

Structural Study of *p*-Nitrophenylhydrazonomalononitrile and its Conjugate Base. Evidence for Extensive Charge Delocalization in the Hydrazone Anion

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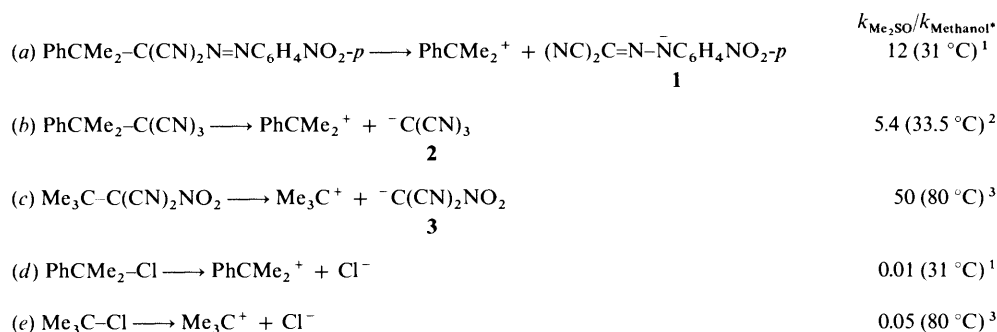
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The molecular structures of *p*-nitrophenylhydrazonomalononitrile and the tetraethylammonium salt of its conjugate base, hydrazone anion, have been determined from X-ray diffraction data. Bond and dihedral angles confirm the planar framework of both the hydrazone and the hydrazone anion. Evidence for extensive charge delocalization in the hydrazone moiety is provided by a comparison of bond lengths between the neutral and anionic species. A quinonoid-type interaction is stronger in the hydrazone than in the hydrazone anion, contrary to the results of AM1 calculations. The observed structural feature is closely related to the function of some arylhydrazonomalononitriles as efficient uncouplers of oxidative phosphorylation in mitochondrial systems.

Recently we reported the first generation of unstable carbocations such as *tert*-cumyl^{1,2} and *tert*-butyl^{2,3} cations via carbon-carbon bond heterolysis as illustrated in reactions (a)–(c) (Scheme 1), in which the substrates produce highly resonance-stabilized anions, *i.e.*, the hydrazone anion (1), the tricyanomethanide ion (2), and the dicyano(nitro)methanide ion (3). The most intriguing feature of these S_N1-E1 reactions is that the heterolysis process is insensitive to hydrogen bonding with protic solvents, in sharp contrast to the hydrogen bond-

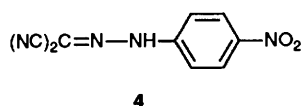
It is well known that some derivatives of phenylhydrazonomalononitrile [FCCP (*p*-CF₃O) and CCCP (*m*-Cl)] serve as efficient uncouplers of oxidative phosphorylation in mitochondrial systems.⁷ These uncouplers are considered to be lipophilic both in neutral and anionic forms, since the anions are expected to be stabilized without strong solvation, contrary to common protophilic anions. Our present data would therefore help understand some structural features of the anionic form of uncouplers of this type.



Scheme 1 *Deuteriated solvents

sensitive nature of common S_N1-E1 reactions [*e.g.*, (d) and (e)]. Carbon-carbon bond heterolysis reactions proceed more rapidly in the dipolar aprotic solvent dimethyl sulfoxide (DMSO) than in the protic solvent methanol whereas substrates bearing Cl as a leaving group undergo heterolytic cleavage much faster in methanol.

The hydrogen bond-insensitive behaviour is attributed to the pronounced charge dispersal in leaving group anions. The first requisite of such an anion is thus to possess a planar structure. Almost planar and charge-dispersed structures have already been confirmed by X-ray analysis in the anions **2**⁴ and **3**⁵ but not yet in the hydrazone anion **1**. The hydrogen bond-insensitive nature of the hydrazone anion was also confirmed by another method, *i.e.*, by measuring the enthalpy of solution of the hydrazone anion as the tetraethylammonium salt in methanol, DMSO, and methanol-acetonitrile binary mixtures.⁶ Our interest in the nature of the hydrazone anion **1** led to the structural study of *p*-nitrophenylhydrazonomalononitrile (**4**) and the tetraethylammonium salt of the anion **1**.



Experimental

Preparation of the Tetraethylammonium Salt of the Hydrazone Anion.—A methanol solution of tetraethylammonium hydroxide was prepared by mixing freshly precipitated silver oxide (1.2 equiv.) with finely granulated tetraethylammonium iodide (1.0 equiv.) in methanol with efficient stirring. After insoluble materials had been removed by filtration, a solution of the hydrazone **4** (1.0 equiv.) in acetone was added to the solution. The mixture was evaporated to dryness under reduced pressure. The residue was dissolved in acetonitrile and the resulting solution was dehydrated with CaH₂. Evaporation of the solvent gave the salt, which was dried *in vacuo*, and recrystallized three times from methyl ethyl ketone-hexane and once from dichloromethane-hexane to give reddish-brown crystals (Found: C, 59.1; H, 7.0; N, 24.3. Calc. for C₁₇H₂₄N₆O₂: C, 59.28; H, 7.02; N, 24.40%).

An attempted preparation of the tetraethylammonium salt of the conjugate base of phenylhydrazonomalononitrile was unsuccessful.

X-Ray Structure Analyses.—The cell dimensions and diffraction intensities were measured on a Rigaku Denki AFC-4 automatic four-circle diffractometer using graphite monochromated

Table 1 Crystal data

Compound	Hydrazone	Salt
Formula	C ₉ H ₅ N ₅ O ₂	C ₁₇ H ₂₄ N ₆ O ₂
<i>M</i>	215.18	344.43
Crystal system	Monoclinic	Monoclinic
Space group	<i>P</i> 2 ₁ / <i>c</i>	<i>P</i> 2 ₁ / <i>n</i>
<i>a</i> /Å	6.150(1)	14.387(1)
<i>b</i> /Å	10.936(1)	12.142(3)
<i>c</i> /Å	14.935(2)	11.309(1)
β /°	97.25(1)	108.05(1)
<i>U</i> /Å ³	996.4(2)	1878.4(5)
<i>Z</i>	4	4
<i>D</i> _{calc} /g cm ⁻³	1.43	1.22
Crystal dimensions/mm ³	0.8 × 0.3 × 0.2	0.5 × 0.2 × 0.3
<i>F</i> (000)	440	736
μ /cm ⁻¹	1.16	0.91
$2\theta_{\max}$ /° ($\lambda = 0.71069$ Å)	55	55
No. of reflections used	1629	2064
$ F_o \geq 3\sigma F_o $		
No. of independent collected reflections	2320	4300
No. of parameters	165	278
<i>R</i> (= $\Sigma\Delta/\Sigma F_o $)	0.051	0.077
<i>R</i> _w	0.059	0.066
<i>S</i>	0.772	1.141
w Hydrazone: [18.74(sin θ/λ) ² - 19.19(sin θ/λ) + 4.96] ⁻¹		
Salt: [0.0030 <i>F</i> _o ² - 0.041 <i>F</i> _o + 0.945] ⁻¹		

Table 2 Positional parameters (× 10⁴) for the hydrazone (esds in parentheses)

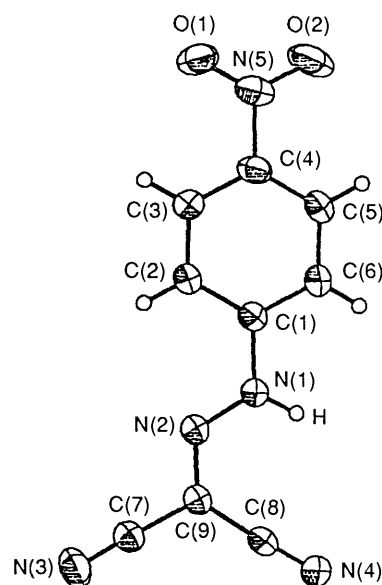
Atom	<i>x</i>	<i>y</i>	<i>z</i>
C(1)	4 716(3)	3 435(2)	6 035(1)
C(2)	5 599(3)	4 595(2)	6 181(2)
C(3)	4 615(4)	5 403(2)	6 711(2)
C(4)	2 780(4)	5 029(2)	7 086(1)
C(5)	1 900(4)	3 878(2)	6 950(2)
C(6)	2 870(4)	3 073(2)	6 416(2)
C(7)	10 199(4)	2 398(2)	4 266(2)
C(8)	7 394(4)	852(2)	4 445(2)
C(9)	8 250(3)	2 049(2)	4 635(1)
N(1)	5 651(3)	2 578(2)	5 498(1)
N(2)	7 400(3)	2 854(2)	5 132(1)
N(3)	11 751(4)	2 655(3)	3 972(2)
N(4)	6 633(6)	-88(2)	4 324(3)
N(5)	1 756(4)	5 906(2)	7 648(2)
O(1)	2 317(4)	6 974(2)	7 638(2)
O(2)	378(6)	5 521(3)	8 092(3)
H(-N1)	5 016(77)	1 886(48)	5 420(31)

Mo-K α radiation at room temperature. The structure was solved by MULTAN 78⁸ and the Fourier techniques. The hydrogen atoms were located in a difference Fourier map except the hydrogen atoms belonging to the Et₄N ion. The structural parameters were refined by a full-matrix least-squares method, using the UNICS III system.⁹ Crystal data and the final *R* values are given in Table 1. Methylene carbon atoms in the Et₄N ion, which were found to be disordered, were represented in terms of two orientations in the Fourier map (Fig. 2). The site occupancy factors were estimated from peak heights in the Fourier map and were refined, being constrained to sum up to 1.0 in the first stage of the least-squares calculation. Later the refinement was carried out, fixing these site parameters at 0.67 and 0.33, respectively. The parameters for ethyl hydrogen atoms were not refined.

Atomic coordinates are listed in Table 2 for the hydrazone **4** and in Table 3 for the salt. Full lists of hydrogen atom

Table 3 Positional parameters (× 10⁴) for the hydrazono anion as the tetraethylammonium salt (esds in parentheses)

	<i>x</i>	<i>y</i>	<i>z</i>
C(1)	2917(3)	4283(5)	86966(4)
C(2)	2309(5)	5023(5)	9001(5)
C(3)	1410(4)	4659(6)	9150(5)
C(4)	1202(3)	3552(5)	9011(4)
C(5)	1825(4)	2818(5)	8720(5)
C(6)	2674(4)	3184(5)	8556(5)
C(7)	5128(3)	7020(5)	8741(4)
C(8)	5531(3)	5185(4)	8173(4)
C(9)	4875(3)	5892(4)	8516(4)
N(1)	3831(3)	4587(4)	8488(3)
N(2)	4009(3)	5597(4)	8677(3)
N(3)	5330(3)	7923(4)	8891(4)
N(4)	6068(3)	4633(4)	7893(4)
N(5)	303(3)	3140(5)	9181(4)
O(1)	-325(3)	3810(5)	9223(5)
O(2)	186(3)	2143(4)	9195(4)
N(6)	1994(2)	3807(3)	4020(3)
C(10)	2145(5)	3888(6)	2755(5)
(C10')	2406(10)	2788(12)	3713(14)
C(11)	2511(4)	2810(5)	2338(5)
C(12)	1340(5)	2858(5)	4111(7)
C(12')	952(10)	4080(13)	2971(13)
C(13)	281(4)	3011(5)	3060(6)
C(14)	1625(5)	4902(5)	4288(6)
C(14')	1769(10)	3670(12)	5236(12)
C(15)	1463(4)	4916(5)	5616(5)
C(16)	2990(5)	3537(6)	5009(6)
C(16')	2668(12)	4808(13)	4086(14)
C(17)	3716(4)	4527(6)	5119(6)

**Fig. 1** ORTEP drawing of (NC)₂C=NNHC₆H₄NO₂-*p*

coordinates and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC).*

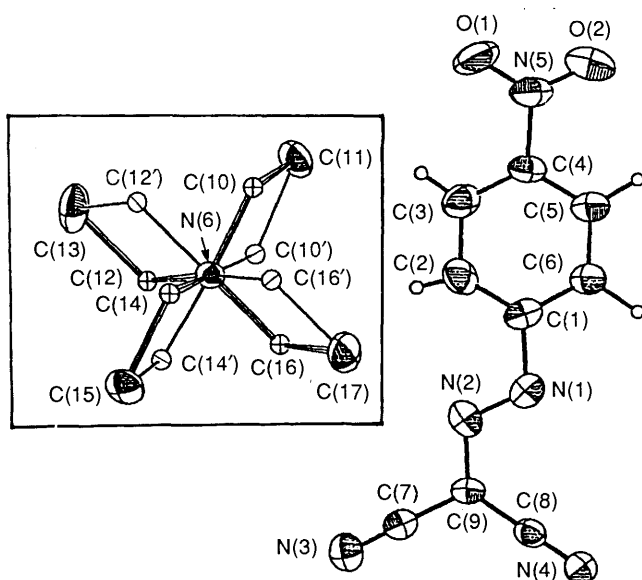
Results and Discussion

Bond lengths and bond angles of the hydrazone **4** and the hydrazono anion **1** are compiled in Tables 4 and 5, respectively. The numbering of the atoms is the same for the two compounds. ORTEP drawings of these structures are given in Figs. 1 and 2.

* For details of the CCDC scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1992, in the January issue.

Table 4 Bond lengths/Å obtained from crystal structures and AM1 calculations

	Hydrazone	Hydrazono anion	Hyd(Calc.)	Anion(Calc.)
C(1)–C(2)	1.387(3)	1.371(9)	1.411	1.425
C(2)–C(3)	1.377(3)	1.425(10)	1.390	1.380
C(3)–C(4)	1.383(3)	1.377(9)	1.404	1.409
C(4)–C(5)	1.375(3)	1.374(8)	1.404	1.411
C(5)–C(6)	1.374(3)	1.365(8)	1.388	1.378
C(6)–C(1)	1.390(3)	1.376(8)	1.416	1.430
C(1)–N(1)	1.402(2)	1.453(7)	1.417	1.396
N(1)–N(2)	1.302(3)	1.257(6)	1.309	1.278
N(2)–C(9)	1.302(3)	1.361(7)	1.324	1.345
C(9)–C(7)	1.426(3)	1.420(7)	1.433	1.423
C(7)–N(3)	1.114(4)	1.134(7)	1.163	1.165
C(9)–C(8)	1.433(3)	1.417(7)	1.431	1.423
C(8)–N(4)	1.135(4)	1.138(7)	1.162	1.165
C(4)–N(5)	1.469(3)	1.454(8)	1.485	1.465
N(5)–O(1)	1.215(5)	1.228(8)	1.202	1.208
N(5)–O(2)	1.219(3)	1.224(8)	1.202	1.208
N(1)–H	0.853(51)		1.007	

**Fig. 2** ORTEP drawing of the salt $[(\text{NC})_2\text{CNNC}_6\text{H}_4\text{NO}_2\text{-}p]^- \text{Et}_4\text{N}^+$. Occupation factors in two Et_4N^+ moieties (methylene carbons are represented by arbitrary spheres): 1.0 for nitrogens and terminal carbons of both cations; 0.67 for methylene carbons of one cation; and 0.33 for methylene carbons of the other cation.

The dihedral angle data indicate that both the hydrazono anion and the hydrazone itself are planar.

A comparison of the bond lengths of the hydrazone and the hydrazono anion provides evidence that the framework of the hydrazono anion is well suited to extensive charge delocalization throughout the hydrazono moiety. The bond in the hydrazono anion corresponding to the single bond in the hydrazone, *i.e.*, N(1)–N(2) 1.26 Å, is shorter than that in the hydrazone (1.30 Å), while the C–CN bond distances [C(7)–C(9) and C(8)–C(9)] are close to each other (1.42 Å in the hydrazono anion and 1.43 Å in the hydrazone). The C(9)–N(2) bond (1.36 Å) in the hydrazono anion corresponding to the double bond in the hydrazone is considerably longer than that in the hydrazone (1.30 Å). The lengths of C=N triple bonds are less sensitive to the change from a neutral to an anionic form. However, the C≡N bond lengths in the hydrazono anion are within the range of those in the anions **2** and **3** (1.15–1.17 and 1.13–1.16 Å, respectively).^{4,5} The lengths of the C–CN bonds in the hydrazono anion are slightly closer to those in **2** and **3** (1.37–

Table 5 Bond angles/° from crystal structures

	Hydrazone	Hydrazono anion
C(1)–C(2)–C(3)	119.1(2)	120.4(5)
C(2)–C(3)–C(4)	118.9(2)	117.6(6)
C(3)–C(4)–C(5)	122.5(2)	121.7(6)
C(4)–C(5)–C(6)	118.7(2)	120.0(6)
C(5)–C(6)–C(1)	119.5(2)	120.3(5)
C(2)–C(1)–C(6)	121.3(2)	120.4(5)
C(2)–C(1)–N(1)	121.4(2)	123.6(5)
C(6)–C(1)–N(1)	117.3(2)	116.0(5)
C(1)–N(1)–N(2)	120.4(2)	111.6(4)
N(1)–N(2)–C(9)	119.7(2)	112.4(4)
N(2)–C(9)–C(7)	124.7(2)	115.1(4)
N(2)–C(9)–C(8)	117.0(2)	126.4(4)
C(9)–C(7)–N(3)	176.4(3)	178.4(6)
C(9)–C(8)–N(4)	178.8(3)	178.8(6)
C(3)–C(4)–N(5)	118.0(2)	119.5(5)
C(5)–C(4)–N(5)	119.6(2)	118.8(5)
C(4)–C(5)–O(1)	117.7(3)	118.2(6)
C(4)–N(5)–O(2)	118.4(2)	118.3(5)
O(1)–N(5)–O(2)	123.9(3)	123.3(6)
C(1)–N(1)–H	117(3)	
N(2)–N(1)–H	122(3)	

1.41 and 1.38–1.41 Å, respectively) than those in the hydrazone as a result of charge dispersion.

Interestingly, the C(phenyl)–N(amino) bond [C(1)–N(1)] in the hydrazone (1.40 Å), which is formally a single bond, is significantly shorter than that in the hydrazono anion. The result suggests that there exists a strong quinonoid-type interaction between the *p*-nitrophenyl group and the lone-pair electrons on the amino nitrogen atom in the hydrazone, while such an extra-resonance effect is depressed in the hydrazono anion presumably because the negative charge is attracted more strongly to the cyano groups. This view is consistent with the kinetic behaviour of heterolysis of arylazo-*tert*-cumylmalononitriles, in which the substituent effect correlates with σ rather than σ^- .¹

The length of the C(phenyl)–N(nitro) bond [C(4)–N(5)], however, shows no trend supporting a stronger quinonoid-type interaction in the hydrazone, because the bond in the hydrazone does not appear shorter than that in the hydrazono anion. A similar situation has been reported in structural studies of

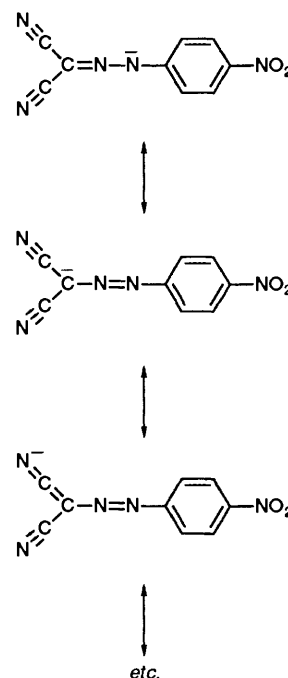
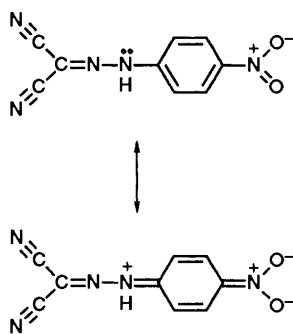
Resonance forms of the hydrazono anion **1**

Table 6 Bond lengths in *p*- and *m*-nitroanilines obtained from crystal structures and AM1 calculations^a

	<i>para</i> (Obs.) ¹⁰	<i>meta</i> (Obs.) ¹¹	<i>para</i> (Calc.)	<i>meta</i> (Calc.)
C(1)–C(2)	1.408(6)	1.419(15)	1.421	1.417
C(2)–C(3)	1.377(7)	1.366(16)	1.384	1.414
C(3)–C(4)	1.390(6)	1.381(12)	1.406	1.400
C(4)–C(5)	1.395(6)	1.409(15)	1.406	1.402
C(5)–C(6)	1.373(7)	1.348(16)	1.384	1.394
C(6)–C(1)	1.415(7)	1.380(13)	1.421	1.389
C(1)–N(1)	1.371(7)		1.378	
C(2)–N(1)		1.406(11)		1.394
C(4)–N(5)	1.460(7)	1.440(16)	1.478	1.490
N(5)–O(1)	1.246(7)	1.242(11)	1.204	1.202
N(5)–O(2)	1.247(7)	1.211(10)	1.204	1.202

^a The numbering is the same as that given for the hydrazone.



The quinonoid structure of the hydrazone 4

nitroanilines. *p*-Nitroaniline, which undoubtedly includes a strong contribution from the quinonoid structure due to an extra-resonance term, has a shorter C–N(amino) bond (1.37 Å) but a longer C–N(nitro) bond (1.46 Å)¹⁰ than *m*-nitroaniline [C–N(amino), 1.41; C–N(nitro), 1.44 Å],¹¹ while the bonds in *N,N*-dimethyl-*p*-nitroaniline exhibit both the shortest values [C–N(amino), 1.36; C–N(nitro), 1.41 Å] among these nitroanilines.¹²

The quinonoid contribution in 1,4-disubstituted benzene derivatives naturally shortens the C(2)–C(3) and C(5)–C(6) bond lengths. Krygowski introduced a parameter Δ composed of the bond lengths in a benzene ring, in which Δ is either $2 \times [C(2)–C(3)] - [C(1)–C(2)] - [C(3)–C(4)]$ or $2 \times [C(5)–C(6)] - [C(4)–C(5)] - [C(6)–C(1)]$, and demonstrated that the extent of quinonoid contribution is correlated with Δ , *i.e.*, the smaller the parameter Δ the greater the quinonoid contribution.¹³ The parameters Δ (Å, as mean values) for the above *p*-nitrophenyl derivatives increase in the order: *N,N*-dimethyl-*p*-nitroaniline (–0.11, –0.06) < *p*-nitroaniline (–0.06, –0.04) < hydrazone (–0.02, –0.02) < hydrazone anion (–0.02, 0.10). This order is in agreement with that of C(phenyl)–N(amino) bond lengths. With the hydrazone anion, however, it seems difficult to hold such a discussion based on the analytical data for the benzene ring, since the shape of the ring is too unsymmetrical with respect to the 1,4-axis, presumably because there exists a negatively-charged unsymmetrical hydrazone moiety as the substituent, which produces ambiguity due to a large difference between two Δ -values for the anion.

Molecular orbital calculations by the AM1 method were performed with MOPAC version 5.01¹⁴ and the results for the hydrazone and its anion are compared in Table 4. The calculated structures for both compounds are planar. There appears to be a distinct divergence between calculated and crystal structures, since the MO calculation predicts a larger

contribution of a quinonoid form for the hydrazone anion than for the hydrazone: both amino and nitro C–N bonds are shorter in the anion than in the hydrazone. As mentioned above, it is likely that the electron-withdrawing effect of cyano groups in the actual anion is much stronger than that estimated from this type of calculation and causes charge dispersal mainly restricted to the hydrazone moiety, which prevents the formation of a quinonoid structure. A similar comparison is given for *p*- and *m*-nitroanilines in Table 6. As expected, the MO calculation points to the quinonoid form of *p*-nitroaniline. The result that the lengths of both amino and nitro C–N bonds are shorter in *p*-nitroaniline than in the *meta*-isomer is, however, different from that of crystal structures. Although we cannot explain the origin of this difference, it is suggested that only the length of amino C–N bonds in crystal structures may be correlated with the extent of contribution of quinonoid resonance forms.

Conclusions

A planar and highly resonance-stabilized structure of the hydrazone anion, confirmed by X-ray analysis of the tetraethylammonium salt, is exactly what is expected from its hydrogen bond-insensitive nature. This was previously observed during investigations on the formation of the hydrazone anion *via* S_N1-E1-type reactions¹ and on the enthalpy of solution of the salt.⁶ The charge of the hydrazone anion is delocalized mainly within the hydrazone moiety, but little through the *p*-nitrophenyl group. The hydrogen bond-insensitive nature of hydrazone anions appears to have *a priori* been assumed, since some hydrazone malononitriles have been utilized as efficient uncouplers.⁷ Our results are in favour of Mitchell's chemiosmotic theory in which uncouplers act as proton carriers across the mitochondrial bilayer membrane.

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