Extended lithium ion pair indicator scale in tetrahydrofuran[1]

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Abstract: The lithium pK scale has been extended to 25 indicators with a pK range of 9.7–24.4. The resulting scale is compared with the cesium ion pair acidities and to ionic pK's in DMSO and aqueous DMSO.

Key words: ion pair acidity, organolithium compounds, indicator, acidity scale.

Résumé : On a étendu l'échelle pK du lithium à 25 indicateurs couvrant une plage de pK allant de 9,7 à 24,4. On a établi une comparaison entre l'échelle qui en résulte et les acidités des paires d'ion du césium et aux pK ioniques dans le DMSO et de DMSO aqueux.

Mots clés : acidité d'une paire d'ion, composés organolithium, indicateur, échelle d'acidité.

Several years ago we proposed a scale of proton transfer indicators in THF based on the solvent separated (SSIP) lithium ion pair salts of hydrocarbons whose UV–vis spectral characteristics are convenient (1). Equilibrium constants for the individual ion pair proton transfer equilibria in eq. [1] were converted to a numerical pK scale, eq. [2], by arbitrarily assigning to the lithium SSIP of fluorene its free ion pK value in DMSO of 22.90 (per hydrogen) (2).

[1] $\quad \text{RH} + \text{R}'^- \text{Li}^+ \overset{K}{\rightleftharpoons} \text{R}^- \text{Li}^+ + \text{R}'\text{H}$

[2] $\quad \text{p}K(\text{RH}) = \text{p}K(\text{R}'\text{H}) - \log K$

The resulting pK values were related to a corresponding scale involving the contact ion pairs (CIP) of the cesium salts by conductivity measurements of the dissociation of both the lithium and cesium ion pairs to the free ions in THF (3).

The resulting lithium scale has been used in a number of studies of the ion pair acidities of various substrates in THF, including fluorenes with chelating groups (4), dilithiated carboxylic acids (5), silanes (6), dithianes (7), dilithiated 9,9′-bifluorenyl (8), diphenylamine (9), acetylenes (10), polyhalobenzenes (11), ketones. (12–14), and carbazole (15). In the course of these and other studies we have added a number of new indicators to the lithium scale. The present paper presents a summary of the published and unpublished results in a convenient form.

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Other ion pair scales have been proposed in THF solution. Fraser et al. used NMR measurements of equilibria to determine the effective pK's of a number of types of compounds (16–21). This work required measurements at high concentration and no account was taken of the possible role of ion pair aggregation; such aggregation is known to lower measured pK values (22). We have published an extended scale of cesium salts of indicators (23). Buncel and Menon used reactions of 18-crown-6 complexed potassium salts of indicators to determine the ion pair pK of dihydrogen in THF (24). Antipin et al. developed a scale of [2.1.1]-cryptated lithium salts of indicators in THF (25–27).

Results and discussion

The most precise measurements of the equilibria in eq. [1] are those of the so-called double-indicator method. In this approach, both lithium salts have conveniently measurable spectra and the concentrations of both are determined directly. Stoichiometry from the known starting amounts of RH and R′H then provides the equilibrium constant without interference from the traces of adventitious water generally present even with careful work. For example, we have found that with the use of Pyrex glassware the water content cannot be reduced below about 5×10^{-5} M because THF extracts water even from carefully dried and baked glassware. Lower water levels are possible with the use of quartz glassware and storage over molecular sieves in a glovebox. In many cases, the lithium salts were generated by adding 9-lithio-9,10,10-trimethyldihydroanthracene (LiTMDA) to the mixture. LiTMDA is a strong base that readily metallates the indicators on this scale.

UV–visible spectroscopic measurements of eq. [1] require that the two lithium salts have significantly different spectra. Moreover, good precision is not possible if K is too large or too small. These are the primary reasons for having a number of different indicators.

Table 1 summarizes the lithium indicator scale. Included in this table are the abbreviations for the indicators used in many of our papers, together with the absorption λ_{max} and the extinction

Table 1. The lithium indicator pK scale. All pK's are on a per-hydrogen basis.

Symbol	Compound	pK	λ_{max}, nm	(ε)
PTFI	1-Phenyl-3-(2′,3′,5′,6′-tetrafluorophenyl)indene	9.66[a]	448	(37 900)
BBP	1,1,3,3-Bis(biphenylene)propene	10.38	557.5	(112 500)
PePC	1,2,3,4,5-Pentaphenyl-1,3-cyclopentadiene	11.07	346	(41 200)
DPI	1,3-Diphenylindene	12.32	450	(32 900)
			380	(22 000)
TeFPFl	9-(2′,3′,5′,6′-Tetrafluorophenyl)-fluorene	14.12	452	(21 000)
PDP	1,12-(o-Phenylene)-7,12-dihydropleiadene	14.44	401	(20 500)
TPI	1,2,3-Triphenylindene	14.67	436	(16 200)
			393.5	(17 500)
			325.5	(27 000)
Ph-3,4-BF	9-Phenyl-3,4-benzofluorene	14.84	418	(26 000)
			394	(23 900)
9-BpFl	9-Biphenylylfluorene	16.99	526	(25 600)
			498	(33 400)
			373	(14 300)
Ph-1,2-BF	9-Phenyl-1,2-benzofluorene	17.38	472	(11 500)
PhFl	9-Phenylfluorene[b]	17.6	411	(25 300)
Ph-2,3-BF	9-Phenyl-2,3-benzofluorene	17.84	442	(52 000)
DMAPhFl	9-(p-Dimethylaminophenyl)fluorene	19.02	383	(27 800)
3,4-BF	3,4-Benzofluorene[b]	19.29	410	(6 650)
			387	(7 740)
1,2-BF	1,2-Benzofluorene[b]	19.7	454	(8 530)
BA	Benzanthrene[b]	20.13	661	(800)
			447	(35 000)
BnMP	9-Benzyl-9H-benzo[def]fluorene[b]	21.35	535	(6 700)
BnFl	9-Benzylfluorene[b]	21.36	381	(15 400)
IPF	9-Isopropylidenefluorene	22.33	535	(1 730)
			498	(2 200)
			379	(27 700)
BFl	9-Butylfluorene[c]	22.4	387	(16 000)
MeFl	9-Methylfluorene	22.46	387	(16 200)
			517	(1 670)
DiBF	2:3,6:7-Dibenzofluorene[b]	22.68	497	(56 200)
Fl	Fluorene[b,d]	(22.90)	373	(9 300)
2,3-BF	2,3-Benzofluorene[b]	22.95	430	(25 500)
TBFl	9-tert-Butylfluorene	24.41	509	(1 350)
			387	(13 100)
BPDT	Biphenylyldithiane	29.30	485	(27 500)[e]

[a] Referred to the equilibrium mixture of the two indene isomers.

[b] References 1 and 3.

[c] Reference 4.

[d] The reference is taken as the Li SSIP salt of fluorene. Since fluorenyllithium in THF at 25°C is about 70% SSIP and 30% CIP the composite pK(SSIP+CIP) = 22.75 (3).

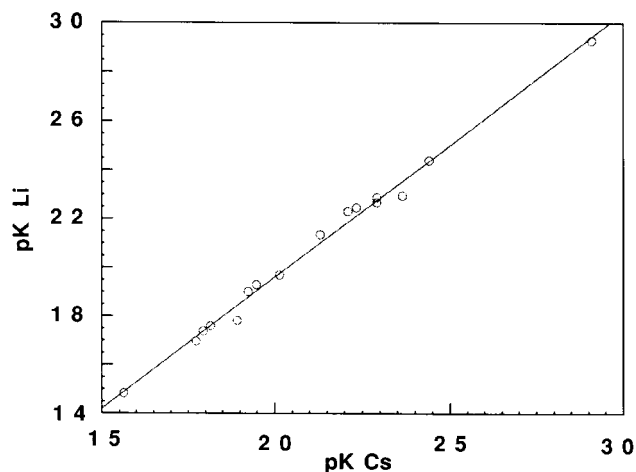[e] CIP pK = 28.20, λ_{max} 388 nm (27 500) (7).

coefficient. The pK values are statistically corrected to be on a per-hydrogen basis; that is, the uncorrected pK of benzanthrene is lower by 0.30 (log 2), 1,3-diphenylindene is higher by 0.30 (the anion has two equivalent positions to which a proton can return), and 9-phenylfluorene is unchanged. The scale ends just below the pK value of 25. Above this value the proton transfer equilibria are inconveniently slow. The dithiane shown was measured by a special technique (7). The exchange rates of cesium salts are much higher and this scale goes up to pK's in the high 30s (23).

The indicators were generally compared with more than one reference. Agreement was generally a few parts in the
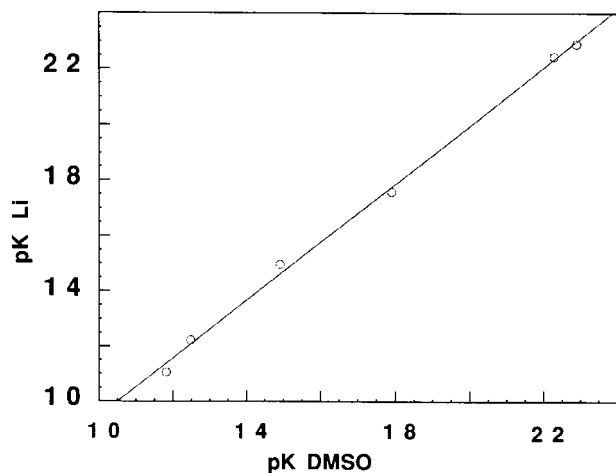
second decimal. Accordingly, the assigned pK's in Table 1 should be accurate to about ± 0.1 units.

The lithium and cesium scales in THF were interrelated by measuring the dissociation constants of several systems (3). The dissociation constants of the SSIP lithium salts of delocalized carbanions are relatively constant at 1×10^{-5} M; the cesium CIP dissociation constants show more variation with structure and are generally in the range $(1-20) \times 10^{-8}$ M. Accordingly, there is generally an excellent correlation between pK's on the two ion pair scales (Fig. 1), but there is some scatter because of the variation in ion pair dissociation constants. Note that both scales are based on fluorene as a standard,

Fig. 1. Comparison of lithium SSIP and cesium CIP acidities in THF at 25°C. The equation of the line shown is $pK(Li) = -1.984 + 1.080\ pK(Cs)$; $R^2 = 0.993$.

Fig. 2. Comparison of Li ion pair pK's in THF with absolute pK's in DMSO. The line shown is $pK(Li) = -0.963 + 1.046\ pK(DMSO)$; $R^2 = 0.998$.

Table 2. Comparison of pK's.

Symbol	Li, THF	Cs, THF[a]	DMSO[b]	aq. DMSO[d]
PePC	11.07		11.8	
DPI	12.32		12.47[c]	
Ph-3,4-BF	14.84	15.62		16.60
TPI	14.67		14.60[c]	
9-BpFl	16.99	17.72		18.21
Ph-1,2-BF	17.38	17.94		
PhFl	17.60	18.15	17.9	18.59
Ph-2,3-BF	17.84	18.92		
DMAPhFl	19.02	19.23		19.61
3,4-BF	19.29	19.47		19.92
1,2-BF	19.70	20.13		
BnFl	21.36	21.30		21.20
IPF	22.33	22.08		
MeFl	22.46	22.32	22.3	21.80
DiBF	22.68	22.91		
Fl	(22.90)	(22.90)	22.90	22.40
2,3-BF	22.95	23.63		
TBFl	24.41	24.39		23.41
BPDT	29.30	29.1		

[a] Reference 23.
[b] Reference 2.
[c] Reference 29.
[d] Reference 28.

ion pair values in THF (Fig. 3) shows an excellent correlation but with a slope of only 0.70. The range of pK's of these delocalized carbanions is highly attenuated in the aqueous medium.

Some of the results show features of special interest. The powerful inductive effect of fluorine is shown by comparing PTFl with DPI and TeFPFl with PhFl. The four fluorine substituents increase acidity by 2.6–3.5 pK units. Steric hindrance to conjugation can play an important role. A phenyl substituent in the 9-fluorenyl position of 2,3-benzfluorene (11*H*-benzo[*b*]fluorene) and 3,4-benzfluorene (7*H*-benzo[*c*]fluorene) increases acidity by 4.5–5.1 pK units, but a similar substitution in 1,2-benzfluorene (7*H*-benzo[*a*]fluorene) has only a 2.3 pK unit effect, undoubtedly because of steric interaction between the benzo group and the phenyl ring. In agreement with the DMSO results of Bordwell and Drucker (30), triphenylindene (TPI) is 2.3 pK units less acidic than 1,3-diphenylindene (DPI), probably in part because the central phenyl substituent impedes conjugation of the terminal phenyls.

Conclusions

The lithium scale of SSIP indicators in THF has been extended to 25 compounds. This scale should find use in ion pair acidity measurements of lithium salts in THF, particularly in the region of convenient proton transfer rates below $pK = 25$.

Experimental section

The syntheses of many of the indicators have been reported previously (30–35) or were available from our past work or commercially. In general, the aromatic hydrocarbons were recrystallized from hexane or an ethanol–hexane mixture and

the Li SSIP in one case and the Cs CIP in the other. Because of the relative insensitivity to structural variation of the ion pair dissociation constants of the lithium salts of these delocalized carbanion indicators, the free ion acidities in THF should closely parallel the SSIP acidities. The slope of the correlation in Fig. 1, 1.08, shows that the Cs scale is slightly compressed compared to the Li scale; this result is probably due to the slightly higher electrostatic attraction of the carbanion to a cesium cation, which is effectively smaller than the solvent-separated lithium cation. There is an excellent correlation with the absolute pK as in DMSO with a slope close to unity (Fig. 2). This correlation shows that the choice of any other standard than fluorene would result in but little change in the lithium scale. Note that a number of compounds on the Li scale are not on the Cs and DMSO scales.

A number of the same compounds were studied in aqueous DMSO mixtures by the H_ method and should represent the pK's for the dilute aqueous standard state (28). These values are also summarized in Table 2; a comparison with the lithium

Fig. 3. Comparison of aqueous DMSO pK's (H_ method) with lithium ion pair pK's. The correlation line shown is pK(aq DMSO) = 6.26 + 0.701 pK(Li, THF); R^2 = 0.998.
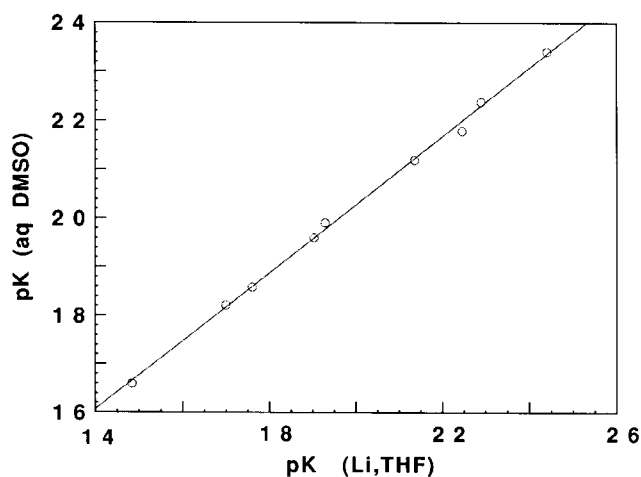
then vacuum sublimed. Purity was assessed by spectroscopic methods, melting point, and (or) elemental analysis as necessary. The details of the procedure of pK measurement have been described in previous publications.

1,1,3,3-Bis(biphenylene)propene (BBP)
This compound was prepared following Kuhn et al. (36) and was purified by multiple recrystallizations from benzene–hexane to remove the last traces of fluorene and, finally, from toluene. Sublimation afforded a white powder, mp 215–216°C (lit. (36) mp 205–206°C); ^{1}H NMR (300 MHz, CDCl$_3$) δ: 8.33 (d, J = 7.5 Hz, 1H), 7.20–7.85 (m, 15H), 6.51 (d, J = 10 Hz, 1H), 5.87 (d, J = 10 Hz, 1H).

1-Phenyl-3-(2′,3′,5′,6′-tetrafluorophenyl) indene (PTFI)
To a 250 mL flame-dried three-necked flask containing 100 mL of dry THF and 2 g (13.3 mmol) of 1,2,4,5-tetrafluorobenzene was added 5.7 mL of n-BuLi (2.1 M in hexanes) dropwise at –78°C. After 20 min, 2.08 g (10 mmol) of 3-phenylindanone was added. The solution was stirred for an additional 1 h at –50°C and then quenched with water. An NMR spectrum of the crude product showed a mixture of the desired carbinol and starting material (probably through enolization of the ketone by the tetrafluorophenyllithium) in a ratio of 60/40. The crude mixture of carbinol and ketone was dissolved in 60 mL of benzene and a few drops of concentrated H$_2$SO$_4$ were added. The mixture was refluxed for 5 h until TLC showed no carbinol remaining. The indene was isolated by flash column chromatography using hexane–ether in a ratio of 10/1 as an eluant, recrystallized from methanol, and finally sublimed; mp 104–106°C. ^{1}H NMR: 7.18–7.33 (m, 9H), 7.13 (tt, J_1 = 9.6 Hz, J_2 = 7.3 Hz), 6.81 (d, J = 1.8 Hz), 4.82 (d, J = 1.8 Hz). ^{19}F NMR (H-decoupled): –138.78 (m, 2F), –139.09 (m, 2F) relative to CFCl$_3$. HRMS, calcd.: 340.0882; found: 340.0875.

General procedure for the preparation of the lithium bases
Lithium diisopropylamide (LDA) was freshly prepared, twice sublimed under vacuum, and placed in the glovebox. The neutral indicator, 9,9,10-trimethyldihydroanthracene (5.3 mg, 0.024 mmol), was added to a vacuum-adapted storage flask. To this flask, THF (2 mL) and LDA (2.1 mg, 0.020 mmol) were added, resulting in an orange solution. The deprotonation reaction is slow and it was necessary for reaction to proceed for a minimum of 3 days with occasional stirring. The flask was then taken out of the glovebox and directly attached to a vacuum line. The THF was removed via vacuum and the flask was returned to the glovebox. The resulting red semi-solid was dissolved with an appropriate amount of THF to give a 0.1 M concentration. The resulting base was stored at –10°C and checked periodically for decomposition.

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