Introduction of Bridgehead Functionality via Lead(IV) Oxidation of Hydrocarbons

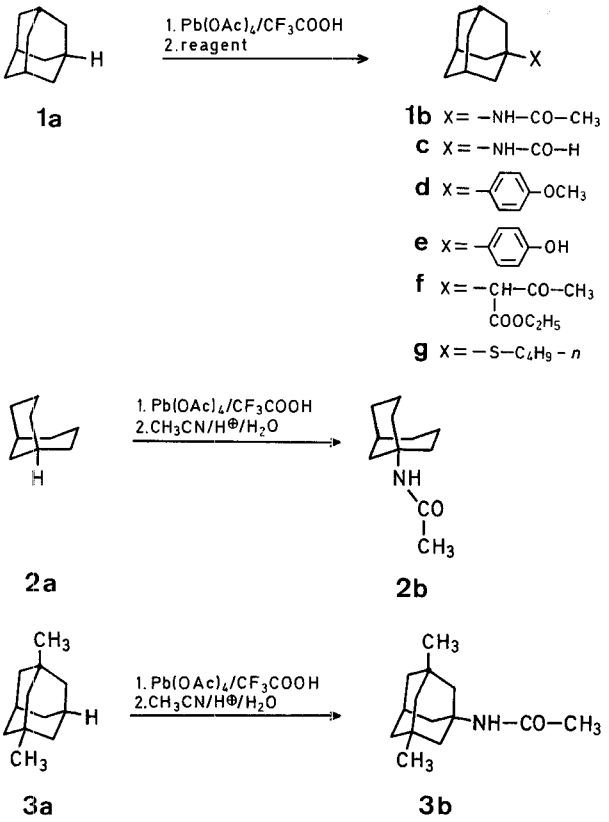
Stephen R. JONES, John M. MELLOR

Department of Chemistry, The University, Southampton S09 5NH, England

Introduction of a functionality into saturated hydrocarbons rarely results in high yields of a single product. Bridged hydrocarbons are an exception, and selective halogenation proceeds in high yield[1]. Nitrogen functionality has been introduced into such hydrocarbons either by a two step process of the Ritter reaction[2] via the previously prepared halogenated derivative, or by the use of nitrogen trichloride[3]. Oxygen functionality may be introduced directly with chromium trioxide[4] in moderate yield, by the use of sulfuric acid[5] in the case of adamantanes, and recently we have shown[6] that bridgehead trifluoroacetates may be obtained in high yield by oxidation with Pb(IV) salts. Direct introduction of a sulfur functionality has not been described. We now describe a one pot reaction sequence whereby a hydrocarbon may be directly functionalised with carbon, nitrogen, or sulfur containing substituents.

Reaction of the hydrocarbon with Pb(IV) acetate in trifluoroacetic acid/dichloromethane at room temperature[6] followed by addition of a nucleophile and where appropriate, a mineral acid catalyst led to the respective products in high yields as reported in the Table. In no case did the presence of lead salts interfere with reaction. Use of the trifluoroacetoxy group as the leaving group permits efficient acid catalysis, which is desirable for the introduction of a nitrogen functionality or for efficient alkylation of ethyl acetoacetate, or of aromatics. The formation of sulfides does not require acid catalysis.

The possibility of direct introduction of a carbon, nitrogen, oxygen, or sulfur functionality without isolation of the intermediate trifluoroacetate from the crude oxidation mixture is of interest in view of, for example, the anti-viral activity[7] of adamantylamines. Successful extension to bridged hydrocarbons other than adamantanes (**1** and **3**) is indicated by functionalisation of bicyclo[3.3.1]nonane (**2a**).



***N*-(1-Bicyclo[3.3.1]nonyl)-acetamide (2b):**

Bicyclo[3.3.1]nonane (**2a**; 0.61 g) and lead(IV) acetate (B.D.H.; 2.80 g) were stirred at room temperature for 24 h in dichloromethane (12 ml) and trifluoroacetic acid (12 ml). Acetonitrile (1.5 ml) and concentrated sulfuric acid (0.68 ml; 98%) were added to the solution. Addition of the acid caused insoluble lead(II) salts to precipi-

tate from solution. The solution was stirred for an additional 8 h. The reaction mixture was poured on to chloroform (50 ml) and water (50 ml) and the trifluoroacetic acid was decomposed by slow addition of solid sodium carbonate until effervescence had stopped. The insoluble lead salts were filtered off and washed with chloroform. Further extraction of the water layer with chloroform (50 ml) and drying the combined chloroform extracts ($MgSO_4$) followed by removal of solvent gave an oil; yield: 0.83 g. Crystallisation from hexane gave pure *N*-(1-bicyclo[3.3.1]nonyl)-acetamide (**2b**); yield: 0.60 g; m.p. 85–86°. Further purification of the mother liquor by T.L.C. afforded a further crop (0.10 g); total yield: 78%.

I.R. (nujol): $\nu_{max} = 3300$, 3000, 1635, and 1555 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 1.9$ (s, 3H, $NHCOCH_3$), 1.4–2.3 (15H, complex), and 5.2 ppm (broad, 1H, $NHCOCH_3$).

M.S.: $m/e = 181$ ($M^{\oplus}$, 31%), 138 ($M^{\oplus} - C_2H_3O$, 92%), 122 ($M^{\oplus} - C_2H_5NO$, 17%), and 96 ($M^{\oplus} - C_4H_7NO$, 100%).

Table. Functionalisation of Bridgehead Hydrocarbons

Substrate	Reagent	Product[a]	Yield (%)[b]	b.p. or m.p.
1a	$CH_3CN/H^{\oplus}$	**1b**	85	m.p. 148–149°
1a	KCN	**1c**	82	m.p. 138–139°
1a	$H_3COC_6H_5/H^{\oplus}$	**1d**[c]	84	m.p. 82–83°
1a	$C_6H_5OH/H^{\oplus}$	**1e**[c]	81	m.p. 180–181°
1a	$H_3CCOCH_2COOC_2H_5/H^{\oplus}$	**1f**	87	b.p. 165–170°/ 2 torr
1a	n-C_4H_9SH	**1g**	97	b.p. 194–196°/ 40 torr
2a	$CH_3CN/H^{\oplus}$	**2b**	78	m.p. 85–86°
3a	$CH_3CN/H^{\oplus}$	**3b**	85	m.p. 112–112.5°

[a] All products gave satisfactory physical data.
[b] Based on the distilled or recrystallised products.
[c] *para* isomer.

N-(1-Adamantyl)formamide (1c):
Adamantane (0.68 g) and lead(IV) acetate (2.90 g) in trifluoroacetic acid (12 ml) and dichloromethane (12 ml) were stirred as above for 36 h. Addition of solid potassium cyanide (1.27 g) over 1 h, stirring for 5 h and work up as above afforded a white solid. Recrystallisation from cyclohexane gave pure *N*-(1-adamantyl)-formamide (**1c**); yield: 0.73 g (82%); m.p. 138–139° (Lit.[8] 139–140°).
I.R. (nujol): $\nu_{max} = 3170$, 3070, and 1685 cm^{-1}.
^{1}H-N.M.R. ($CDCl_3$): $\delta = 1.6$–2.3 (complex, 15H), 6.6 (broad, 1H, NHCHO), 8.05, 8.20, and 8.40 ppm (1H, NHCHO).
M.S.: $m/e = 179$ ($M^{\oplus}$, 52%) and 122 (100%).

4-(1-Adamantyl)-anisole (1d):
Adamantane (0.68 g) was stirred with lead(IV) acetate (2.90 g) in dichloromethane (12 ml) and trifluoroacetic acid (12 ml) for 36 h as above. Excess anisole (5.4 ml) and concentrated sulfuric acid (0.68 ml) were added to the cooled reaction mixture. An aliquot removed after 1 h showed the absence of adamantyl trifluoroacetate (G.L.C. on OV1) and formation of two products (19:1) with longer retention times. The reaction mixture was stirred for a further 3 h when analysis showed a single product of longer retention time. The reaction mixture was poured on to ether (50 ml) and ice-water (50 ml) containing sodium hydroxide (5 g). The insoluble lead salts were filtered and washed thoroughly with additional ether. Further extraction of the water layer with ether (50 ml), drying the ether extract ($MgSO_4$), and removal of solvent gave an oil (5 g). Removal of excess anisole under reduced pressure gave a white solid (1.10 g) which was recrystallised from methanol to give 4-(1-adamantyl)-anisole (**1d**); yield: 1.00 g (84%); m.p. 82–83° (Lit.[9] 80–83°).

I.R. (nujol): $\nu_{max} = 1615$ and 1520 cm^{-1}.

N.M.R.: $\delta = 1.67$–2.20 (m, 15H), 6.88 (d, 2H), and 7.33 ppm (d, 2H).

M.S.: $m/e = 243$ ($M+1^{\oplus}$, 18%), 242 ($M^{\oplus}$, 97%), 186 (17%), and 185 (100%).

Ethyl (Adamant-1-yl)acetoacetate (1f):
Adamantane (0.69 g) was stirred with lead tetraacetate (2.90 g) at room temperature for 36 h in dichloromethane (12 ml) and trifluoroacetic acid (12 ml). Ethyl acetoacetate (2.8 ml) and concentrated sulfuric acid (0.68 ml) were added to the reaction mixture and stirring was continued for 4 h. The reaction mixture was worked up as for **2b** to afford an oil. Removal of the excess ethyl acetoacetate followed by distillation gave ethyl (adamant-1-yl)-acetoacetate (**1f**); yield: 1.17 g (87%); G.L.C. showed 96% purity.
I.R. (liquid film): $\nu_{max} = 1720$ cm^{-1}.
N.M.R. ($CDCl_3$): $\delta = 1.27$ (t, 3H), 1.57–2.10 (complex, 15H), 2.22 (s, 3H), 3.19 (s, 1H), and 4.14 ppm (q, 2H).
M.S.: $m/e = 264$ ($M^{\oplus}$, 3%), 222 ($M^{\oplus} - C_2H_2O$, 16%), 135 ($M^{\oplus} - C_6H_9O_3$, 100%).

1-Adamantyl *n*-Butyl Sulfide (1g):
Adamantane (0.69 g) was stirred with lead(IV) acetate (2.90 g) at room temperature for 36 h as above and *n*-butylthiol (2.4 ml) was added and stirring continued for a further 3 h. Work up as before afforded by bulb to bulb distillation 1-adamantyl *n*-butyl sulfide; yield: 1.10 g; G.L.C. showed 96% purity.
N.M.R. ($CDCl_3$): $\delta = 0.8$–2.75 ppm (complex).
M.S.: $m/e = 224$ ($M^{\oplus}$, 9%), 135 ($M^{\oplus} - C_4H_9S$, 100%).

Note added in proof: It was subsequently found that the reproducibility of the oxidation of the hydrocarbons was dependent on the source of the lead(IV) acetate. Differences in chloride concentration was suspected. Consistent results were obtained by the addition of 0.25 mol of lithium chloride per mol of lead(IV) acetate.

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