

# Reactivity of the Mutagen 1,4-Dinitro-2-methylpyrrole as an Alkylating Agent

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**Supporting Information**

<b>1. FREE ENERGIES .....</b>	<b>3</b>
<b>2. CARTESIAN COORDINATES OF THE EQUILIBRIUM GEOMETRIES.....</b>	<b>5</b>
<b>3. IDENTIFICATION OF INTERMEDIATES.....</b>	<b>22</b>

Supporting Information - For Review Only - Not for Publication

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## 1. Free Energies

**TABLE 1. Free Energies in Aqueous Solution\***

	<i>G</i> (hartree)
<b>NMP</b>	-658.47517
<b>OH<sup>-</sup></b>	-75.954271
<b>1</b>	-734.45613
<b>TS2</b>	-734.43765
<b>2</b>	-529.19122
<b>NO<sub>2</sub><sup>-</sup></b>	-205.30622
<b>7</b>	-529.23549
<b>8</b>	-529.23061
<b>9</b>	-529.22720
<b>10</b>	-529.22239
<b>11</b>	-529.21795
<b>12</b>	-529.20565
<b>13</b>	-529.20117
<b>9<sup>b</sup></b>	-529.180898
<b>OH<sup>-</sup>+2H<sub>2</sub>O<sup>a</sup></b>	-228.84057
<b>TS1+2H<sub>2</sub>O<sup>a</sup></b>	-887.238844
<b>NMP<sup>a</sup></b>	-658.429218
<b>Pyridine<sup>b</sup></b>	-248.245115
<b>TS 9+Pyridine<sup>b</sup></b>	-777.398807

\* All structures were checked to have either zero (minima) or one imaginary frequencies (transition states)

<sup>a</sup> Two explicit water molecules were added to the calculation in order to take into account the close range interactions of the charged OH<sup>-</sup> with the solvent. The energy barrier for the formation of TS2 was calculated from the difference in free energy between NMP+OH<sup>-</sup>+2H<sub>2</sub>O and TS1+2H<sub>2</sub>O. Due to the size of the system energies were calculated at the B3LYP 6-31++G(d,p) level.

<sup>b</sup> Due to the size of the molecules, calculations were carried at the B3LYP 6-31++G(d,p) level

## 2. Cartesian Coordinates of the Equilibrium Geometries\*

\* All structures were checked to have either zero (minima) or one imaginary frequencies (transition states)

TABLE 2. Cartesian Coordinates of NMP

Atom type	X (Å)	Y (Å)	Z (Å)
C	0	0	0
C	0	0	1.36586
C	1.358495	0	1.805927
C	2.196325	0	0.728276
N	1.366466	0	-0.374005
H	-0.871053	0	2.000096
H	3.267478	0	0.645162
N	1.894561	0	-1.701825
O	3.102496	0	-1.784997
O	1.084102	0	-2.601653
N	1.803692	0	3.179519
O	3.012436	0	3.387775
O	0.935229	0	4.045332
C	-1.160545	0	-0.937425
H	-1.166488	0.879154	-1.584841
H	-1.166486	-0.879152	-1.584845
H	-2.073399	0	-0.340525
Bq	0.984257	0	0.705212
Bq	0.984257	1.000000	0.705212
Bq	0.984257	-1.000000	0.705212

**TABLE 3. Cartesian Coordinates of TS2**

Atom type	X (Å)	Y (Å)	Z (Å)
C	0	0	0
C	0	0	1.389189
C	1.325318	0	1.843783
C	2.218498	-0.166088	0.64294
N	1.279326	0.031779	-0.501964
H	-0.879363	-0.034567	2.019211
N	1.756204	0.081204	3.122422
O	3.005097	0.092453	3.362227
O	0.921335	0.145681	4.080644
N	1.635523	1.77814	-0.977154
O	2.698886	1.970254	-1.537085
O	0.697902	2.549038	-0.942005
C	-1.179058	-0.044073	-0.919068
H	-1.230162	0.853011	-1.541721
H	-1.120304	-0.904051	-1.591486
H	-2.107616	-0.115257	-0.352478
H	3.041884	0.545395	0.578428
O	2.706162	-1.495092	0.601033
H	3.292445	-1.578465	-0.180205

**TABLE 4. Cartesian Coordinates of 2**

Atom type	X (Å)	Y (Å)	Z (Å)
C	-0.605022	-1.101744	-0.047263
C	0.415084	-0.242589	0.05301
C	-0.119276	1.161697	0.279999
C	-1.830133	-0.267376	0.047548
N	-1.571687	0.989821	0.18269
H	-0.569792	-2.178864	-0.159829
H	0.101539	1.459442	1.316739
O	0.328568	2.125855	-0.632344
H	0.973673	2.715048	-0.18994
N	1.807456	-0.576144	0.045256
O	2.593649	0.291373	0.428535
O	2.150364	-1.691459	-0.344983
C	-3.20715	-0.835744	-0.014293
H	-3.332967	-1.424232	-0.926843
H	-3.372053	-1.515213	0.82642
H	-3.952442	-0.043531	0.014153



**TABLE 5. Cartesian Coordinates of 3**

Atom type	X (Å)	Y (Å)	Z (Å)
C	0	0	0
C	0	0	1.367252
C	1.353329	0	1.845826
C	2.182004	0	0.767393
N	1.364342	0	-0.364496
H	-0.893195	0	1.973246
H	3.25156	0	0.664765
N	1.893498	-0.000185	-1.667981
O	3.10727	-0.000021	-1.752615
O	1.095971	-0.000483	-2.58682
C	-1.157547	0.000076	-0.941945
H	-1.162887	0.878169	-1.591405
H	-1.163274	-0.878261	-1.591076
H	-2.073254	0.000389	-0.348343
H	1.671682	0	2.876449
Bq	0.979939	0	0.723188
Bq	0.97995	0.999996	0.72312
Bq	0.979928	-1.000004	0.723256

**TABLE 6. Cartesian Coordinates of 4**

Atom type	X (Å)	Y (Å)	Z (Å)
C	0	0	0
C	0	0	1.372946
C	1.363919	0	1.780154
C	2.169544	0	0.661098
N	1.326819	0	-0.409363
H	-0.858538	0	2.023252
H	3.241821	0	0.570959
N	1.849843	0	3.129686
O	3.068694	0	3.303585
O	1.016659	0	4.033129
C	-1.124085	0	-0.982632
H	-1.101411	0.885078	-1.62715
H	-1.101409	-0.885077	-1.627151
H	-2.077064	0	-0.452975
H	1.629444	0	-1.370961
Bq	0.972056	0	0.680967
Bq	0.972056	1	0.680967

**TABLE 7. Cartesian Coordinates of 5**

Atom type	X (Å)	Y (Å)	Z (Å)
C	0	0	0
C	0	0	1.379101
C	1.35634	0	1.820854
C	2.15154	0	0.699864
N	1.319377	0	-0.398914
H	-0.881819	0	2.001831
H	3.223694	0	0.589538
C	-1.125006	0	-0.983621
H	-1.106448	0.884529	-1.630484
H	-1.106408	-0.884495	-1.63053
H	-2.078773	0	-0.454044
H	1.705118	0	2.841795
H	1.630288	0	-1.356403
Bq	0.965452	0	0.700181
Bq	0.965454	0.999993	0.700183

**TABLE 8. Cartesian Coordinates of 7**

Atom type	X (Å)	Y (Å)	Z (Å)
C	-1.795545	-0.393088	0.003452
C	-0.658694	-1.142543	-0.001216
C	0.45334	-0.228858	0.000305
C	-0.073078	1.077385	-0.005954
N	-1.415526	0.957696	-0.001671
H	-0.593506	-2.218353	0.005088
N	1.798105	-0.569649	0.00197
O	2.666596	0.325967	0.033831
O	2.103906	-1.781126	-0.026061
C	-3.233983	-0.78178	0.010034
H	-3.754356	-0.383639	0.885605
H	-3.755634	-0.411599	-0.877093
H	-3.321455	-1.867192	0.026977
H	-2.055163	1.757755	-0.037077
O	0.569679	2.234007	-0.011932
H	-0.071626	2.989226	-0.012015

**TABLE 9. Cartesian Coordinates of 8**

Atom type	X (Å)	Y (Å)	Z (Å)
C	0.624207	-1.085199	-0.510792
C	-0.517262	-0.128579	-0.688917
C	1.686883	-0.398972	-0.063243
H	-0.891073	-0.036633	-1.712114
N	1.359096	0.963882	0.125005
H	1.996379	1.680686	0.48578
H	0.59019	-2.133421	-0.768622
C	0.06495	1.223166	-0.186457
O	-0.529633	2.282984	-0.099002
N	-1.724569	-0.507257	0.149586
O	-1.616678	-0.447732	1.368058
O	-2.732584	-0.872713	-0.442296
C	3.073656	-0.859062	0.214751
H	3.792103	-0.324783	-0.412541
H	3.342445	-0.66431	1.256653
H	3.16483	-1.926357	0.022573

TABLE 10. Cartesian Coordinates of 9

Atom type	X (Å)	Y (Å)	Z (Å)
C	0.519622	-1.096509	-0.276489
C	-0.435153	-0.175305	-0.103707
C	1.846605	-0.414123	-0.392098
H	2.24049	-0.601956	-1.404232
H	0.398044	-2.172625	-0.313549
C	0.154399	1.209112	-0.100192
O	-0.408155	2.292432	-0.009755
N	-1.834802	-0.479402	0.064987
O	-2.56433	0.395766	0.518001
O	-2.221244	-1.60522	-0.246329
N	1.484804	0.98804	-0.250001
H	2.153164	1.754204	-0.352022
C	2.880168	-0.888336	0.640021
H	3.100497	-1.945712	0.489283
H	3.805293	-0.324051	0.520134
H	2.508498	-0.743184	1.654931

**TABLE 11. Cartesian Coordinates of 10**

Atom type	X (Å)	Y (Å)	Z (Å)
C	-1.782108	-0.125632	0.025913
C	-0.707887	-1.053155	0.553394
C	0.490008	-0.12654	0.672432
N	-1.398315	1.078141	-0.256088
H	-1.000192	-1.48869	1.511225
C	-3.180898	-0.586593	-0.152018
H	-3.575131	-0.937768	0.806424
H	-3.81449	0.205406	-0.543497
H	-3.200764	-1.447615	-0.82677
H	-0.542638	-1.874359	-0.147715
C	-0.024952	1.201056	0.021415
O	0.647575	2.17566	-0.192234
N	1.723794	-0.567937	-0.058052
O	2.796707	-0.208512	0.404465
O	1.591227	-1.212151	-1.090369
H	0.805816	0.076817	1.697595

**TABLE 12. Cartesian Coordinates of 11**

Atom type	X (Å)	Y (Å)	Z (Å)
C	-1.835966	-0.23136	-0.00003
C	-0.660359	-1.171981	0.000065
C	0.46463	-0.189661	-0.000014
C	-0.092044	1.072918	-0.000041
N	-1.488573	1.022891	-0.000167
H	-0.677983	-1.826871	0.878622
C	-3.252344	-0.677654	0.000045
H	-3.450298	-1.299378	0.877765
H	-3.928869	0.174338	-0.001599
H	-3.449616	-1.302452	-0.87561
H	-0.677999	-1.827028	-0.878378
N	1.808034	-0.528095	0.000009
O	2.675435	0.365442	0.000142
O	2.10324	-1.741255	-0.000152
O	0.516374	2.230908	0.00008
H	-0.15536	2.96349	-0.000402



**TABLE 13. Cartesian Coordinates of 12**

Atom type	X (Å)	Y (Å)	Z (Å)
C	1.743377	-0.301305	-0.080583
C	0.740811	-1.049963	-0.57443
C	-0.459556	-0.162462	-0.688359
C	0.098189	1.126242	-0.082114
N	1.33955	1.046543	0.226913
H	0.771728	-2.079045	-0.90138
C	3.163019	-0.67406	0.161226
H	3.830204	-0.042686	-0.431623
H	3.423068	-0.513126	1.210979
H	3.345542	-1.717084	-0.093409
N	-1.675248	-0.621396	0.101297
O	-1.501369	-1.015448	1.244562
O	-2.763509	-0.551733	-0.451578
O	-0.698901	2.169816	0.050408
H	-0.203384	2.925264	0.464391
H	-0.822088	-0.001144	-1.707997

TABLE 14. Cartesian Coordinates of 13

Atom type	X (Å)	Y (Å)	Z (Å)
C	-1.880447	-0.309653	-0.414724
C	-0.626979	-1.122382	-0.303602
C	0.374152	-0.24855	-0.107762
C	-0.208325	1.112587	-0.084844
N	-1.481451	1.093021	-0.251813
H	-0.563922	-2.201815	-0.374208
C	-2.976437	-0.720589	0.581872
H	-2.622875	-0.615074	1.608175
H	-3.846522	-0.079386	0.444739
H	-3.273289	-1.756457	0.414959
O	0.476918	2.240796	0.08503
H	1.425595	2.042243	0.197478
N	1.763355	-0.566472	0.050101
O	2.120497	-1.735776	0.006326
O	2.539064	0.38214	0.225031
H	-2.275935	-0.441105	-1.435893

TABLE 15. Cartesian Coordinates of TS1+2H<sub>2</sub>O

Atom type	X (Å)	Y (Å)	Z (Å)
C	0.810789	-1.357268	0.792412
C	-0.532844	-1.542552	0.902515
C	-1.175846	-0.850646	-0.184154
C	-0.221155	-0.165831	-0.924765
N	0.988291	-0.546377	-0.376996
H	-1.025799	-2.109011	1.683759
N	2.192157	-0.142376	-0.938737
O	2.124043	0.590943	-1.920649
O	3.221788	-0.562842	-0.421475
N	-2.538645	-0.819405	-0.459364
O	-3.316486	-1.456965	0.290937
O	-2.954259	-0.160469	-1.44166
C	1.905452	-1.843899	1.682579
H	2.592457	-2.520217	1.165735
H	2.498573	-1.018515	2.087672
H	1.442588	-2.38362	2.512976
H	-0.285114	0.290829	-1.898456
O	-0.277817	2.000001	-0.151784
H	-0.28558	2.515853	-0.980859
H	-1.586787	2.286211	0.73348
O	-2.369214	2.499755	1.344184
H	-3.164526	2.17193	0.894088
H	1.122663	2.188658	0.596377
O	2.024834	2.283962	1.052927
H	1.857415	2.141077	1.999553

**TABLE 16. Cartesian Coordinates of Pyridine**

Atom type	X (Å)	Y (Å)	Z (Å)
C	-1.880447	-0.309653	-0.414724
C	-0.626979	-1.122382	-0.303602
C	0.374152	-0.24855	-0.107762
C	-0.208325	1.112587	-0.084844
N	-1.481451	1.093021	-0.251813
H	-0.563922	-2.201815	-0.374208
C	-2.976437	-0.720589	0.581872
H	-2.622875	-0.615074	1.608175
H	-3.846522	-0.079386	0.444739
H	-3.273289	-1.756457	0.414959
O	0.476918	2.240796	0.08503
H	1.425595	2.042243	0.197478
N	1.763355	-0.566472	0.050101
O	2.120497	-1.735776	0.006326
O	2.539064	0.38214	0.225031
H	-2.275935	-0.441105	-1.435893

TABLE 17. Cartesian Coordinates of TS9+PYR

Atom type	X (Å)	Y (Å)	Z (Å)
C	-0.070718	-0.068841	-0.004859
C	0.009759	0.030804	1.370857
C	1.344721	-0.088017	-0.547259
H	1.480131	0.660243	-1.337999
H	-0.884309	-0.540083	-0.547075
C	1.411301	0.297317	1.793486
O	1.876162	0.505566	2.92088
N	-1.100552	-0.09047	2.21802
O	-0.94048	-0.067144	3.454906
O	-2.232319	-0.21956	1.698265
N	2.125704	0.27701	0.632205
H	3.144357	0.393245	0.61996
C	1.718095	-1.476213	-1.098666
H	1.101432	-1.716841	-1.972142
H	2.76856	-1.47698	-1.409121
H	1.577208	-2.252422	-0.33855
N	-0.830074	1.807019	-0.794573
C	-0.500438	2.977652	-0.234863
C	-1.516812	1.784758	-1.944635
C	-0.842178	4.196228	-0.821964
H	0.046478	2.933533	0.708752
C	-1.897312	2.956765	-2.599595
H	-1.762155	0.800425	-2.348548
C	-1.549142	4.183638	-2.027338
H	-0.556588	5.130478	-0.340579
H	-2.455335	2.901895	-3.53314
H	-1.827215	5.118821	-2.513283

Supporting Information - For Review Only - Not for Publication

### **3. Identification of Intermediates**

### 1,4-Dinitro-2-methylpyrrole (NMP)

UV  $\lambda_{\max}$  in nm ( $\epsilon$ ,  $M^{-1}cm^{-1}$ ): 209 (11621  $\pm$  123), 229 (17428  $\pm$  135), 270 (13551  $\pm$  107), 329 (8764  $\pm$  66), 385 (1806  $\pm$  19).

$^1H$ -NMR ( $CDCl_3$ ):  $\delta$  2.64 (s, 3H,  $CH_3$ ), 7.9 (d, 1H,  $CH-C-NO_2$ ), 8.8 (d, 1H,  $CH-N-NO_2$ ).

Accurate mass calculated for  $C_5H_5N_3O_4Na$  ( $M^+Na$ ): 194.017227, found: 194.0187.

### 5-Methyl-3-nitro-1H-pyrrol-2-ol (Isomer 7)

The identification of the intermediates was performed in water medium.

$^1H$ -NMR ( $D_2O$ ):  $\delta$  2.5 (s, 3H,  $CH_3$ ), 8.2 (s, 1H, CH).

$^{13}C$  (D<sub>2</sub>O):  $\delta$  20 ( $CH_3$ ), 120 ( $-CH=$ ), 130 (C-OH), 140 (C- $CH_3$ ), 146 (C- $NO_2$ ).

**Comment [m1]:** Hay que poner los valores exactos. Mirar espectros originales

Mass-charge relation:  $m/z = 144$

### 4-Hydroxy-5-methyl-3-nitro-pyrrolidin-2-one (14)

Mass-charge relation:  $m/z = 161$