Elimination and Addition Reactions. Part 34.[1] The Effect of Activating Group and Medium on Leaving Group Rank in Elimination from Carbanions

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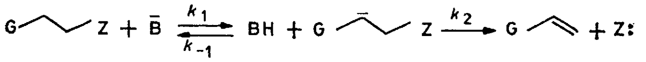
Ranking of leaving groups in 1,2-elimination from carbanions has been extended to cyano-activated systems and, in a few cases, to oxo-activated systems. The ranks are compared with those found earlier for sulphonyl-activated eliminations. The results suggest that there is little cleavage of the bond to the leaving group in the transition state for the process in which the leaving group is expelled; these conclusions are reinforced by the insensitivity of the rates of these reactions to change of solvent and to intervention in any degree of ion-association in the media studied.

In Part 30,[2] absolute leaving-group abilities (ranks) of a wide range of leaving groups were determined for the reaction in which a sulphonyl-stabilised carbanion (2; G = SO_2Ph) expels a leaving group, Z, from the adjacent atom (Scheme). The rank ($\log k_{obs.} - \log k_1$) is equivalent to $\log (k_2/k_{-1})$ but because k_{-1} is close to being diffusion controlled for sulphonyl-stabilised[3] carbanions, rank differentials are essentially equivalent to differentials in $\log k_2$ and hence define absolute leaving-group abilities.



(1) (2)

Scheme

It was seen that leaving-group abilities do not correlate simply with any molecular parameters. Several questions remained. (i) Does leaving-group rank vary with the group, G, which stabilises the carbanion? (ii) What is the nature of the transition state for expulsion of the leaving group and does it vary with the activating group, G? (iii) Does leaving-group rank vary with solvent or with ion–solvent equilibria? (iv) What general conclusions can be drawn about the nature of the process in which the leaving group is expelled? This paper deals with these questions.

(i) *Variation of Leaving-group Rank with Activating Group.*—For measurement of leaving-group ability in elimination reactions two criteria must be fulfilled.[2] First, elimination by the $(E_1cB)_R$[4] mechanism (k_2 rate determining) must be studied because either departure of the leaving group is irrelevant as for the $(E_1cB)_I$ mechanism (k_1 rate determining),[5] or departure of the leaving group is concerted with β-C–H bond fission (E_2), and departure of the leaving group cannot be separately considered. Second, the effect of the leaving group on

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[1] K. N. Barlow, D. R. Marshall, and C. J. M. Stirling, *J.C.S. Perkin II*, 1977, 1920.

[2] D. R. Marshall, P. J. Thomas, and C. J. M. Stirling, *J.C.S. Perkin II*, 1977, 1898.

[3] J. Hine, J. C. Philips, and J. I. Maxwell, *J. Org. Chem.*, 1970, **35**, 3943.

[4] F. G. Bordwell, M. M. Westling, and K. C. Yee, *J. Amer. Chem. Soc.*, 1970, **92**, 5950.

[5] D. R. Marshall, P. J. Thomas, and C. J. M. Stirling, *J.C.S. Perkin II*, 1977, 1914.

the equilibrium which precedes leaving-group expulsion must be assessable so that direct comparisons of k_2 may be made.

The first criterion is exacting and demands the study of eliminations from carbanions which inherently repronate rapidly. For these ions k_{-1} is large and likely to exceed k_2. This is the requirement for the $(E_1cB)_R$ mechanism to operate.[2] For only two types of carbanion accessible in the base–solvent system (ethanolic sodium ethoxide) that we have used can this criterion be at all generally met. Carbanions derived from nitriles [6] and sulphones [3] reprotonate very much more rapidly than those derived from ketones [7] or nitro-compounds.[8] In this paper, the ranks for expulsion of leaving groups from cyano-stabilised carbanions are compared with those for sulphones derived earlier.[2] Ranking of leaving groups from oxo-stabilised carbanions, however, cannot generally be accomplished because the carbanion reprotonates slowly, k_2 generally exceeds k_{-1},[5] and the $(E_1cB)_I$ mechanism is observed. When the leaving group is poor, however, k_2 is small. Ranking becomes possible for such groups because the $(E_1cB)_R$ mechanism ($k_{-1} \gg k_2$) is then adopted.

The second criterion can be met if the sensitivity of the carbon acid to polar effects on deprotonation rate is known. Detritiation measurements on ketones, nitriles, and sulphones [9] have provided this information which now allows the rank order to be derived for nitriles and, in a restricted number of cases, ketones.

Elimination of a series of groups, Z, from ten nitriles, (**1**; G = CN) and five ketones (**1**; G = Bz) in ethanolic sodium ethoxide has been studied. Results are in Table 1. For the cyano- and sulphonyl-activated series, the groups $Ph\overset{+}{N}Me_2 > OPh > SPh > OMe > CMe_2NO_2$ are ranked in the same order. The groups $OMe > NRAc > CN, CMe_2NO_2$ are in the same order in the sulphonyl- and benzoyl-activated series. Similar ranges of rank and generally similar rank differentials suggest similar transition states for k_2 in the two systems. Earlier,[10,11] it was concluded that bond extension in the transition state of k_2 for sulphonyl-activated systems was low.

The phenylsulphonyl group has a markedly low rank in the sulphone series.[2] This may be due to the destabilising interaction between the sulphonyl group and the partially developed carbon–carbon double bond.[12] In the bis-sulphone (**1**; $G = Z = PhSO_2$), two sulphonyl groups interact with the carbon–carbon double bond in the transition state for k_2. This has the effect of further raising the energy of the transition state for the expulsion of the leaving group.

The rank values of the three groups $\overset{+}{N}Me_2Ph$, SO_2Ph, and N(Me)Ac are all substantially lower in the sulphone series than in the nitrile series. For the first two groups this may be due to electrostatic destabilisation of the developing double bond and these substituents have high polar and low resonance effects in their interaction with p/π systems.[13] The acetamido-group has not been

TABLE 1

Leaving-group ranks in elimination from carbanions [a]

G	Z	$k_{obs.}$ [b]	log k_1	Rank [c,d]	Rank [c] (G = SO_2Ph)	Rank ($PhSO_2$–CN)
CN	$\overset{+}{N}Me_2Ph$	1.21×10^4	4.5 [f]	10.7	9.2	−1.5
CN	SePh	3.5×10^{-1}	0.25 [g]	10.0	10.4	+0.4
CN	SO_2Ph	17.1	2.66 [h]	9.6	8.7	−0.9
CN	OPh	9.44×10^{-2} [i]	1.74 [h]	8.2	8.9	+0.7
CN	$P(O)(OEt)_2$	7.31×10^{-4}	−0.15 [g,k]	8.0		
CN	SPh	1.04×10^{-2} [j]	1.09 [h]	7.9	8.7	+0.8
CN	N(Me)Ac	2.54×10^{-5}	0.84 [g]	6.6	5.0	−1.4
CN	OMe	1.65×10^{-4}	0.96 [h]	6.3	6.1	−0.2
CN	CN		−0.82 [h]	<0.5 [l]		
CN	$C(Me_2)NO_2$		0.62 [g,m]	n	n	
PhCO	$P(O)(OEt)_2$	1.17×10^{-3}	0.36	7.7		
PhCO	OMe	9.85×10^{-4} [o]	1.14	6.8	6.1	
CH_3CO	$N(CH_2Ph)Ac$	3.20×10^{-4}	1.16 [g,p,q]	6.3	5.0 [r]	
PhCO	CN		1.63 [h]	<0.5 [l]	<0.5 [l]	
PhCO	$C(Me_2)NO_2$		0.74 [g,m]	n	n	

[a] Reactions with ethanolic sodium ethoxide at 25 °C; $(E_1cB)_R$ mechanisms assigned, unless otherwise stated, from $k_{obs.} : k_1$ comparisons *cf.* ref. 5. [b] Units: l mol^{-1} s^{-1}. [c] log $k_{obs.}$ − log k_1 + 11. [d] This work. [e] Values from Part 30, ref. 2. [f] Calculated from rate of detritiation in Et_3N–EtOH. [g] Calculated from $\rho^*\sigma^*$ plot for detritiation, Part 31, ref. 9. [h] From detritiation rate constant and k_H/k_T ref. 9. [i] Value from Part 19, ref. 22. [j] Value determined by Dr. R. P. Redman. [k] Value derived from pK_a $(EtO)_2P(O)CH_2CO_2H$ = 3.97 (this work) giving σ^* $[(EtO)_2P(O)CH_2]$ = 0.40. [l] Maximum values; no observable reaction. [m] σ^* Value derived from pK_a of 4-nitrobutyric acid = 3.76 (P. Walden, *Z. Phys. Chem.*, 1892, **10**, 652). [n] See footnote on page 1132. [o] k_H/k_D = 1.01. [p] σ^* Value of $AcN(CH_2Ph)$ assumed equal to that of AcN(Me). [q] No corrections applied; ρ^* for detritiation when G = Ac assumed equal to that for G = PhCO. [r] Rank for Z = AcN(Me).

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[6] F. Hibbert, F. A. Long, and E. A. Walters, *J. Amer. Chem. Soc.*, 1971, **93**, 2829.

[7] R. P. Bell, 'The Proton in Chemistry,' 2nd edn., Chapman and Hall, London, 1973, ch. 10.

[8] D. J. Cram, 'Fundamentals of Carbanion Chemistry,' Academic Press, New York, 1965, ch. 1.

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[11] J. Crosby and C. J. M. Stirling, *J. Chem. Soc. (B)*, 1970, 679.

[12] J. Hine and N. W. Flachskam, *J. Amer. Chem. Soc.*, 1973, **95**, 1179.

[13] F. G. Bordwell, M. Van Der Puy, and N. R. Vanier, *J. Org. Chem.*, 1976, **41**, 1883.

evaluated in this respect[14] but probably does not share these characteristics.

In all three series, the ranks of OMe and N(Me)Ac are the lowest measurable but the order N(Me)Ac > OMe for G = $PhSO_2$ and Bz is reversed when G = CN. In the oxo-series, k_{-1} is much lower than for sulphones and nitriles but a more stable carbanion is produced;[15] k_2 should then also be lower because of the reduced tendency of the more stable carbanion to expel the leaving group. The fact that ranks in the oxo-series are similar to the values for sulphones and nitriles suggests compensation between k_2 and k_{-1}.

In all three series, expulsion of the relatively ' stable ' ion $\bar{C}Me_2NO_2$ [$pK_a(H_2O)Me_2CHNO_2 \simeq 10$] fails to occur.* Expulsion of cyanide ion from neither succinonitrile nor 2-benzoylpropionitrile can be observed; in 2-phenylsulphonylpropionitrile, elimination of benzenesulphinate ion is the sole reaction. The phenomenon of very low rank for carbon-connected groups is thus general.[2]

As found previously for the sulphonyl-activated series, rank orders in the nitrile and oxo-activated series do not correlate with simple molecular parameters. In the next section of this paper it is seen that correlation of leaving-group ability with pK_a of ZH is possible over a narrow range of pK_a and for a single type of leaving group. Further investigation of narrow ranges of leaving-group type is in progress and will be reported later.

TABLE 2

Leaving-group β-values for elimination of aryloxy-groups from sulphones and nitriles

Aryloxy-nitriles, $CN{\cdot}CH_2CH_2OC_6H_4$-*p*-Z

Z	Me	H	Cl	CO_2Et	CN	NO_2
k_{obs} [a]	0.036	0.094	0.36	1.05	3.16	21.1
σ [b]	−0.10	0.00	+0.28	+0.60		+0.96
			ρ = 2.4			

Values for equation (1)

$\Delta \log k_{\mathrm{obs.}}{}^{c} = \rho^{*\,d}{}_{\mathrm{detrit}} \cdot (\sigma^{*\,e}{}_{p\text{-}NO_2C_6H_4OCH_2} - \sigma^{*\,e}{}_{PhOCH_2}) + \rho_{k_2}(\sigma^{\,b}{}_{NO_2} - \sigma_H{}^{b})$
$(NO_2\text{–}H)$
G = $PhSO_2$ $2.0^{f} = 4.9 \cdot 0.16 + \sigma_{k_2} \cdot 0.96$
G = CN $2.3 = 3.8 \cdot 0.16 + \sigma_{k_2} \cdot 0.96$
Giving for G = $PhSO_2$; $\rho_{k_2} = 1.26$ $\beta_{LG} = \rho_{k_2}/\rho_{ArOH}{}^{g} = 0.40$
G = CN; $\rho_{k_2} = 1.76$ $\beta_{LG} = \rho_{k_2}/\rho_{ArOH}{}^{g} = 0.55$

[a] Units = l mol^{-1} s^{-1}. [b] σ Values of *p*-substituents required to correlate dissociation constants of phenols in 95% EtOH–H_2O (ref. 16). [c] Points well correlated by Hammett plot in both series. [d] Values from ref. 9. [e] Derived from pK_a values of $ArOCH_2CO_2H$ and $\Delta pK_a = 1.76\ \Delta\sigma^*$. [f] From ref. 11. [g] From pK_a values in ref. 16 and σ values in ref. 17.

(ii) *The Transition State for Expulsion of the Leaving Group*.—Elimination of aryloxy-groups in the sulphonyl-[11] and cyano-activated series has been compared. Results are given in Table 2. For each series, Hammett ρ values for $k_{obs.}$ have been measured. σ-Values for the substituents used were derived from a Hammett plot of pK_a values of phenols in 95% aqueous ethanol[16] against Verkade's[17] limited range of σ-values. This procedure ensures a common basis for the comparison of the kinetic and equilibrium data.

For elimination by the $(E_1cB)_R$ mechanism, the effect of substituents in the leaving group on $k_{obs.}$ is composite *viz*:

$$\Delta \log k_{\mathrm{obs.}} = \Delta \log k_1 + \rho_{k_2}\,\Delta\sigma - \Delta \log k_{-1} \qquad (1)$$

Because reprotonation (k_{-1}) of sulphonyl- and cyano-stabilised carbanions is very rapid, $\Delta \log k_{-1} \simeq 0$.

i.e. $$\frac{\Delta \log k_{\mathrm{obs.}} - \Delta \log k_1}{\Delta\sigma} = \rho_{k_2} \qquad (2)$$

(Δ Refers to the differences in designated values between two specific substituents.)

The value of $\Delta \log k_1$ is given by equation (3).

$$\Delta \log k_1 = \rho_{k_1}{}^{*}{\cdot}\Delta\sigma^{*} \qquad (3)$$

The groups *p*-NO_2 and H have been chosen as designated substituents. The values of $\Delta\sigma^*$ for the *p*-nitrophenoxymethyl and phenoxymethyl groups are derived from the dissociation constants of the corresponding aryloxyacetic acids[18] using $\rho_{pK_a}{}^{*} = 1.72$.[19a] Δσ refers to the difference between the values of σ required to correlate *p*-NO_2 and *p*-H substituents on a Hammett plot for dissociation constants of substituted phenols. β_{LG} is then given by $\rho_{k_2}/\rho_{K_a(ArOH)}$.

For aryloxy-leaving groups, $\rho_{k_2}^{CN}$ is substantially greater than $\rho_{k_2}^{SO_2Ph}$ and $\beta_{LG}^{CN}(0.55)$ is thus greater than $\beta_{LG}^{SO_2Ph}(0.40)$. The results suggest that the degree of bond extension to the leaving group and hence of double bond formation in the transition state is small in each case but greater for

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* *Note added in proof*: The rate constant for elimination of $\bar{C}Me_2NO_2$ in the G = $PhSO_2$ series has recently been measured at *85 and 95* °C leading to an estimated rank of +2.6 at 25 °C.

[14] J. Hine, ' Structural Effects on Equilibria in Organic Chemistry,' Wiley–Interscience, New York, 1975, Section 6-5.

[15] W. S. Matthews, J. E. Bares, J. E. Bartmess, F. G. Bordwell, F. J. Cornforth, G. E. Drucker, Z. Margolin, R. J. McCollum, G. J. McCollum, and N. R. Vanier, *J. Amer. Chem. Soc.*, 1975, **97**, 7006.

[16] G. Swarzenbach and E. Rudin, *Helv. Chim. Acta*, 1939, **22**, 360.

[17] H. van Bekkum, P. E. Verkade, and B. M. Wepster, *Rec. Trav. chim.*, 1959, **78**, 815.

[18] N. V. Hayes and G. E. K. Branch, *J. Amer. Chem. Soc.*, 1943, **65**, 1555.

[19] (*a*) R. W. Taft in ' Steric Effects in Organic Chemistry,' ed. M. S. Newman, Wiley, New York, 1956, p. 607; (*b*) M. B. Davy, K. T. Douglas, J. S. Loran, A. Steltner, and A. Williams, *J. Amer. Chem. Soc.*, 1977, **99**, 1196.

G = CN than for G = SO_2Ph. In related work on the alkaline hydrolysis of aryl phenylmethanesulphonates in water,[19b] formation of sulphenes by an $(E_1cB)_R$ process is observed. Rate constants for the expulsion of aryloxide from the intermediate carbanion are derived and the corresponding value of $\beta_{LG} = 1.9$ shows the very much larger extension of the bond to the leaving group than in the present system. The low sensitivity of rank values to activating group, G, is also consistent with a small degree of extension of the leaving group bond in the transition state.

(iii) *The Effect of Solvent and Ion-association on Rank*.—The effect of solvent on activated eliminations is profound. No reaction can be detected in the system (1; G = Z = CN) in ethoxide–ethanol.[2] When potassium hydroxide in hexamethylphosphoramide is used, however, reactions occur readily.[20] We have, so far, made no extensive tests of the sensitivity of rank to medium. In Table 3, the effect of the addition of 50% water to the standard reaction medium is seen for three different leaving groups in two activation series, all reactions proceeding by the $(E_1cB)_R$ mechanism. In all cases, $k_{obs.}$ is depressed to a small extent by the change from pure ethanol to 50% aqueous ethanol. Pre-equilibrium formation of the carbanion is depressed [21] in the less basic aqueous system. No firm conclusions can be derived from the small differences observed, whose magnitudes are insensitive to change of activating group or rank of the leaving group. Earlier studies of solvent effects on the elimination of phenoxide ion in carbanionic eliminations [11] show that for an uncharged activating group, change from ethoxide–ethanol to hydroxide ion–water typically produced a ten-fold rate depression for a series of activating groups spanning a reactivity range of 10^8.[22]

TABLE 3

Effect of medium change on carbanionic elimination

Substrate	Medium	$k_{obs.}$ [a, b]
$NC{\cdot}CH_2CH_2SePh$ [c]	NaOEt–EtOH	35.4
$NC{\cdot}CH_2{\cdot}CH_2SePh$	NaOEt–EtOH–H_2O	20.3
$NC{\cdot}CH_2CH_2{\cdot}SPh$ [c]	NaOEt–EtOH	10.4
$NC{\cdot}CH_2CH_2{\cdot}SPh$	NaOEt–EtOH–H_2O [d]	8.75
$NC{\cdot}CH_2CH_2{\cdot}SPh$	KOEt–EtOH	20.4
$NC{\cdot}CH_2{\cdot}CH_2{\cdot}SPh$	KOEt–EtOH–crown [e]	19.4
$PhSO_2{\cdot}CH_2{\cdot}CH_2OPh$ [c]	NaOEt–EtOH	361
$PhSO_2{\cdot}CH_2{\cdot}CH_2{\cdot}OPh$	NaOEt–EtOH–H_2O [d]	145
$PhSO_2{\cdot}CH_2CH_2{\cdot}SPh$ [c]	NaOEt–EtOH	22.8
$PhSO_2{\cdot}CH_2{\cdot}CH_2{\cdot}SPh$	NaOEt–EtOH–H_2O [d]	8.76
$PhSO_2{\cdot}CH_2{\cdot}CH_2{\cdot}SPh$	KOEt–EtOH	36.6
$PhSO_2{\cdot}CH_2CH_2{\cdot}SPh$	KOEt–EtOH–crown	33.3
$PhSO_2{\cdot}CH_2{\cdot}CH_2{\cdot}Cl$ [f]	NaOEt–EtOH	798 000
$PhSO_2{\cdot}CH_2{\cdot}CH_2Cl$	KOEt–EtOH	773 000
$PhSO_2{\cdot}CH_2{\cdot}CH_2Cl$	KOEt–EtOH–crown	776 000

[a] Units: l mol^{-1} s^{-1}. [b] × 10^3. [c] Mechanism = $(E_1cB)_R$. [d] 50 : 50 v/v. [e] Dicyclohexyl-18-crown-6 equimolar with base. [f] $(E_1cB)_I$ mechanism assigned (Part 32), ref. 5.

It was also of interest to examine the effect of any ion-association upon the behaviour of the intermediate carbanion. Effects of this type have been discussed recently [23] and it was important to establish whether ion-association was a significant factor in determining the reactivity differences between carbanions bearing different stabilising groups (G) and leaving groups (Z). The effect of dicyclohexyl-18-crown-6 upon reactions promoted by potassium ethoxide in ethanol in two $(E_1cB)_R$ reactions (G = CN and SO_2Ph and Z = SPh) and one $(E_1cB)_I$ reaction [5] (G = $PhSO_2$ and Z = Cl) have been examined. Results in Table 3 show that for the $(E_1cB)_R$ processes, the change from sodium ethoxide to potassium ethoxide in ethanol roughly doubles the rate constant. For the $(E_1cB)_I$ reaction of the chlorosulphone, this change makes no difference and none of the reactions with potassium ethoxide are affected by the addition of the crown ether.

It is clear from this evidence that solvent effects and ion-association to the extent that it is present in the media used in this work, are unimportant in determining the ranks of leaving groups.

Conclusions.—For eliminations activated by groups at the middle of the activation range,[11] the values of β_{LG} and the variation of leaving-group rank with activating group are small. These factors point to a small degree of double-bond formation and leaving-group departure in the transition state of the process in which the leaving group is ejected. Ejection of a group such as SPh from a sulphonyl-stabilised carbanion occurs very rapidly; the rank of SPh in the sulphone series suggests a k_2 value of $\simeq 10^7$ s^{-1} and it is not surprising that an early transition state is indicated.

These conclusions match those developed by Winey and Thornton [24] for phenethyl derivatives in the extreme case of the (E_1cB)-like E_2 process.

The leaving-group series delineated earlier (Part 30) [2] referred to a single activating group (G = $PhSO_2$) in a single medium (ethanolic sodium ethoxide). The present studies of the significance of solvent change and ion-association suggest that not only is the structure of the carbanion unimportant in deciding leaving-group rank but so is change of solvent and intervention in whatever association there may be between cations present and the conjugate base either of the substrate or solvent. The results suggest that the original leaving-group series [2] may have some generality and be adhered to even with substantial changes in substrate structure and reaction medium.

The general conclusions are strengthened by the response of the system to structural effects; these are reported in the following paper.[25]

EXPERIMENTAL

For general directions on kinetics, synthesis, and product analysis see Part 30,[2] and on detritiation measurements see Part 31.[9]

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[24] D. A. Winey and E. R. Thornton, *J. Amer. Chem. Soc.*, 1975, **97**, 3102.

[25] P. J. Thomas and C. J. M. Stirling, following paper.

Reactions with $CNCH_2CH_2\overset{+}{N}Me_2Ph\overset{-}{I}$ [1] were carried out as for the sulphone.[2]

For details of reactions with $CNCH_2CH_2SO_2Ph$ and $CNCH_2CH_2SPh$ see Part 32.[5] For reactions with $CNCH_2CH_2OPh$ see Part 19;[22] product analyses for phenoxynitriles in the present work were analogous.

Substrates.—2-Methoxypropanenitrile had b.p. 72/15 mmHg (lit.,[26] b.p. 85.5/49 mmHg, n_D^{20} 1.4032). Conversion into 2-ethoxypropanenitrile was followed by g.l.c.[2] as for 2′-methoxypropiophenone. Reactions were followed both by appearance of product and disappearance of substrate. 4-Methyl-4-nitropentanenitrile had b.p. 100 °C/0.1 mmHg; n_D^{17} 1.4509 (lit.,[27] b.p. 89 °C/0.07 mmHg). Diethyl 2-benzoylethylphosphonate had b.p. 72 °C/0.1 mmHg, n_D^{20} 1.5074 (lit.,[28] b.p. 161—164 °C/0.04 mmHg, n_D^{20} 1.5060). The phosphonate, on treatment with ethanolic 0.3M-sodium ethoxide, gave 2′-ethoxypropiophenone (93%), b.p. 121 °C/12 mmHg.[2] 3-Benzoylpropanenitrile had m.p. 75.7 (lit.,[28] m.p. 76 °C).

TABLE 4

Substrates and products

G	Z	B.p. (°C)/ mmHg n_D^{20}	Yield %	Found (%)			Formula	Reqd. (%)				
				C	H	N		C	H	N		
CN	SePh [a]	71/0.2 1.5957	93	51.5	4.4	6.6	C_9H_9NSe	51.4	4.3	6.7	$CNCH_2CH_2OEt$ (94)	PhSeSePh (78)
CN	$C_6H_4CO_2Et$-*p* [c]	56.2 [b]	24	65.6	5.7	6.3	$C_{12}H_{13}NO_3$	65.8	5.9	6.4	*d*	
CN	OC_6H_4Me-*p* [c]	47.1 [b]	19	74.2	6.75	8.6	$C_{10}H_{11}NO$	74.1	6.8	8.6	*d*	
CN	OC_6H_4Cl-*p* [c]	44.3 [b]	15	60.0	4.4	7.9	C_9H_8ClNO	59.5	4.4	7.7	$CNCH_2CH_2OEt$ (97)	*p*-ClC_6H_4OH (83)
CN	OC_6H_4CN-*p* [c]	61.1 [b]	32	76.7	5.0	17.7	$C_{10}H_8N_2O$	76.9	5.1	17.9	*d*	
CN	$OC_6H_4NO_2$-*p* [c]	53.1 [b]	8	56.4	4.3	14.9	$C_9H_8N_2O_3$	56.3	4.2	14.6	*d*	
CN	N(Me)Ac [e]	144/0.2	82	57.3	8.0	22.3	$C_6H_{10}N_2O$	57.1	7.9	22.2	$CNCH_2CH_2OEt$ [f]	
Bz	$N(CH_2Ph)Ac$ [g]	125/0.06	73	76.9	6.9	4.9	$C_{18}H_{19}NO_2$	76.9	6.8	5.0	$PhCOCH_2CH_2OEt$	
Ac	$C(Me_2)NO_2$ [h]	79/0.1 1.4532	85	52.4	8.0	8.8	$C_7H_{13}NO_3$	52.8	8.2	8.8	*i*	

[a] By addition of PhSe to propenenitrile, see Experimental section. [b] M.p. [c] By cyanoethylation of the phenol. Details in Part 19 ref. 22. Dioxan was used as solvent in reaction with *p*-nitrophenol. [d] Stoicheiometry checked by u.v. [e] By acetylation of propenenitrile–methylamine adduct. [f] G.l.c. [g] By acetylation of phenyl vinyl ketone–benzylamine adduct. See Experimental section. [h] By addition of 2-nitropropane to methyl vinyl ketone. [i] >95% Recovery from M-NaOEt–EtOH at 25 °C after 10 days.

3-*Phenylselenopropanenitrile*.—Sodium borohydride (0.02 mol) was added slowly to diphenyl diselenide (0.01 mol) in dry ethanol (75 ml) under N_2. Acrylonitrile (0.02 mol) and triethylamine hydrochloride (0.02 mol) were added. When no yellow colouration [of $(PhSe)_2$] was produced on addition of a portion of the reaction mixture to aqueous hydrogen peroxide, extraction gave the *selenide*.

The selenide (0.01 mol) was kept with ethanol 0.67M-sodium ethoxide (150 ml) for 3 h at 20 °C. The mixture was poured into saturated brine and extraction gave 2-ethoxypropanenitrile (94%), b.p. 61 °C/12 mmHg, n_D^{19} 1.4073 (lit.,[26] b.p. 65 °C/15 mmHg, n_D^{20} 1.4068). Acidification and re-extraction of the brine after oxidation in an air stream gave diphenyl diselenide (89%), m.p. and mixed m.p. 63 °C.

3-(N-*Methylacetamido*)*propanenitrile*.—Ethanolic 33% methylamine (0.5 mol) was stirred for 15 h with propenenitrile (0.1 mol) at 22 °C. Distillation gave 3-methylaminopropionitrile (85%), b.p. 79 °C/20 mmHg (lit.,[29] 74 °C/16 mmHg; n_D^{20} 1.4320). Acetylation with acetic anhydride in toluene (at 100 °C for 12 h) gave the *amide* (Table 4).

2-(N-*Benzylacetamido*)*ethyl Phenyl Ketone*.—Benzylamine (10 mmol) was added to ethenyl phenyl ketone prepared *in situ* from 2-chloroethyl phenyl ketone (10 mmol) and triethylamine (10 mmol) in toluene (20 ml). After 12 h at 20 °C, the mixture was evaporated and the residue of crude amine adduct was heated under reflux with acetic anhydride (2 g) in toluene (100 ml). Evaporation and distillation gave the *amide* (Table 4).

5-*Methyl*-5-*nitrohexan*-2-*one*.—Methyl vinyl ketone (0.2 mol) was added dropwise to 2-nitropropane (0.2 mol) in aqueous 33% potassium hydroxide (10 ml). The mixture was kept at 100 °C for 1 h when extraction gave the *nitroketone* (Table 4).

Diethyl Carboxymethylphosphonate.—Ethyl bromoacetate (5 mmol) and triethylphosphite (5.5 mmol) were refluxed in diglyme under nitrogen. After 36 h, distillation gave *ethyl diethylphosphonylacetate* (93%), b.p. 150 °C/0.4 mmHg, n_D^{22} 1.4298 (Found: C, 42.2; H, 7.4. $C_8H_{17}O_5P$ requires C, 42.3; H, 7.6%). Hydrolysis of the ester was with methanolic sodium hydroxide at 65 °C. The saponification mixture was evaporated and an ethereal suspension of the residue was saturated with dry hydrogen chloride. Evaporation of the ethereal solution gave the *acid* (86%) (Found: C, 36.6; H, 6.4. $C_6H_{13}O_5P$ requires C, 36.7; H, 6.6%), $\tau(D_2O)$ 5.85 (4 H, q, *J* 7 Hz), 7.05 (2 H, d, *J* 21 Hz), 8.65 (3 H, t, *J* 7 Hz). The acid decomposed on attempted distillation.

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