Table I. Reduction of Ketones and Aldehydes to Hydrocarbons with Sodium Cyanoborohydride and *p*-Toluenesulfonyl Hydrazide in Dimethylformamide–Sulfolane at 100–105°

Entry	Carbonyl compound[a]	Time, hr	Product	% yield[b] (isolated)
1	$CH_3(CH_2)_8C{=}NNHTs(CH_3)$	3.5	$CH_3(CH_2)_9CH_3$	95
2	Cholestan-3-one tosylhydrazone	1.0	Cholestane	93
3	*N*-Benzylpiperidone 4-tosylhydrazone	4.0	*N*-Benzylpiperidone	79
4	$CH_3(CH_2)_8COCH_3$	4.0	$CH_3(CH_2)_9CH_3$	91 (86)
5	Cholestan-3-one	2.0	Cholestane	98 (88)
6	4-*tert*-Butylcyclohexanone	3.0	*tert*-Butylcyclohexane	77
7	$CH_3(CH_2)_9CHO$	4.0	$CH_3(CH_2)_9CH_3$	66
8	$CH_3CO(CH_2)_3CO_2(CH_2)_7CH_3$	2.0	$CH_3(CH_2)_4CO_2(CH_2)_7CH_3$	87 (80)
9	$CH_3CO(CH_2)_2CO_2(CH_2)_9CH_3$[c]	2.0	$CH_3(CH_2)_3CO_2(CH_2)_9CH_3$	80
10	$CH_3(CH_2)_2COCH_2CO_2(CH_2)_7CH_3$	2.0	$CH_3(CH_2)_4CO_2(CH_2)_7CH_3$	62
11	$CH_3COCH_2CO_2(CH_2)_9CH_3$	4.0	$CH_3(CH_2)_2CO_2(CH_2)CH_3$	65
12	$CH_3CO(CH_2)_3CO_2(CH_2)_8CN$	2.0	$CH_3(CH_2)_4CO_2(CH_2)_8CN$	75
13	$PhCOCH_2CO_2(CH_2)_7CH_3$	16	$Ph(CH_2)_2CO_2(CH_2)_7CH_3$	Trace

[a] Reaction solutions were 0.2 *M* in the carbonyl compound, 0.8 *M* in $NaBH_3CN$ in a 1:1 mixture of DMF and sulfolane acidified with 500 mg of *p*-toluenesulfonic acid monohydrate per 100 ml of solvent unless specified otherwise. [b] Yields of products were determined by glpc using internal standards and detector response factors. [c] 1.6 *M* in $NaBH_3CN$, 1.00 g of *p*-toluenesulfonic acid per 100 ml of solvent.

maximum yields. The rate plots for 2-undecanone tosylhydrazone (Figure 1) illustrate that increasing the acid concentration markedly accelerates the rate of reduction, but destruction of cyanoborohydride apparently competes with reduction at greater acid concentrations and lowers the final yield. The prior preparation of tosylhydrazones is unnecessary since the slow rate of carbonyl reduction[7] permits the generation of these intermediates *in situ* from the carbonyl compound and the *p*-toluenesulfonylhydrazide.

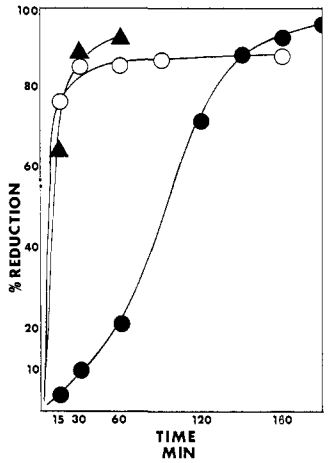

Figure 1. Reduction of 2-undecanone and cholestan-3-one tosylhydrazones with sodium cyanoborohydride in 1:1 dimethylformamide–sulfolane at 100°. All solutions were 0.2 *M* in tosylhydrazone and 0.8 *M* in sodium cyanoborohydride. The per cent reduction was determined by glpc analysis using internal standards: ●, 2-undecanone tosylhydrazone, solvent contained 500 mg of *p*-toluenesulfonic acid monohydrate per 100 ml, pH *ca.* 1.4; ○, 2-undecanone tosylhydrazone, solvent contained 1000 mg of *p*-toluenesulfonic acid monohydrate per 100 ml, pH *ca.* 0.8; ▲, cholestan-3-one tosylhydrazone, solvent contained 500 mg of *p*-toluenesulfonic acid monohydrate per 100 ml, pH *ca.* 1.4.

With the above in mind, the following general synthetic procedure was developed to effect a number of reductions which are shown in Table I. The aldehyde or ketone (1 mmol) and *p*-toluenesulfonylhydrazide (1.25 mmol) were dissolved in 5 ml of 1:1 DMF–sulfolane containing 25 or 50 mg of *p*-toluenesulfonic acid (see Table I). To this was added $NaBH_3CN$ (4 mmol), and the solution was heated at 100–105°. After completion,[9] the reactions were worked up by simply diluting with water and extracting with cyclohexane. Isolation of products is easily accomplished by washing with water to remove residual sulfolane and DMF followed by evaporation of the cyclohexane.

Several noteworthy features of the procedure are apparent from Table I. First, the yields of deoxygenated products are good to excellent (62–98% in 1–4 hr). Furthermore, in no cases studied were alkene or other side products detected by glpc or nmr. The superior selectivity possible is demonstrated by the conversions of keto esters (entries 8–11) and a cyano keto ester (entry 12) to the corresponding esters and cyano ester, respectively.[10] In fact, this procedure is so mild that aromatic ketones are not affected (entry 13), thus allowing aliphatic ketones to be removed in their presence. A wide variety of other functional groups should also be inert toward cyanoborohydride, and we are currently exploring the scope of possible selective conversions.

In conclusion, the procedure described offers a convenient, high-yield, relatively mild, and rapid method for the selective reduction of aliphatic ketones and aldehydes to hydrocarbons and should be applicable to a wide scope of structural types.

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(9) The reductions were conveniently monitored by adding an internal standard and 10 ml of cyclohexane to the reactions. At appropriate intervals, small samples of cyclohexane solution were removed and analyzed by glpc.

(10) For other procedures used to convert β-keto esters to saturated esters, see R. M. Coates and J. E. Shaw, *J. Org. Chem.*, **35**, 2601 (1970), and references cited therein. These authors used a two-step procedure involving methoxymethylation followed by lithium-in-ammonia reduction to the esters in 23–61% yields.

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Acidity of Hydrocarbons. XXXV. Equilibrium Acidities of Phenylacetylene and *tert*-Butylacetylene in Cyclohexylamine

Sir:

Measures of the equilibrium acidity of acetylenes are presently available only for phenylacetylene in

Table I. Acidity of Phenylacetylene

Run	Indicator[a] RH	Indicator pK[b]	Concn at equil, 10^3 M R⁻	RH	PhA⁻	PhA	Total change in R⁻, 10^6 mol[c]	pK PhA
23A	4,5-MP	22.60	0.345	16.8	0.698	175	21	23.31
29A			0.256	0.787	1.36	131	50	23.10
27	9-MF	22.70[d]	2.34	39.3	3.89	172	63	23.23
28A			1.92	25.4	5.28	222	88	23.20
28B			2.53	20.4	4.65	112	76	23.18
29C	1,2-BF	19.97	0.864	0.505	0.281	313	11	23.25
30H			0.928	0.626	0.265	329	10	23.24
30B	2,3-BF	23.16	2.58	20.8	6.26	44.2	116	23.10
31			1.35	15.1	3.80	40.1	81	23.19
							Av	23.20 ± 0.05

[a] 4,5-MP = 4,5-methylenephenanthrene; 9-MF = 9-methylfluorene; 1,2-BF = 1,2-benzfluorene; 2,3-BF = 2,3-benzfluorene. [b] Reference 3. These values are approximately based on the aqueous solution as standard state. As such, ΔpK's are far more accurate than the absolute pK values. [c] Decrease in the total quantity of indicator anion on addition of the PhA. [d] Reference 5.

ether[1] and for acetylene in ammonia.[2] We report here the equilibrium acidities of phenylacetylene (PhA) and *tert*-butylacetylene (BuA) toward lithium cyclohexylamide (LiCHA) in cyclohexylamine (CHA). In previous work we reported[3] relative acidities of hydrocarbons toward LiCHA by spectrometric measurements of the equilibria

$$R^-Li^+ + R'H \rightleftharpoons RH + R'^-Li^+ \qquad (1)$$

The lithium salts of acetylenes have no visible spectrum but equilibrium constants for the equilibria 1 could be obtained from the reduction in absorbance of a suitable hydrocarbon indicator when a known amount of the acetylene was added. Control experiments established the amount of indicator lost from the simultaneous admission of adventitious moisture. The results in Table I for PhA with four different hydrocarbon indicators demonstrate the self-consistency and reproducibility of this technique. Because of its lower acidity, BuA was measured against only a single indicator but reproducible results were obtained for a range of concentrations (Table II).

Table II. Acidity of *tert*-Butylacetylene

Run	Concn at equil, 10^3 M R⁻[a]	RH[a]	BuA⁻	BuA	K
40A	2.88	14.4	3.94	91.8	4.66
51	10.1	12.6	8.62	50.9	4.75
58	5.33	36.0	5.43	180	5.21
105	8.72	11.3	12.3	85.7	5.40
				Av	5.01 ± 0.30
				pK	25.48 ± 0.03

[a] Indicator is 9-*tert*-butylfluorene, pK = 24.79 (ref 5). See also Table I, footnote *b*.

For convenience, the equilibrium constants for the equilibria (1) have been converted to "pK" values, PhA, 23.20 ± 0.05, BuA, 25.48 ± 0.03, relative to the value, 18.49, for 9-phenylfluorene. The latter value is approximately that for the aqueous standard state[4] based on the usual H_- assumptions. The lithium salts of localized acetylenic carbanions are not expected to have the same activity coefficient behavior as those of delocalized fluorenyl anions so that the acetylenic pK's may differ substantially from a water basis; nevertheless, toward LiCHA in CHA, the assigned values may be compared with other structures having comparable acidity: fluorene, 22.6,[4] and 9-*tert*-butylfluorene, 24.8.[5]

McEwen[1] estimated the acidity of PhA to be about that of 9-phenylfluorene with respect to the sodium salts in ether, whereas we find a difference of almost 10^5 in acidity with respect to the lithium salts in CHA. In both cases ion-pair equilibria are involved and it appears that the difference can best be accounted for in terms of increased cation solvation in CHA compared to ether. By simple electrostatic attraction, the more concentrated charge of the essentially localized acetylenic carbanion provides more effective solvation of the metal cation in an ion pair than does a delocalized fluorenyl anion; hence, the acetylenic ion pair is less sensitive to the cation-solvating power of the solvent. Consequently, the 9-phenylfluorenyllithium ion pair is stabilized more by the better cation-solvating solvent than is the phenylacetylenyllithium ion pair. This difference emphasizes the impossibility of setting up a universal acidity scale for hydrocarbons of different types.

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Molecular Conformation of Orotidine, a Naturally Occurring Nucleoside, in the Syn Conformation in Aqueous Solution

Sir:

We report here a complete analysis of the 100-MHz spectrum of orotidine (6-carboxyuridine, O) and a comparison of the data with those of uridine (U) and β-cyanuric acid riboside (β-CAR), Figure 1. O