A New Leaving Group in Acetolysis Reactions: the Synthesis of Alkyl Picrates

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IN solvolysis reactions the effects of changes in leaving group have received little attention; in systems of moderate reactivity choice has virtually been confined to arenesulphonate and halide ions and fragmenting residues. We now report that alkyl picrates (alkyl 2,4,6–trinitrophenyl ethers) can be made from the alcohols at least as readily as the corresponding toluene-*p*-sulphonates, and undergo unimolecular solvolysis only slightly more slowly. Further, alkyl picrates have u.v.

absorption spectra which differ from those of ionised or un-ionised picric acid, so the reaction can readily be followed.

Although the synthesis of picrates from low molecular-weight primary alcohols[1] and phenols[2] presents no difficulty, the preparation of those having secondary or large primary alkyl groups has hitherto been difficult and unreliable. However, picryl fluoride (1·2 mol.) reacts with alcohols (1·0 equiv.) in the minimum volume of dry methylene dichloride in the presence of tertiary amines (1·0 mol.) at room temperature to give good yields of alkyl picrates. Yields of *trans*-4-t-butylcyclohexyl picrate of 55, 60, and 70% were obtained with triethylamine, pyridine, and DABCO (1,4-diazabicyclo[2,2,2]octane) respectively. As the reaction with DABCO alone is self-indicating (the red colour of the DABCO–picryl fluoride charge-transfer complex fades to yellow when the reaction is complete), this is the base of choice. Reaction times vary from a few seconds to 18 hr. The product is isolated by washing the methylene dichloride with dilute acid and aqueous sodium hydrogen carbonate, evaporation, and recrystallisation. The following alcohols, chosen so as to include compounds with hydroxy-groups in varied environments and representative of the major classes of natural products, were converted into their fully picrylated derivatives by this procedure; percentage yield, followed by m.p., is given in parentheses: octan-1-ol (60, 27°), 2,2-dimethylpropan-1-ol (62, 61°), allyl alcohol (55, 89°), propargyl alcohol (45, 101°), 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (85, 150°), *N*-2,4-dinitrophenyl-DL-serine methyl ester (57, 165°), pentan-3-ol (93, 79°), cyclohexanol (95, 100°), *trans*-4-t-butylcyclohexanol (70, 143°), *cis*-4-t-butylcyclohexanol (55, 131°), DL-*trans*-*cis*-bicyclo-[4,4,0]decan-2-ol (60, 106°), DL-*cis*-*trans*-bicyclo-[4,4,0]decan-2-ol (55, 137°), DL-*endo*-norbornan-2ol-(77, 82°), DL-*exo*-norbornan-2-ol (51, 101°), adamantan-2-ol (45, 140°), DL-1-phenylethanol [45, *ca.* 83° (decomp.)], cholesterol [60, 165° (decomp)], DL-*trans*-2-acetamidocyclohexanol (70, *ca.* 160°; after decomp. *ca.* 138°), DL-*trans*-2-benzamidocyclohexanol [79°, 115—119° (decomp.)], adamantan-1-ol [68, 150° (decomp.)], 1,4:2,6-dianhydro-D-mannitol (97, 242°) and DL-propane-1,2-diol (50, 181°). Especially noteworthy is the ready production of 1-adamantyl and 1-phenylethyl picrates: adamantyl toluene-*p*-sulphonate is only obtained pure with difficulty[4] and 1-phenylethyl toluene-*p*-sulphonate not at all.[5] All new compounds gave acceptable analyses. The reaction in neat pyridine was illustrated by the conversion of dextrin into a derivative with 1·8 picryl groups per glucose residue. Other alkyl picrates are highly crystalline solids which are almost colourless when pure, but rapidly turn brown on exposure to light. Despite the use of methyl picrate as an explosive,[6] these compounds have resisted even deliberate attempts to detonate them.

Data on the kinetics and kinetically controlled products of the acetolysis of *cis*- and *trans*-4-t-butylcyclohexyl picrates are contrasted with those for the corresponding toluene-*p*-sulphonates in the Table. Data for toluene-*p*-sulphonate products are taken from ref. 7, rates are calculated from ref. 8, and activation parameters from ref. 9.

The rate of acetolysis of each picrate is about one-eighth that of the corresponding toluene-*p*-sulphonates, and the products are similar but

Acetolysis of 4-t-butylcyclohexyl derivatives

	trans		*cis*	
	Toluene-*p*-sulphonate	Picrate	Toluene-*p*-sulphonate	Picrate
Products (normalised percentage yields; in 0·15M-NaOAc)				
trans-4-OAc	0·4	0·27 ± 0·05	7·9	5·1 ± 0·2
cis-4-OAc	19·2	15·9 ± 0·6	0·8	0·33 ± 0·04
trans-3-OAc	0·6	0·26 ± 0·04	4·3	1·92 ± 0·07
cis-3-OAc	1·5	0·47 ± 0·03	0·4	0·19 ± 0·01
4-$\mathrm{Bu^t}$-cyclohexene	73·4	80·7 ± 1·2	83·5	91·3 ± 0·4
3-$\mathrm{Bu^t}$-cyclohexene	4·5	2·9 ± 0·1	2·8	1·45 ± 0·07
1-$\mathrm{Bu^t}$-cyclohexene	0·5	0·25 ± 0·02	0·2	0·07 ± 0·02
Recovery	94·7	100·5 ± 0·3	91·5	103·0 ± 1·3
Total rearranged products	7·1	3·9 ± 0·2	7·7	3·6 ± 0·1
Kinetics				
10^4k (sec.$^{-1}$) (100·0°)	6·14 ± 0·13	0·71 ± 0·03	14·3 ± 0·04	1·69 ± 0·07
10^4k in 0·15M-NaOAc	—	0·80 ± 0·04	—	2·30 ± 0·04
$\Delta H\pm$ (kcal.)	28·1 ± 0·3	29·0 ± 0·6	28·7 ± 0·2	29·6 ± 0·6
$\Delta S\pm$ (e.u.)	−0·1 ± 0·8	0·1 ± 1·6	2·8 ± 0·5	4 ± 2

significantly different. These results establish the limiting, S_N1 nature of the acetolyses of the 4-t-butylcyclohexyl picrates, as the following criteria are obeyed:

(1) Occurrence of products derived from hydride shift.[7]

(2) Near-zero entropy and high energy of activation.[10]

(3) Insensitivity of the rate to added base.[11]

An important difference between alkyl picrates and alkyl toluene-*p*-sulphonates is that picrates may be cleaved under very mild conditions with retention of configuration. Aqueous ethanolic ammonia at room temperature or even passage down an alumina chromatographic column[12] regenerates the alcohol virtually quantitatively, the former reagent giving picramide. In view of the high crystallinity of picryl derivatives, the picryl residue may find application both for the protection of hydroxy-groups and in synthetic intermediates which react by S_N1 and S_N2 processes.[13]

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