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FURTHER STUDIES ON THE ACTIVATION OF THE C-H BOND IN SATURATED HYDROCARBONS

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Summary : Various saturated aliphatic and alicyclic hydrocarbons have been regioselectively oxidised with surprising efficiency by a system containing iron powder and a carboxylic acid in aqueous pyridine under an atmosphere of oxygen. A trace of hydrogen sulphide initiates the reaction.

In a recent Communication[1] we described our initial studies of a system for the oxidation of saturated hydrocarbons. In particular the reaction of adamantane with iron powder and molecular oxygen in a solvent system containing pyridine, acetic acid and a little water was studied. Hydrogen sulphide was used as an initiator.

We have made a systematic study of various organic acids. The results (Table) display several features of interest. Within a given series of monocarboxylic acids increasing acid strength appears to favour a higher relative ratio of attack at the secondary methylene positions of adamantane (C^2/C^3 ratio). The formation of a heteroatom linked chelate, probably achieved by use of lactic acid, picolinic acid and thiosalicylic acid, does not appear to confer enhanced reactivity on the system. Among the simpler dicarboxylic acids, malonic acid gives the best yield. Of the various dicarboxylic acids possessing additional hydroxyl groups inexpensive tartaric acid is particularly noteworthy for its high overall yield (27.8%) and selectivity.

It is perhaps appropriate at this stage to make some comment on the C^2/C^3 ratio. This parameter is a function not only of the chosen reagents and solvent but also of the manner in which the experiment is performed. Thus, as exemplified in the reactions of tartaric acid, introduction of oxygen by passing a current of gas over a well stirred mixture leads to a higher overall yield but a poorer relative ratio of attack at the secondary position. In contrast reaction, under a static positive pressure of oxygen gives the converse result. It may well be that two different mechanisms are operating for the formation of the tertiary alcohol (radical oxygenation) and the ketone (non-radical oxygenation).

We have also succeeded in isolating a yellow complex from the reaction of tartaric acid with iron powder in aqueous pyridine under an argon atmosphere. Subsequent reaction of this complex with adamantane (and iron powder) in acetic acid under oxygen gave adamantan-1-ol (0.6%), adamantan-2-ol (6%) and adamantanone (5%), thus demonstrating exceptionally high selectivity (C^2/C^3 = 19).

Table[a)]

ACID	TIME (h)	PRODUCTS[b)] (% Yield) Adamantan 1-ol	2-ol	one	TOTAL (% yield)	C^2/C^3[c)]
Acetic	15.5	3.5		9.5	13.0	2.7
Trichloroacetic	16.5	2.5		6.0	8.5	2.4
Trifluoroacetic	17.5	1.5		9.0	10.5	6.0
(+)-Lactic	16	3.0		5.0	8.0	1.7
Picolinic	17	3.5		7.0	10.5	2.0
Thiosalicylic	15	2.0	0.2	1.0	3.2	0.6
Oxalic	21.5	1.5		4.5	6.0	3.0
Malonic	19.5	4.0		15.5	19.5	3.9
Succinic	16	3.5		4.5	8.0	1.3
(+)-Malic	19	1.0		3.0	4.0	3.0
Diglycolic	17	3.5		12.0	15.5	3.4
Mucic	27.5	8.0		12.5	20.5	1.6
Citric	15	6.0		15.5	21.5	2.6
meso-Tartaric	17.5	8.5		16.5	25.0	1.9
(+)-Tartaric	15	9.0		17.5[d)]	26.5	1.9
(+)-Tartaric	2	7.0		14.5	21.5	2.0
	3[e)]	1.5		14.5	16.0	9.6
	49[f)]	1.5		13.5	15.0	9.0

a) In a typical experiment iron powder (10 atom equiv) and the organic acid (10 m equiv.) were added to a solution of adamantane (1 mmol) in pyridine containing 6.6% water (10 ml). Hydrogen sulphide (0.05 mmol) in pyridine was added and a slow stream of oxygen was passed over the vigorously stirred reaction mixture which was maintained in a bath at 30°C.

b) Determined by g.l.c. analysis which slightly underestimates the adamantanone.

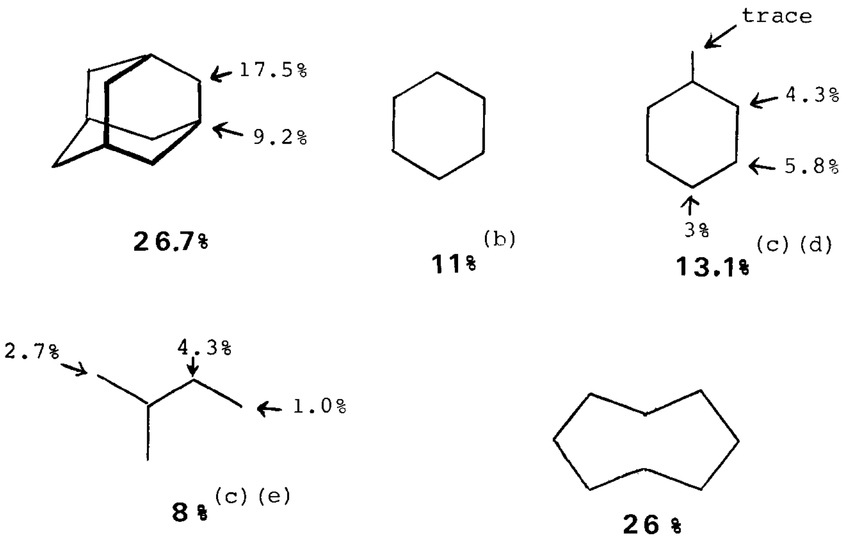
c) C^2/C^3 represents the relative ratio of attack at the secondary and tertiary positions respectively.

d) The crystalline DNP derivative of adamantanone was isolated in 18.5% yield

e) Reaction performed under a static oxygen atmosphere.

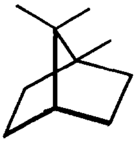
f) Reaction performed under a static oxygen atmosphere using 20 ml of solvent

Yield and Site Selectivity in the Functionalisation of Saturated Hydrocarbons[(a)]

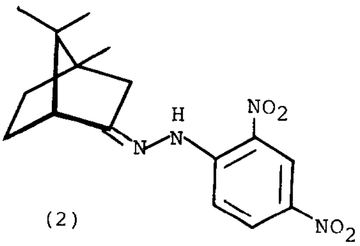


Scheme

(a) The indicated yields refer to isolated 2,4-dinitrophenylhydrazone derivatives of the corresponding carbonyl compounds. The general experimental procedure was as indicated in Table 1.
(b) Cyclohexanol (0.5%) was detected by g.l.c. analysis.
(c) G.l.c. analysis of the crude reaction mixture failed to detect appreciable amounts of the tertiary alcohol.
(d) The relative proportions of the various 2,4-dinitrophenylhydrazone derivatives was determined by H.P.L.C. and 400 MHz n.m.r. comparison with authentic samples.
(e) 2,4-Dinitrophenylhydrazone derivatives separated by semi-preparative H.P.L.C.



(1)



(2)

The tartaric acid system was accordingly chosen to examine the scope of the oxidation. The results for a variety of hydrocarbons (Scheme) indicate that an acceptable conversiion can be achieved with acyclic, linear, branched and unbranched hydrocarbons. It is of interest that the pattern of carbonyl site selectivity in 2-methylbutane and methylcyclohexane is different from that observed *in vivo* for cytochrome P-450 oxidation of the same substrates[2]. Recent interest in the possibilities of organoiron carbenoid intermediates[3] prompted us to study cyclooctane, since a derived carbene intermediate might reasonably be expected[4] to undergo 1,5 insertion to the bicyclo [3,3,0] octane skeleton. In the event, no derivatives of this type were detected.

We have also examined the possibility of asymmetric induction. Camphane (**1**) gave a surprisingly complex reaction mixture[5]. It was possible to isolate and characterise essentially racemic *epi*camphor 2,4 dinitrophenylhydrazone[6] (2), ($[\alpha]_D^{20}$ = − 2° (c, 0.5, $CHCl_3$). (+)-Epicamphor 2,4-dinitrophenylhydrazone has $[\alpha]_D^{20}$ = + 175° (c, 0.437 $CHCl_3$).

The results outlined in this communication suggest that the mechanism of our reaction does not involve a transition metal oxenoid nor is radical behaviour predominant. The apparent preference for a methylene group over a methine is that to be expected from reactions involving insertion of a co-ordinatively unsaturated transition metal complex into the C-H bond of an alkane[7].

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