Tetrahedron Letters,Vol.28,No.7,pp 763-766,1987
Printed in Great Britain

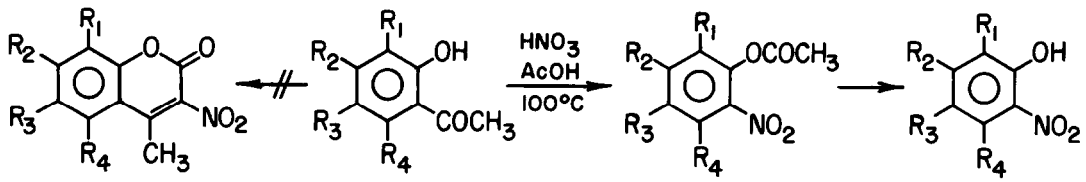
0040-4039/87 $3.00 + .00
Pergamon Journals Ltd.

INTRAMOLECULAR ELECTROPHILIC DISPLACEMENT OF ACYL BY NITRO GROUP DURING ATTEMPTED SYNTHESIS OF 3-NITROCOUMARINS

George M. Benedikt* and Lee Traynor
BFGoodrich Research and Development Center
Brecksville, Ohio 44141

Summary: 2-Hydroxyacetophenones undergo upon nitration in acetic acid a substitution of the acyl by nitro group followed by an intramolecular 1,3-acyl shift reminescent of a retro-Fries rearrangement to yield phenyl esters.

In the context of our investigations of photosensitive polymeric systems for microlithography[1], we attempted to prepare 3-nitrocoumarins according to a recently published procedure[2]. The reaction of several 2-hydroxyacetophenones with nitric acid in acetic acid for 30 minutes at 100°C, followed by precipitation of the products upon dilution with cold water, was reported to yield substituted coumarins in moderate yields.



2 1 3 6

R_1, R_2, R_3, R_4 = See Table I

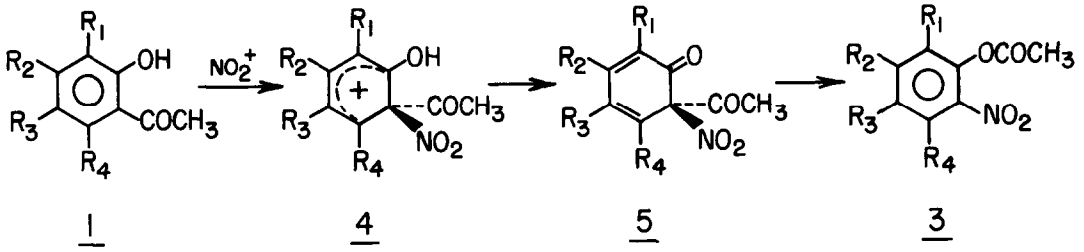
We report here that no coumarin could be isolated in the above reaction. Instead, we have found that the reaction products of compounds 1a and 1b obtained in fairly low yields (see Table 1), are actually the nitrophenyl acetates 3a and 3b, in which a nitro group replaced the acyl group, the latter being shifted to the phenolic oxygen to form an ester. Nitration of the unsubstituted ortho-phenolic position in 1b also occurred. The structure of the compound 3a was demonstrated by ^1H and ^{13}C NMR, by molecular weight determination using field desorption mass spectrometry as well as by hydrolysis to 3,4-dimethyl-2,6-dinitrophenol, 6a. Due to the difficulty in nitrating 3,4-dimethylphenol to 3,4-dimethyl-2,6-dinitrophenol[3] we could not independently obtain compound 3a. Nitration of 3,4-dimethylphenyl acetate with

nitric acid in acetic acid following the procedure described above lead to 3,4-dimethyl-6-nitrophenyl acetate 7. Compounds 6a and 7 were characterized by ^{1}H-NMR and by IR Spectroscopy.

The structure of compound 3b was demonstrated by the same techniques as well as by unambiguous synthesis[3] from 2,4-dichloro-6-nitrophenol.

The 1,3-shift of the ortho-acetyl group to the phenolic oxygen is intramolecular. Compounds 1a and 1b yielded identical products 3a and 3b, respectively, when the nitration was performed in propionic acid. The reaction is reminescent of the retro-Fries rearrangement[5].

The reaction mechanism probably involves formation of the typical aromatic electrophilic substitution intermediate 4, by nitronium ion attack on the acyl-bearing carbon, which upon losing a proton yields dienone 5. A 1,3-acyl shift in 4, the driving force for which is the rearomatization of the six membered ring, is responsible for the formation of compound 3.



1 4 5 3

The electrophilic displacement of the acyl by nitro group in ortho-acylphenols seems to be general. On the other hand, the hydrolytic stability of the resulting phenyl esters during the aqueous work-up, depends on the substitution of the aromatic ring[6]. This could explain the low yields in esters 3a and 3b as well as why compounds 1c and 1d yielded under the same reaction conditions the free 4-chloro-2,6-dinitrophenol 6c and 3,5-dimethyl-2,4,6-trinitrophenol 6d, respectively.

We subjected further, the parent 2-hydroxyacetophenone 1e to the same reaction and isolated as the only solid product 2,4,6-trinitrophenol 6e. A shorter reaction time revealed by ^{1}H NMR the presence of 3,5-dinitro-2-hydroxyacetophenone, the normal nitration product of 1h, together with compound 6e.

Since we could not observe in any of the above reactions a product in which the acyl group migrated to form the phenyl ester without being replaced by a nitro group we conclude that the 1,3-acyl shift follows attack by the nitronium ion.

Further work is under way to elucidate whether 4-hydroxyacylphenones behave similarly during the nitration reaction.

Experimental Data: A solution of 20 mmol substituted 2-hydroxyacetophenone (Table 1) in 20 ml glacial acetic acid was placed in a 250 ml Ehrlenmeyer flask provided with magnetic stirring. 10 ml of nitric acid (d = 1.49) was added quickly at room temperature, the flask was connected to a reflux condenser and placed in a boiling water bath. After the vigorous evolution of nitrogen oxide fumes ceased, the flask was kept for another 25 minutes, after which it was cooled to room temperature and 100 ml of ice-water mixture was added. The formed precipitate was filtered, dried without rinsing in order to avoid losses, and analyzed.

Table 1. Compound Substitution, Solvent and Reaction Yields

Compound	R_1	R_2	R_3	R_4	Product	R_1	R_2	R_3	R_4	Solvent	Yield
1a	H	CH_3	CH_3	H	3a	NO_2	CH_3	CH_3	H	A*	10%
1a	H	CH_3	CH_3	H	3a	NO_2	CH_3	CH_3	H	P*	11%
1b	Cl	H	Cl	H	3b	Cl	H	Cl	H	A*	13%
1b	Cl	H	Cl	H	3b	Cl	H	Cl	H	P*	10%
1c	H	H	Cl	H	6c	NO_2	H	Cl	H	A*	35%
1d	H	CH_3	H	CH_3	6d	NO_2	CH_3	NO_2	CH_3	A*	60%
1e	H	H	H	H	6e	NO_2	H	NO_2	H	A*	20%

* A = Acetic Acid, P = Propionic Acid

Table 2. Physical Data for Compounds of Interest

Compound	m.p. (°C)	^{1}H-NMR (ppm vs. TMS, all in $CDCl_3$ except 6e, in dmso-d_6)	IR (cm^{-1}, in CCl_4 except 6e, in KBr)
3a	137	2.31, 2.36, 2.44 (3s, 9H, R_2, R_3 and CH_3CO), 8.1 (s, 1H, R_4)	1340 (NO_2), 1544 (NO_2), 1800 (CO)
3b	77	2.4 (s, 3H, CH_3CO), 7.7 and 8.0 [2d (J=3.5Hz), 2H, R_2 and R_4]	1345 (NO_2), 1540 (NO_2), 1790 (CO)
6c	81[7]	8.5 (s, 2H, R_2 and R_4), 11.2 (Broad s, 1H, OH)	1350 (NO_2), 1545 (NO_2), 3200-Broad (OH)
6d	106[8]	2.4 (s, 6H, R_2 and R_4), 9.5 (Broad s, 1H, OH)	1365 (NO_2), 1550 (NO_2), 3200-Broad (OH)
6e	120[9]	9.0 (s, 2H, R_2 and R_4), 10.8 (Broad s, 1H, OH)	1340 (NO_2), 1540 (NO_2), 3200-Broad (OH)
6a	125[3]	2.3 and 2.35 (2s, 6H, CH_3), 8.0 (s,1H, aromatic) 10.65 10.65 (s,1H, OH)	1330 (NO_2), 3200-Broad (OH)
7	79	2.32, 2.33, 2.35 (3s, 9H, CH_3) 7.0 and 7.9 (2s, 2H, aromatic)	1340 (NO_2), 1530 (NO_2), 1785 (CO)

Compound	m/e(M+)	^{13}C-NMR (ppm vs. TMS)
3a	254	15.1, 20.0, 20.34 (3 CH3), 127.5 (aromatic CH), 135.2, 136.6, 137.5, 139.7, and 146.9 (aromatic C), 167.2 (CO)
3b	249	20.3 (CH3), 124.5 and 135.0 (aromatic CH), 131.9, 132.3, 140.4, and 143.5 (aromatic C), 167.1 (CO)
6c	218	124.6 (C-Cl), 131.2 (2 CH), 138.1 (2 C-NO_2), 148.2 (C-OH)[10]
6d	257	14.9 (2 CH3), 130.6 (2 aromatic C), 137.5 and 145.8 (aromatic C), 147.5 (2 aromatic C)
6e	229	125.1 (2 C-H), 126.1 (C-NO_2), 141.9 (2 C-NO_2), 150.7 (C-OH)[10]

Acknowledgements: Thanks are due to Professor Leo A. Paquette and Dr. Paul Nicholas for helpful discussions.

References:

1. Benedikt, G. M., SPIE Proceedings, 539, 242 (1985).
2. Cascaval, A., Synthesis, 428 (1985).
3. Stanek, J., Ledvinova, M., Kalina, O., Racek, V., Czechoslovakian Patent 143881 (1971), Chem. Abstr., 78:25366x (1971).
4. Raiford, L. C., Kaiser, D. W., J. Org. Chem., 4, 555 (1939).
5. Effenberger, F., Gutmann, R., Chem. Ber., 115, 1089 (1982) and literature cited therein.
6. Bell, J. A., Gov. Rep. Announce. (U.S.), 12, 53 (1972), Chem. Abstr., 78:3871f (1973).
7. Lin C. T., et al, J. Chem. Soc., Perkin Trans. 2, 957 (1978), m.p. = 80°C.
8. Moore, C. E., Peck, R., J. Org. Chem., 20, 673 (1955), m.p. = 106.5°C.
9. Ibid, m.p. = 122°C.
10. Ilczyszyn, M., Latajka, Z., Ratajszak, H., Org. Magn. Res., 13, 132 (1980).

(Received in USA 6 November 1986)