6.15 (d, J = 11 Hz) and 2.67 (dq, J = 11 and 7 Hz), respectively. The chemical shifts are reported using internal THF-d_7 (δ 3.58) or internal toluene-d_7 (δ 2.09 or 6.98) as reference.

Hydrolysis of 3. To a reaction flask containing 2.0 mmol of **3** at room temperature was introduced 1.0 mL of water. After 1 h of stirring, the reaction mixture was treated with 5 mL of 3 N NaOH and 5 mL of 30% H_2O_2. After the usual workup and purification by column chromatography (silica gel-pentane) and distillation, 0.23 g (83%) of 4-(trimethylsilyl)-2-pentene (**23**) was isolated as a colorless liquid (Z:E = 10:1): IR (neat) 1640 (w), 1450 (m), 1400 (m), 1250 (s), 850 (s), 725 (s), 690 (s), 670 (s) cm^{-1}. Z isomer: ^{1}H NMR δ 5.30 (1 H, dq, J = 10.8 and 6.4 Hz), 5.18 (1 H, tq, J = 10.8 and 1.5 Hz), 1.83 (1 H, m), 1.54 (3 H, dd, J = 6.4 and 1.5 Hz), 0.99 (3 H, d, J = 7.1 Hz), -0.06 (9 H, s); ^{13}C NMR δ 134.20, 119.84, 21.39, 14.92, 13.12, -3.54; MS m/e 142 (M^+), 127, 99, 85, 73. The isomer ratio was determined by the integration of the ^{1}H NMR spectrum and by gas chromatography.

Hydrolysis of 4. To a reaction flask containing 1.6 mmol of **4** at room temperature was introduced 10 mL of water. After 2 h of stirring, the reaction mixture was treated with 5 mL of 3 N NaOH and 5 mL of 30% H_2O_2. After the usual workup and purification by silica gel chromatography (hexane), 0.235 g of 4-(trimethylsilyl)-2-octene (**24**) (79% yield, Z:E = 9:1) was isolated as a colorless liquid: IR (neat) 1635 (w), 1450 (m), 1390 (m), 1370 (m), 1240 (s), 1120 (w), 1080 (m), 960 (m), 830 (s), 780 (m), 740 (m), 720 (m), 680 (m) cm^{-1}. Z isomer: ^{1}H NMR δ 5.40 (1 H, dqd, J = 10.8, 6.6, and 1 Hz), 5.14 (1 H, tq, J = 10.8 and 1.7 Hz), 1.79 (1 H, tdd, J = 11, 3, and 1 Hz), 1.56 (3 H, dd, J = 6.7 and 1.7 Hz), 1.5-1.1 (6 H, br m), 0.88 (3 H, t), -0.03 (9 H, s); ^{13}C NMR δ 132.92, 121.22, 31.98, 29.41, 28.06, 22.61, 14.12, 13.28, -3.11. Anal. Calcd for $C_{11}H_{24}Si$: C, 71.65; H, 13.12. Found: C, 71.09; H, 12.47. The isomer ratio was determined by the integration of the ^{1}H NMR spectrum and by gas chromatography.

Hydrolysis of 17. To a reaction flask containing 1.98 mmol of **17** at 0 °C was introduced 1.0 mL of water. After 1 h of stirring at room temperature, the reaction mixture was treated with 5 mL of 3 N NaOH and 5 mL of 30% H_2O_2. After the usual workup and purification by column chromatography (silica gel-pentane) and distillation, 0.21 g (75%) of (E)-4-(trimethylsilyl)-2-pentene[26] (**25**) was isolated as a colorless liquid: ^{1}H NMR δ 5.45 (1 H, ddq, J = 15.2, 7.8, and 1.5 Hz), 5.23 (1 H, dqd, J = 15.2, 6.2, and 1.1 Hz), 1.67 (3 H, dt, J = 6.2 and 1.5 Hz), 1.51 (1 H, m), 1.04 (3 H, d, J = 7.3 Hz), -0.03 (9 H, s); ^{13}C NMR δ 134.04, 120.62, 26.11, 18.17, 13.79, -3.50; MS m/e 142 (M^+), 127, 99, 85, 73. The Z isomer was not detected by the ^{1}H and ^{13}C NMR spectra and gas chromatography.

Hydrolysis of 18. To a reaction flask containing 1.4 mmol of **18** at 0 °C was introduced 10 mL of water. After 2 h of stirring at room temperature, the reaction mixture was treated with 5 mL of 3 N NaOH and 5 mL of 30% H_2O_2. After the usual workup and purification by silica gel chromatography (hexane), 0.175 g of (E)-4-(trimethylsilyl)-2-octene (**26**) (67% yield) was isolated as a colorless liquid: IR (neat) 1640 (w), 1440 (m), 1370 (m), 1240 (s), 1120 (w), 1080 (m), 960 (s, E geometry), 830 (s), 740 (m), 680 (m) cm^{-1}; ^{1}H NMR δ 5.2 (2 H, m), 1.66 (3 H, d, J = 4.8 Hz), 1.4-1.1 (7 H, br m), 0.88 (3 H, t), -0.05 (9 H, s); ^{13}C NMR δ 132.67, 122.25, 33.09, 31.73, 28.73, 22.65, 18.14, 14.10, -3.11. The Z isomer was not detected by the ^{1}H and ^{13}C NMR spectra and gas chromatography.

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Evidence in Favor of Lithium-Halogen Exchange Being Faster Than Lithium-Acidic Hydrogen (Deuterium) Exchange

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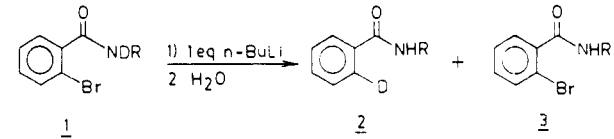
Abstract: Treatment of 2-iodo-3-(deuterioxymethyl)quinoline with 1.5 equiv of n-butyllithium in ether, followed by aqueous work up, furnished 2-deuterio-3-(hydroxymethyl)quinoline in greater than 50% yield, confirming our earlier report,[2] which has been questioned by Beak and co-workers in this journal.[1] A mechanism is proposed, in which the reaction of n-butyllithium is faster with C-I bond than with acidic deuterium. Further experiments are described in which the reaction of n-butyllithium is also faster with the C-I bond than with the ester carbonyl group.

In a recent paper[1] Beak and co-workers report that when N-deuterio-N-isopropyl-2-bromobenzamide (**1**) is treated with 1 equiv of n-butyllithium, N-isopropyl-2-deuteriobenzamide (**2**), and N-isopropyl-2-bromobenzamide (**3**) are formed in 1:1 ratio, each in 33% yield (Scheme I).

They propose a mechanism (Scheme II) which, in particular, is to explain the formation of **2** and **3** in the ratio 1:1.

In the above mechanism, n-butyllithium reacts first with the acidic deuterium of the N-deuterium bond to give the N-lithioamide **4**. Another mole of n-butyllithium then reacts further with the C-Br bond to furnish the dilithiated species **5**. The preference for the n-butyllithium to react with the C-Br of **4** rather than with acidic deuterium of the unreacted **1** is attributed to the local concentration of n-butyllithium in the vicinity of the N-lithiated amide **4** and the fastness of this reaction with respect to mixing of n-butyllithium with the unreacted **1**. Since only 1 equiv of

Scheme I



1 2 3

R = i-Pr

n-butyllithium is used, all the reagent is consumed in its reaction with 50% of **1**. The dilithiated species **5** formed then reacts with the unreacted **1** to give **2** and **3** in the ratio 1:1, the deuterated species **3** itself being formed in no greater than 50% yield.

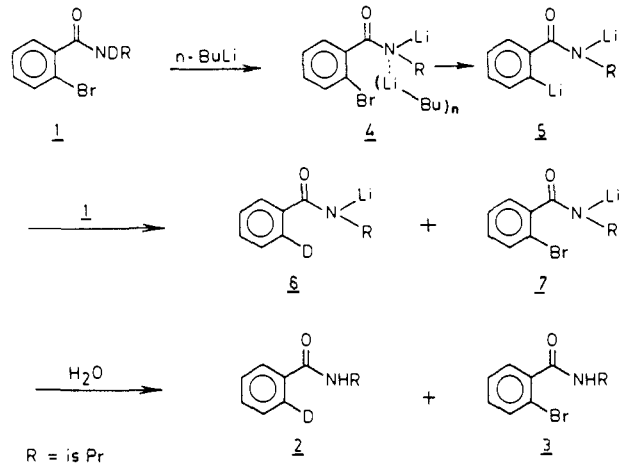
An alternate pathway for the formation of **3** was considered by the authors. This (Scheme III) is similar to what we had proposed[2] for the lithiation of 2-iodo-3-(hydroxymethyl)quinoline **9**.

(1) Beak, P.; Musick, T. J.; Chen, C.-w. *J. Am. Chem. Soc.* **1988**, *110*, 3538.

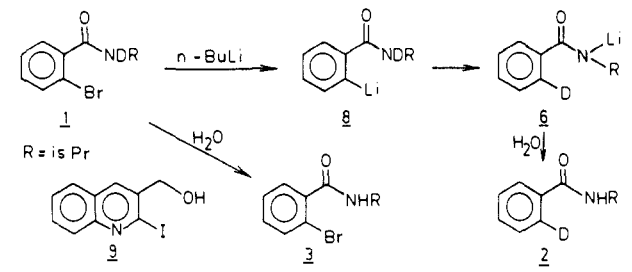
(2) Narasimhan, N. S.; Ammanamanchi, R. *J. Chem. Soc., Chem. Commun.* **1985**, 1368.

0002-7863/90/1512-4431$02.50/0

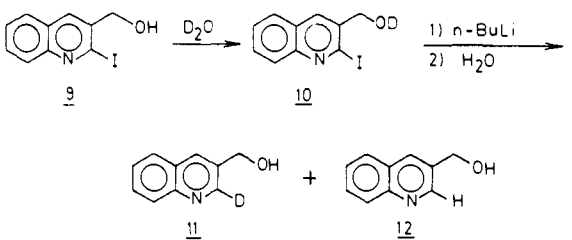
Scheme II



Scheme III



Scheme IV



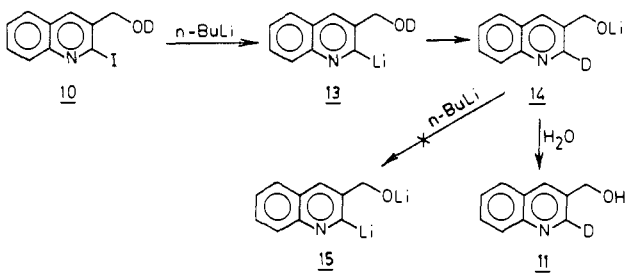
In this mechanism *n*-butyllithium reacts first with the C–Br bond to give the nuclear lithiated amide **8**, which then undergoes an intramolecular D, Li exchange to give **6**. The latter on aqueous workup yields **3**. In this mechanism, formation of **2** would be explained by proposing that the reaction of *n*-butyllithium with **1** was incomplete. This explanation was not satisfactory; but more so was the fact that the mechanism did not explain, specifically, why the reaction always gave **2** and **3** in 1:1 ratio, as observed by Beak and co-workers. For this reason Beak and co-workers rejected the mechanism and more particularly the postulate that *n*-butyllithium reacts first with the C–Br bond then with the acidic deuterium, which is central to the mechanism (Scheme III).

There are several reports in literature[3] where again it is postulated that alkyllithium compounds react faster with the C–halogen bond than with acidic hydrogen. Beak and co-workers investigated two of them. Once again they found that it was not necessary to postulate that *n*-butyllithium reacted faster with the C–halogen bond than with the acidic hydrogen and that these cases were in accord with their mechanism.

Recently we had reported[2] that when 2-iodo-3-(hydroxymethyl)quinoline (**9**) was converted to the O-deuterated derivative **10** and treated with 2 equiv of *n*-butyllithium, a mixture of **11** and **12** was obtained in a total yield of 91% (Scheme IV). In the mixture, **11** was present to the extent of 83%. Unfortunately, there was an error in the calculation, which was based on the comparison of the intensity of the methylene proton signal at δ 4.91 with the C_2-H signal at δ 8.95, and the percentage of **11** in the mixture was only 66% and not 83% as reported. The absolute

(3) References cited in 1.

Scheme V



yields of **11** and **12**, on the basis of NMR analysis, were thus 60 and 31%, respectively. (Our mistake was due to an oversight to subtract the contribution of **12** from the total intensity of the methylene proton signal at δ 4.91 to calculate the contribution of **11**.)

The formation of **11**, in greater than 50% absolute yield, was explained by a mechanism, in which the reaction of *n*-butyllithium was faster with the C–I bond than with the acidic deuterium (Scheme V).

The mode of formation of **12** was not clear at that time (for explanation, vide infra).

The formation of **11**, in greater than 50% absolute yield (actually 60%), in the above reaction was clearly inconsistent with a mechanism similar to that of Beak and co-workers. Beak and co-workers were aware of our work but had dismissed it with a statement, in a footnote of their paper, that they were "unable to repeat the conversion of i (**10**) to ii (**11**) in high yield, (and) so (we) cannot comment on the report".

In the present paper we affirm that our work is entirely reproducible. We also show that the principal results of Beak and co-workers can indeed be explained by a mechanism in which, once again, the reaction of *n*-butyllithium is faster with C–Br bond than with an acidic hydrogen. Finally we give further interesting examples where the reaction of *n*-butyllithium is also faster with C–halogen bond than with an electrophilic carbonyl group.

Results and Discussion

Reaction of *n*-Butyllithium with 10. In our experiments we used *n*-butyllithium in ether solution freshly prepared from *n*-BuBr and Li of 99.8% purity.

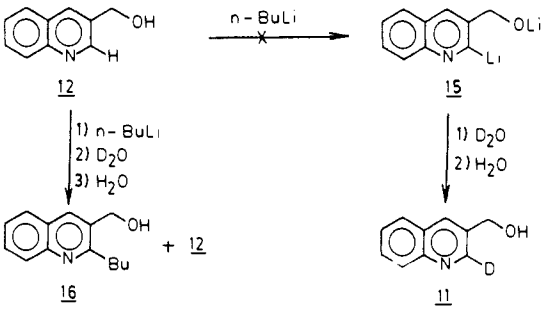
We had difficulties in estimating accurately the concentration of *n*-butyllithium in the ether solution. The concentration varied between 0.48 M and 0.58 M, and the values determined were only approximate. Fortunately in our reaction the end point of addition of the reagent to the substrate **10** was discernible by a fairly sharp color change which occurred when about 1.5 equiv of the reagent had been added. This was then used as the guideline to discontinue the addition of the reagent.

In a typical experiment, 2 equiv of a solution of *n*-butyllithium in ether was taken in the addition funnel and added dropwise to a solution of **10** in THF at −78 °C. When about 1.5 equiv of the reagent had been added, a red color developed. The addition of the reagent was discontinued and the stirring continued for 10 min. Aqueous workup gave **11** and **12** in a total yield of 90%. The starting compound **9** was not present in any detectable amount (TLC, NMR). With use of the intensity of the methylene proton signal at δ 4.91 and the C_2-H signal at δ 8.95, the ratio of **11** and **12** was calculated as 66:34.[9]

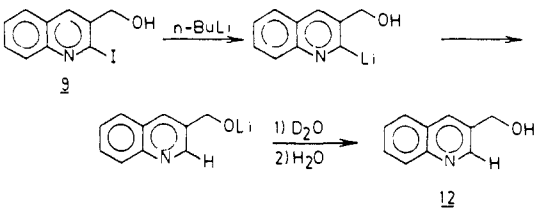
As stated earlier the above result cannot be explained by a mechanism in which the *n*-butyllithium reacts first with the acidic deuterium. However, the results were in agreement with a mechanism (Scheme V) where *n*-butyllithium reacts first with the C–I bond rather than with the acidic deuterium.

We now comment on the formation of **12**. Its obtention via the dilithio compound **15**, obtained by lithiation of **14** (Scheme V), can be ruled out as, under the same experimental conditions, the C_2–H analogue of **14**, i.e. **12**, did not give **11**, on treatment with *n*-butyllithium and quenching with D_2O. The reaction gave only the starting compound **12** and the 2-butyl derivative **16**, in 47% and 40% yields, respectively. Had the C_2–Li derivative been

Scheme VI



Scheme VII



formed, **11** should have resulted (Scheme VI).

Another possibility for formation of **12** is from **9**, present in the starting compound, due to the incomplete conversion of **9** to **10** in the deuteration reaction, by a process analogous to that shown in Scheme VII. This was not viewed with favor since the deuteration reaction was not expected to be incomplete and in any case **9** was not expected to be present in such a high proportion as to give 34% of **12** in the total mixture. The absence of **9** in the starting compound was also established as follows. In one experiment, after lithiation, the reaction mixture was divided into two parts. One part was quenched with saturated NH_4Cl while the other with D_2O followed by aqueous workup. The first reaction gave, as earlier, a mixture of **11** and **12** in the ratio 66:34, while the second gave exclusively **11**. If compound **9** had been present in the starting compound, the second reaction, i.e. D_2O workup, would have resulted in the formation of some **12** (Scheme VII).

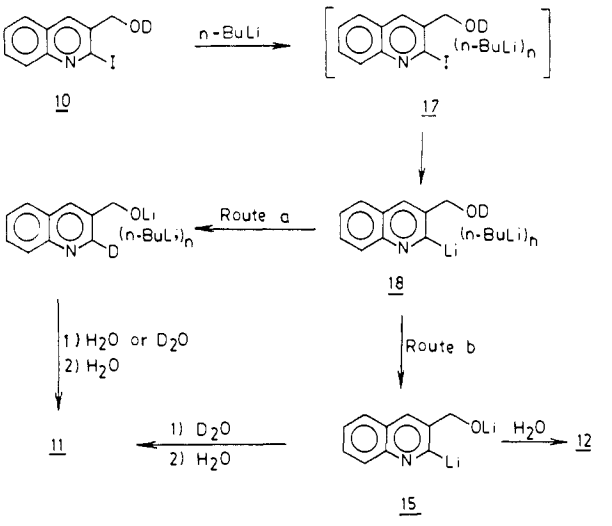
We may now propose a generalized mechanism which explains the formation of all the products in our lithiation reaction. This is shown in Scheme VIII.

In this mechanism, *n*-butyllithium first complexes with **10** (complex **17**), through the electron-donor atoms present in the latter. It then reacts with the C–I bond to give complex **18**. The latter still has a high local concentration of *n*-butyllithium in the vicinity of the C_2–Li bond. Complex **18** can undergo intramolecular C_2-Li,D exchange (route a) to give **14**, which on reaction with either H_2O or with D_2O, followed by aqueous workup would give only **11**. Alternatively, **18** can undergo a Bu-Li,D exchange (route b) to give the dilithiated species **15**, which on aqueous workup would give **12**, but on treatment with D_2O, followed by aqueous workup, only **11**. Thus the lithiation reaction when worked up with H_2O would give **11** and **12**, but when worked up with D_2O, followed by aqueous workup, only **11**, which is what was observed.

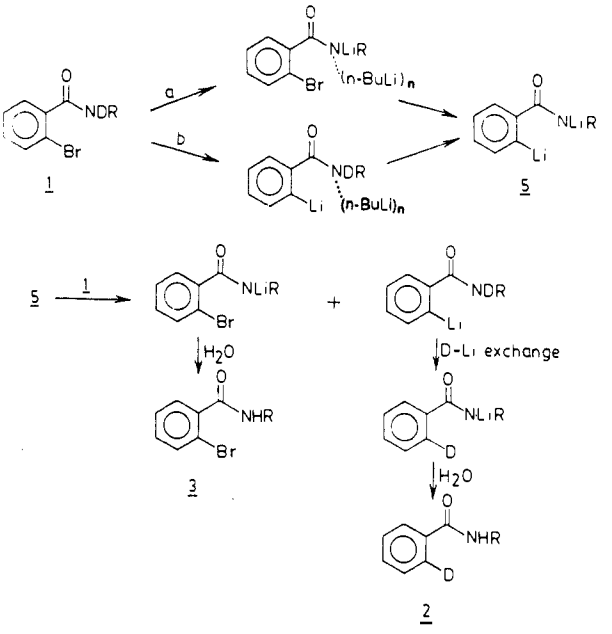
It is obvious that the reaction, involving as it does complexes **17** and **18**, and more specifically **18**, would depend upon several factors such as solvent, temperature, presence (sometimes inadvertently) of salts of lithium (halides, carbonates, etc.), and also speed of stirring, size of droplets of reagent added, etc. In any case the point to be noted is that the *the first reaction is that of n-butyllithium with C–I bond rather than with the acidic deuterium.*

A Reinterpretation of the Results of Beak and Co-Workers. The only valid conclusion that may be reasonably drawn from the results of Beak and co-workers, is that *the dilithiated species* **5** *is an intermediate in their reaction.* Beak and co-workers visualize its formation via a prior reaction of *n*-butyllithium with the acidic deuterium of the N–deuterium bond (Scheme IX, route a). According to our results, however, this is formed by a prior reaction of the *n*-butyllithium with the C–Br bond (Scheme IX, route b).

Scheme VIII



Scheme IX



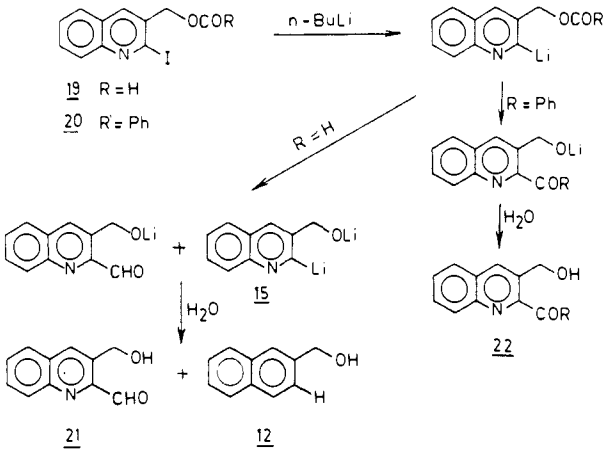
The dilithiated species **5** further reacts with the unreacted amide **1**, once again by a metal–halogen exchange reaction, which is followed by intramolecular C_2-Li,D exchange (Scheme IX).

Reaction of *n*-Butyllithium with the *O*-Acyl Derivatives of 9. In order to explain why *n*-butyllithium reacts faster with the C–halogen bond than with an acidic hydrogen, a distinction was sought between these two reactions. It was noted that while the reaction of *n*-butyllithium with an acidic hydrogen was an acid–base reaction, the reaction of *n*-butyllithium with a C–halogen bond could be a radical reaction.[4,10] If this is so, the latter reaction could be faster than the former. Further the reaction of *n*-butyllithium with a C–halogen bond could be faster than even its nucleophilic reaction with a carbonyl group. (Indeed metal–halogen exchange initiated cyclization of iodo carbonyl compounds has been recently reported.[5]) To test this, the reaction of *n*-butyllithium with the formyl (**19**) and benzoyl (**20**) derivatives of **9** was studied. On treatment of **19** and **20** with 2 equiv (approximately) of *n*-butyllithium at −78 °C, a blood red color developed which intensified toward the end of the addition. On stirring of the mixture for a further period of 30–90 min, the color

(4) Russel, G. A.; Lamson, D. W. *J. Am. Chem. Soc.* **1964**, *91*, 3967. Ashby, E. C.; Pham, T. N. *J. Am. Chem. Soc.* **1987**, *52*, 1291. Barker, P. J.; Winter, J. N. In *The Chemistry of the Metal-Carbon Bond*; Hartley, F. R., Patai, S., Eds.; John Wiley and Sons: New York, 1985; Vol. 2, p 164.

(5) Cooke, M. P.; Honpis, N. *Tetrahedron Lett.* **1988**, *26*, 4987.

Scheme X



faded slightly. Aqueous workup furnished the C_2-acyl derivatives **21** and **22**, in 57% and 72% yields, respectively. Some amount of compound **12** was also obtained in the first reaction. The formation of these compounds can be rationalized by a sequence in which the *n*-butyllithium reacts first with the C–I bond (Scheme X). When R = H, the formate group also reacts with BuLi to give **15**, which then leads to the formation of **12** on treatment with water.

Conclusions

Our results provide examples in which *n*-butyllithium reacts faster with a C–halogen bond than with an acidic hydrogen or with an ester carbonyl group. It is possible that this is because, while the reaction of *n*-butyllithium with an acidic hydrogen is an acid–base reaction and the reaction with an ester carbonyl is an ionic nucleophilic reaction, the reaction with a C–halogen bond is a radical reaction. The radical nature of the reactions of alkyllithium with alkyl halides is now well recognized.[4]

Experimental Section

^{1}H NMR were recorded on JEOL FX-90 Q (90 MHz) in deuteriochloroform unless otherwise mentioned. Melting points recorded on a Gallenkamp apparatus are uncorrected. Peak multiplicities are given with the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broadened. Diethyl ether was dried over sodium metal; THF was dried from sodium and benzophenone. Lithium metal (99.8%) was obtained from Aldrich. All reactions were carried out under an atmosphere of dry nitrogen. IR was recorded with Nujol mulls on a Perkin-Elmer 337 instrument.

Preparation of 2-Chloro-3-(hydroxymethyl)quinoline (23). A solution of 2-chloro-3-formylquinoline[6] (1.916 g, 10 mmol) in THF (15 mL) and water (1 mL) was cooled to 10 °C. $NaBH_4$ (0.4 g, 10 mmol) was then added in small lots over a period of 5 min. After stirring for a further period of 1 h, the reaction mixture was slowly poured onto 30 g of crushed ice with good agitation. Filtration, drying, and crystallization from EtOAc yielded 2-chloro-3-(hydroxymethyl)quinoline (**23**) (1.89 g, 98%); mp 162–163 °C. ^{1}H NMR ($CDCl_3$, DMSO-d_6): δ 8.32 (1 H, s, C_4-*H*), 8.0–7.4 (4 H, m, Ar*H*), 5.55 (1 H, t, exch. -O*H*), 4.67 (2 H, d, J = 5.5 Hz, ArCH_2OH, collapses to singlet after D_2O). Anal. Calcd for $C_{10}H_8ClNO$: C, 62.03; H, 4.16. Found: C, 62.27; H, 4.23. IR: 3400 cm^{-1}.

2-Iodo-3-(hydroxymethyl)quinoline (9). A solution of 2-chloro-3-(hydroxymethyl)quinoline (**23**) (1 g, 5.2 mmol) and NaI (2 g, 13 mmol) in dry acetonitrile (20 mL) was refluxed for 36 h and then concentrated to 5 mL, cooled, and poured onto saturated $NaHCO_3$ (15 mL). Filtration, drying, and crystallization from EtOAc yielded 2-iodo-3-(hydroxymethyl)quinoline (**9**) (1.18 g, 80%), mp 189 °C. ^{1}H NMR ($CDCl_3$): δ 8.3–7.54 (5 H, m, Ar-*H*), 4.82 (2 H, d, J = 6.5 Hz, collapses to singlet after D_2O exchange, ArCH_2OH), 2.22 (1 H, brt, exchanges with D_2O, O*H*). Anal. Calcd for $C_{10}H_8INO$: C, 42.13; H, 2.83. Found: C, 42.11; H, 2.93. IR: 3350 cm^{-1}.

Formate Ester (19) of 2-Iodo-3-(hydroxymethyl)quinoline. A solution of 2-iodo-3-(hydroxymethyl)quinoline (**9**) (0.860 g, 3 mmol), formic acid (2 mL, 98%), and BF_3·Et_2O (1 mL) was stirred for 8 h and then basified with cold saturated $NaHCO_3$. The resulting solid was filtered, dried, and crystallized from 10% EtOAc/hexane to yield **19** (0.86 g, 91%), mp 94–96 °C. ^{1}H NMR ($CDCl_3$): δ 8.31 (1 H, s, C*H*O), 8.23–7.5 (5 H, m, Ar-*H*), 5.43 (2 H, s, ArCH_2O). Anal. Calcd for $C_{11}H_8INO_2$: C, 42.20; H, 2.56. Found: C, 42.37; H, 2.40. IR: 1720 cm^{-1}.

Benzoate Ester (20) of 2-Iodo-3-(hydroxymethyl)quinoline. A solution of 2-iodo-3-(hydroxymethyl)quinoline (**9**) (0.57 g, 2 mmol) in dry THF (20 mL), triethylamine (0.84 mL), and benzoyl chloride (0.4 mL) was stirred for 8 h and evaporated to dryness in vacuo. Saturated $NaHCO_3$ (5 mL) was then added. Extraction with CH_2Cl_2, drying (Na_2SO_4), evaporation of solvent and column chromatography, using silica gel and 10% EtOAc/hexane as eluant, gave **20** (0.680 g, 87%), mp 144–145 °C (10% EtOAc/hexane). ^{1}H NMR ($CDCl_3$): δ 8.37–7.3 (10 H, m, Ar-*H*), 5.6 (2 H, s, ArCH_2). Anal. Calcd for $C_{17}H_{12}INO_2$: C, 52.46; H, 3.11. Found: C, 52.62; H, 3.08. IR: 1720 cm^{-1}.

Preparation of *n*-Butyllithium in Ether. Dry ether (20 mL) was placed in a two-necked flask. Finely cut pieces of lithium metal (0.43 g, 62 mmol) were introduced. *n*-BuBr (0.3 mL) was then added, and the reaction was stirred until a cloudiness appeared. The reaction was then cooled in an ice–salt bath, and a solution of *n*-BuBr (2.7 mL) in ether (15 mL) was then added dropwise over a period of 30 min and stirred at the same temperature for 45 min. The entire supernatant was drawn into a calibrated syringe, and the required amount was transferred to the addition funnel. The concentration of *n*-BuLi was about 0.48–0.58 M.[7]

O-Deuteration of 2-Iodo-3-(hydroxymethyl)quinoline (9). The iodo alcohol **9** (1 g) in dry THF (5 mL) was stirred with D_2O (2 mL) for 3 h. The solution was evaporated to dryness in vacuo. The resulting solid was again dissolved in dry THF (5 mL), and D_2O (2 mL) was added. Stirring for further 12 h and evaporation to dryness in vacuo gave the deuterated compound **10** (1 g, 99%), mp 188–189 °C.

Reaction of 2-Iodo-3-(deuterioxymethyl)quinoline (10) with *n*-Butyllithium. A solution of 2-iodo-3-(deuterioxymethyl)quinoline (**10**) (0.858 g, 3 mmol) in dry THF (30 mL) was cooled to −78 °C. *n*-BuLi (6 mmol in 10 mL of ether) was taken in the addition funnel and added dropwise to the cooled solution. When a pale red solution resulted (after addition of about 7.5 mL), the addition was stopped (about 15 min was required for this). Stirring the reaction mixture for a further period of 10 min, quenching with saturated NH_4Cl (5 mL), separating the THF layer, and extracting the aqueous layer with methylene chloride (10 mL) gave in the combined organic extracts, after drying (Na_2SO_4) and removal of solvent, a residue, which when chromatographed over silica gel, using chloroform/methyl alcohol (98:2) as eluant, yielded 3-(hydroxymethyl)quinolines C_2-D and C_2-H (0.432 g, 90%), mp 83–84 °C (lit.[8] mp 84 °C) (40% EtOAc/hexane). ^{1}H NMR ($CDCl_3$): δ 8.95 (d, J = 2 Hz, C_2-*H*), 8.0–8.14 (2 H, m, C_4-*H*, C_8-*H*), 7.42–8.0 (3 H, m, C_5-*H*, C_6-*H*, C_7-*H*), 4.91 (2 H, s, ArCH_2OH), 3.05 (1 H, brs, O*H* exchanges with D_2O).

The intensity of the methylene proton signal at δ 4.91 and the C_2H signal at δ 8.95 were in the ratio 5.9:1. This indicated that C_2-D compound was about 66% and C_2H was 34%.

Reaction of 2-Iodo-3-(deuterioxymethyl)quinoline (10) with *n*-Butyllithium: Quenching One Part with Water and the Other with D_2O Followed by H_2O. The *n*-BuLi solution in ether used for this and the following experiment was from the *same freshly prepared stock*, and all the experiments were carried out on the same day. The concentration of *n*-BuLi was approximately 0.6 M.

A solution of 2-iodo-3-(deuterioxymethyl)quinoline (**10**) (0.572 g, 2 mmol) in dry THF (25 mL) was cooled to −78 °C. *n*-BuLi (4.8 mmol in 8 mL of ether) was taken in an addition funnel and added to the cooled solution dropwise. When 5 mL had been added (about 10 min), a pale red color developed. The addition of *n*-BuLi was discontinued, and the reaction mixture was stirred for a further period of 10 min.

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(7) *n*-BuLi was estimated according to the method given: Gilman, H.; Morton, J. W. *Org. Reactions (New York)* **1954**, *8*, 258.

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(9) One of the referees has suggested that *n*-butyllithium may be titrated with the tosylhydrazone of diphenylacetone as the indicator. We have now done this to measure the concentration of *n*-butyllithium in ether. When **10** (0.286 g, 1 mmol) was treated with 1 equiv of *n*-butyllithium, a mixture of **11** and **12** was obtained in the ratio of 66:33 (i.e. 2:1) and in a total yield of 66%. The starting compound **10** was recovered (as the CH_2OH compound instead of the CH_2OD due to aqueous workup) in 18% yield. On the other hand, when 1.5 equiv of the reagent was employed, the reaction gave a mixture of **11** and **12**, once again in the ratio of 66:33, but now in a total yield of 90% with no starting compound being recovered.

(10) Another referee has suggested that "the metal halogen exchange is a four centred reaction which may possess an electron transfer component but does not give rise to radical intermediates". The reaction indeed could be so but the fact that the lithium reagent has reacted faster with the C–halogen bond than with the carbinol moiety stands.

One part of the reaction mixture (2 mL) was quenched with H_2O and the other (25 mL) with D_2O followed by water. Usual workup gave from the first part a mixture (0.02 g) of **11** and **12** in a ratio of 66:34 (NMR), and from the second only **11** (0.256 g). The total yield of **11** and **12** was 89%.

Reaction of 3-(Hydroxymethyl)quinoline with 1.0 Equiv and 1.5 Equiv of *n*-Butyllithium. The *n*-butyllithium used was from the same stock as above. A solution of 3-(hydroxymethyl)quinoline (**12**) (0.318 g, 2 mmol) in dry THF (25 mL) was cooled to −78 °C. *n*-BuLi (~2 mmol in 3.3 mL of ether) was added to the cooled solution over a period of 10 min. The reaction mixture was stirred for a further period of 10 min and quenched with D_2O. Usual workup and isolation gave a compound (mp 84 °C). The ratio of the C_2-H at δ 8.95 and methylene proton signal at δ 4.91 were in the ratio 1:2, indicating that the compound was only **12** (0.27 g, 85%) and no **11** was present.

The experiment was repeated by adding 5 mL of *n*-BuLi over a period of 10 min. Stirring for an additional 10 min, followed by treatment with D_2O and aqueous workup, gave **16** (0.172 g, 40% as a thick liquid). ^1H NMR ($CDCl_3$): δ 8.3–7.3 (5 H, m, Ar-*H*), 4.85 (2 H, s, $ArCH_2OH$), 2.9 (2 H, t, J = 7 Hz, $ArCH_2R$), 1.4–2.0 (5 H, m, exch $ArCH_2CH_2C$-H_2CH_3, $ArCH_2OH$), 1.0 (3 H, t, CH_3). Anal. Calcd for $C_{14}H_{17}NO$: C, 78.1; H, 7.96. Found: C, 78.07; H, 7.67. IR: 3300 cm^{-1}. Workup also gave a compound (mp 84 °C) whose NMR had the C_2-H proton signal at δ 8.95 and the methylene proton signal at δ 4.91 in the ratio 1:2, indicating it was only **12** (0.150 g, 47%) with no **11** being present.

Reaction of the Formate Ester (19) of 2-Iodo-3-(Hydroxymethyl)-quinoline with *n*-Butyllithium. A solution of the formate ester (**19**) of 2-iodo-3-(hydroxymethyl)quinoline (0.940 g, 3 mmol) in dry THF (50 mL) was cooled to −78 °C. *n*-BuLi (6 mmol in ether) was added to the cooled solution dropwise over a period of 15 min when a deep red coloration resulted. Stirring for a further period of 2 h at −78 °C, quenching with saturated NH_4Cl (15 mL), separating the THF layer, and extracting the aqueous layer with ethyl acetate (10 mL) gave in the combined organic extracts after drying (Na_2SO_4), concentration, and column chromatography of the residue over silica gel, using chloroform/methanol (98:2) as eluant, first 2-formyl-3-(hydroxymethyl)quinoline (**21**) (0.316 g, 56%), mp 155 °C (2% methanol/chloroform) and then 3-(hydroxymethyl)quinoline (**12**) (0.146 g, 30%). **21**: ^1H NMR ($CDCl_3$) (keto/lactol 1:10): δ 10.61 (1 H, s, C*H*O), 8.43–7.5 (10 H, m, Ar-*H*), 6.77 (2 H, brs, exch OH, keto and lactol), 6.57 (1 H, s, C*H*OH lactol), 5.43 (2 H, q, J = 13 Hz, $ArCH_2O$, lactol), 5.17 (2 H, q, $ArCH_2OH$, keto). Anal. Calcd for $C_{11}H_9NO_2$: C, 70.58; H, 4.85. Found: C, 70.49; H, 4.80) IR: 3150 cm^{-1}.

Reaction of the Benzoyl Ester (20) of 2-Iodo-3-(hydromethyl)quinoline with n-Butyllithium. A solution of the benzoyl ester (**20**) of 2-iodo-3-(hydroxymethyl)quinoline (1.012 g, 2.6 mmol) in dry THF (50 mL) was cooled to −78 °C. *n*-BuLi (5.2 mmol in ether) was added to the cooled solution dropwise over a period of 15 min when a deep red coloration resulted. Stirring for a further period of 30 min at −78 °C and workup as above gave, on crystallization, 2-benzoyl-3-(hydroxymethyl)quinoline **22** (0.493 g, 72%), mp 94–95 °C (40% EtOAc/hexane). ^1H NMR ($CDCl_3$): δ 8.43–7.37 (10 H, m, Ar*H*), 4.81 (2 H, s, $ArCH_2OH$), 3.67 (1 H, brs, exch OH). Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98. Found: C, 77.45; H, 5.28. IR: 3330, 1665 cm^{-1}.

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Mechanism of Solvolysis of 1-(1-Adamantyl)ethyl Sulfonates

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Abstract: In contrast to the pinacolyl (3,3-dimethyl-2-butyl) sulfonate esters, the solvolyses of 1-(1-adamantyl)ethyl sulfonates produce significant proportions of unrearranged substitution products indicating that a strong steric bias exists against what is, for the pinacolyl esters, a facile rearrangement of the secondary cation to the tertiary cationic isomer. In addition, the α-*d* and β-d_3 isotope rate effects vary with solvent. This is a strong indication of a change in mechanism which can only occur if internal return is significant. The unusually small isotope effects in trifluoroethanol/water solvents indicate that a proportion of the reaction proceeds through a transition state having the rearranged structure. Observations of extensive oxygen scrambling during solvolysis confirm the existence of internal return. The solvolytic substitutions starting with either the chiral secondary sulfonate or the chiral tertiary heptafluorobutyrate reveal that the rearrangement in both directions is stereospecific as is the unrearranged substitution from the tertiary ester which gives retained chirality. The unrearranged substitution product from solvolysis of the secondary ester, although predominantly of retained configuration, contains a proportion of the inverted enantiomer which increases with solvent nucleophilicity to a maximum of 50% found in ethanol. A steady-state analysis based on a mechanism which involves equilibrating secondary and tertiary carbocations successfully correlates the observed isotope effects with the product yields and the isotope effects expected for the various single steps. Since the steady-state treatment gives unassisted ionization rates which are 2.3 (80E) to 7.7 (97T) times faster than those for the pinacolyl analogue, it seems clear that the ionization rates of the latter are also unassisted.

Some years ago it was suggested that 3,3-dimethyl-2-butyl (pinacolyl) sulfonate esters **1** are useful reference reactants for the estimation of unassisted ionization rates of secondary sulfonate esters in the absence of internal return.[1] The magnitude and constancy of the observed secondary deuterium rate effects in a wide range of solvents of varying nucleophilicity and ionizing power indicate that pinacolyl sulfonates solvolyze by unassisted, irreversible ionization followed by rapid Wagner–Meerwein rearrangement to the more stable tertiary ion; that is rearrangement of the secondary to the tertiary cation in the ion pair is faster than ion recombination. Consistent with this interpretation are the facts that all of the products have rearranged structures[2] and that no ^{18}O scrambling can be detected in recovered unreacted ester.[3] Since internal return and S_N2 attack are insignificant for this ester,[4] the comparison of its solvolytic rates and isotope effects

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