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Supporting Information

69451 Weinheim, Germany

The Guareschi Reaction (1897). Alkyl Radical Generation in Water under Ambient Conditions

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GENERAL PROCEDURE

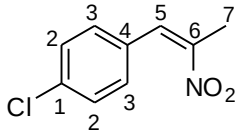
Solvents of HPLC grade were purchased from Fisher or Rathburn. Where dry solvents were required they were purified by expression through an activated alumina column build after the procedures described by Grubbs.[1] Column chromatography was performed on Merck silica gel 60 (0.040 – 0.063 nm), using standard flash chromatographic methods. ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$, DMSO-d_6 or D_2O. ^{1}H NMR spectra were recorded on Bruker DPX250 (250 MHz), DPX400 (400 MHz), AV400 (400 MHz) or AV500 (500 MHz) spectrometers and were referenced against the residual solvent peaks. Assignments were aided by the use of COSY, HMQC, DEPT and HMBC experiments. Mass spectra were recorded on a Fisons VG and Bruker MicroTOF spectrometers. Infrared spectra were recorded on a Bruker Tensor 27 FT spectrometer on potassium bromide matrix. UV spectra were recorded on a Lambda 25 UV/V spectrometer. Melting points were measured out on a Reicher-Koffler block apparatus and are uncorrected. Unless noted below, all other compounds were reported in literature or were supplied by Aldrich and used without further purification.

Aqueous deuterated buffer solutions were used prepared from KH_2PO_4 and Na_2HPO_4 (pH 6.9) and $Na_2B_4O_7.10H_2O$ and 0.1M DCl solution in D_2O (pH 8.0, 9.2, and 9.6).

Cyclic voltametry was carried out in 10 ml voltametric cell equipped with Pt-electrode (square surface 2 mm^2), glass fabric auxiliary electrode and saturated calomel reference electrode. Solution of of substrates (2.0 mM) in 0.1 M Et_4NClO_4 solution in acetonitrile was used for the study at sweep rate 0.1 – 1.0 $V.s^{-1}$.

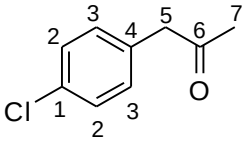
SYNTHESIS OF STARTING MATERIALS

Synthesis of 1-chloro-4-(2-nitroprop-1-enyl)benzene[2]



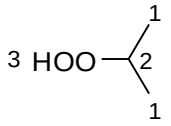
A solution of 4-chlorobenzaldehyde (10.0 g, 71 mmole), nitroethane (8.15 ml, 114 mmole) and ammonium acetate (6.05 g, 78 mmole) in glacial acetic acid (58.50 ml) was refluxed for 3 hours. After cooling to RT, the solution was kept at –19 °C overnight, during that time crystal formation was observed. Crystals were filtered and washed with ice cold ethanol (200 ml). A second crop was collected from the filtrate, filtered out and washed with ice cold water (100 ml) and ice cold ethanol (50 ml). Two crops were combined and dried, giving the desired product: 1-chloro-4-(2-nitroprop-1-enyl)benzene (6.54 g, 47%), as a yellow powder, m.p. 86-87 °C (lit[3] 86-87 °C); δ_H (400 MHz, $CDCl_3$) 8.03 (1H, s, H-5), 7.43 (2H, d, $J_{2,3}$ 8.6, H-2), 7.37 (2H, d, $J_{2,3}$ 8.6, H-3), 2.43 (3H, d, $J_{5,7}$ 0.9, H-7); d_C (101 MHz, $CDCl_3$) 148.0 (C-6), 136.1 (C-1), 132.2 (C-5), 131.2 (C-3), 130.8 (C-4), 129.2 (C-2), 14.0 (C-7). Lit.[2] δ_H (200 MHz, $CDCl_3$, TMS) 8.04 (1H, s), 7.35–7.47 (4H, m), 2.44 (3H, s).

Synthesis of 1-(4-chlorophenyl)propan-2-one[4]



Raney Nickel slurry in water (2.5 ml) was added dropwise to a mixture of an aqueous solution of sodium hypophosphite (14.0 g, 163 mmol in 60 ml) and a solution of 1-chloro-4-(2-nitroprop-1-enyl)benzene (2.77 g, 14 mmol) in ethanol-sodium acetate buffer pH 5 (2:1, 400 ml) at RT. The solution was then heated to 60 °C for 3 hours, and the catalyst was filtered off and washed with water. The filtrate was extracted with diethyl ether (4 x 600 ml). The organic layers were combined and dried over $MgSO_4$. The solvent was removed *in vacuo* to give a red oil. Purification by flash chromatography (Et_2O/pentane,4:6) to afford the pure 1-(4-chlorophenyl)propan-2-one as a red oil (1.12 g, 47%). d_H (400 MHz, $CDCl_3$) 7.30 (2H, d, $J_{2,3}$ 8.5, H-3), 7.12 (2H, d, $J_{2,3}$ 8.6, H-2), 3.67 (2H, s, H-5), 2.16 (3H, s, H-7); d_C (101 MHz, $CDCl_3$) 205.6 (C-6), 133.0 (C-1), 132.5 (C-4), 130.7 (C-2), 128.8 (C-3), 50.0 (C-5), 29.4 (C-7). Lit.[4] d_H (60 MHz, $CDCl_3$): 7.2 (4H, q), 3.6 (2H, s), 2.1 (3H, s).

Synthesis of 2-hydroperoxypropane



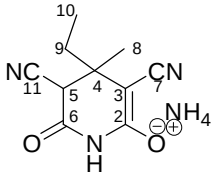
2 N isopropyl magnesium chloride (0.50 ml, 1.0 mmole) in THF was added dropwise to anhydrous diethyl ether (2.0 ml), saturated with oxygen, at -78° C during the course of 2 hrs and stirred for further 15 min. The mixture was allowed to warm up to 0 °C and was quenched with saturated aqueous NH_4Cl (2.0 ml). The organic layer was transferred via cannula and the excess of solvent was cautiously removed *in vacuo* at –20 °C to give colorless oil, which was used immediately. d_H (400 MHz, D_2O) 4.20 (1H, m, H-2), 1.16 (6H, d, $J_{1,2}$ 6.3, H-1); d_C (100 MHz, D_2O) 79.05 (C-2), 19.92 (C-1).

SYNTHESIS OF GLUTARIMIDES

Procedure A: A round-bottom flask was charged with the ketone (28 mmole), ammonia 2M NH_3/MeOH (37 ml, 75 mmole), and ethyl cyanoacetate (5.3 ml, 50 mmole) at 0 ^{0}C. The reaction mixture was stirred at 0 0C for 1 hour and then at room temperature for 24 hours. White precipitate was filtered and washed with cold methanol (50 ml) and diethyl ether (200 ml) to afford pure 1

Procedure B: A round-bottomed flask was charged with the ketone (13 mmol), ethyl cyanoacetate (3.0 ml, 26 mmole) and 7 N NH_3/MeOH (5.60 ml, 39.45 mmol) in ethanol (14 ml). A mixture was then stirred at RT for 7 days. The reaction mixture was then dissolved in water (500 ml) and extracted with diethyl ether (3 x 400 ml). To the combined aqueous layers 1.2 equivalence of 2 M HCl (7.80 ml) was added. The resulted white precipitate was filtered, washed with ice cold ethanol (100 ml) and dried under vacuum to give the product.

Ammonium 3,5-dicyano-4-ethyl-4-methyl-6-oxo-1,4,5,6-tetrahydro-pyridin-2-olate (3a)[5] (procedure A, 48% yield)



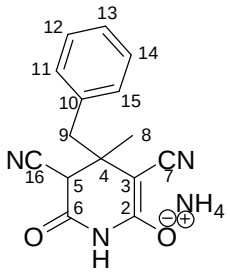
Diastereomer A: d_H (400 MHz, D_2O) 1.49 (2H, m, H-9), 1.23 (3H, s, H-8), 0.78 (3H, t, $J_{10,9}$ 7.4, H-10); d_C (100 MHz, D_2O) 167.6 (C-2), 165.0 (C-6), 126.7 (C-7), 116.4 (C-11), 60.4 (C-3), 37.1 (C-4), 31.1 (C-9), 24.9 (C-8), 8.4 (C-10); d_H (500 MHz, DMSO-d_6) 9.41 (1H, s, N-H), 7.25 (4H, s, NH_4^+), 4.11 (1H, s, H-5), 1.44 (2H, m, H-9), 1.16 (3H, s, H-8), 0.84 (3H, m, H-10); d_C (125 MHz, DMSO-d_6) 164.7 (C-2), 163.3 (C-6), 126.1 (C-7), 116.8 (C-11), 55.3 (C-3), 48.4 (C-5), 36.6 (C-4), 31.1 (C-9), 25.3 (C-8), 8.7 (C-10);

Diastereomer B: d_H (400 MHz, D_2O) 1.49 (2H, m, H-9), 1.09 (3H, s, H-8), 0.83 (3H, t, $J_{10,9}$ 7.5, H-10); d_C (100 MHz, D_2O) 167.6 (C-2), 165.6 (C-6), 127.4 (C-7), 116.6 (C-11), 61.1 (C-3), 37.9 (C-4), 31.4 (C-9), 23.8 (C-8), 8.4 (C-10); d_H (500 MHz, DMSO-d_6) 9.45 (1H, s, N-H), 7.25 (4H, s, NH_4^+), 3.95 (1H, s, H-5), 1.44 (2H, m, H-9), 1.03 (3H, s, H-8), 0.84 (3H, m, H-10); d_C (125 MHz, DMSO-d_6) 164.7 (C-2), 163.8 (C-6), 125.3 (C-7), 116.6 (C-11), 55.9 (C-3), 44.8 (C-5), 37.3 (C-4), 31.7 (C-9), 25.0 (C-8), 8.7 (C-10);

Diastereomer C: d_H (400 MHz, D_2O) 1.73 (2H, q, $J_{9\text{-}10}$ 7.6, H-9), 1.21 (3H, s, H-8), 0.89 (3H, t, $J_{10,9}$ 7.5, H-10);

IR (n_{max}/cm^{-1}): 3087 (m broad, N-H), 2174 (m, C=N), 1678 (m, CO-N-CO), 1587 (s, CO-N-CO), 1357 (m, C-Me); HRMS(ESI) calculated for $[M\text{-}NH_4]^{-3}$ 204.0773; Found: 204.0771

Ammonium 4-benzyl-3,5-dicyano-4-methyl-6-oxo-1,4,5,6-tetrahydro-pyridin-2-olate (3b) (procedure A, 7 % yield)



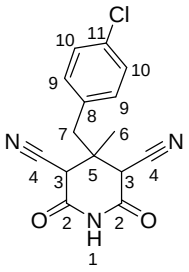
m.p. 259-262ºC;

Diastereomer A: d_H (400 MHz, D_2O) 7.19 (5H, m, H-11 and H-15), 2.68 (1H, s, H-9), 1.32 (3H, s, H-8); d_C (100 MHz, D_2O) 166.4 (C-2), 165.2 (C-6), 136.7 (C-10), 130.8 (C-12, C-14), 128.3 (C-11, C-15), 127.5 (C-13), 126.8 (C-7), 116.6 (C-16), 60.2 (C-3), 43.6 (C-5), 38.9 (C-9), 27.2 (C-8);

Diastereomer B: d_H (400 MHz, D_2O) 7.19 (5H, m, H-11 and H-15), 2.72 (1H, dd, J 13.6, 46.6, H-9), 1.25 (3H, s, H-8);

IR (n_{max}/cm^{-1}) 3027 (s broad, N-H), 2165 (s, C=N), 1674 (s, CO-N-CO), 1586 (vs, CO-N-CO), 1356 (s, C-Me); HRMS(ESI) estimated for $[M\text{-}NH_4]^{-3}$ 266.0930, found 266.0930.

4-(4-Chlorobenzyl)-4-methyl-2,6-dioxopiperidine-3,5-dicarbonitrile (3c) (procedure B, 29% yield)



A viscous dark brown oil was observed after the addition of 2 M HCl to the combined aqueous layers. Upon the addition of DCM (10 mL) to the oil, a white solid was formed, which was the desired product, 4-(4-chlorobenzyl)-4-methyl-2,6-dioxopiperidine-3,5-dicarbonitrile, m.p. 272-274 °C.

Three diastereoisomers were observed in DMSO-d_6.

Diastereoisomer A: d_H (500 MHz, DMSO-d_6) 12.10 (1H, s, H-1), 7.53 (2H, d, $J_{9,10}$ 8.4, H-10), 7.27 (2H, d, $J_{9,10}$ 8.4, H-9), 4.29 (2H, s, H-3), 2.95 (2H, s, H-7), 1.35 (3H, s, H-6); d_C (126 MHz, DMSO-d_6) 164.4 (C-2), 132.8 (C-8), 132.3 (C-11) 131.7 (C-9), 129.2 (C-10), 114.4 (C-4), 43.7 (C-3), 42.7 (C-7), 40.2 (C-5) 19.9 (C-6);

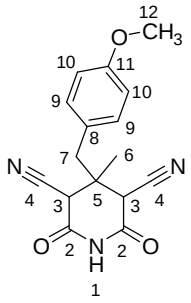
Diastereoisomer B: d_H (500 MHz, DMSO-d_6) 11.61 (1H, s, H-1), 7.37 (2H, d, $J_{9,10}$ 8.3, H-10), 7.18 (2H, d, $J_{9,10}$ 8.4, H-9), 4.82 (2H, s, H-3), 2.96 (2H, s, H-7), 1.45 (3H, s, H-6); d_C (125 MHz, DMSO-d_6) 164.1 (C-2), 132.8 (C-8), 132.2 (C-11) 131.8 (C-9), 128.6 (C-10), 114.5 (C-4) 45.0 (C-3), 40.4 (C-5), 40.1 (C-7), 26.7 (C-6);

The amount of diastereoisomer C present in the solution is too insignificant for the full assignment. Observed peaks are: d_H (500 MHz, DMSO-d_6): 12.06 (1H, s, H-1), 7.39 (2H, d, $J_{9,10}$ 8.5, H-10), 7.22 (2H, d, $J_{9,10}$ 8.5, H-9), 4.73 (2H, s, H-3) and 1.31(3H, s, H-6).

IR (ν_{max}/cm^{-1}) 3207 (m, -CONH-), 3108 (m, -CONH-), 2250 (w, -C=N), 1750 (s, -CO-N-CO), 1700 (s, -CO-N-CO). ?$_{max}$ (MeOH)/nm 275, 268, 260, 222, 213.16 (e = 710, 772, 716, 9370 and 8840 dm^3.cm^{-1}.mol^{-1} respectively). HRMS(ESI) calculated for [M-H]$^{-3}$ 300.0518, found: 300.0534.

4-(4-methoxybenzyl)-4-methyl-2,6-dioxopiperidine-3,5-dicarbonitrile (3d)

(procedure B, 48% yield)



m.p. 192-197 °C. Three diastereoisomers of the product were observed in DMSO-d_6.

Diastereoisomer A: d_H (500 MHz, DMSO-d_6) 12.06 (1H, s, H-1), 7.18 (2H, d, $J_{9,10}$ 8.8, H-9), 7.04 (2H, d, $J_{9,10}$ 8.8, H-10) 4.26 (2H, s, H-3), 3.77 (3H, s, H-12), 2.90 (2H, s, H-7), 1.34 (3H, s, H-6). d_C (125 MHz, DMSO-d_6) 164.6 (C-2), 159.0 (C-11), 130.9 (C-9), 125.1 (C-8), 114.7 (C-10), 114.5 (C-4), 55.1 (C-12), 43.7 (C-3), 42.5 (C-7), 40.5 (C-5), 19.9 (C-6);

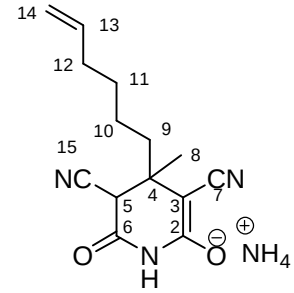
Diastereoisomer B: d_H (500 MHz, DMSO-d_6) 11.47 (1H, s, H-1), 7.09 (2H, d, $J_{9,10}$ 8.5, H-9), 6.84 (2H, d, $J_{9,10}$ 8.5, H-10), 4.79 (2H, s, H-3), 3.74 (3H, s, H-12), 2.91 (2H, s, H-7), 1.45 (3H, s, H-6). d_C (125 MHz, DMSO-d_6) 164.1 (C-2), 158.9 (C-11), 131.0 (C-9), 125.5 (C-8), 114.5 (C-4), 114.0 (C-10), 55.0 (C-12), 44.9 (C-3), 40.9 (C-5), 40.0 (C-7), 26.9 (C-6);

The amount of diastereoisomer C present in the solution is too insignificant for the full assignment. Observed peaks are: d_H (500 MHz, DMSO-d_6): 12.00 (1H, s, H-1), 3.75 (3H, s, H-12), 1.31 (3H, s, H-6).

IR (ν_{max}/cm^{-1}) 3196 (m, -CONH-), 3124 (m, -CONH-), 2265 (w, -C=N), 1750 (s, -CO-N-CO), 1715 (s, -CO-N-CO). ?$_{max}$ (MeOH)/nm 283, 277, 227, 211, 209, 207 (e = 1829, 1918, 8496, 8661, 9525 and 9290 dm^3.cm^{-1}.mol^{-1} respectively); HRMS(ESI) calculated for [M-H]$^-$: 296.1035, found: 296.1030.

Ammonium 3,5-dicyano-4-(5-hexenyl)-4-methyl-6-oxo-1,4,5,6-tetrahydro-pyridin-2-olate (3e)

(procedure A, 30% yield)



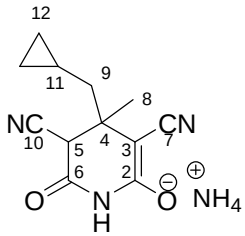
Ketone[6] was prepared from ethyl 2-acetyl-7-heptenoate[7], followed by hydrolysis in aqueous NaOH and decarboxylation using aqueous H_2SO_4 50%.

Diastereomer A d_H (500 MHz, DMSO-d_6) 7.09 (1H, s, NH), 5.86-5.74 (1H, m, H-13), 5.05 (1H, d, $J_{14,13}$ 17.4, H-14), 4.98 (1H, d, $J_{14,13}$ 9.7, H-14), 2.06 (2H, m, H-12), 1.62-1.00 (9H, m, H-8, H-9, H-10 and H-11); d_C (125 MHz, DMSO-d_6) 169.4 (C-2), 163.3 (C-6), 138.4 (C-13), 118.9 (C-7), 115.1 (C-14), 114.7 (C-15), 81.9 (C-3), 48.0 (C-5), 44.0 (C-4), 33.0, 29.1, 23.4 (C-10, C-11 and C-12), 19.4 (C-8), 17.7 (C-9);

Diastereomer B d_H (500 MHz, DMSO-d_6) 5.86-5.74 (1H, m, H-13), 5.01 (1H, d, $J_{14,13}$ 17.0, H-14), 4.94 (1H, d, $J_{14,13}$ 9.8, H-14), 4.76 (1H, s, NH), 2.00 (2H, m, H-12), 1.62-1.00 (9H, m, H-8, H-9, H-10 and H-11);

HRMS(ESI) calculated for $[M\text{-}NH_4]^-$ 258.1242, found 258.1237.

3,5-Dicyano-4-cyclopropylmethyl-4-methyl-6-oxo-1,4,5,6-tetrahydro-pyridin-2-ol; ammonium salt (3f) (procedure A, 41% yield)



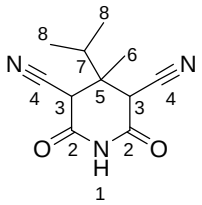
Ketone was synthesized according to Bloodworth and Despoina.[8]

Diastereomer A d_H (500 MHz, D_2O) 1.91 (1H, dd, $J_{9a,9b}$ 14.8, $J_{9a,11}$ 3.5, H-9a), 0.97 (1H, dd, $J_{9b,9a}$ 14.8, $J_{9b,11}$ 9.6, H-9b), 0.66 (1H, m, H-11), 0.41 (2H, m, H-12a), 0.04 (2H, m, H-12b);

Diastereomer B d_H (500 MHz, D_2O) 1.43 (1H, dd, $J_{9a,9b}$ 14.2, $J_{9a,11}$ 6.0, H-9a), 1.25 (1H, dd, $J_{9b,9a}$ 14.2, $J_{9b,11}$ 7.8, H-9b), 0.56 (1H, m, H-11), 0.36 (2H, m, H-12a), 0.02 (2H, d, $J_{12a,12b}$ 4.8, H-12b);

HRMS(ESI) calculated for $[M]^-$ 230.0930, found 230.0924.

4-Isopropyl-4-methyl-2,6-dioxopiperidine-3,5-dicarbonitrile (3g)



Procedure described by McElvain *et al*[9] was followed using (*E*)/(*Z*)-ethyl 2-cyano-3,4-dimethylpent-2-enoate (32)[10] as starting material to receive the title compound as a white solid (0.71 g, 58%). Recrystallization from absolute ethanol gave colourless plate crystals.

m.p. 252-254 °C (lit.[11] 232-234 °C)

Three diastereoisomers were observed by NMR in DMSO-d_6.

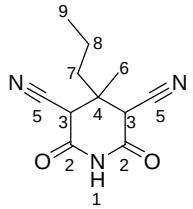
Diastereoisomer A: d_H (400 MHz, d_6-DMSO): 12.16 (1H, s, H-1), 4.69 (2H, s, H-3), 1.95 (1H, septet, $J_{7,8}$ 7.0, H-7), 1.25 (3H, s, H-6), 1.09 (6H, d, $J_{7,8}$ 7.0, H-8). d_c (100 MHz, DMSO-d_6) 165.3 (C-2), 115.2 (C-4), 43.2 (C-3), 41.4 (C-5), 35.5 (C-7), 18.4 (C-6), 17.2 (C-8).

Diastereoisomer B. d_H (400 MHz, DMSO-d_6): 12.23 (1H, s, H-1), 4.72 (2H, s, H-3), 2.07 (1H, m, H-7), 1.19 (3H, s, H-6), 1.03 (6H, d, $J_{7,8}$ 6.8, H-8). d_c (100 MHz, DMSO-d_6): 165.0 (C-2), 115.3 (C-4), 42.3 (C-3), 34.0 (C-7), 19.9 (C-6), 15.3 (C-8).

The amount of diastereoisomer C present in the solution is too insignificant for a full assignment. Observed peaks are d_H (400 MHz, d_6-DMSO) 12.21 (H-1) and 0.99 **(**H-8).

IR (n_{max}/cm^{-1}) 3204 (s, -CONH), 3127 (s, -CONH-), 2268 (m, -C=N), 1750 (s, -CO-N-CO),1706 (s, -CO-N-CO).

4-Methyl-2,6-dioxo-4-propylpiperidine-3,5-dicarbonitrile (3h) (procedure B, 17% yield)



Recrystallisation from ethanol gave colourless plate crystals

m.p. 194-196 °C (lit.[12] 190-192 °C)

Three diastereoisomers were observed in DMSO-d_6.

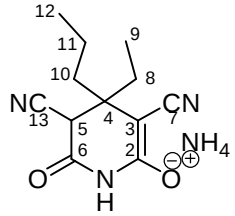
Diastereoisomer A: d_H (400 MHz, DMSO-d_6) 12.12 (1H, s, H-1), 4.75 (2H, s, H-3), 1.57 (2H, m, H-6), 1.35 (2H, m, H-7), 1.17 (3H, s, H-5), 0.94 (3H, t, $J_{7,8}$ 7.1, H-8). d_c (100 MHz, DMSO-d_6): 165.1 (C-2), 114.3 (C-5), 44.2 (C-3), 40.5 (C-6), 20.4 (C-5), 16.0 (C-7), 14.2 (C-8).

Diastereoisomer B: d_H (400 MHz, DMSO-d_6): 12.14 (1H, s, H-1), 4.77 (2H, s, H-3), 1.57 (2H, m, H-6), 1.35 (2H, m, H-7), 1.20 (3H, s, H-5), 0.89 (3H, t, $J_{7,8}$ 7.2, H-8). d_c (100 MHz, DMSO-d_6): 165.0 (C-2), 114.5 (C-5), 46.1 (C-3), 37.8 (C-6), 20.5 (C-5), 17.6 (C-7), 14.6 (C-8).

The amount of diastereoisomer C present in the solution is too insignificant for a full assignment. Observed peaks are d_H (400 MHz, DMSO-d_6) 12.21 (H-1) and 4.74 (H-3).

IR (n_{max}/cm^{-1}) 3205 (m, -CONH-), 3126 (m, -CONH-), 2271 (w, -C=N), 1751 (s, -CO-N-CO), 1703 (s, -CO-N-CO).

Ammonium 3,5-dicyano-4-ethyl-6-oxo-4-propyl-1,4,5,6-tetrahydro-pyridin-2-olate (3i)[13] (procedure A, <1% yield)



Filtration did not give the product. The filtrate was concentrated *in vacuo* and ethyl acetate was used to dissolve the residue. Filtration followed by solvent evaporation and washing with dichloromethane gave a solid, which was dried and washed with warm diethyl ether to give pure product.

m.p. 221-227ºC, (lit.[2] 216-217ºC);

Diastereomer A: d_H (400 MHz, DMSO-d_6) 7.65 (1H, s, H-N), 4.78 (2H, s, H-3 and H-5), 1.64 (4H, m, H-8 and H-10), 1.35 (2H, m, H-11), 0.96 (3H, t, $J_{9,8}$ 7.4, H-9), 0.88 (3H, t, $J_{12,11}$ 7.4, H-12); d_C (100 MHz, DMSO-d_6) 165.3 (C-2, C-6), 114.2 (C-7, C-11), 42.6 (C-3, C-5), 41.8 (C-4), 38.0 (C-10), 28.5 (C-8), 17.0 (C-11), 14.5 (C-9), 7.3 (C-12);

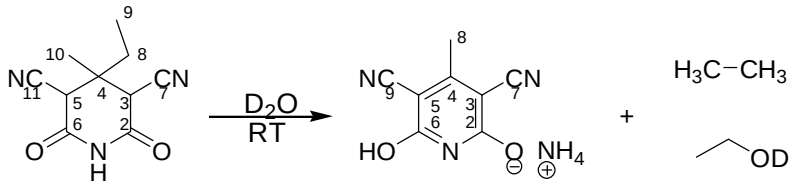
Diastereomer B: d_H (400 MHz, DMSO-d_6) 7.34 (1H, s, H-N), 4.77 (2H, s, H-3 and H-5), 1.64 (4H, m, H-8 and H-10), 1.35 (2H, m, H-11), 0.97 (3H, t, $J_{9,8}$ 7.4, H-9), 0.96 (3H, t, $J_{12,11}$ 7.4, H-12); d_C (100 MHz, DMSO-d_6) 165.3 (C-2, C-6), 114.2 (C-7, C-11), 43.0 (C-3, C-5), 41.6 (C-4), 38.3 (C-10), 29.3 (C-8), 15.8 (C-11), 14.1 (C-9), 8.5 (C-12);

HRMS(ESI) estimated for $[M\text{-}NH_4]^-$ 232.1086, found 232.1082.

DECOMPOSITION STUDY OF GLUTARIMIDES

All decomposition experiments were carried out in $Na_2B_4O_7$/DCl pH 8 buffer solution with substrate concentration 1.0 $g.l^{-1}$, unless otherwise specified. In all ^1H NMR spectra the original peaks of investigated glutarimides remained and characterisation data for decomposition products are listed below for each reaction.

Decomposition of 3a



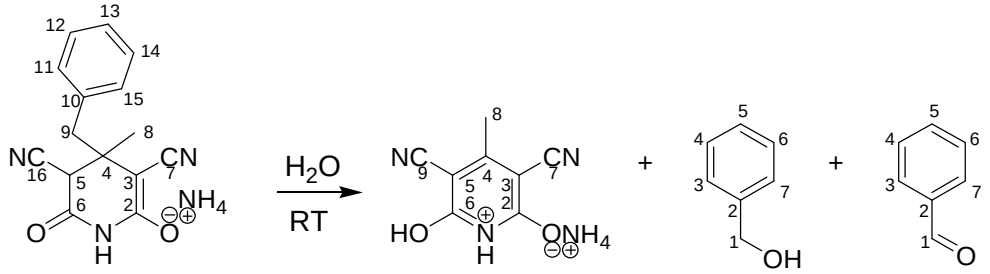
3a **2**

Compound **2** m.p. >275ºC (lit.[5] >320ºC); d_H (400 MHz, DMSO-d_6) 10.38 (1H, s, H-N), 7.08 (4H, s, NH_4^+), 2.18 (3H, s, H-8); d_C (100 MHz, DMSO-d_6) 163.3 (C-2, C-6), 159.5 (C-4), 118.8 (C-7, C-9), 82.0 (C-3, C-5), 19.5 (C-8); IR (n_{max}/cm^{-1}) 3540 (m, N-H), 3113 (m, N-H), 2208 (s, C=N), 1619 (s, -O-C-N-C-O-), 1399 (s, C-Me); HRMS(ESI) estimated for $[M\text{-}NH_4]^-$ 174.0304, found 174.0302.

C_2H_6 d_H (400 MHz, D_2O) 0.67 (s); HRMS(ESI) calculated for $[C_2H_5]^+$ 29.0391, found 29.0390; calculated for $[C_2H_4D]^+$ 30.0453, found 30.0442; calculated for $[C_2H_5D]$ 31.0533, found 31.0535.

C_2H_5OH d_H (400 MHz, D_2O) 3.51 (2H, q, *J* 7.1), 1.04 (3H, t, *J* 7.1) (matched those of commercial ethanol);

Decomposition of 3b



3b **2**

Compound **9** d_H (400 MHz, D_2O) 2.24 (3H, s, H-8);

Benzyl alcohol d_H (400 MHz, D_2O) 4.51 (2H, s, H-1) (matched that of commercial sample);

Benzaldehyde d_H (400 MHz, D_2O) 9.80 (1H, s, H-1), 7.82 (2H, d, $J_{3,4}$, $J_{7,6}$ 8.2, H-3 and H-7), 7.62 (1H, t, $J_{5,4}$, $J_{5,6}$ 8.1, H-5), 7.49 (2H, t, $J_{4,3}$, $J_{4,5}$, $J_{6,5}$, $J_{6,7}$ 7.7, H-4 and H-6) (matched those of commercial sample);

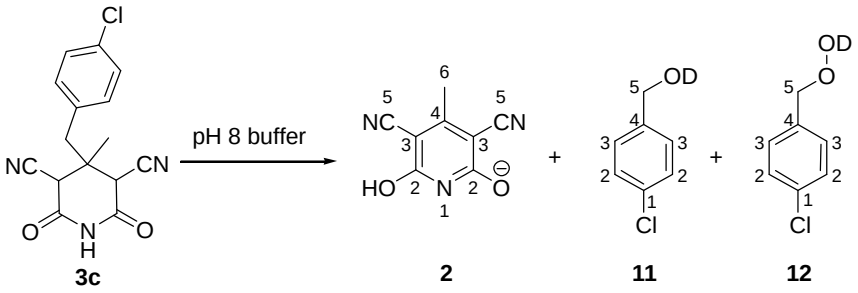
Decomposition of 3b in degassed D_2O

Decomposition of compound **3b** in degassed D_2O (0.7ml) was monitored for two and a half weeks by ^{1}H NMR. During this period, there was no significant change observed in the spectra.

A steady, slow stream of O_2 was then bubbled through the sample for five minutes, after which the sample was vigorously agitated, and the spectrum recorded 16 hours later. The intensity of the product peaks doubled in the presence of oxygen during

that time. Finally the spectrum was recorded 40 hours after the addition of oxygen, after which time a five fold increase in the product of interest **2** was observed.

Decomposition of 3c

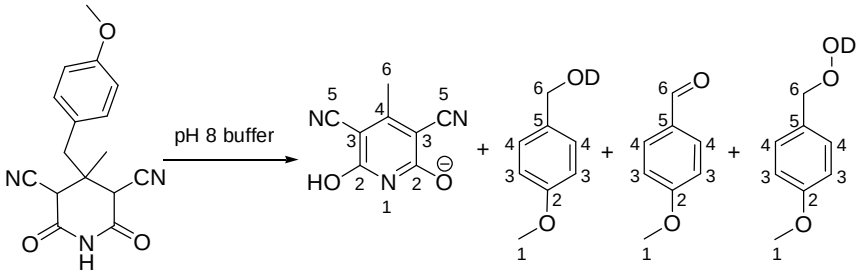


Compound **2** d_H (500 MHz, D_2O): 2.45 (3H, s, H-6);

Compound **11** d_H (500 MHz, D_2O): 7.47 (2H, d, $J_{2,3}$ 8.5, H-3), 7.32 (2H, d, $J_{2,3}$ 8.5, H-2), 4.66 (2H, s, H-5);

Compound **12** d_H (500 MHz, D_2O): 7.47 (2H, d, $J_{2,3}$ 8.5, H-3), 7.18 (2H, d, $J_{2,3}$ 8.5, H-2), 5.03 (2H, s, H-5);

Decomposition of 3d



3d **2** **13** **14** **15**

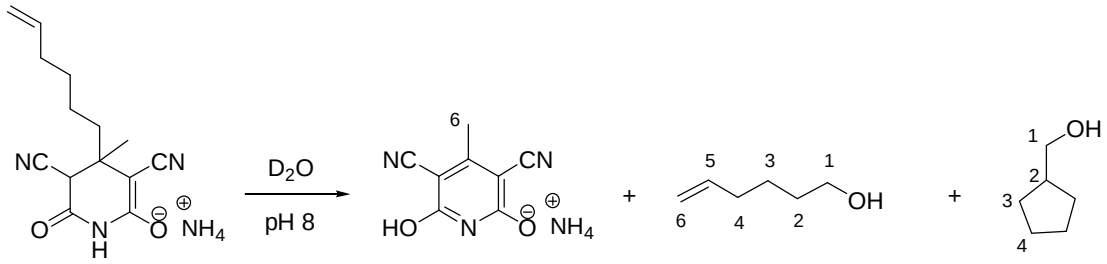
Compound **2** d_H (500 MHz, D_2O): 2.45 (3H, s, H-6);

Compound **13** d_H (500 MHz, D_2O): 7.40 (2H, d, $J_{3,4}$ 8.8, H-4), 7.06 (2H, d, $J_{3,4}$ 8.8, H-3), 4.62 (2H, s, H-6), 3.89 (3H, s, H-1);

Compound **14** d_H (500 MHz, D_2O): 9.82 (1H, s, H-6), 7.99 (2H, d, $J_{3,4}$ 8.7, H-4), 7.20 (2H, d, $J_{3,4}$ 8.8, H-3), 3.98 (3H, s, H-1);

Compound **15** d_H (500 MHz, D_2O): 7.46 (2H, d, $J_{3,4}$ 8.7, H-4), 7.07 (2H, d, $J_{3,4}$ 8.1, H-3), 4.99 (2H, s, H-6), 3.89 (3H, s, H-1);

Decomposition of 3e



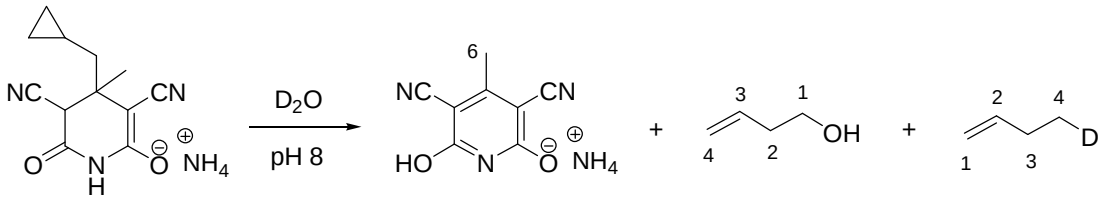
2

Compound **2** d_H (500 MHz, D_2O) 2.45 (3H, s, H-6);

Hex-5-en-1-ol d_H (500 MHz, D_2O) 3.66 (2H, t, $J_{1,2}$ 6.4, H-1) (matched that of commercial sample), other peaks were overlapping with those of **3e**;

Cyclopentylmethanol d_H (500 MHz, D_2O) 3.52 (2H, d, $J_{1,2}$ 7.0, H-1) (matched that of commercial sample), other peaks were overlapping with those of **3e**;

Decomposition of 3f



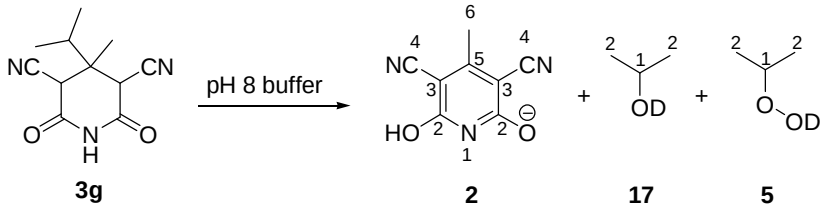
2

Compound **2** d_H (500 MHz, D_2O) 2.45 (3H, s, H-6);

But-3-en-1-ol d_H (500 MHz, D_2O) 5.78 (1H, tdd, $J_{3,4}$ 17.4, $J_{3,4}$ 10.3, $J_{3,2}$ 6.8, H-3), 5.07 (1H, d, $J_{4,3}$ 17.4, H-4), 5.03 (1H, d, $J_{4,3}$ 10.3, H-4), 3.58 (2H, t, $J_{1,2}$ 6.5, H-1), 2.23 (2H, dt, $J_{2,1}$ 6.5, $J_{2,3}$ 6.8, H-2) (matched those of commercial sample);

[4-^{2}H]but-1-ene d_H (500 MHz, $CDCl_3$) 2.07 (2H, dt, $J_{3,2}$ 7.0, $J_{3,4}$ 7.4, H-3) 0.95 (2H, td, $J_{4,3}$ 7.4 , J_{HD} 1.2, H-4) (matched those of commercial butene);

Decomposition of 3g



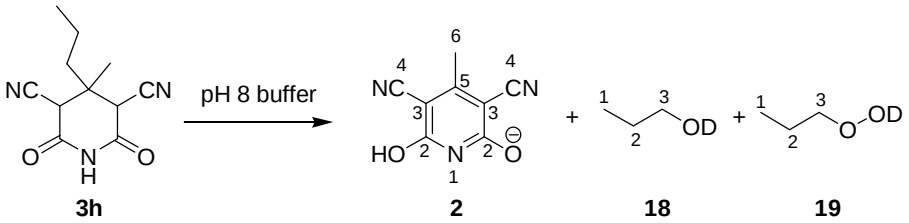
3g **2** **17** **5**

Compound **2** d_H (400 MHz, D_2O): 2.39 (3H, s, H-6);

Compound **17** d_H (400 MHz, D_2O): 3.99 (1H, m, H-1), 1.15 (6H, d, $J_{1,2}$ 6.3, H-2) (matched those of commercial sample);

Compound **5** d_H (400 MHz, D_2O): 4.20 (1H, h, $J_{1,2}$ 6.2, H-1), 1.17 (6H, d, $J_{2,1}$ 6.2, H-2);

Decomposition of 3h

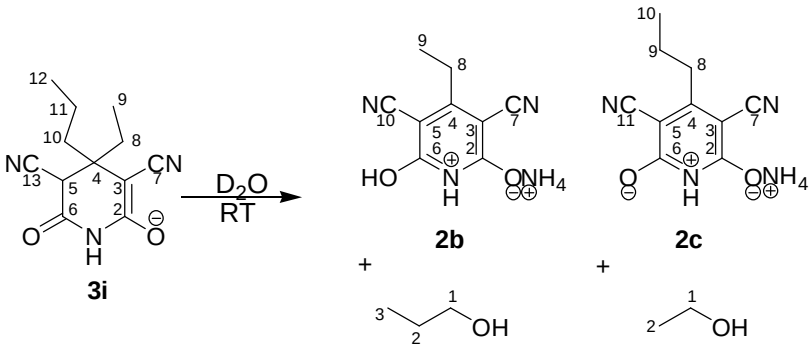


Compound **2** d_H (400 MHz, D_2O) 2.39 (3H, s, H-6);

Compound **18** d_H (400 MHz, D_2O) 3.53 (3H, t, $J_{1,2}$ 6.8, H-1) (matched that of commercial sample);

Compound **19** d_H (400 MHz, D_2O) 3.95 (3H, t, $J_{1,2}$ 6.5, H-1);

Decomposition of 3i



Ethanol d_H (400 MHz, D_2O) 3.53 (2H, q, $J_{1,2}$ 7.2, H-1), 1.05 (3H, t, $J_{2,1}$ 7.2, H-2) (matched those of commercial sample);

Propanol d_H (400 MHz, D_2O) 3.43 (2H, t, $J_{1,2}$ 6.7, H-1), 0.77 (3H, t, $J_{3,2}$ 7.0, H-3) (matched those of commercial sample);

Compound **2b** d_H (400 MHz, D_2O) 2.58 (2H, q, $J_{8,9}$ 8.3, H-8), 1.13 (3H, t, $J_{9,8}$ 8.3, H-9);

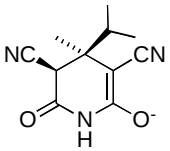
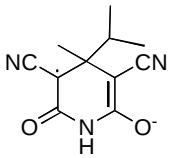
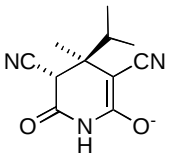
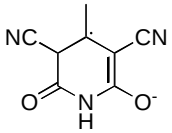
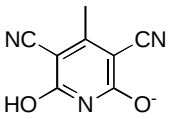
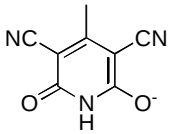
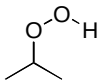
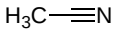
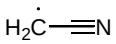
Compound **2c** d_H (400 MHz, D_2O) 2.57 (2H, t, $J_{8,9}$ 7.7, H-8), 1.59 (2H, tq, $J_{9,8}$ 7.7, $J_{9,10}$ 7.4, H-9), 0.87 (3H, t, $J_{10,9}$ 7.4, H-10); HRMS(ESI) calculated for $[M\text{-}NH_4]^+$ 202.0617, found 202.0620.

DFT CALCULATIONS ON THE GUARESCHI IMIDE DECOMPOSITION PATHWAY

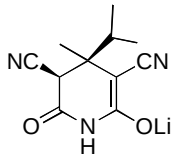
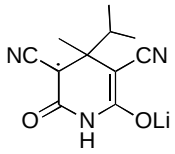
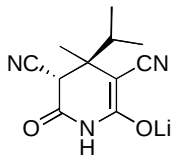
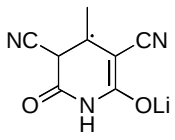
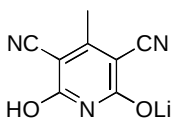
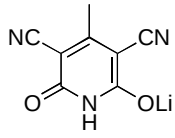
All calculations were carried out using the Gaussian 03 package. Prior conformational analysis of all structures was done by initial semi-empirical calculations at the PM3 level. The most stable conformers found (within 1.0 kcal/mole) were then optimised using DFT at the B3LYP/6-31G(d,p) level of theory, and the lowest energy species tabulated. Recorded energies were include zero-point energy correction.

A. Energies of the contributing species (1 Hartree = 627.5 Kcals mol^{-1})

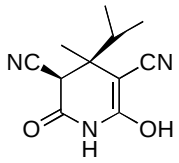
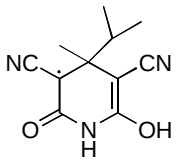
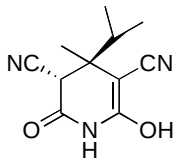
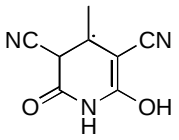
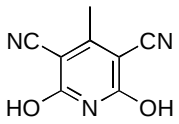
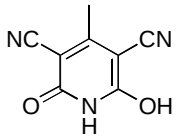
Enolate pathway (most favourable)

	Energy (Hartrees)*		Energy (Hartrees)
	-740.957845		-740.337708
	-740.956181		-622.477105
	-621.927249		-621.952049
	-119.051648		-118.399946
	-269.387848		-268.765030
	-132.713705		-132.066633

Li-Enolate pathway

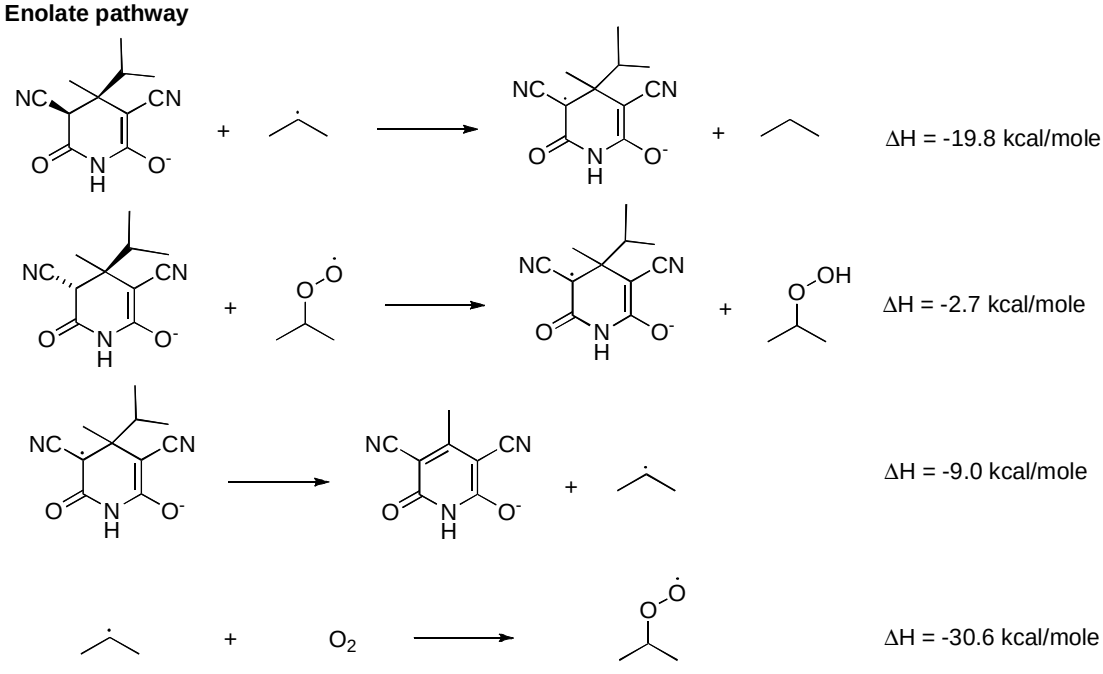
	Energy (Hartrees)		Energy (Hartrees)
	-748.489398		-747.866132
	-748.491634		-630.003457
	-629.456371		-629.466959

Enol pathway

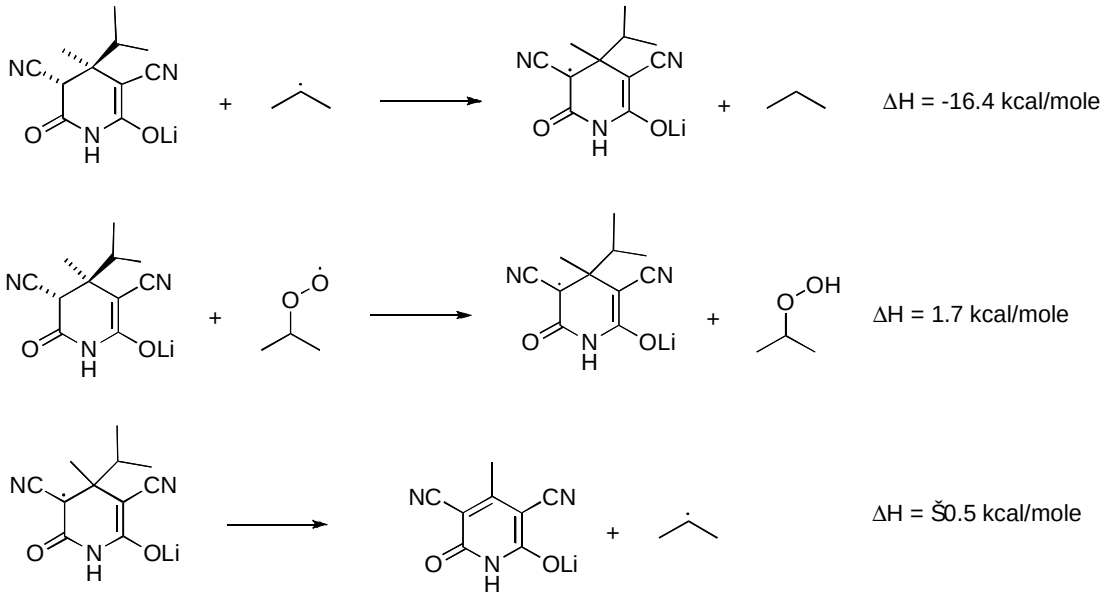
	Energy (Hartrees)		Energy (Hartrees)
	-741.464278		-740.839090
	-741.462686		-622.977424
	-622.439566 (preferred isomer)		-622.436514

B. Enthalpy changes in contributing reactions (most stable conformers/diastereomers) only.

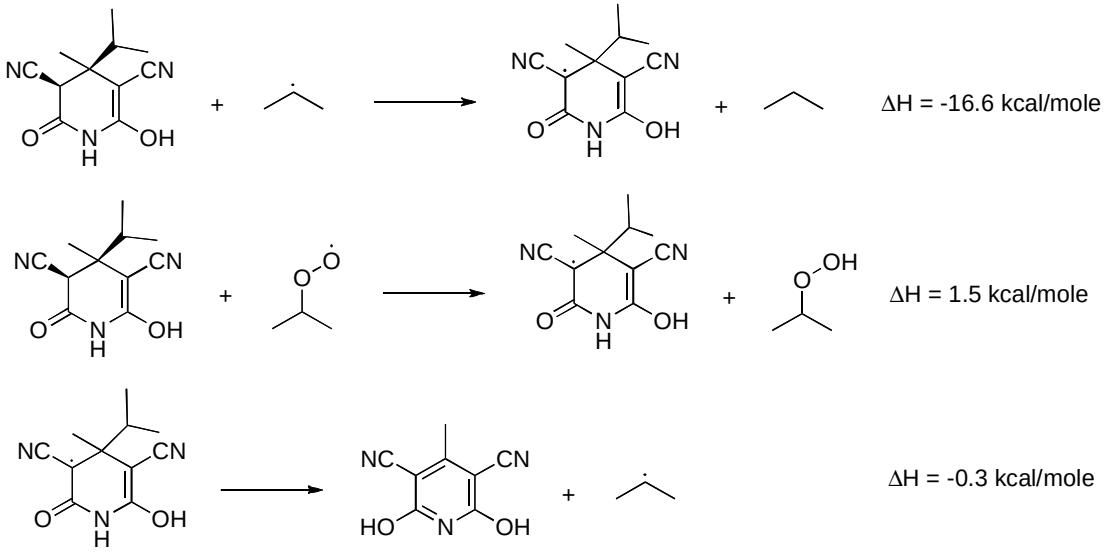
Enolate pathway



Lithium enolate pathway

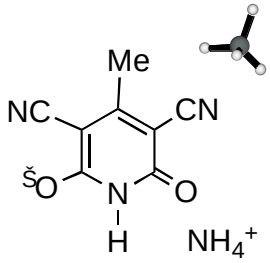


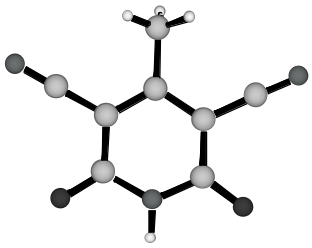
Enol pathway

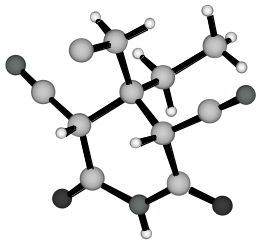


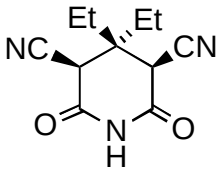
X-RAY STRUCTURES

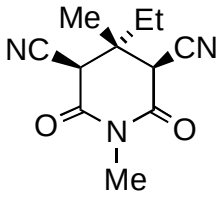
X-ray structures of neutral Guareschi imides and the aromatization product (as ammonium salt). Structure analysis was carried out by Dr. A. Cowley, and the data will be submitted to the Cambridge Structural Database on acceptance. Copies of CIF files are available from the authors.

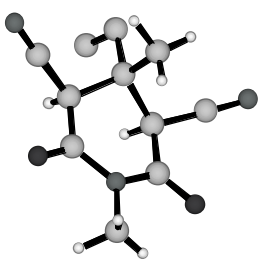


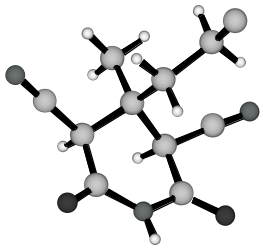


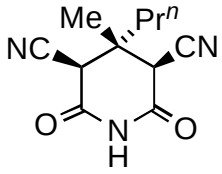


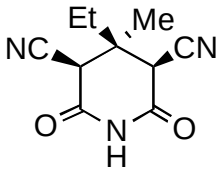


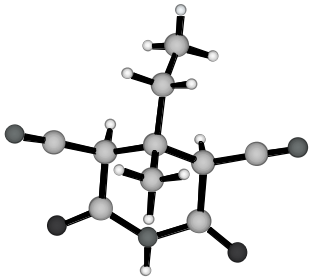


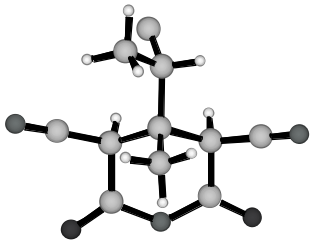


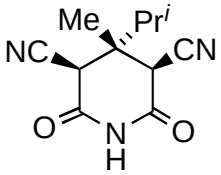












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