# An Unusual Rearrangement and its Dependence on Configuration[1])

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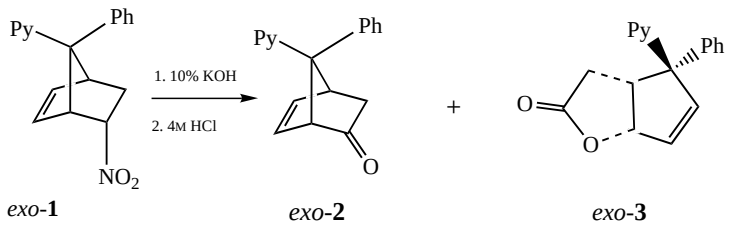
In honor of *Edgar Heilbronner* and his 80th birthday. While this is not one of our theoretical publications, we remember that *Edgar* did begin his career as a traditional organic chemist.

In the course of a synthetic study, we encountered an unusual rearrangement that we now report, one that involves a 5-nitronorbornenyl system having 7-*endo*- and 7-*exo*-pyridin-2-yl groups being treated under *Nef*-reaction conditions. The stereoisomers differ in their *Nef*-reaction behavior: the isomer with the pyridin-2-yl group *exo* to the $NO_2$ moiety primarily affords the *Nef* reaction, however, with formation of a rather unusual rearrangement side-product. The *endo*-pyridyl stereoisomer proceeded exclusively with rearrangement.

**Introduction and Results.** – Our research has ranged from theoretical to synthetic. In continuing our research on the stereochemistry of kinetic protonation of delocalized carbanions, which now has stretched over five decades [2], we recently turned to the question of intramolecular delivery. The intent was to reverse the normal delivery to the less-hindered side of the carbanions [2c]. In the course of this research, we utilized the two phenyl-pyridyl-nitro norbornenes *exo*-**1** and *endo*-**1**, which differ only in the *endo*- *vs.* *exo*-configuration of the phenyl (Ph) and pyridin-2-yl (Py) groups. Our objective was the transformation of the two $NO_2$ isomers into the corresponding ketones *exo*-**2** and *endo*-**2** by use of the *Nef* reaction[2]). Serendipitously, this led to an unanticipated and interesting reaction.

Thus, as shown in *Scheme 1*, the *exo*-2-Py stereoisomer *exo*-**1** under typical *Nef* conditions, afforded the desired ketone *exo*-**2** in 67% yield. However, a second product, *exo*-**3** was obtained in 15% yield along with some reactant (*ca.* 13%).

*Scheme 1*




*exo*-**1** *exo*-**2** *exo*-**3**

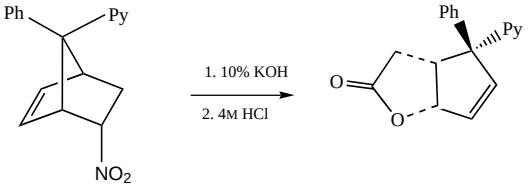
[1]) Part 262 of our general series; Part 260: [1a]; Part 261: [1b].

[2]) It has been suggested that the *Nef* reaction of 5-nitrobornenes does not operate [3a]; however, it has been reported [3b] that 7-silyl derivatives do undergo the *Nef* reaction successfully.

The second product (m.p. 111–112°) had a C=O peak in the IR at 1773 $cm^{-1}$ that clearly did not correspond to a norbornyl ketone. A high-resolution mass spectrum gave molecular weight of 277.1101, indicating a molecular formula of $C_{18}H_{15}NO_2$. Thus, the mass was subjected to a convenient program 'Analyzer'[3]), which suggested one Ph group, one Py group, one vinyl group, two methines, one $CH_2$, one COO group, and one extra C-atom. The NMR spectrum was consistent with this result, and one structure suggested by the NMR spectrum was that of *exo*-**3**. This was confirmed by X-ray analysis. Thus, we may write the reaction as in *Scheme 1* and the structure as shown. It is seen that this product results from an unexpected rearrangement.

Interestingly, the stereoisomeric nitronorbornene *endo*-**1**, having the 2-Py group *endo*, gave *only* the rearranged type product, here *endo*-**3** (*Scheme 2*). Also, in all of these reactions, a transient blue color, characteristic of nitroso compounds, was observed.

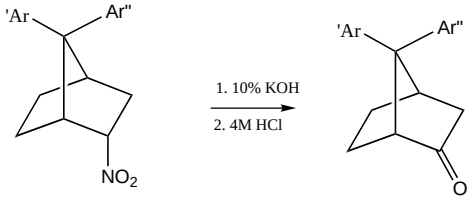
*Scheme 2*




*endo*-**1** *endo*-**3**

It was found that the norbornene C=C bond was requisite for the rearrangement. Thus, the corresponding nitronorbornanes *endo*-**4** and *exo*-**4** gave only the normal *Nef* ketones *endo*-**5** and *exo*-**5**, respectively (*Scheme 3*). Curiously, the reaction of the dihydro *endo*-pyridyl stereoisomer *endo*-**4** was found to be considerably slower than the reactions of the other nitro compounds.

*Scheme 3*




*endo*-**4** Ar' = Ph, Ar'' = Py *endo*-**5**
*exo*-**4** Ar' = Py, Ar' = Ph *exo*-**5**

**Discussion.** – The reaction has some uncertain precedent in the literature, having been reported by *Ranganathan* and co-workers [4], where products resulting from

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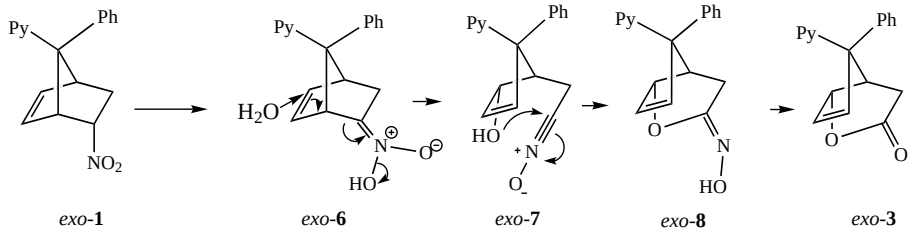
[3]) H. E. Zimmerman, Analyzer, a program that determines which linear combination of potentially available groups sums up to the given high-resolution mass.

fragmentation of a norbornene ring were reported with the formation of hydroxamic esters and their conversion to $\gamma$-lactones, along with a variety of other products.

The reaction mechanism for the abnormal *Nef* rearrangement of *exo*-**1** is proposed in *Scheme 4*. The curious pattern of reactivity encountered is outlined in the *Table.*

Scheme 4. *Proposed Mechanism for Lactone Formation from* exo-**1**, *under* Nef *Conditions*




*exo*-**1** *exo*-**6** *exo*-**7** *exo*-**8** *exo*-**3**

Table. *Pattern of Reactivity*

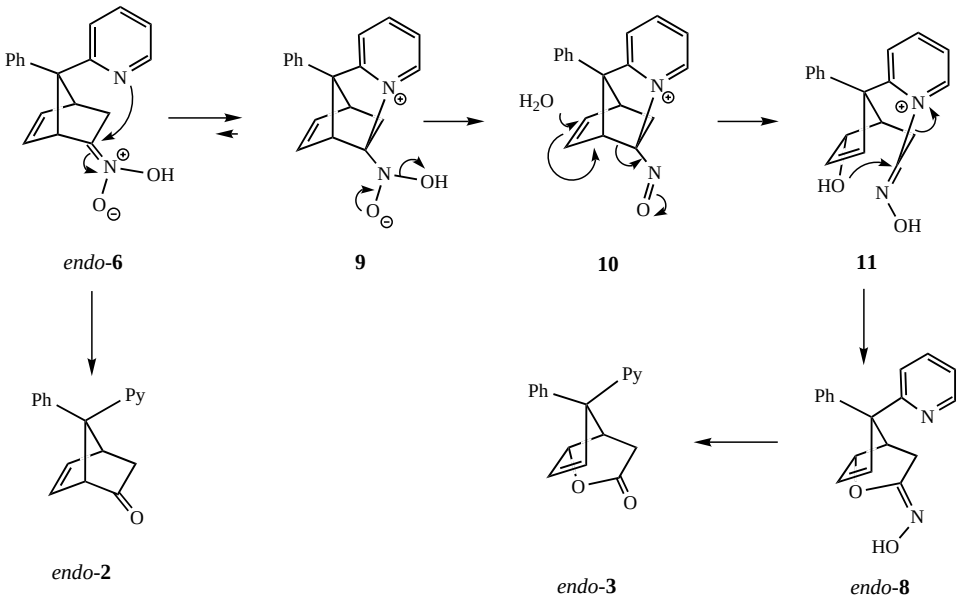
| Reactant | *Nef* product (yield/%) | Rearrangement product (yield/%) | Qualitative rate[a]) |
|---|---|---|---|
| *endo*-**1** | None | *endo*-**3** (83%) | Fast |
| *exo*-**1** | *exo*-**2** (82%)[b]) | *exo*-**3** (18%)[b]) | Fast |
| *endo*-**4** | *endo*-**5** (53%) | None | Slow |
| *exo*-**4** | *exo*-**5** (78%)[b]) | None | Fast |

[a]) Fast dissipation of blue color in 1 h; slow dissipation in 50 h. [b]) Based on 82% conversion.

The reaction sequence for *endo*-**1** is outlined in *Scheme 5*. The overall situation is summarized by the statement that an *endo*-2-Py group inhibits the *Nef* reaction while not affecting the fragmentation rearrangement. Thus, in the case of *endo*-**1**, with its *endo*-Py moiety, no *Nef* reaction occurs, and only the rearrangement proceeds. However, in the case of *exo*-**1** with a Ph group proximate to the $NO_2$ function, both the *Nef* reaction and the fragmentation rearrangement compete. With no C=C bond present, as in the dihydro reactants *endo*-**4** and *exo*-**4**, no rearrangement of the type depicted in *Scheme 4* is possible, and only the *Nef* reaction occurs. However, again, the *endo*-Py group of *endo*-**4** is *Nef*-inhibiting, and the reaction rate is slow. The inhibition of the *Nef* reaction by the *endo*-Py group is understood to proceed by the same mechanism depicted in *Scheme 5* for the *endo* dehydro system, in which the 2-Py N-atom adds to the nitronic acid $\pi$-bond, thus eliminating the possibility of $H_2O$ addition and ketone formation. Throughout, we assume the normal *Nef* mechanism for the *endo*-Py compounds but recognize that it is possible that nucleophilic $H_2O$ attack may instead intervene at a later stage.

Hence, in conclusion, we find that an *endo*-2-Py inhibits (slows) the *Nef* reaction but not the rearrangement. If both are *a priori* possibilities, one obtains only the rearrangement due to inhibition of the *Nef* reaction. If there is no C=C bond and only the *Nef* reaction is a possibility, it does proceed, but slowly due to the inhibition. Thus, our mechanistic reasoning leads us to the conclusion that, on abstracting a proton, the nitronate may rearrange directly as in *Scheme 4* or, instead, in the case of the *endo*-Py nitronate, may rearrange after Py bridging.

Scheme 5. *Selective Inhibition of the* Nef *Reaction*




**Conclusion.** – This report is a good illustration of serendipity. In the course of synthetic efforts aimed at precursors desired for one mechanistic study, some particularly interesting mechanistic and synthetic observations were encountered. Additionally, it seems that the present synthetic method constitutes an interesting example of a norbornene to norbornenone transformation under *Nef* conditions.

## Experimental Part

*General*. Column chromatography (CC) was performed on silica gel *60 Geduran* 35–75 μm and slurry packed into column. M.p.: uncorrected. IR Spectra ($CDCl_3$): $\tilde{\nu}$ in $cm^{-1}$. $^1$H- and $^{13}$C-NMR spectra: *Bruker AC-300*, $CDCl_3$ as solvent, $\delta$ in ppm, $J$ in Hz.

*7*-endo-*Phenyl-7*-exo-*(pyridin-2-yl)bicyclo[2.2.1]hept-5-en-2-one* (*exo*-**2**) *and 3,3a,4,6a-Tetrahydro-4*-endo-*phenyl-4*-exo-*(pyridin-2-yl)-2*H-*cyclopenta[*b*]furan-2-one* (*exo*-**3**). *5-Nitro-7*-endo-*phenyl-7*-exo-*(pyridin-2-yl)-bicyclo[2.2.1]hept-2-ene* (*exo*-**1**; 1.5 g, 5.1 mmol) was stirred in 85 ml of 10% KOH overnight at r.t., HCl (120 ml, 4M) was then added. The yellow suspension became green-blue. The mixture was stirred for 1.5 h. The color changed to light yellow, and then the mixture was heated at 90° for 2.5 h. The soln. was cooled, neutralized with $NaHCO_3$, and extracted with $CH_2Cl_2$. The combined org. layers were dried ($MgSO_4$) and concentrated to yield a brown oil, which was chromatographed (silica gel; $CH_2Cl_2/Et_2O$ 9:1). Crystallization yielded 0.20 g (15%) of *exo*-**3** and 0.90 g (67%) of *exo*-**2**.

*Data of* exo-**3** Colorless needles. M.p. 111–112°. $R_f$ 0.58. IR ($CDCl_3$): 1773. $^1$H-NMR ($CDCl_3$): 8.54 (*d*, $J$ = 5.0, 1 H); 7.50 (*td*, $J$ = 8.0, 2.0, 1 H); 7.38–7.09 (*m*, 6 H); 6.85 (*d*, $J$ = 8.0, 1 H); 6.44 (*d*, $J$ = 6.0, 1 H); 5.99 (*d*, $J$ = 6.0, 1 H); 5.87 (*d*, $J$ = 7.0, 1 H); 4.58 (*m*, 1 H); 2.20 (*dd*, $J$ = 13.5, 10.0, 1 H); 1.99 (*dd*, $J$ = 13.5, 9.0, 1 H). $^{13}$C-NMR ($CDCl_3$): 176.76; 164.56; 148.72; 143.50; 140.28; 136.35; 129.91; 128.83; 127.87; 127.27; 123.22; 121.64; 89.25; 66.70; 46.03; 32.43. HR-MS: 277.1101 ($M^+$, $C_{18}H_{15}NO_2^+$; calc. 277.1103).

*Data of* exo-**2**: White powder. M.p. 178°. $R_f$ 0.45. IR ($CDCl_3$): 1742. $^1$H-NMR ($CDCl_3$): 8.49 (*d*, $J$ = 5.0, 1 H); 7.55–6.95 (*m*, 8 H); 6.60 (*dd*, $J$ = 6.0, 3.0, 1 H); 5.96 (*dd*, $J$ = 6.0, 3.0, 1 H); 4.19 (*s*, 1 H); 4.09 (*m*, 1 H); 1.95 (*s*, 2 H). $^{13}$C-NMR ($CDCl_3$): 213.26; 162.37; 148.81; 143.93; 141.45; 136.00; 128.84; 127.98; 127.09; 126.98; 122.02; 121.00; 62.65; 46.79; 35.91. HR-MS: 261.1153 ($M^+$, $C_{18}H_{15}NO_2^+$; calc. 261.1154).

*3,3a,4,6a-Tetrahydro-4-*exo*-phenyl-4-*endo*-(pyridin-2-yl)-2*H*-cyclopenta[*b*]furan-2-one* (*endo*-**3**). *5-Nitro-7-*exo*-phenyl-7-*endo*-(pyridin-2-yl)bicyclo[2.2.1]hept-2-ene* (*endo*-**1**; 60 mg, 0.2 mmol) was stirred mechanically in 4.0 ml of 10% KOH overnight at r.t. in a 25-ml flask to afford a yellow soln. HCl (5.6 ml, 4M) was added, the mixture became light blue, then the color disappeared in 5 min. The mixture was stirred at r.t. for 1 h, then at 90° for 2.5 h. The soln. was cooled and neutralized with $NaHCO_3$ to pH *ca.* 8 and extracted with $CH_2Cl_2$. The combined org. layers were dried ($MgSO_4$) and concentrated to yield a brown oil, which was subjected to CC ($CH_2Cl_2$/hexane/$Et_2O$ 2:2:1) to yield 45 mg (83%) of *endo*-**3**. Yellow oil, $R_f$ 0.20. IR ($CDCl_3$): 1775. $^1$H-NMR ($CDCl_3$): 8.61 (*d*, *J* = 5.0, 1 H); 7.63 (*td*, *J* = 8.0, 1.8, 1 H); 7.33–7.14 (*m*, 6 H); 7.10 (*d*, *J* = 8.0, 1 H); 6.73 (*d*, *J* = 6.0, 1 H); 6.00 (*dd*, *J* = 6.0, 1.5, 1 H); 5.73 (*d*, *J* = 7.0, 1 H); 4.01 (*td*, *J* = 9.0, 7.0, 1 H); 2.38 (*dd*, *J* = 18.0, 9.0, 1 H); 2.07 (*dd*, *J* = 18.0, 9.0, 1 H). $^{13}$C-NMR ($CDCl_3$): 176.15; 163.08; 149.12; 145.62; 141.50; 136.58; 128.69; 127.82; 126.77; 126.39; 122.74; 121.83; 88.15; 65.67; 47.86; 32.75. HR-MS: 277.1101 ($M^+$, $C_{18}H_{15}NO_2^+$; calc. 277.1103).

*7-*endo*-Phenyl-7-*exo*-(pyridin-2-yl)bicyclo[2.2.1]heptan-2-one* (*exo*-**5**). Compound *exo*-**1** (2.0 g, 6.9 mmol) and potassium azodiformate (4.0 g, 20.6 mmol) were stirred in 70 ml of MeOH in an ice-bath. A soln. (5.0 ml) of AcOH (48.0 mmol) in MeOH was slowly added during 3 h, then stirred for an additional 3 h. The mixture was added to 60 ml of dilute $NaHCO_3$ soln. and extracted with $CH_2Cl_2$. The combined org. layers were dried ($MgSO_4$) and concentrated to yield 1.98 g solid, which was used for the *Nef* reaction without further purification. The crude product was treated with 100 ml of 10% KOH, stirred for 36 h, then treated with 140 ml of 4M HCl. The soln. became blue immediately and was stirred for 1 h at r.t., then at 90° for 2.5 h. The mixture was cooled, neutralized with $NaHCO_3$ powder to pH of *ca.* 7–8, extracted with $CH_2Cl_2$, and concentrated to yield a solid, which was subjected to CC (silica gel; $CH_2Cl_2$/hexane/$Et_2O$ 2:2:1) to yield 1.4 g (78%) of *exo*-**5**, which was crystallized from $Et_2O$/hexane soln. Colorless crystals. M.p. 196°. $R_f$ 0.33. IR ($CDCl_3$): 1732. $^1$H-NMR ($CDCl_3$): 8.54 (*d*, *J* = 5.0, 1 H); 7.55 (*td*, *J* = 8.0, 1.8, 1 H); 7.49–7.01 (*m*, 7 H); 3.64 (*m*, 2 H); 2.20–1.50 (*m*, 6 H). $^{13}$C-NMR ($CDCl_3$): 216.22; 162.01; 149.37; 141.92; 136.50; 128.72; 127.71; 126.72; 121.63; 121.22; 64.99; 56.41; 44.19; 41.97; 26.54; 22.58. HR-MS: 263.1310 ($M^+$, $C_{18}H_{17}NO^+$; calc. 263.1310).

*7-*exo*-Phenyl-7-*endo*-(pyridin-2-yl)bicyclo[2.2.1]heptan-2-one (endo-***5***)*. Compound *endo*-**1** (1.1 g, 3.8 mmol) and potassium azodiformate (2.0 g, 10.0 mmol) were stirred in 40 ml of MeOH in an ice-bath. A soln. (5.0 ml) of AcOH (24 mmol) in MeOH was slowly added during 2 h, and then stirred for 1.5 h. The mixture was poured into 50 ml of $H_2O$, neutralized with $NaHCO_3$, and extracted with $CH_2Cl_2$. Combined org. layers were dried ($MgSO_4$) and concentrated to yield the crude product that was used for the *Nef* reaction without further purification. The crude product was stirred with 70 ml of 10% KOH overnight, and then treated with 98 ml of 4M HCl, the soln. became blue immediately. Stirred for 2 h at r.t., then heated in an oil bath (100–105°) for 50 h. The color changed slowly from blue to green, and, finally, a yellow-green soln. was obtained. The soln. was cooled and neutralized with $NaHCO_3$ to pH of *ca.* 7–8, and extracted with $CH_2Cl_2$. The combined org. layers were dried ($MgSO_4$) and concentrated to yield the crude product, which was subjected to CC (silica gel; $CH_2Cl_2$/hexane/$Et_2O$ 2:2:1) to yield 0.53 g (53%) of *endo*-**5**. M.p. 157–159°. $R_f$ 0.32. IR ($CDCl_3$): 1744. $^1$H-NMR ($CDCl_3$): 8.45 (*d*, *J* = 5.0, 1 H); 7.48–7.12 (*m*, 7 H); 6.94 (*ddd*, *J* = 7.5, 5.0, 1.0, 1 H); 3.64 (*d*, *J* = 4.0, 1 H); 3.58 (*m*, 1 H); 2.12–1.80 (*m*, 4 H); 1.62–1.46 (*m*, 2 H). $^{13}$C-NMR ($CDCl_3$): 215.90; 162.21; 148.98; 141.33; 136.33; 128.53; 126.90; 126.44; 122.38; 121.15; 65.24; 56.23; 44.15; 41.86; 26.41; 22.30. HR-MS: 263.1311 ($M^+$, $C_{18}H_{17}NO^+$; calc. 263.1310).

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