Oxidation of Alkyl Carbazates: a New Method for Replacement of the Hydroxy-group by Halogen

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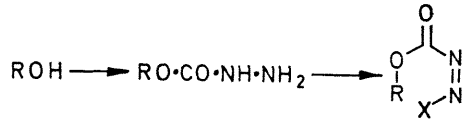
Summary Conversion of alcohols into carbazates followed by oxidation with *N*-halogenosuccinimides in the presence of pyridine is a new preparative route to alkyl halides.

SUBSTITUTION at a bridgehead is often difficult.[1] However, in the particular case of replacement of OH by halogen, we considered that carbazates are correctly constituted to provide an adequate driving force for the reaction. Conveniently, such esters can be made from alcohols under mild conditions[2] by successive treatment with phosgene and hydrazine, and oxidation with a source of positive halogen could produce an azo-intermediate (**1**) which could collapse



(1)

in various ways, including a pericyclic process (when X = halogen), with expulsion of CO_2 and N_2 to afford an alkyl halide. In the event, we have found essentially neutral conditions for effecting this overall transformation.

Addition of adamantyl carbazate[2] in CH_2Cl_2 to a solution in the same solvent of *N*-bromosuccinimide (2 mol.) and pyridine (1 mol.) gave 1-bromoadamantane[3]† (49%) after 20 min at room temperature. (Anhydrous materials were used; the minimum reaction time was not established). Similar use of *N*-iodosuccinimide gave 1-iodoadamantane[4]† (63%) but with *N*-chlorosuccinimide little, if any, alkyl chloride was formed.‡

Application of the process to cyclohexyl carbazate[6]§ afforded cyclohexyl iodide and bromide (*ca.* 39 and 42% respectively). The bromide was accompanied by *trans*-1,2-dibromocyclohexane (*ca.* 38 mole % of product bromides) which probably arises from cyclohexene. Such a possibility suggests, at least for the dibromide, intervention of the cyclohexyl carbonium ion or elimination *via* an azo-intermediate (**1**) and on this basis the reaction is best suited as a synthetic procedure to those cases where olefin formation is difficult. In this respect application to 1-apocamphanol is a demanding test because the bridgehead position of the bicyclo[2,2,1]heptyl system is known[7] to be an extremely unfavourable site for replacement by normal nucleophilic substitution. Techniques have been devised for replacing the hydroxy-group of 1-apocamphanol by iodine in a free-radical process[8] and by fluorine *via* a cationic intermediate.[9] We find that 1-apocamphanol can be converted[6] smoothly into its carbazate§ (84% yield) and oxidation, best carried out in diethyl ether with iodine–pyridine, affords 1-iodoapocamphane (39%).¶

† (>99% pure by g.l.c.). Identified by comparison with an authentic sample

‡ Contrast this sequence of reactivity with the observation that in highly acidic media ($HX–X_2$; X = Cl, Br, or I) benzhydrazide is converted[5] into benzoyl chloride, benzhydrazidium tribromide, and benzhydrazidium tri-iodide, respectively. $HCl–Cl_2$ converts[5] benzyl carbazate into benzyl chloride. For oxidation of hydrazides under basic conditions see *e.g.*, Y. Wolman, P. M. Gallop, A. Patchornik, and A. Berger, *J. Amer. Chem. Soc.*, 1962, **84**, 1889.

§ Analytical values agree to within ±0·2%.

¶ Iodine (4 mol.) and pyridine (5 mol.) were used per mol. carbazate but the optimum proportion of reagents was not established. The product was identical with an authentic sample.[10]

Although the mechanistic details are unclear, the reaction is, therefore, of preparative use where usual substitution processes are difficult.[7,4]

This work was begun during tenure of an I.C.I. Research Fellowship at Imperial College (D.L.J.C.) and was subsequently supported by a grant from Shell Research.

(*Received, June 25th,* 1971; *Com.* 1045.)

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