Tetrahedron Vol 37, pp. 789 to 793
Pergamon Press Ltd., 1981 Printed in Great Britain

0040-4020/81/0215-0789/$02.00/0

DERIVATIVES AND REACTIONS OF GLUTACONALDEHYDE—XII

PHOTOCHEMICAL AND THERMAL PREPARATION OF 5-AMINO-2,4-PENTADIENENITRILES†

J. BECHER, L. FINSEN and I. WINCKELMANN
Department of Chemistry, Odense University, Campusvej 55, DK-5230 Odense M, Denmark.
and
R. RAO KOGANTY and O. BUCHARDT
Chemical Laboratory II, The H. C. Ørsted Institute, University of Copenhagen, Universitetsparken 5, DK-2100 Copenhagen, Denmark.

(*Received in U.K. 15 May* 1980)

Abstract—Irradiation of pyridine N-oxide (**1**) in the presence of secondary amines in aqueous solution produces mixtures of isomeric 2*Z*,4*E* and N,N-disubstituted *all-E* 5-amino-2,4-pentadienenitriles (**3** and **4**), in fair yields, and with an ease to render the reaction preparatively useful. Furthermore, such compounds can be prepared thermally by dehydration of 5-amino-2,4-pentadienal oximes.

In a recent paper we described the photochemical ring-opening of pyridine N-oxide, in aqueous or alcoholic base, to give the anion of 5-hydroxy-2,4-pentadienenitrile (**2a**).[1] In the same paper it was shown that if the pyridine N-oxide irradiation was carried out in the presence of a number of secondary amines, the corresponding N,N-disubstituted 5-amino-2,4-pentadienenitriles, *cf*,[2] were generated, albeit not in synthetically useful amounts. The detailed structures were discussed in a second paper.[3] The reaction appears at the present time to be specific for 2- (or 6-) unsubstituted pyridine N-oxides.[1] Thus, a series of other heteroaromatic N-oxides did not behave similarly. However, it may very well be found for other monocyclic N-oxides since, e.g. pyrimidine N-oxides are known to undergo related light-induced ring-openings,[4] whereas the only light-induced reaction between bicyclic N-oxides and secondary amines is the formation of the corresponding N-aminocarbostyrils.[5]

The 5-amino-2,4-pentadienenitriles are of interest as potential synthons, and the apparently quite facile manner by which they could be generated photochemically prompted a preparative photochemical study, which is presented here. Although preparative yields are not very high, the ease of obtaining amounts of the order of 4–6 g, starting with pyridine N-oxide and a suitable amine, should render the method quite attractive.

A serious obstacle for the progress of synthetic photochemistry are the difficulties in scaling up. We have not tried to overcome this photochemically, but instead developed a fairly simple thermochemical method[1,3], which could be used for larger scale preparations.

† This paper is also part XXIII in the series "Photochemical Studies", for part XXII see Ref. 1.

RESULTS AND DISCUSSION

Photochemical preparations

The irradiations can be carried out with a "Rayonet" photoreactor (method a). However, it was found that a photoreactor with pumped circulation (method b) was superior due to the short irradiation times necessary.

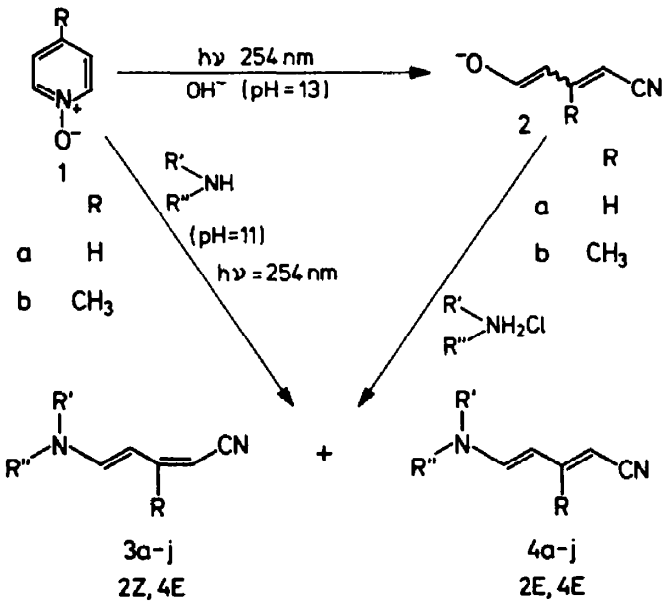
The irradiations were preferentially followed by UV spectroscopy, and the irradiation stopped immediately upon consumption of all the N-oxide. In a typical run, 10 g of pyridine N-oxide was consumed in 3 h, resulting in a turbid yellow mixture (the photoproduct often separates out). The products, which were isolated by extraction were >95% pure, and thus could be used directly without further purification; analytically pure material was obtained by vacuum distillation, but this led to rather drastic losses due to polymerization.

^{1}H NMR spectra (Table 1) demonstrated that the nitriles are mixtures of **3** and **4**, the 2*Z*,4*E* and 2*E*,4*E* isomers, respectively, which under the reaction conditions used (method b and c), gave the isomers **3**/**4** in ratios of 1.5–1.6/1.0. GC-MS determinations of **3e** and **4e** as well as **3g** and **4g** confirmed this ratio, since **3** and **4**, which are easily separated by GC, gave identical mass spectra. Especially the morpholino derivatives (**3g** and **4g**; **3h** and **4h**) showed large differences in retention time. During batch distillation of the samples, higher ratios of the isomers **3** were found in the first fraction, i.e. the 2*Z*,4*E* isomers have the lower boiling points, as expected.

As seen from the flash experiments described previously,[1] the photoreaction consists of several steps, where formation of the anion and subsequent reaction with the amine leads to a mixture of **3** and **4**. The reactions between glutaconaldehydes and amines are well-known.[6] The anion (**2**) as well as the final products, **3** and **4**, are all stable under the reaction conditions used (water at 20° and pH = 10–13); thus in each case a high OH ion concentration appears to be necessary for stabilizing the anion (**2**). Irradiation of

Chemical shifts of protons in δ (ppm) from TMS in $CDCl_3$. Coupling constants, J, in Hz

Compound	H(2)	H(3)	H(4)	H(5)	C(3)-CH_3	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	Alkyl groups at nitrogen
3a	4.38(d)	6.75(d,d)	5.36(d,d)	6.72(d)	-	10.8	12.0	12.0	2.90(s)
4a	4.68(d)	6.98(d,d)	5.09(d,d)	6.63(d)	-	15.4	12.0	12.0	2.93(s)
3b	4.38(s)	-	5.41(d)	6.76(d)	1.93(s)	-	-	13.2	2.89(s)
4b	4.66(s)	-	5.04(d)	6.69(d)	2.07(s)	-	-	13.2	2.85(s)
3c	4.36(d)	6.80(d,d)	5.35(d,d)	6.85(d)	-	10.4	12.1	12.1	3.31(m) and 1.95(m)
4c	4.66(d)	6.94(d,d)	5.05(d,d)	6.68(d)	-	15.4	12.2	12.2	3.31(m) and 1.95(m)
3d	4.40(s)	-	5.44(d)	7.06(d)	1.97(s)	-	-	13.6	3.30(m) and 2.80(m)
4d	4.68(s)	-	5.05(d)	6.99(d)	2.12(s)	-	-	13.6	3.30(m) and 2.80(m)
3e	4.40(d)	6.70(d,d)	5.52(d,d)	6.60(d)	-	10.4	12.2	12.2	3.19(m) and 1.61(m)
4e	4.68(d)	6.92(d,d)	5.20(d,d)	6.53(d)	-	15.3	12.1	12.1	3.19(m) and 1.61(m)
3f	4.44(s)	-	5.61(d)	6.71(d)	1.94(s)	-	-	13.5	3.20(m) and 1.62(m)
4f	4.71(s)	-	5.23(d)	6.65(d)	2.10(s)	-	-	13.5	3.20(m) and 1.62(m)
3g	4.53(d)	6.71(d,d)	5.56(d,d)	6.57(d)	-	10.4	12.2	12.8	3.71(m) and 3.18(m)
4g	4.79(d)	6.91(d,d)	5.24(d,d)	6.50(d)	-	15.3	12.2	12.8	3.71(m) and 3.18(m)
3h	4.61(s)	-	5.72(d)	6.66(d)	2.01(s)	-	-	13.5	3.80(m) and 3.22(m)
4h	4.82(s)	-	5.29(d)	6.60(d)	2.15(s)	-	-	13.5	3.80(m) and 3.22(m)
3i	4.64(d)	6.80(d,d)	5.79(d,d)	7.09(d)	-	10.4	12.2	12.2	N-CH_3: 3.23(s)
4i	4.91(d)	6.99(d,d)	5.46(d,d)	7.08(d)	-	15.6	11.3	12.8	N-CH_3: 3.26(s)



3a–j
2Z, 4E

4a–j
2E, 4E

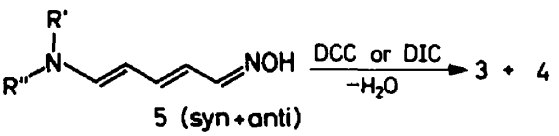
	R	R'	R''
a	H	CH_3	CH_3
b	CH_3	CH_3	CH_3
c	H	$-(CH_2)_4-$	
d	CH_3	$-(CH_2)_4-$	
e	H	$-(CH_2)_5-$	
f	CH_3	$-(CH_2)_5-$	
g	H	$-CH_2CH_2OCH_2CH_2-$	
h	CH_3	$-CH_2CH_2OCH_2CH_2-$	
i	H	CH_3	C_6H_5
j	H	H	2,4-dinitrophenyl

pyridine N-oxide in 0.1 M NaOH to produce the anion (**2**), followed by addition of a secondary amine hydrochloride, also produced the nitriles (**3** and **4**), in yields similar to those obtained by direct photolysis. This variety of the reaction may be used as an alternative route for the preparation of the nitriles. The irradiations described here are all preparatively superior to the previously reported irradiations in dichloromethane,[1] which gave rise to dark by-products.

Thermal preparations

Thermal preparations of the nitriles from the oximes (**5**) were performed by the method described previously.[3] However, reagents such as acetic anhydride as well as phosphorous pentoxide led to extensive decomposition of the oximes.

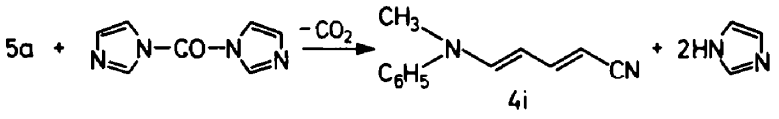
The mild dehydrating reagents, N,N'-dicyclohexylcarbodiimide (DDC) and N,N'-diisopropylcarbodiimide (DIC), were found to give the nitriles in fair yields. The products in these reactions were a mixture of the isomers **3** and **4**. However, the pure *all-E* isomer **4i** could be obtained from **5a** with N,N'-carbonyldiimidazole, and it was the key component



5 (syn+anti)

	R'	R''
a	CH_3	C_6H_5
b	$-CH_2CH_2OCH_2CH_2-$	
c	H	2,4-dinitrophenyl

for the assignment of structures to the nitriles **3** and **4**,[3] obtained by the other methods as mixtures of isomers.



The applicability of these compounds in synthesis is presently under scrutiny in the authors' laboratories.

EXPERIMENTAL

General photochemical procedures for the preparation of isomeric N,N-disubstituted 5-amino-2,4-pentadienenitriles (**3** *and* **4**)

Method a. Irradiation in the "Rayonet" reactor. A quartz flask containing a solution of pyridine N-oxide (0.022 mol), 25 ml aqueous dialkylamine soln (40%) and 300 ml water was irradiated under N_2 with 254 nm light in a Rayonet reactor, type RPR 208.

The disappearance of the pyridine N-oxide was followed by UV spectroscopy. When the pyridine N-oxide had been consumed the mixture was extracted with ether (3 × 150 ml). The ether phase was subsequently washed with water, dried (Na_2SO_4) and concentrated *in vacuo* to give quite pure **3** and **4** as evidenced by ^{1}H NMR. This should be suitable for a number of preparative experiments. If necessary, further purification was undertaken as follows. The dark yellow residue was chromatographed through a short column of silica gel with ether as eluent. Concentration *in vacuo* of the resulting solution gave the title compounds (**3** and **4**) as pale yellow oils or in semicrystalline form, see table 2.

Method b. Irradiation in a quartz NORMAG 9346 photoreactor (Otto Fritz GmbH) equipped with a 700 W high pressure mercury lamp. Pyridine N-oxide (0.09 mol) was dissolved in 900 ml of a 1.3 M soln of the appropriate secondary amine. This mixture was irradiated for 3 hr at 20°, after which all pyridine N-oxide was consumed.

During the reaction the pH was kept between 11–12. The resulting yellow turbid mixture was extracted with ether (3 × 300 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The resulting dark red oil was distilled through a short path distillation apparatus or in a Büchi "Kugelrohr aparatus", which gave the title compounds (**3** and **4**) as viscous yellow oils.

Method c. In two steps: step 1—preparation of the anion **2**; step 2—reaction with the appropriate amine. Pyridine N-oxide (0.014 mol) was irradiated in 1000 ml 0.1 M NaOH as described previously.[8] To the resulting orange soln was added the appropriate secondary amine hydrochloride (0.07 mol). After stirring for a few min, the mixture was processed as described above to give the title compounds (**3** and **4**).

Thermal preparations

4-Morpholinyl-2,4-pentadienenitriles (**3g** *and* **4g**). The oxime **5b** (1.46 g) and N,N'-diisopropylcarbodiimide (DIC, 1.12 g) was refluxed in dry benzene (150 ml) for 48 hr in the presence of a catalytic amount of cuprous chloride dihydrate. The N,N'-diisopropylurea which separated upon cooling was filtered off, whereupon the filtrate was concentrated *in vacuo*.

Table 2. Experimental data on the mixture of isomers. (a) Pressure in mmHg. (b) The yields of distilled products could be drastically increased by decreasing the amounts of pyridine N-oxide to *ca.* 1 g. (c) Lit.[7] 123–125° (0.5). (d) Lit.[7] 168–170° (2)

Compound	IR(cm^{-1}) (CN)	UV(abs.EtOH) λ_{max}(nm)	UV(abs.EtOH) logε	Ratio 3/4	Analysis C,H,N	b.p. (pressure)[a]	Yield
3a+4a	2182	333.0	4.65	1.55	$C_7H_{10}N_2$	90-2°C (0.01)	Crude: 25% Dist.: 16%
3b+4b	2184	337.5	4.49	1.61	$C_8H_{12}N_2$	95-6°C[c] (0.01)	Crude: 53% Dist.: 15%
3c+4c[7]	2180	337.5	4.74	1.55	$C_9H_{12}N_2$	138-9°C (0.025)	Crude: 43% Dist.: 7%
3d+4d	2182	343.5	4.37	1.00	$C_{10}H_{14}N_2$	142-4°C (0.3)	Crude: 33% Dist.: 3%
3e+4e	2181	334.5	4.62	1.50	$C_{10}H_{14}N_2$	130-5°C (0.03)	Crude: 24% Dist.: 3%
3f+4f	2183	338.5	4.61	1.52	$C_{11}H_{16}N_2$	133-5°C[d] (0.08)	Crude: 33% Dist.: 13%
3g+4g	2185	329.0	4.51	1.60	$C_9H_{12}N_2O$	148°C (0.04)	Crude: 24% Dist.: 4%
3h+4h	2184	331.5	4.82	1.57	$C_{10}H_{14}N_2O$	148°C (0.04)	Crude: 40% Dist.: 10%

This gave a yellow semicrystalline residue (0.95 g), which was column chromatographed (Al_2O_3 (30 g), Merck, neutral, activity 2) with methylene chloride as eluent. The main fraction was collected, treated with activated carbon, filtered, and concentrated *in vacuo* to give pale yellow crystals of a 1:4 mixture of **3g** and **4g** as shown by ^{1}H NMR, yield 0.71 g (54%), m.p. 50–55°. IR (KBr): 2195 cm^{-1} (CN). UV (abs. EtOH): λ_{max} (log ε): 330 nm (5.25). Found: C, 65.65; H, 7.46; N, 16.82. Calc. see Table 2.

The independently run mass spectra of **3g** and **4g** were identical; *m/e* (%): 165 (10.9), 164 (100.0) ($M^{+\cdot}$), 133 (7.8), 124 (55.6), 107 (12.6), 106 (34.4), 105 (41.6), 96 (8.3), 94 (15.6), 92 (8.7), 85 (13.3), 80 (20.6), 79 (67.3), 78 (24.7), 67 (10.1), 66 (8.7), 65 (9.1), 57 (13.8), 56 (8.9), 55 (33.4), 54 (9.1), 53 (14.5) and 52 (35.2).

5-(*N-Methylanilino*)-2E,4E-*pentadienenitrile* (**4i**). *A* suspension of the oxime **5a** (5.05 g) and N,N'-carbonyldiimidazole (5.00 g) was refluxed for 48 hr in dry ether (100 ml). Collection of the evolved CO_2 yielded 0.54 l (90% of the theoretical amount). The precipitated imidazole was filtered off, whereupon the filtrate was washed with phthalate buffer (pH = 5, 2 × 25 ml). Evaporation of the dried ($MgSO_4$) ether soln yielded a yellow oil (3.82 g). Preparative layer chromatography (silica gel, 60 PF, Merck) with $CHCl_3$:MeOH (15:1) as eluent of this oil, gave one main band (R_f = 0.6). Isolation of this band, and recrystallization from methylcyclohexane gave 3.2 g (70%) of the pure 2*E*,4*E*-isomer, **4i**, as yellow crystals (no trace of the other isomer was seen). m.p. 50.5–51.0°. IR (KBr): 2195 cm^{-1} (CN). UV (abs. EtOH): λ_{max} (log ε): 344 nm (4.63), 231 nm (3.73). (Found: C, 78.17; H 6.43; N, 15.39. Calc. for $C_{12}H_{12}N_2$: C 78.23; H 6.57; N 15.21%).

5-(2,4-*Dinitroanilino*)-2E,4E-*pentadienenitrile* (**4j**). Prepared as described above for **4i**. The oxime **5c** (2.78 g) and N,N'-carbonyldiimidazole (1.78 g) in $CHCl_3$ (50 ml) gave the title compound as red crystals, 0.22 g (8.5%), m.p. 172–175° (ether-pentane). IR (KBr): 220 cm^{-1} (CN). (Found: C 51.03; H 3.17; N 21.45. Calc. for $C_{11}H_8N_4O_4$: C 50.77; H 3.10; N 21.53%).

Instrumentation. Microanalyses were carried out in the Microanalytical Department of the University of Copenhagen by Mr. Preben Hansen and his staff.

IR (as film on NaCl or KBr), Perkin Elmer 580 spectrograph. UV: Varian Cary 219 spectrograph. ^{1}H NMR (60 MHz): Jeol JNM-PMX 60 spectrograph. ^{1}H NMR (270 MHz): Bruker HX-270 spectrometer. ^{13}C NMR: Jeol JNM FX 60 Q spetrometer. MS: Varian Mat CH7A spectrometer coupled with a Varian 2800 gas chromatograph (column, 2 m glass, 3% OVI at 160° and 16 ml He/min).

Irradiations: Rayonet Rector type RPR 208 or RPR 100 with 254 nm lamps of a Normag Quartz 9346 photoreactor (Otto Fritz GmbH) with a 700 W Atlas high pressure mercury lamp.

Acknowledgements—We thank the Danish Foreign Ministry for the support of Dr. R. Rao Koganty as a DANIDA stipendiate and Dr. Jens Eriksen, Århus University for the loan of a Rayonet reactor. The 270 MHz spectrometer, the mass spectrometer and the RPR 100 photoreactor were provided by the Danish Natural Science Research Council.

REFERENCES

[1] O. Buchardt, J. J. Christensen, P. E. Nielsen, R. R. Koganty, L. Finsen, C. Lohse and J. Becher, *Acta Chem. Scand.* **B34** (1980) 31.

[2] M. Nakagawa, T. Kaneko and J. Yamagushi, *Chem. Commun.* 603; (1971) M. Nakagawa, T. Kaneko, H. Yamagishi, T. Kawashima and T. Hino, *Tetrahedron* **30** (1974) 2591.

[3] L. Finsen, J. Becher, R. R. Koganty and O. Buchardt, *Acta Chem. Scand.* in press.

[4] F. Bellamy, P. Martz and J. Streith, *Tetrahedron Letters* 3189: (1974) J. Streith and P. Martz, *Ibid.* 4899); J. Streith, C. Leibovici and P. Martz, *Bull. Soc. Chim. Fr* 4152 (1971).

[5] C. Kaneko, I. Yokoe and M. Ishikawa, *Tetrahedron Letters* 5237 (1967).

[6] J. Becher, *Synthesis*, 589 (1980).

[7] N. V. Koshmina and F. Ya. Perveev, *Zh. Org. Khim.* **12** 2074 (1976).

[8] O. Buchardt, J. J. Christensen, C. Lohse, J. J. Turher and J. R. Dunkin, *Chem. Commun.* 837 (1977).