

CARBANION MECHANISMS

VII *. METALLATION OF HYDROCARBON ACIDS BY POTASSIUM AMIDE AND POTASSIUM METHYLAMIDE IN TETRAHYDROFURAN AND THE RELATIVE HYDRIDE ACIDITIES

ERWIN BUNCEL * and BALACHANDRAN MENON

Department of Chemistry, Queen's University, Kingston K7L 3N6 (Canada)

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Summary

The metallation of a series of arylmethanes of decreasing acidity has been studied in tetrahydrofuran medium. Potassium amide has been found to metallate triphenylmethane, diphenylmethane and di-2,4-xilylmethane to completion, di-*p*-tolylmethane to partial completion, while toluene is unreactive. Correspondingly, potassium methylamide in tetrahydrofuran metallates to completion 2,4-dixilylmethane and di-*p*-tolylmethane, but is unreactive towards toluene. From these results one can estimate the relative acidities of ammonia and of methylamine, with respect to these hydrocarbon acids, in tetrahydrofuran. The effect of ion association phenomena on acidity constants in these systems is considered. The results pertain to the utility of the KNH₂/THF and KNHCH₃/THF basic systems as metallating agents.

Introduction

We reported recently [1,2] on the metallation of a series of hydrocarbon acids as effected by potassium hydride in tetrahydrofuran (THF) in the presence of 18-crown-6 polyether according to eq. 1. The study served



to provide information concerning the metallating properties of the KH/crown ether/THF system, and also afforded the first experimental approach towards determination of the acidity of molecular hydrogen. The pK_a of H₂ is of funda-

* For Part VI, see ref. 1.

mental importance [3,4] and is also requisite in studies of isotopic exchange of D_2 in basic systems [5-10].

It appeared of interest to extend the method that we developed in the study of reaction 1 to metallation by potassium amide, with respect to the information that would be gained concerning the acidity of ammonia, and thereby on the synthetic potential of the KNH_2/THF system. Similar considerations would apply to the $KNHCH_3/THF$ system. In contrast to the wealth of information that is available concerning the basicities of amines, there is a dearth of data relating to their acidities. A pK_a value of 35 has been assigned to NH_3 by indirect methods [11] and there appear to be no experimentally determined pK_a values reported for aliphatic amines. However, the acidities of binary hydrides are of fundamental importance in the understanding of the effect of structural changes on molecular properties, as well as having application in synthesis. For example, knowledge of the acidity of a hydride XH_n would enable one to utilize to maximum advantage the alkali metal hydride MXH_{n-1} in metallation processes. Although KNH_2 has in the past found wide usage as a metallating agent in synthetic sequences involving carbanion intermediates (e.g. in alkylation [2]) this use has largely been limited to substrates in the medium acidity range such as ketones and nitriles [13]. Metallation by $KNHCH_3$ has not previously been studied systematically.

Results and discussion

We report now the results of a systematic study of metallation by KNH_2 and by $KNHCH_3$, in THF solvent, of a series of arylmethanes of decreasing acidity (eq. 2 with $R' = H$ or CH_3).



The arylmethanes used, with their abbreviated notation and pK_a values (determined in the cesium cyclohexylamide/cyclohexylamine system [14]) are: triphenylmethane (TPM, 31.5), diphenylmethane (DPM, 33.1), di-2,4-xyllylmethane (DXM, 36.3), *p*-phenyltoluene (PPT, 38.7) and toluene (TOL, 41.0). A spectrophotometric method has been used to estimate the formation of the carbanion alkali metal salts, RK, which are known to have characteristic absorptions in the UV-visible region.

Potassium amide metallations

The experimental procedure involved use of a glass reaction vessel equipped with a vacuum stopcock and a quartz cuvette to facilitate the spectrophotometric measurements under anaerobic conditions and in the absence of traces of moisture. Dry THF was transferred under vacuo into the reaction vessel containing potassium amide, prepared in situ from potassium metal and liquid ammonia. The hydrocarbon was introduced under nitrogen and the development of the carbanion spectrum was monitored. The time required to reach maximum absorbance with the various hydrocarbons was found to be as follows: TPM, 5 min; DPM, 40 min; DXM, 100 min; PPT, 50 min *. The stabilities of the car-

* Although there is an approximate correlation between the rates of these reactions and the hydrocarbon acidities, it should be emphasized that the results of the present work (Tables 1 and 3) are interpreted only in terms of the equilibrium acidities (see Table 2).

TABLE 1
METALLATION OF ARYLMETHANES BY POTASSIUM AMIDE IN THF

RH	[RH] × 10 ³ (M)	[KNH ₂] ^a (M)	λ _{max} (nm)	A	% R _{rxn} .
TPM	0.666	0.0379	486	1.47	104 ^c
DPM	0.230	0.0268	440	1.00	101 ^c
DXM	0.185	0.0279	442	0.56	100 ^d
	0.481	0.0246 ^b	442	1.34	100 ^d
PPT	2.070	0.0302 ^b	470	0.33	10 ^c
	1.083	0.0344	470	0.30	17 ^e
	0.546	0.0229	470	0.12	14 ^e
TOL	1.700	0.0359	—	—	0

^a Calculated from the amount of potassium used, assuming complete reaction with NH₃; the KNH₂ is only partly soluble in THF and the [KNH₂] values are given only for purposes of comparison. The measured solubility of KNH₂ in THF is 1.3 × 10⁻⁴ M (see Experimental). ^b Fe₂O₃ was not used as a catalyst in the preparation of KNH₂ in these cases only. ^c The percent reaction was calculated as % rxn = (A_{obs}/C₀l) × 100, where *c* is the extinction coefficient of RK, C₀ is the initial concentration of RH and *l* is the cell path length (0.1 cm). For TPM⁻K⁺ and DPM⁻K⁺, the *c* values used are 21,300 and 43,000 respectively [2]. ^d A plot of absorbance vs. concentration gives a straight line Beer's law plot passing through the origin. From the slope of the line, *c* for DXM⁻K⁺ is calculated as 29,000. ^e Calculated using for PPT⁻K⁺, *c* = 16,200 (see Table 3).

banions in this system were evaluated by following the decrease of the spectral absorptions with time. In the case of TPM⁻K⁺ there was no decrease in the absorption during several hours while the absorptions of DPM⁻K⁺, DXM⁻K⁺ and PPT⁻K⁺ showed a decrease of 10% during 1 h.

The complete results on the metallation reaction of the hydrocarbons RH by KNH₂ in THF are given in Table 1. It is seen that KNH₂/THF is completely effective in metallating TPM, DPM and DXM, partially effective in metallating PPT, and completely unreactive towards TOL. From eq. 2 it can be inferred that the acidity of NH₃ must be intermediate between those of DXM and TOL and comparable to that of PPT in the THF medium.

An apparent pK_a value for NH₃

The data that we have obtained can be used to calculate an apparent pK_a value for NH₃ in this system according to eq. 3:



For the case of PPT one can calculate via eq. 4 an equilibrium constant *K*_{rel}, and hence pK_{app}^{NH₃} via eq. 5:

$$K_{\text{rel}} = \frac{[\text{R}^-\text{K}^+]_e [\text{NH}_3]_e}{[\text{K}^+\text{NH}_2^-]_e [\text{RH}]_e} \quad (4)$$

$$\text{pK}_{\text{app}}^{\text{NH}_3} = \text{pK}_a^{\text{RH}} - \text{p}K_{\text{rel}} \quad (5)$$

The results for the three separate experiments performed with this hydrocarbon are given in Table 2. [RK]_e is the experimentally determined equilibrium carbanion concentration, [KNH₂]_e is the measured solubility of potassium amide in THF, and [RH]_e = [RH]₀ - [RK]_e. Also, [RK]_e = [NH₃]_t, the total ammonia

TABLE 2
 CALCULATION OF $pK_{app}^{NH_3}$ FROM THE REACTION BETWEEN *p*-PHENYLTOLUENE, (PPT) AND KNH_2 IN TETRAHYDROFURAN USING DATA IN
 TABLE 1

$[PPT]_0^a$ $\times 10^3 (M)$	$[PPT]_e^b$ $\times 10^3 (M)$	$[NH_3]_i^d$ $\times 10^3 (M)$	$[NH_3]_e^d$ $\times 10^3 (M)$	$[PPT]_e^c$ $\times 10^{-3} (M)$	$(KNH_2) /$ $\times 10^4 (M)$	$K_{rel}^{\#}$	$pK_{rel}^{\#}$	$pK_{app}^{NH_3}$
2.070	0.203	0.203	0.180	1.867	(1.34 ± 0.46)	0.169 ± 0.042	0.818 ± 0.110	37.78 ± 0.11
1.088	0.185	0.185	0.164	0.898	(1.34 ± 0.46)	0.274 ± 0.072	0.580 ± 0.110	38.01 ± 0.10
0.646	0.0740	0.0740	0.0657	0.472	(1.34 ± 0.46)	0.0836 ± 0.0222	1.099 ± 0.108	37.53 ± 0.12

^a Initial concentration of PPT. ^b Spectrophotometrically measured carbanion concentration at equilibrium. ^c Total ammonia produced. ^d Equilibrium concentration of ammonia in solution phase. ^e Equilibrium concentration of PPT. / Measured concentration of KNH_2 in THF. [#] Error limits for K_{rel} , pK_{rel} and $pK_{app}^{NH_3}$ are based on the experimental error in the measurement of the solubility of KNH_2 in THF.

produced, and this will be partitioned between the solution and gaseous phases, i.e. $[\text{NH}_3]_e = [\text{NH}_3]_l - [\text{NH}_3]_g$ where $[\text{NH}_3]_e/[\text{NH}_3]_g = 7.95$ from the measured solubility of ammonia in THF. This enables pK_{rel} to be evaluated and hence $pK_{\text{app}}^{\text{NH}_3}$. One thus obtains $pK_{\text{app}}^{\text{NH}_3} = 37.8 \pm 0.2$.

It should be noted however that the calculation for K_{rel} according to eq. 4 is based on overall concentrations of KNH_2 and RK . In the low dielectric constant THF medium these metal salts are expected to be present as ion pairs and higher aggregates [15]. The state of association will, moreover, be different for the charge delocalized carbanionic species and for the charge localized metal amide. Noting that the pK_a of a species AH in solvent S refers to the ionization process giving the free ions $(\text{A}^-)_{\text{in S}}$ and $(\text{SH}^+)_{\text{in S}}$, it follows that it is not possible in the present system to obtain a pK_a for NH_3 which would be a valid measure of the true ionization process. The problems in obtaining valid pK_a 's from measurements in media of low dielectric constant, have been discussed by Bordwell [16], Streitwieser [17], and others [11,18,19].

Although, as we have shown, the present results do not yield an absolute pK_a for NH_3 , they do provide valid information with respect to the relative acidity of NH_3 and the hydrocarbons under examination in the THF medium. Since these experimental conditions typically apply to metallation processes of a variety of organic molecules, the present observations provide useful guidelines for the application of potassium amide in organic syntheses [12].

Potassium methylamide metallations

These experiments were performed using the technique which has been described for the $\text{RH}/\text{KNH}_2/\text{THF}$ reactions. However, the hydrocarbon series examined with the $\text{KNHCH}_3/\text{THF}$ system was truncated, only the less acidic members being studied. It was found that the maximum absorbance of the carbanions was reached more quickly compared with the KNH_2/THF system, i.e. 20 min for $\text{DXM}^- \text{K}^+$ and 8 min for $\text{PPT}^- \text{K}^+$ [2]. The carbanion species were also relatively less stable in this basic system, reaching 90% decomposition in 30 min in the case of $\text{PPT}^- \text{K}^+$.

The detailed results for the $\text{RH}/\text{KNHCH}_3/\text{THF}$ system are given in Table 3. It is seen that DXM and PPT are completely metallated but TOL is unreactive.

TABLE 3
METALLATION OF ARYLMETHANES BY POTASSIUM METHYLAMIDE IN THF

RH	$[\text{RH}] \times 10^3$ (M)	$[\text{CH}_3\text{NHK}]^a$ (M)	λ_{max} (nm)	A	% Rxn
DXM	0.511	0.0317	442	1.42	96
PPT	0.440	0.0305	470	0.60	100 ^c
	1.089	0.0264	470	1.84	100 ^c
	0.658	0.0383	470	1.10	100 ^c
	0.342	0.0416 ^b	470	0.50	100 ^c
TOL	1.393	0.0305	—	—	—

^a As footnote ^a in Table 1: measured solubility of KNHCH_3 in THF is $7.8 \times 10^{-3} \text{ M}$. ^b Fe_2O_3 was not used as a catalyst in the preparation of CH_3NHK in this case only. ^c A plot of absorbance vs. concentration is given a straight line Beer's law plot through the origin. From the slope of the line, ϵ for $\text{PPT}^- \text{K}^+$ is calculated as 16,200.

It follows from these results that CH_3NH_2 is less acidic than PPT but more acidic than TOL, under the experimental conditions. These results may be compared with those for KNH_2/THF in Table 1.

It can be concluded from the results of this study that the KNH_2/THF and $\text{KNHCH}_3/\text{THF}$ basic systems are capable of metallating efficiently hydrocarbons of very low acidity. In the arylmethane series, the carbanions generated exhibit satisfactory stability for the KNH_2/THF basic system but not for the $\text{KNHCH}_3/\text{THF}$ system. The results also yield the relative acidity order $pK_a^{\text{CH}_3\text{NH}_3} > pK_a^{\text{NH}_3}$ in the tetrahydrofuran medium.

Experimental

Materials

Ammonia and methylamino (Matheson) were dried and stored over metallic sodium, as liquids, prior to use. THF was dried by distilling from calcium hydride, and then stored over *n*-butyllithium containing a few mg of triphenylmethane, which acted as an indicator via the trityl anion. Hydrocarbon acids were procured commercially, except for DXM which was prepared according to ref. 20.

Procedure

A glass ampoule containing a known weight of potassium (25–35 mg) sealed under vacuo was placed in the cylindrical reaction vessel (~120 ml) equipped with a "Rotaflo" stopper and 0.1 cm cuvette [21]. Following evacuation of the vessel the ampoule was broken by shaking, and ammonia (or methylamine), 1–2 g, dried over sodium, was distilled in under vacuo. A small quantity of Fe_2O_3 (1–3 mg) in a vial was then introduced into the reaction vessel under nitrogen. In the case of the potassium-ammonia solution the blue color changed into pale yellow in 15–30 min at -30°C indicating the formation of KNH_2 (as compared to 4–6 h in the absence of Fe_2O_3). For the case of the potassium-methylamine solution the blue color changed into pale in 20 h at 5°C (as compared to 72 h in the absence of Fe_2O_3). The reaction vessel was then attached to the vacuum line, the ammonia (or methylamine) was distilled back into the storage vessel, and dry THF introduced by distillation under vacuo. A weighed quantity of the hydrocarbon was then introduced into the reaction vessel in a small vial under nitrogen, the vessel was shaken and placed into the cell compartment of a Unicam SP800 spectrophotometer for intermittent monitoring.

Solubility of potassium amide and potassium methylamide in THF

Potassium amide (potassium methylamide) was prepared in the reaction vessel as described above and dry THF distilled in. The contents of the vessel were shaken vigorously at room temperature for 1 h and filtered under vacuo through a glass fritted disc into another receiver. The filtrate was evaporated to dryness, the residue dissolved in water and titrated with standard 0.01 *N* HCl. The results obtained were $(1.34 \pm 0.46) \times 10^{-4} M$ for KNH_2 in THF and $(7.77 \pm 0.31) \times 10^{-3} M$ for KNHCH_3 in THF.

Attempts were made to measure the solubility of KNH_2 and KNHCH_3 in THF by filtering the KNH_2/THF ($\text{KNHCH}_3/\text{THF}$) suspension through the

fritted disc into another reaction vessel containing triphenylmethane so as to generate TPM^-K^+ which would then be estimated spectrophotometrically and thereby yield the concentration of KNH_2 (KNHCH_3). However the characteristic color of TPM^-K^+ was in fact not obtained in the filtrate, apparently due to reaction of KNH_2 (KNHCH_3) with the THF solvent during the slow filtration process. This result also suggests that the solubility data for KNH_2 (KNHCH_3) given above may be too high, since the titrimetric procedure yields the total base content of the solutions.

Solubility of ammonia in THF

The solubility of ammonia in THF was determined by a titrimetric method. 20 ml of anhydrous THF was saturated with dry NH_3 gas. Aliquots of 1.0 ml were then withdrawn using a gas-tight syringe, quenched by adding to 25.0 ml of 0.1 N aq. HCl, and titrated with 0.1 N aq. NaOH. Based on three separate experiments, the mean value of the solubility of NH_3 in THF is $0.355 \pm 0.005 M$. The solubility coefficient of NH_3 in THF can then be expressed as the volume of gas dissolved by unit volume of liquid, i.e. $22.4 \times 0.355 = 7.95$.

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