Acyl Cyanides as Carbonyl Heterodienophiles

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Abstract: Acyl cyanides have been shown to behave as carbonyl dienophiles in reactions with electron-rich o-quinodimethanes. This represents the first observation of an acyl cyanide carbonyl group reacting in such a manner.

Heterodienophiles have proven to be of considerable value in the synthesis of six membered ring heterocycles.¹ In the area of carbonyl dienophiles, Danishefsky and co-workers have shown that aldehydes react efficiently with electron-rich dienes, especially in the presence of mild Lewis acid catalysts, to give dihydropyrans.² Fewer examples exist in which ketones act as dienophiles, the major class being ketomalonates.³ According to recent reviews, one example exists⁴ in which an ester acts as a dienophile in an intramolecular Diels-Alder; to the best of our knowledge there appear to be no reports concerning the use of acyl cyanides as carbonyl dienophiles.

As part of ongoing work we had occasion to re-examine the photoenolisation of 2methylbenzoyl cyanide 1, the subject of a brief early account by Sammes,⁵ who reported the isolation of 4 after irradiation in the presence of maleic anhydride. The authors concluded that 4 arose from the unstable adduct, 3, via loss of HCN and decarboxylation during hydrolytic workup. In view of the recent conclusions concerning the mechanistic role of steric crowding in photoenols which lead to benzocyclobutenols,⁶ we anticipated that in the absence of maleic anhydride, 2 might undergo electrocyclisation to benzocyclobutenone cyanohydrin, analogus to the known cyclisation of the photoenol derived from 2-methylacetophenone.



In the event, irradiation of 1 (0.1-1.0 M in benzene) furnished a new product in up to 65% yield whose spectroscopic and analytical properties indicated structure 6.7 In particular the proton spectrum of 6 showed diagnostic signals at 2.68 ppm, (aromatic methyl) and an AB quartet centered at 3.71 ppm (JAB = 16.5 Hz) in addition to the

aromatic hydrogens. The infrared spectrum showed an ester carbonyl absorbance at 1747 cm⁻¹ but did not show a nitrile peak in the 2200 - 2250 cm⁻¹ range. Curiously, none of the other adducts we isolated during the course of our study exhibited peaks in this region;⁸ the presence of this group was verified by a combination of elemental analysis, mass, proton and carbon nmr spectra, as well as an X-ray structure determination of the related adduct 12a.

The formation of 6 can be rationalised by assuming a hetero Diels-Alder cycloaddition in which the carbonyl group acts as dienophile toward the photochemically generated o-quinodimethane 2 initially yielding 5a, which upon loss of HCN, produced the observed product. Interestingly, since nitriles have been observed to act as dienophiles with o-quinodimethanes, 9,10 the above result indicates that in the case where the two functional groups are joined in the form of an acyl cyanide, the carbonyl group is more reactive.



Irradiation of benzene or acetonitrile solutions of 1 in the presence of two equivalents of benzoyl cyanide afforded 8^{11} in 73% yield. Subsequent treatment with NaOH in aqueous acetonitrile yielded 2-benzoylmethylbenzoic acid, which helped to confirm its stuctural assignment. Similar irradiation of an acetonitrile solution of 2-methylacetophenone (9) led to the tertiary alcohol 10^{12} in 45% isolated yield.

Benzoyl cyanide also reacts cleanly with thermally generated electron-rich oquinodimethanes. Thus, heating 11^{13} with two equivalents of benzoyl cyanide in refluxing toluene afforded a 3 : 1 mixture of the isomeric adducts 12a and 12b¹⁴ in 90% yield. Under the same conditions, the sulfone 13^{12} gave 14a and 14b,¹⁵ also as an isomeric mixture; when benzoyl cyanide was replaced with acetyl cyanide, the adducts 15a and 15b¹⁶ were formed.

Extrusion of sulfur dioxide from 11 is known to give the E,E-diene $11a.^{13} A 4\pi s + 2\pi s$ cycloaddition between 11a and benzoyl cyanide should afford 12a and 12b, having the 1,4 -methoxy and phenyl groups cis to each other. The X-ray structure determination¹⁷ of 12a, the major isomer resulting from the thermolysis of 11, is shown in Fig.1. The structure confirms the stereochemistry predicted by. Diels-Alder mechanism. Although not specifically proven, we suggest that 12a is isomeric with

12b at the carbon bearing the cyano group and not at the methoxy carrying carbon. This is based on the observation that cycloaddition of 11a and 13a with either benzoyl or acetyl cyanide yielded, in each case, only two isomers even though four were possible for 11a. Such a result is expected only if 11a maintains its stereochemical integrity, and the isomers are due to the endo/exo ratio in the addition of the acyl cyanides to the diene system.



The adducts reported herein have considerable potential as intermediates. For example, reaction of 8 with methyllithium in THF afforded, after aqueous workup, 3phenylnaphth-1-ol (85%) while heating with DBN in cyclohexane gives 3phenylisochromanone. A wider investigation of the dienophilicity of acyl cyanides is in progress.



Fig. 1. Ortep drawing of compound 12a

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(7) 6: mp 126.5-127.5 oC;1H NMR (CDCl3) d 2.68 (s, 3H), 3.71 (q, 2H, J = 16.5 Hz), 7.23-7.40 (m, 4H), 7.46-7.70 (m, 3H), 8.16 (d, 1H, J = 7.7 Hz).

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(11) 8: mp 144.6-146.1 oC;1H NMR (CDCl3) d 3.54 (q, 2H, J = 16.7 Hz), 7.34 (d, 1H, J = 7.5 Hz), 7.45-7.55 (m, 4H), 7.61-7.71 (m, 3H), 8.19 (d,1H, J = 7.7 Hz).

(12) 10: Colorless plates (ether); 1H NMR (CDCl3) d 2.63 (s, 3H), 3.44 (q, 2H, J = 13.9 Hz), 6.90 (s, 1H), 6.98 (d, 1H, J = 8.4 Hz), 7.30-7.60 (m, 7H), 7.73 (d, 1H, J = 8.2 Hz).

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(14) 12a: mp 237.2-238.4 oC; 1H NMR (CDCl3) d 3.83 (s, 3H), 4.36 (s, 1H), 6.23 (s, 1H), 6.73 (dd, 2H, J = 1.7 Hz, 7.5 Hz), 6.90-7.00 (m, 3H), 7.03 (d, 1H, J = 8.1 Hz), 7.15-7.27 (m, 6H), 7.37 (d, 1H, J = 7.4 Hz), 7.51 (d, 1H, J = 7.7 Hz);12b: (CH2Cl2/Hexane) mp 123.5-124.8 oC; 1H NMR (CDCl3) d 3.70 (s, 3H), 4.36 (s, 1H), 5.90 (s, 1H), 6.88 (d, 1H, J = 7.9 Hz), 6.96 (d, 2H, J = 6.6 Hz), 7.13-7.34 (m, 9H), 7.38 (d, 1H, J = 8.1 Hz), 7.48 (d, 1H, J = 6.7 Hz).

(15) 14a:mp 80.1-82.6 oC; 1H NMR (CDCl3) d 3.36 (q, 2H, J = 16.0 Hz), 3.64 (s, 3H), 6.04 (s, 1H), 7.15-7.24 (m, 1H), 7.30-7.51 (m, 6H), 7.69 (dd, 2H, J = 1.6, 8.2 Hz); 14b: mp 91.8-92.6 oC; 1H NMR (CDCl3) d 3.32 (q, 2H, J = 16.4 Hz), 3.70 (s, 3H), 5.81 (s, 1H), 7.11-7.18 (m, 1H), 7.30-7.49 (m, 6H), 7.65 (dd, 2H, J = 2.4, 8.2 Hz).

(16) 15a: oil; 1H NMR (CDCl3) d 1.79 (s, 3H), 3.10 (q, 2H, J = 16.1 Hz), 3.54 (s, 3H), 5.80 (s, 1H), 7.08-7.20 (m, 1H), 7.21-7.36 (m, 3H);15b: oil; 1H NMR (CDCl3) d 1.76 (s, 3H), 3.06 (q, 2H, J = 15.6 Hz), 3.65 (s, 3H), 5.57 (s, 1H), 7.08-7.20 (m, 1H), 7.21-7.36 (m, 3H). (17) Crystal data for 12a: C23H19NO2, M = 341.41, P 21/n, a = 8.4809 (14), b = 9.2811 (17), c = 22.940 (5), b = 100.528 (15), Z = 4, V = 1775.3 (6) A3; C. Bensimon, unpublished observations.

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