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A NEW SYNTHESIS OF PHENYL KETONES BY INTRAMOLECULAR 'DEOXYBENZOYLATION' OF ENOLS AND PHENOLS

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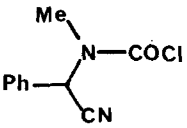
Summary: The phenylcyanocarbamoyl chloride 1 has been used as a benzoyl anion equivalent in an intramolecular process to effect the replacement of the hydroxyl group of enols and phenols by the benzoyl group.

The use of cyanohydrins and aminonitriles as acyl anion equivalents has been exploited for many years and the subject has formed the basis of a recent review.[1]

We now describe the hitherto unknown phenylcyanocarbamoyl chloride 1[2] and in particular its ability to react sequentially, firstly as an electrophile and then following deprotonation as a carbon-nucleophile. In its reactivity the carbamoyl chloride is thus equivalent to the species 2 and we have used this behaviour to deliver a benzoyl anion equivalent in an intramolecular process to form carbon-carbon bonds.



1

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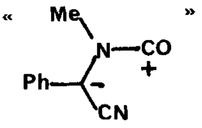
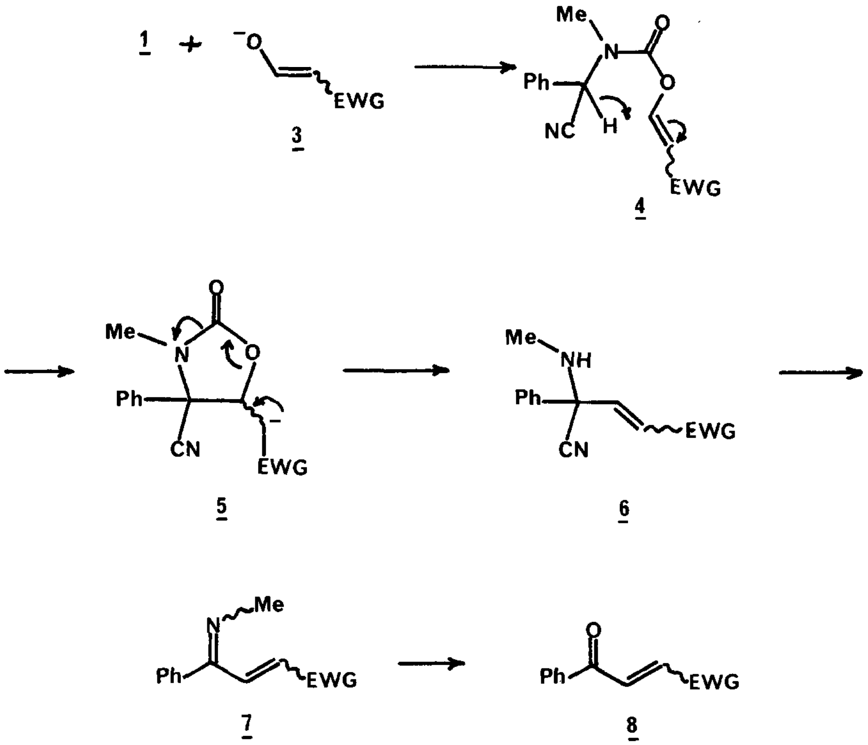


2

Thus 1 reacts with enolate and phenolate anions 3 under basic conditions as in the SCHEME (EWG = electron-withdrawing group), initially to give their carbamic esters 4 which, if suitably activated, undergo cyclisation to oxazolidinone anions 5 (in the case of phenols, to the Meisenheimer intermediate). Expulsion of carbon dioxide from these anions gives aminonitriles 6 which tend, in part, to eliminate hydrogen cyanide under the basic conditions employed to give imines 7. Typically the reaction of equimolar proportions of 1 and the enol or phenol in acetonitrile with an excess of powdered anhydrous potassium carbonate gives variable mixtures of 6 and 7 after 24 h. at room temperature (Method A). The crude mixtures so obtained are readily converted by brief (ca. 30 min.) treatment with silver nitrate in aqueous tetrahydrofuran[3] to give the ketones 8 which are isolated following their purification by chromatography on silica. The scope of the method is illustrated by the examples in the table opposite.

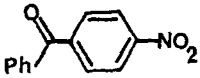
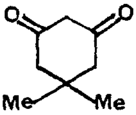
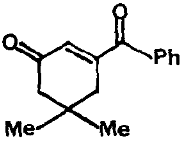
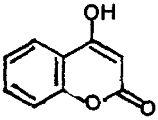
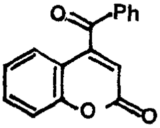
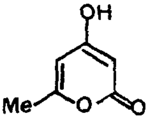
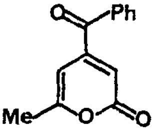
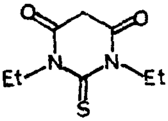
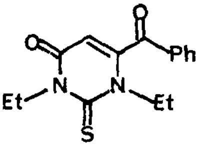
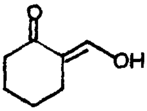
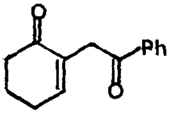
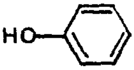
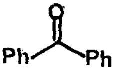
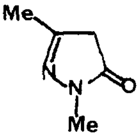
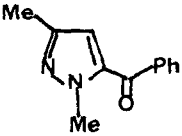
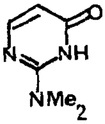
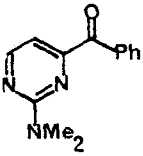
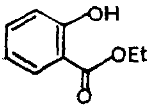
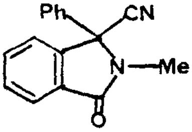


SCHEME

The application of Method A to insufficiently activated substrates yields carbamic esters 4, but we have found that treatment of these with an equivalent of sodium hydride in dimethylformamide (24 h.) in a separate step (Method B) followed by treatment with silver nitrate and isolation as before yields the anticipated ketones (Entries 7 and 8). That such poorly activated esters undergo internal displacement of oxygen is surprising although not wholly without precedent.[4]

Where in the intermediate aminonitrile 6 the electron-withdrawing group is appropriately reactive as well as in a position to interact with the methylamino group then products other than ketones may be formed. Such an example is provided by the single step conversion of ethyl salicylate to the isoindolone as in Entry 10.

The method that we have described here in embryonic form brings about the conversion by intramolecular means of an enol or phenol by replacement of its hydroxyl group by a benzoyl group. Such a process has not as far as we are aware been reported previously, and we have

Entry	Substrate	Method	Product[5]	M.p.	Yield[6]
1		A		135-136°	78%
2		A		118-120°	78%
3		A		124-126°	71%
4		A		68-70°	74%
5		A		79-80°	60%
6		A		54-55°	30%
7		B		48-49°	41%
8		B		(oil)	32%
9		A		57-59°	27%
10		A[7]		102-104°	62%

coined the word 'deoxybenzoylation' to name the transformation. The method clearly has some potential use in synthetic chemistry making readily available certain ketones that may be difficult to obtain by other means. In particular we feel that it may find use for the regiospecific preparation of aryl ketones having substitution patterns which preclude the use of the more usual electrophilic aroylation procedures.

References and notes

1. J.D.Albright, Tetrahedron, 39, 3207 (1983).

2. Formed in 71% yield by the dropwise addition of equimolar proportions of the aminonitrile and N,N-dimethylaniline to one equivalent of phosgene in toluene at 0°, the carbamoyl chloride had b.p. 124°/0.08 mm. Following distillation the compound slowly solidified, and a small sample crystallised from light-petroleum at -60° had m.p. 29-30°. ^{1}H-NMR (90 MHz), δ $CDCl_3$: 3.0 (d,broad due to restricted rotation, 3H), 6.6 (s, broad, 1H), 7.46 (s, 5H). The compound may be kept, protected from moisture, for several months without any detectable deterioration.

3. L.Stella, Tetrahedron Lett., 25, 3457 (1984).

4. See for example the conversion of phenyl ethers to anilides by an intramolecular process: R.Bayles, M.C.Johnson, R.F.Maisey and R.W.Turner, Synthesis, 31, 33 (1977).

5. All products had analytical and ^{1}H-NMR data in accord with the structures shown.

6. Yields reported are not optimised and for the most part are those obtained in a single experiment.

7. Omitting the silver nitrate work-up.

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