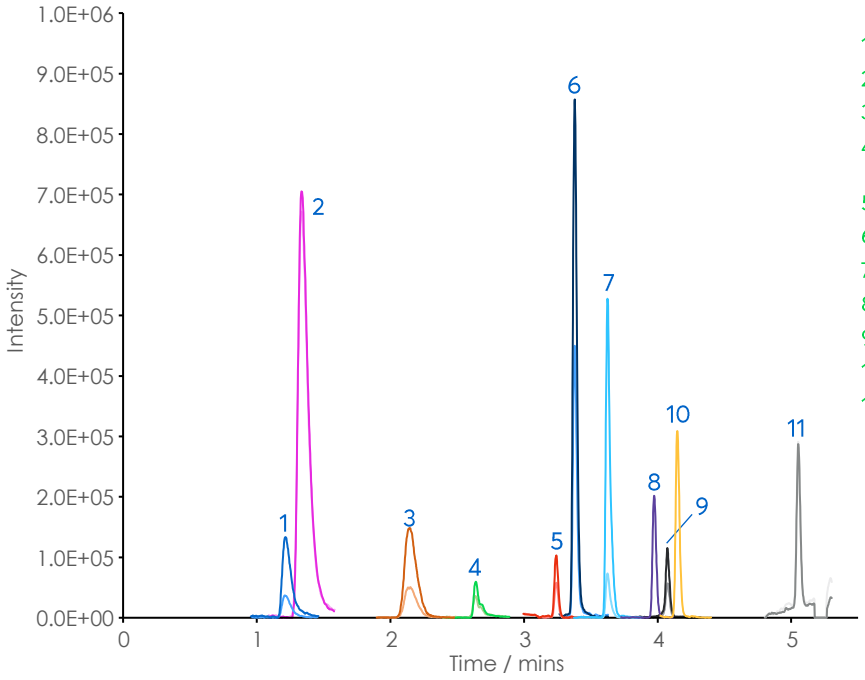
Chromatography Solutions

Application note #7940

LC-MS/MS separation of 10 nitrosamines and DMF in valsartan API on an Avantor® ACE® Excel C18 column



1. N-nitroso-dimethylamine (NDMA)
2. N,N-dimethylformamide (DMF)
3. N-nitroso-morpholine (NMOR)
4. N-nitroso-N-methyl-4-aminobutyric acid (NMBA)
5. N-nitroso-diethylamine (NDEA)
6. N-nitroso-piperidine (NPIP)
7. N-nitroso-ethyl-isopropylamine (NEIPA)
8. N-nitroso-diisopropylamine (NDIPA)
9. N-nitroso-methylphenylamine (NMPA)
10. N-nitroso-di-n-propylamine (NDPA)
11. N-nitroso-di-n-butylamine (NDBA)

Avantor® ACE®

Method Details

CONDITIONS

Column: Avantor® ACE® Excel C18

Particle Size: 2 µm

Dimensions: 100 x 2.1 mm

Mobile Phases: A: 0.1% formic acid in H_2O:MeOH (98:2, v/v)

B: 0.1% formic acid in H_2O:MeOH (2:98, v/v)

Time (mins)	% B
0	0
1	0
2.5	50
5	86.5
5.5	86.5
5.6	0

Flow Rate: 0.5 ml/min

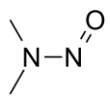
Temperature: 40 °C

Injection volume: 40 µl

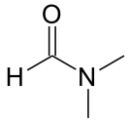
Detection: Sciex QTRAP® 6500+ LC-MS/MS system.

Ionisation mode: APCI, positive mode; Source temperature: 300 °C; Curtain gas: 33 psig; Ion source gas: 30 psig; Needle current: 2 µA

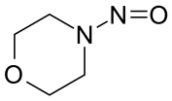
Sample: Valsartan (66.67 mg/ml) spiked with nitrosamines at 1 ng/ml. NDMA-d6, NMBA-d3, NDEA-d10 and NDBA-d18 were used as internal standards.



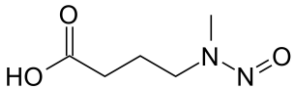
1. NDMA



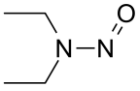
2. DMF



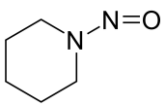
3. NMOR



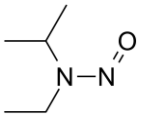
4. NMBA



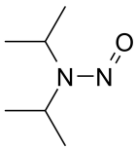
5. NDEA



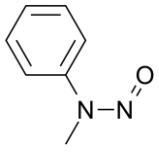
6. NPIP



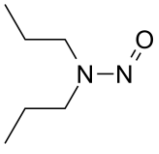
7. NEIPA



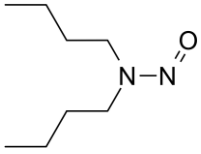
8. NDIPA



9. NMPA



10. NDPA



11. NDBA

MRM TRANSITIONS

Analyte	MRM	Optimised MS Parameters		
		Declustering potential (V)	Collision energy (V)	Cell exit potential (V)
NDMA	+75.0 amu → +43.0 amu	11	19	10
	+75.0 amu → +58.0 amu	11	17	28
NDMA-d6	+81.2 amu → +46.0 amu	40	22	11
	+81.2 amu → +64.1 amu	40	17	12
DMF	+74.0 amu → +42.0 amu	1	46	12
	+74.0 amu → +30.0 amu	1	33	14
NMOR	+117.0 amu → +87.0 amu	11	15	4
	+117.0 amu → +44.9 amu	11	24	4
NMBA	+147.1 amu → +117.1 amu	11	11	12
	+147.1 amu → +87.1 amu	11	17	10
NMBA-d3	+150.1 amu → +120.2 amu	16	11	8
	+150.1 amu → +47.1 amu	21	17	8
NDEA	+103.1 amu → +75.1 amu	16	21	10
	+103.1 amu → +47.1 amu	16	23	22
NDEA-d10	+113.2 amu → +34.2 amu	21	33	6
	+113.2 amu → +49.1 amu	6	23	6
NPIP	+115.0 amu → +69.1 amu	1	21	8
	+115.0 amu → +41.0 amu	1	31	10
NEIPA	+117.1 amu → +75.1 amu	26	17	10
	+117.1 amu → +47.1 amu	21	23	10
NDIPA	+131.1 amu → +89.1 amu	76	15	10
	+131.1 amu → +47.1 amu	71	23	10
NMPA	+137.1 amu →+66.0 amu	21	23	8
	+137.1 amu →+107.1 amu	16	21	12
NDPA	+131.1 amu → +89.1 amu	16	17	10
	+131.1 amu → +43.1 amu	16	21	10
NDBA	+159.2 amu → +57.1 amu	46	17	10
	+159.2 amu → +103.2 amu	51	15	10
NDBA-d18	+177.3 amu → +66.2 amu	46	23	8
	+177.3 amu → +46.2 amu	41	37	22

ORDERING TABLE

Product	Details	Size	Part Number
Avantor® ACE® Excel 2 C18	HPLC Column	100 x 2.1 mm	EXL-101-1002U
Methanol	VWR HiPerSolv CHROMANORM® for LC-MS	2.5 L	83638.320
Water	VWR HiPerSolv CHROMANORM® for LC-MS	2.5 L	83645.320
Formic acid	VWR HiPerSolv CHROMANORM® for LC-MS	10 x 1 mL	85048.001

ORDERING TABLE (US)

Product	Details	Size	Catalog Number
Avantor® ACE® Excel 2 C18	HPLC Column	100 x 2.1 mm	76392-538
Methanol ≥99.9%	ULTRA for LC-MS, tested for UHPLC, J.T.Baker®	1 L	JT9863-2
Water	ULTRA for LC-MS, tested for UHPLC, J.T.Baker®	1 L	JT9823-1