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Improvements in the determination of di-isocyanates using a new gradient elution HPLC methodology

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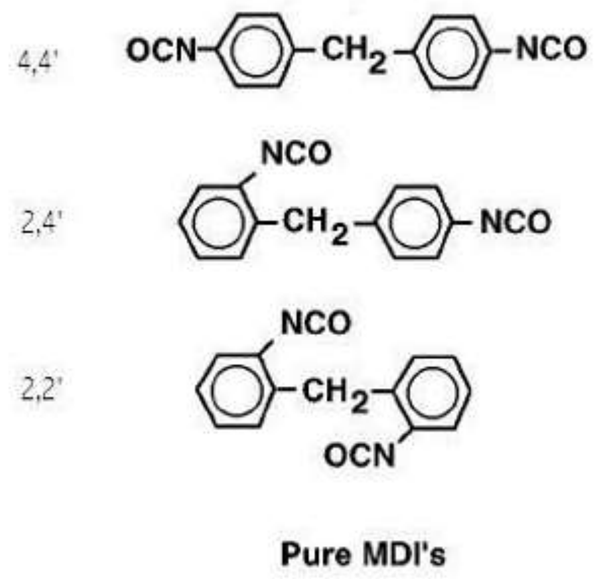
Isocyanates – Industrial uses and chemical structure

Mono isocyanates are industrial chemical precursors

Di-isocyanates are used to manufacture

- Foams
- Adhesives
- Paints

Molecular structures vary widely, all contain the N=C=O group, multiple monomers, each having multiple short chain polymer forms



Isocyanates – Health concerns

- Isocyanates are irritants and potent respiratory sensitisers
- Inhaling even very low levels can result in severe asthma
- Isocyanate exposure is one of the most common causes of occupational asthma

- The UK workplace exposure limit is (WEL) is 0.02 mg/m^3

- The WEL is for all isocyanates combined, known as TRIG – total reactive isocyanate groups

Summary of MDHS 25/4

- Sampled as 1,2-MP derivatives
- Isocratic HPLC
- Dual detector technique, ratio of responses verify isocyanate
- Long run times
- Poor resolution of monomers from reagent peak
- Phosphate buffer / Acetonitrile mobile phase
- Sensitive to small changes in mobile phase composition
- Gradient not possible due to detector back pressure and background signal

Typical MDHS 25/4 chromatogram

- **Motivation for Improvement**

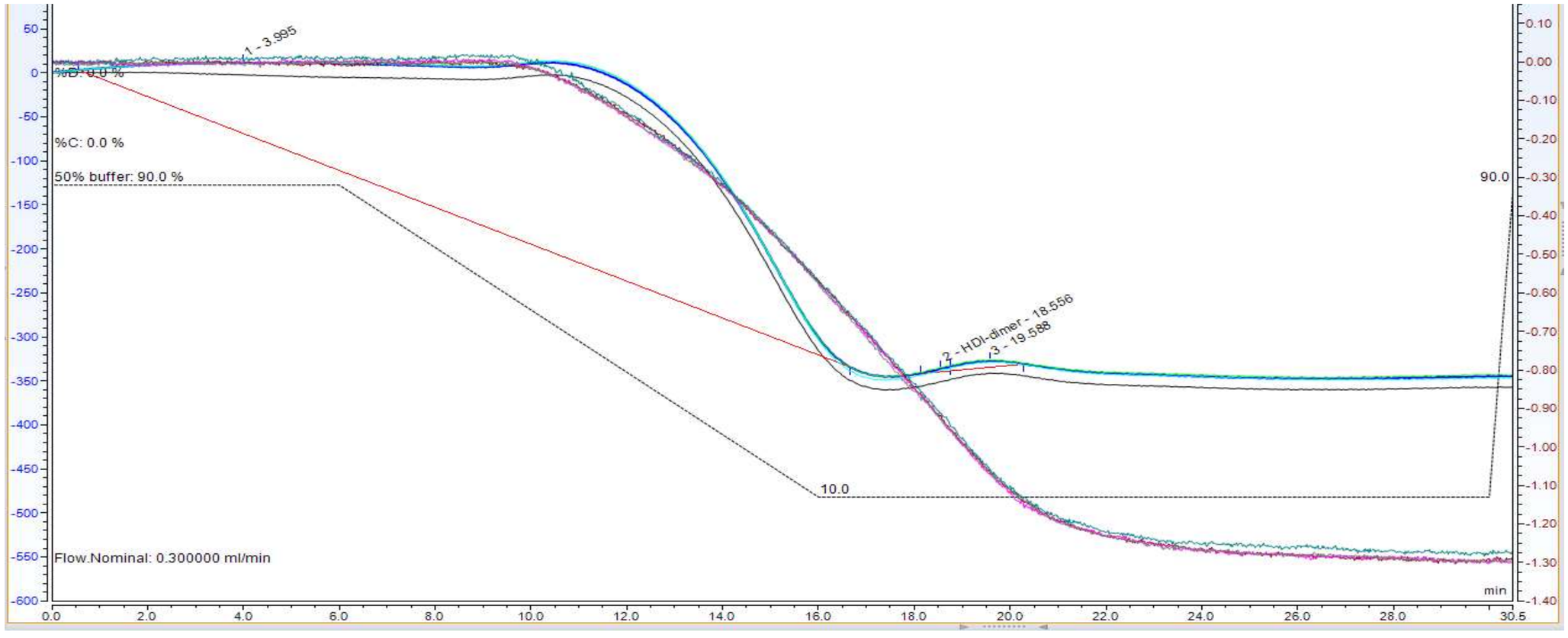
- New instrumentation acquired
- Improved pump performance
- Better detector stability
- Software tools

- **Benefits of Gradient methods**

- Improved resolution
- Greater sensitivity
- Shorter analysis times

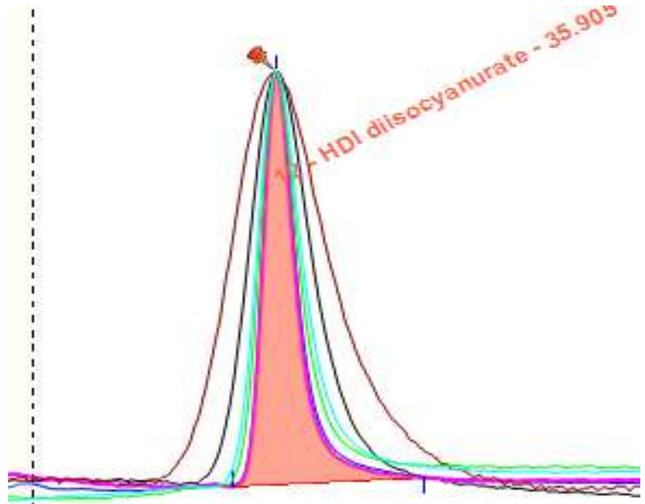
Initial Trials

- Back pressure stability – 130 to 120 bar during gradient
- Detector stability – good consistency across multiple injections in both channels



Gradient Trials

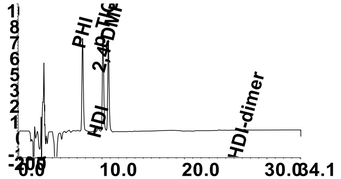
- A selection of gradients were trialled each based on gradients of different concentrations of pre-mixed phosphate buffer / acetonitrile.
- Gradient resulted in dramatically improved peak shape for later eluting peaks.

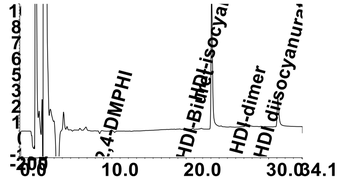


Sequence	Mobile phase composition				[Buffer]		[Real buffer]		Retention times (min)						Diisocyanaurate peak width (50%)	Runtime (min)	Cycle time (min)
	Start ratio	End ration	Start time	Gradient length	A	B	Start	End	HDI	Biuret	Dimer	Isocyanurate	Diisocyanurate	HDI res from 1,2_MP			
20240125jaf gradient	10:90	10:90	6	10	39%	50%	0.489	0.401	4.00	13.94	24.5	17.61	36.79	1.98	0.473	42.5	60
20240308jaf gradient	5:95	95:5	2	22	30%	60%	0.585	0.315	8.50	19.71	26.11	22.08	30.25	5.95	0.154	40.1	58
20240312jaf gradient	10:90	90:10	2	28	30%	60%	0.57	0.33	7.60	21.13	30.18	24.36	35.77	5.15	0.183	40.1	58
20240319jaf 43% isocratic	56.5:43.5	-	-	-	30%	60%	0.4305	-	2.90	7.26	19.19	10.07	41.04	1.06	0.816	45.0	57
20240319jaf 80_20 gradient	20:80	80:20	2	28	30%	60%	0.54	0.36	5.79	19.01	30.61	22.97	38.39	3.54	0.269	45.1	63
20240320jaf 80_20 fast gradient	20:80	80:20	4	18	30%	60%	0.54	0.36	5.81	18.40	26.63	21.40	33.53	3.56	0.264	45.1	63

Further investigations of 95:5 Gradient

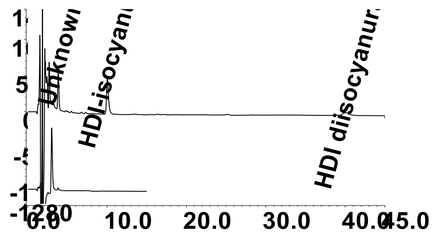
- Able to separate a range of mono isocyanates not previously possible.
- Good resolution of monomers and oligomers and from reagent peak.
- Chromatogram subtraction effective.





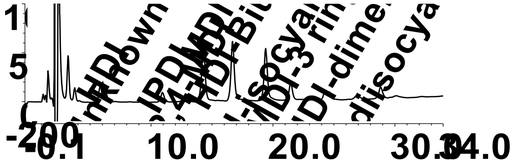
95:5 Gradient on real samples

- Method tested on customer submitted samples.
- An unknown interferent co-elutes with HDI.
- Unknown is resolved in isocratic method



Improved Gradient Conditions

- Trialled a higher proportion of solvent in the starting conditions.
- 80:5 gradient retains good resolution of monomers whilst resolving HDI from the unknown.



Assessing performance on Isocyanate Bulks

- Characterised several bulks using titration, isocratic, gradient and DBA method.
- HDI oligomers quantitatively characterised in bulk hardener samples c.f. titration data.
- MDI oligomers totals do not match titration results. Consistent with isocratic method.
- MDI oligomers also analysed by dibutylamine (DBA) method. 3 different MDI bulks each in triplicate.
- Recoveries for MDI monomer and 3 ring 91 % - 130 % Mean 110 % RSD 10%

Performance of method

- Gradient improves calibration
- Sensitivity improved, especially for HDI and later eluting oligomers
- Response ratios are closer to the 1:1 ideal
- No difference in recovery between isocratic, gradient and DBA methods.

Conclusions

- Gradient offers improvements
- Early results for TDI
- HDI and IPDI can share calibration

Di-isocyanates discussion points

- Use of the MDHS 25/4 reagent 1,2-MP is restricted in several countries
- Primary alternative dibutylamine method cannot measure unknown isocyanates
- Diaminonapthalene method proposed as a universal alternative but development has not progressed.
- A nitrogen specific LC detector would be useful but is not available on the market.