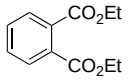
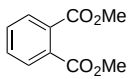
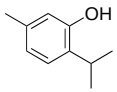
AK Hintermann List of qNMR Standards – Version 1.7

Nuc.	Substance	δ ($CDCl_3$) (D_2O)[a]	*n*	M_r[b]	d(20)	Ref. NMR[c]	Solvent	Mp[d]	Bp[d]	Rec-ov.[e]	Notes[f]	GHS	AKH[g]
^{1}H	***^{1}H NMR***	*^{1}H shifts*											
^{1}H	***Preferred - Generally applicable - [✓ = suitable for crude recoveries]***												
	Benzoesäure (benzoic acid)	7.4–7.7 m 8.13 m	3 2	122.123	–	673	MeOD, DMSO	122	250	–			D3
	(Na)-benzoat {anionic form}	7.39, 7.45 7.80 (m)	2,1 2	144.105	–	LH-157	D_2O	436	–	–	hygr.		D3
	Dibrommethan	4.95 s	2	173.835	2.49	2171	$CDCl_3$ etc	–53	97	(✓)	vol. 13 g/L		H-C_1
	Dichlormethan	5.30 s	2	84.927	1.33	891	not: D_2O	–97	40	✓	vol.		+
	1,2-Dichlorethan	3.73 s	4	98.954	1.25	1280	C_6D_6 (2.90), Me_2CO (3.87), DMSO (3.90), MeOD (3.78)	–36	84	✓	tox., vol.		+
	Dimethylfumarat	3.81 s 6.86 s	6 2	144.126	–	1132	MeOH (3.80, 6.83)	102	193	–	1.6 g/L		H-C_6
	Dimethylsulfon (MSM)	2.94 s	6	94.128	–	LH218	D_2O (3.16), DMSO (3.0), C_6D_6 (x)	110	238	–	150 g/L	–	+
	1,3-Dinitrobenzol (*meta*-dinitrobenzene)	7.87 m 8.62 m 9.08 s	1 2 1	168.108	–	1117	$CDCl_3$	89	291	–	tox.		A1
	1,4-Dioxan	3.71 s	8	88.106	1.03	890	C_6D_6 (3.35), D_2O (3.75)	12	101	✓	vol.		+
	Kalium hydrogenphthalat	7.56 m 7.71 m	2 2	204.222	–	635	MeOD, DMSO (7.53/8.20)	300	–	–		–	A4
	Mesitylen (1,3,5-Trimethylbenzene)	2.26 s 6.78 s	9 3	120.195	0.87	1351	$CDCl_3$	–45	165	–	vol.		H-C_9
	Naphthalin (Naphthalene)	7.48 m 7.84 m	4 4	128.174	–	1350	$CDCl_3$	80	218	–	vol.		M-C_{10}
	1,1,2,2-Tetrachlorethan	5.90 s	2	167.838	1.59	1533	DMSO (6.94), C_6D_6 (4.93)	–43	147	–	tox.		+
	Toluol (toluene)	2.36 s 7.1–7.3	3 5	92.141	0.87	97	DMSO (2.30), MeCN (2.32), MeOH (2.31)	–95	111	✓	vol.		+
	Trichlorethylen	6.45 s	1	131.380	1.46	2151	$CDCl_3$	–86	87	✓	vol.		H-C_2
	1,3,5-Trioxan	5.14 s	6	90.078	–	2156	C_6D_6 (x), D_2O (5.xx),	62	115		220 g/L		H-C_3

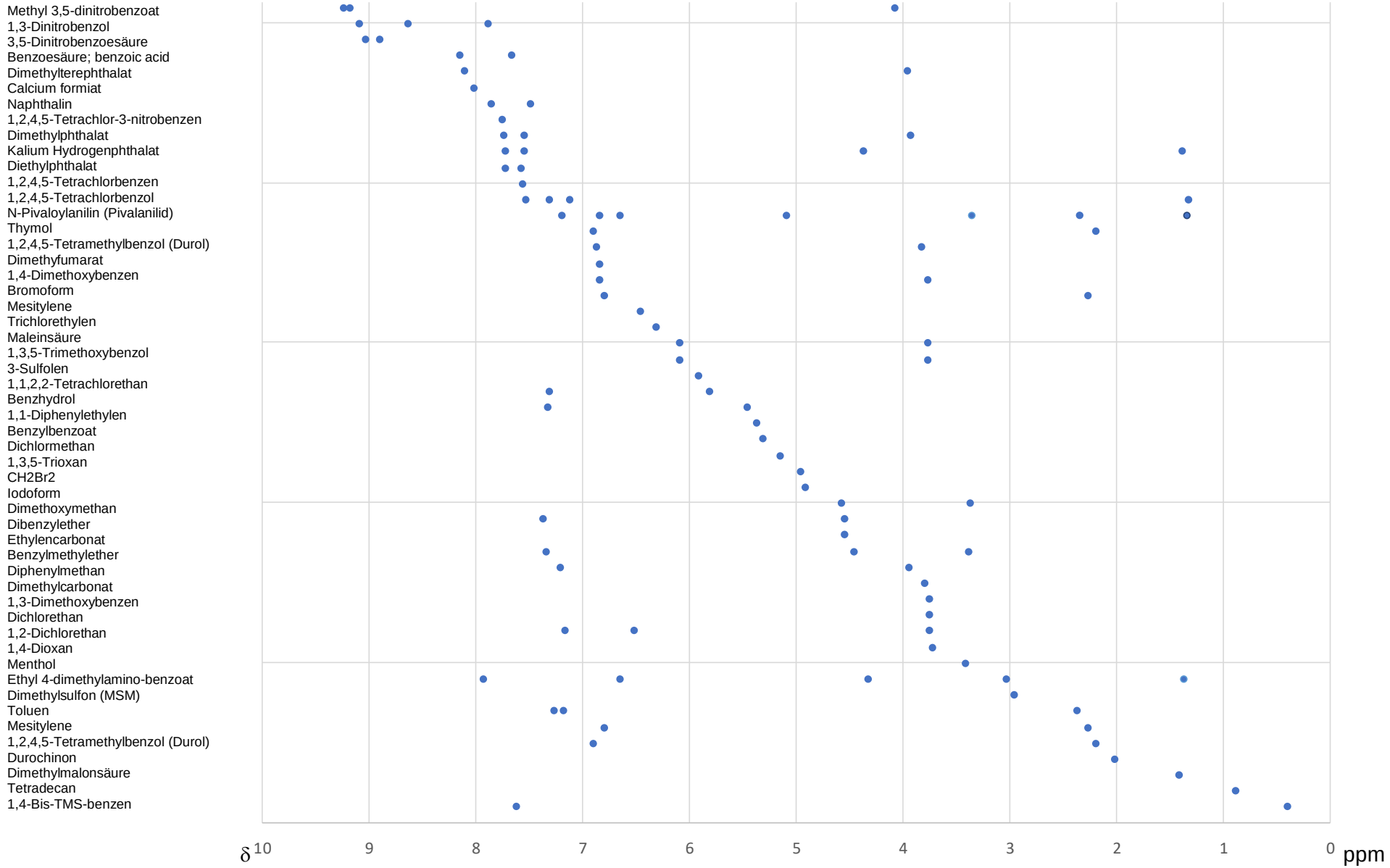
Nuc.	Substance	δ ($CDCl_3$) (D_2O)[a]	*n*	M_r[b]	d(20)	Ref. NMR[c]	Solvent	Mp[d]	Bp[d]	Rec-ov.[e]	Notes[f]	GHS	AKH[g]
	Of Interest / Specific Applications / Present in AKH												
^1H	Benzhydrol (Ph_2CHOH)	5.80 s 7.1–7.5 m	1 10	184.238	–	869	$CDCl_3$ etc	67	298	–			M-C_{13}
	Benzylbenzoat ($PhCO_2Bn$)	5.35 s	2	212.248	1.12	7302	$CDCl_3$ etc	21	323	–			A1
	Benzylmethylether ($Ph\text{-}CH_2\text{-}O\text{-}CH_3$)	3.37 s 4.44 s 7.32 m	3 2 5	122.167	0.987	3571	$CDCl_3$ etc	–52	174	–			H-C_8
	Dibenzylether (Bn-O-Bn)	4.54 s 7.3–7.4 m	4 10	198.265	1.04	1462	$CDCl_3$ etc	4	298	–	reactive		M-C-
	Diethylphthalat 	1.37 t 4.36 q 7.53/7.71	6 4 2/2	222.240	1.11	429	$CDCl_3$ etc	–40	302	–		–	M-C_{12}
	Dimethoxymethan	3.36 s 4.57 s	6 2	76.095	0.859	1213	$CDCl_3$ etc	–105	46	✓	vol.! 330 g/L		H-C_3
	3,5-Dinitrobenzoesäure	8.89 m 9.01 m	2 1	212.117		2230	unlösl. PhH, Et_2O	206	–	–	1.35 g/L		D3
	1,3-Dimethoxybenzen (Resorcin dimethyl ether)	3.74 s 6.50 m 7.15 m	6 3 1	138.166	1.055	2120	$CDCl_3$	–52	217	–	reactive		H-C_8
	1,4-Dimethoxybenzen	3.76 s 6.83 s	6 4	138.166	–	1160	$CDCl_3$	56	213	–	vol.		H-C_8
	Dimethylcarbonat	3.79 s	6	90.078	1.07	2209	D_2O (3.80), DMSO (3.69)	5	90	(✓)	130 g/L		H-C_3
	Dimethylphthalat 	3.91 s 7.53 m 7.73 m	6 2 2	194.186	1.19	423	$CDCl_3$ etc	5	284	–	4 g/L	–	M-C_{10}
	Dimethylterephthalat	3.94 s 8.09 s	6 4	194.186	–	1172	DMSO (8.06/3.87), MeCN (?), MeOD (?)	141	282	–	not D_2O	–	M-C_{10}
	Diphenylmethan (diphenyl methane)	3.93 s 7.1–7.3 m	2 10	168.239	1.01	1257	$CDCl_3$ etc	25	264	–			M-C_{13}
	1,1-Diphenylethylen	5.45 7.31	2 10	180,250	–	1821	$CDCl_3$, etc	6	271	–	selfmade	–	+
	Ethyl 4-dimethylamino-benzoat	1.36 t 3.02 s	3 6	193.246	–	–	MeOD, DMSO	66		–	multi.		M-C_{11}

		4.32 q 6.63 m 7.91 m	2 2 2										
Nuc.	**Substance**	**δ ($CDCl_3$) (D_2O)[a]**	***n***	***M*r[b]**	**d(20)**	**Ref. NMR[c]**	**Solvent**	**Mp[d]**	**Bp[d]**	**Rec-ov.[e]**	**Notes[f]**	**GHS**	**AKH[g]**
^1H	Ethylencarbonat	4.53 s	4	88.062	1.321 (25)	2392	D_2O (4.63), DMSO (4.48), Aceton (4.57)	38	244	–	hygr.		H-C_3
	3-Sulfolen	3.75 m 6.08 m		118.150		3785	$CDCl_3$, C_6D_6, D_2O (x)	66	dec.	–	130 g/L		H-C_4
	1,2,4,5-Tetrachlorbenzen	7.54 s	1	215.882	–	1114	$CDCl_3$, DMSO	140	246	–			H-C_6
	Tetradecan	0.88 t	6	198.394	0.762	3379	$CDCl_3$	5.5	254	–			M-C_{14}
	1,2,4,5-Tetramethylbenzen (Durol)	2.18 s 6.89 s	2 12	134.222	–	2364	$CDCl_3$	79	197	–	vol.		M-C_{10}
	1,3,5-Trimethoxybenzen	3.75 s 6.08 s	9 3	168.192		11035	$CDCl_3$,	53	255	–	reactive		H-C_9
	Others/ Not present												
	1,4-Bis-trimethylsilylbenzen	0.29 s 7.61 s	18 4	222.478	–	–	$CDCl_3$ etc	94	194	–	vol.		–
	Bromoform	6.83 s	1	252.75	2.89	1307	$CDCl_3$ etc	9	150	–	tox., vol.		?
	Calcium formiat	7.5–8.5 s	1	130.112	–	–	D_2O	–	–	–			–
	Dimethylmalonsäure	1.4 s	6	132.115		22178	MeOD, D_2O, DMSO	193		–			–
	Durochinon	2.00 s	12	164.204	–	2123	$CDCl_3$	114	–	–			–
	Iodoform	4.90 s	1	393.732	–	1040	$CDCl_3$ etc.	119	dec.	–	smell, vol.		+
	Maleinsäure (maleic acid)	6.29 s	2	116.072	–	1065	D_2O, MeOD, DMSO	140		–	d1 60 s		–
	Menthol	3.40 m	1	156.269	–	2543	$CDCl_3$, C_6D_6 etc.	43	212	–	multi		+
	Methyl 3,5-dinitrobenzoat	4.07 s 9.17 d 9.23 t	3 2 1	226.144	–	–		109		–	synth.?	–	–
	Pentachlorbenzen	7.53 s	1	250.324	–	10055	C_6D_6 (x)	87	277	–			–
	N-Pivaloylanilin (Pivalanilid)	1.32 s 7.10 m 7.3 m 7.52 m	1 (3) 2	177.247	–	TK-413	Me_2CO	136	–	–	synth. NH var.		M-C_{11}

	2,3,5,6-tetrachloro-1-nitrobenzene.	7.74 s	1	260.879	–	10080	$CDCl_3$, DMSO	101	304	–	cost!		–
	Thymol 	1.33 d 2.35 s 3.34 h 5.08 s 6.63 s 6.83 d 7.18 d	6 3 1 1 1 1 1	150.221	–	–	DMSO (1.13 d, 2.17 s, 3.16 m, 6.5–6.9 m, 9.03 s)	52	232	–	vol. multi. 1 g/L		A1 M-tox
Nuc.	**Substance**	**δ ($CDCl_3$) (D_2O)[a]**	***n***	**M_r[b]**	**d(20)**	**Ref. NMR[c]**	**Solvent**	**Mp[d]**	**Bp[d]**	**Rec-ov.[e]**	**Notes[f]**	**GHS**	**AKH[g]**
^2H	***^2H NMR***	*^2H Shifts*											
^2H	1-Methoxy-4-(D_3-methoxy)benzen	3.72 s	3	141.14		SK314	CH_2Cl_2, δ{C**D**HCl_2} 5.32	61		–	vol.		SK-?
	(D_6)-Benzen	7.16 s	6	84.151	0.950			6.8	79	✓	vol.		+
^{19}F	***^{19}F NMR***	*^{19}F Shifts[1]*											
^{19}F	Benzotrifluorid	–62.61	3	146.112	1.188		$CDCl_3$ etc.	–29	103	(✓)			H-C_7
	4,4′-Difluorobenzophenone	–105.7	2	218.203	–		$CDCl_3$ etc.	105	–	–			–
	Fluorbenzol	–112.96	1	96.104	1.024		$CDCl_3$ etc	–41	85	✓	vol.		H-C_6
	Hexafluorbenzol	–161.64	6	186.056	1.618		$CDCl_3$ etc.	5	81	✓	vol.	?	H-C_6
	Trichlorfluormethan	0.65	1	137.359	1.487		$CDCl_3$ etc	–111	23.7	✓	vol.!		H-C_1 D4
^{31}P	***^{31}P NMR***	*^{31}P Shifts*											
^{31}P	Triphenylphosphat	–17.3	1	326.288	–		$CDCl_3$ etc	49	244(10)	–			M-C_{18}
	Triphenylphosphin	–5.7	1	262.292	–		$CDCl_3$ etc	81	377	–			M-C_{18}
	Triphenylphosphinoxid	30.8	1	278.291	–		$CDCl_3$ etc	157	–	–			M-C_{18}
	Phosphonoessigsäure	16.2	1	140.031	–		D_2O (16.2), CD_3OD (17.7)	146	–	–			–

[a]) Shift of key signals in $CDCl_3$ or D_2O. [b]) M_r with 3 decimals, 2016 values. [c]) Ref. NMR; an SDBS-Link is typically provided - . [d]) Melting point or boiling point, whole number, upper limit of range; bracket number is pressure in torr. [e]) Sample recovery after crude yield determinations: ✓ easy; (✓) possible; – inconvenient. [f]) hygr. = hygroscopic; multi. = multi shift range; *n* g/L = water solubility; synth. = self-synthesized; tox. = toxic; vol. = volatile. [g]) AKH = storage at AK Hintermann.

^{1}H NMR Shift Ranges of Internal Standards (Key Signals) - Graphical Representation - Choose Standard by δ_H Position



^{1}H NMR Shift Ranges - Graphical Representation (Lit.[2])

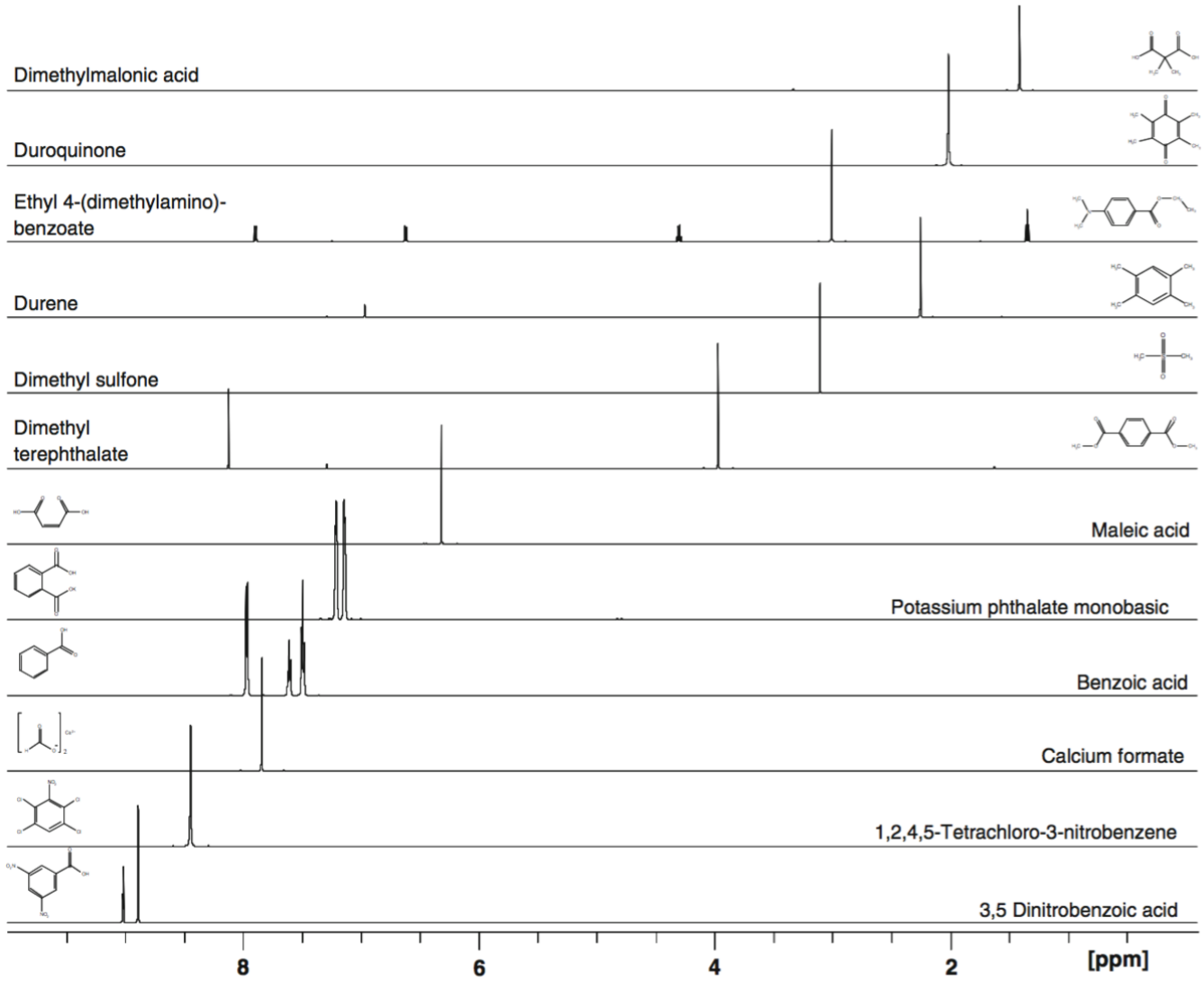


Fig. 4 Set of ^{1}H-NMR spectra of twelve CRM to serve as qNMR standards covering a wide range of chemical shifts and different solubilities. They are all chemically highly stable, non-hygroscopic, and non-volatile

Literature[2, 3, 4, 5, 6, 7, 8]

[1] For ^{19}F Referencing, see: Rosenau, C. P., Jelier, B. J., Gossert, A. D., & Togni, A. "Exposing the Origins of Irreproducibility in Fluorine NMR Spectroscopy". *Angew. Chem. Int. Ed.* **2018**, *57*, 9528–9533. doi:10.1002/anie.201802620

[2] Weber, M., Hellriegel, C., Rück, A., Sauermoser, R., & Wüthrich, J. "Using high-performance quantitative NMR (HP-qNMR®) for certifying traceable and highly accurate purity values of organic reference materials with uncertainties <0.1%". *Accred. Qual. Assur.* **2013**, *18*, 91–98. doi:10.1007/s00769-012-0944-9

[3] G. R. Fulmer, A. J. M. Miller, N. H. Sherden, H. E. Gottlieb, A. Nudelman, B. M. Stoltz, J. E. Bercaw, K. I. Goldberg, "NMR Chemical Shifts of Trace Impurities: Common Laboratory Solvents, Organics, and Gases in Deuterated Solvents Relevant to the Organometallic Chemist", *Organometallics* **2010**, *29*, 2176–2179. doi:10.1021/om100106e

[4] Schönberger, T. "Determination of standard sample purity using the high-precision ^{1}H-NMR process". *Anal. Bioanal. Chem.* **2012**, *403*, 247–254. doi:10.1007/s00216-012-5777-1

[5] Rundlöf, T., Mathiasson, M., Bekiroglu, S., Hakkarainen, B., Bowden, T., Arvidsson, T. "Survey and qualification of internal standards for quantification by ^{1}H NMR spectroscopy". *J. Pharm. Biomed. Anal.* **2010**, *52*, 645–651. doi:10.1016/j.jpba.2010.02.007

[6] Schönberger, T. "Hochpräzise Reinheitsbestimmung analytischer Standards mittels quantitativer ^{1}H-NMR-Spektroskopie". *Toxichem Krimtech* **2012**, *79*, 81; https://www.gtfch.org/cms/images/stories/media/tk/tk79_2/schoenberger1.pdf

[7] Rundlöf, T., McEwen, I., Johansson, M., & Arvidsson, T. (2014). "Use and qualification of primary and secondary standards employed in quantitative ^{1}H NMR spectroscopy of pharmaceuticals". *J. Pharm. Biomed. Anal.* **2014**, *93*, 111–117. doi:10.1016/j.jpba.2013.09.010

[8] Mahajan, S., & Singh, I. P. "Determining and reporting purity of organic molecules: why qNMR". *Magn. Reson. Chem.* **2013**, *51*, 76–81; doi:10.1002/mrc.3906