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The first example of fluoro-Meinwald rearrangement

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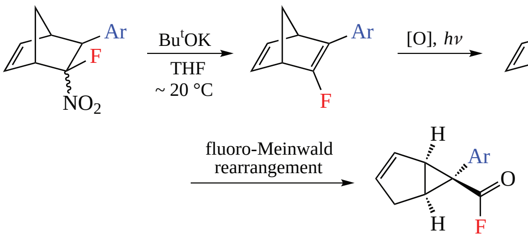
Novel fluorinated norbornadienes were synthesized in up to 95% yield by the base-induced elimination of HNO_2 from 5-fluoro-5-nitro-6-arylbicyclo[2.2.1]hept-2-enes prepared, in turn, by the Diels–Alder reaction of β-fluoro-β-nitrostyrenes with cyclopentadiene. The subsequent epoxidation initiated the Meinwald type rearrangement affording 6-arylbicyclo[3.1.0]hex-2-ene-6-carboxylic acid fluorides as individual (1*SR*,5*RS*,6*RS*)-diastereomers. The transformation is the first example of fluoro-Meinwald rearrangement to form the corresponding acyl fluorides.



Keywords: nitrostyrene, Diels–Alder reaction, norbornene, norbornadiene, epoxidation, Meinwald rearrangement, acyl fluorides, bicyclo[3.1.0]hex-2-ene-6-carboxylic acids, organofluorine compounds.

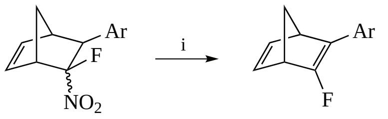
We dedicate this article to Irina Petrovna Beletskaya, a brilliant scientist, whom we always admire and whose achievements in science give us an example in life.

Norbornadiene and its derivatives are important objects of modern organic chemistry and chemical engineering. The strained structure and the presence of homoconjugated double bonds make the norbornadiene molecule highly reactive.[1] Such compounds found a wide application as important synthetic intermediates and useful building blocks in organic synthesis,[2–4] in particular, as active monomers.[5–7] The ability to undergo the valence photoisomerization into quadricyclane makes norbornadiene an effective molecular system for the storage of solar energy.[8–10] On the other hand, fluorinated norbornadienes are very rare and almost unexplored.[11,12] Considering the exceptional importance of fluorine-containing compounds in organic chemistry and chemistry of materials,[13] the development of new routes to fluorinated norbornadienes and study of their chemical properties are essential issues.

Previously, we have described the preparation of 6-aryl-5-fluoro-5-nitronorbornenes **1** *via* the Diels–Alder reaction of β-fluoro-β-nitrostyrenes[14,15] with cyclopentadiene.[16] In this study, we present the effective and selective synthesis of novel 3-aryl-2-fluoronorbornadienes **2** (Scheme 1). Moreover, in the frames of this study we discovered the Meinwald-type rearrangement[17] of 2-fluoro-3-arylnorbornadienes **2** into novel bicyclic acyl fluorides.

To our delight, the base-induced elimination of nitrous acid from 6-aryl-5-fluoro-5-nitronorbornenes **1a–f** occurs selectively leading cleanly to fluorinated norbornadienes **2a–f** (see Scheme 1). No elimination of HF to form the corresponding nitronorbornadienes was observed. These data can be explained by *syn*-elimination which is typical of norbornenes.[18] Since fluoro derivatives **2** turned out to be very unstable, it was necessary to find the optimal conditions for elimination and purification (see Online Supplementary Materials). As a result, a set of novel norbornadienes **2a–f** was obtained in yields up to 95%.

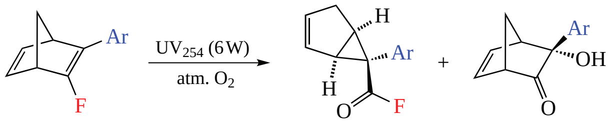
We noticed significant changes in ^{19}F NMR spectrum of compound **2a** upon standing in solution. A new doublet peak at positive area (46.6 ppm) appeared in its ^{19}F NMR spectrum indicating deep structural changes. We found that this transformation proceeds faster and more efficiently with exposure of UV irradiation (Scheme 2). As a result, novel



1a–f **2a–f**

a Ar = 4-ClC_6H_4, 89%
b Ar = 4-BrC_6H_4, 80%
c Ar = Ph, 81%
d Ar = 4-$Bu^tC_6H_4$, 78%
e Ar = 2,6-$Cl_2C_6H_3$, 95%
f Ar = 4-$O_2NC_6H_4$, 77%

Scheme 1 *Reagents and conditions*: **1** (0.2 mmol), Bu^tOK (0.4–0.8 mmol), THF (1 ml), room temperature, ~18 h.



2a–c	**3a–c**	**4a–c**
a Ar = 4-ClC_6H_4	**a** 45% (57%)	**a** 19%
b Ar = 4-BrC_6H_4	**b** 43% (45%)	**b** 18%
c Ar = Ph	**c** 30% (34%)	**c** traces

Scheme 2 Isolated yields; ^{19}F NMR yields are given in parentheses.

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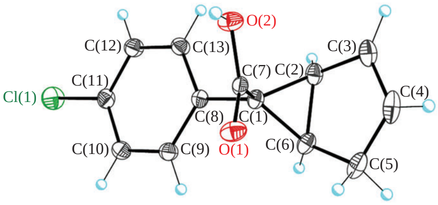
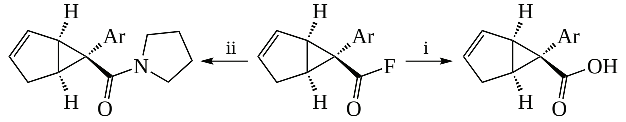


Figure 1 Ellipsoid plot drawing for compound **5a** with 50% probability.

bicyclic acyl fluoride **3a** of bicyclo[3.1.0]hex-2-ene series was isolated in 45% yield. The structure was unambiguously proved by combination of NMR, FTIR (see Online Supplementary Materials) and X-ray diffraction analysis of the corresponding carboxylic acid **5a** (Figure 1).† Bicyclic compound **5a** represents the 1*SR*,2*RS*,6*RS*-diastereomer. Such a transformation looks similar to the Meinwald rearrangement previously discovered in the course of epoxidation of norbornadiene with peroxyacetic acid to form the corresponding bicyclic aldehyde.[19] Therefore, we discovered the first example of fluoro-Meinwald rearrangement. It should be noted that we found no examples of similar rearrangement for other halogenated norbornenes.

In order to confirm the nature of the new rearrangement observed, we treated fluoronorbornadienes **2** with *m*-chloroperoxybenzoic acid in the dark under inert atmosphere. We found that the formation of the same acyl fluoride **3** took place upon epoxidation. Besides, the formation of non-fluorinated hydroxy ketones **4** as side products was observed for both procedures.

We demonstrated some transformation of acyl fluorides **3** (Scheme 3) typical of acyl halides. For example, their hydrolysis afforded the corresponding carboxylic acids **5**. The reaction of **3a,b** with pyrrolidine gave the corresponding amides **6a**,**b**.

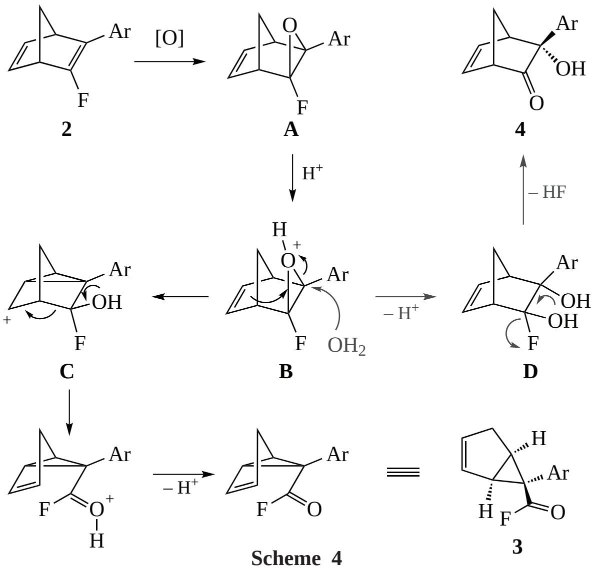


6a,**b**
a 89%
b 95%

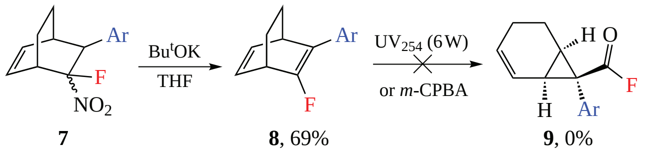
3a,**b**
a Ar = 4-ClC$_6$H$_4$
b Ar = 4-BrC$_6$H$_4$

5a,**b**
a 90%
b 93%

Scheme 3 *Reagents and conditions*: i, NaOH, room temperature, 15 h, then HCl; ii, pyrrolidine, CH$_2$Cl$_2$, room temperature, 5 min.



Scheme 4



Ar = 2,4-Cl$_2$C$_6$H$_3$

Scheme 5

We proposed the following reaction mechanism based on the Meinwald rearrangement that involves the formation of the epoxide intermediate (Scheme 4). We believe that the key step is the ring opening of oxirane **A**. Due to significant strain this intermediate would very easily transform into carbocation **C** by protonation. The intermediate **B** is transformed into **4** by hydration through intermediate **D**, however, the major direction is its rearrangement into **3** through intermediate **C**.

To confirm that strain can be the driving force of the reaction, we decided to study the similar reaction with homologous fluorinated bicyclic system, namely, bicyclo[2.2.2]oct-2-ene (Scheme 5). Elimination of nitrous acid from cycloadduct **7** proceeded smoothly to form the corresponding bicyclo[2.2.2]-octa-2,5-diene **8**. However, our attempt to perform the Meinwald rearrangement into **9** was not successful both under UV-irradiation and in the presence of *m*-CPBA.

In summary, base-induced HNO$_2$ elimination from fluoro(nitro)norbornenes **1** was accomplished to prepare a set of novel fluorinated norbornadienes **2**. The latter were found to undergo the fluoro-Meinwald rearrangement under UV-irradiation to give bicyclic acyl fluorides **3**. The driving force of the transformation is the significant strain of the epoxide intermediate formed *via* oxidation of fluorinated norbornadienes **2**.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2023.02.012.

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† *Crystal data for* **5a**. A colourless prismatic crystal [C$_{13}$H$_{11}$O$_2$Cl (M_r = 234.67)] is triclinic, space group $P\bar{1}$, at T = 100 K, a = 6.7007(1), b = 6.8092(1) and c = 13.0057(3) Å, α = 79.316(1)°, β = 85.340(1)°, γ = 78.852(1)°, V = 571.479(18) Å^3, Z = 2, d_{calc} = 1.364 g cm^{-3}, F(000) = 244, μ = 0.315 mm^{-1}. 10626 reflections (4104 independent reflections, R_{int} = 0.025) were measured and used in the refinement. The refinement converged to R_1 = 0.039 for 3435 observed reflections with $I > 2\sigma(I)$ and wR_2 = 0.102 for all independent reflections, S = 1.026. The measurements were performed on a Bruker D8 QUEST diffractometer using a PHOTON III CCD detector [λ(MoK$_\alpha$)-radiation, graphite monochromator, φ and ω scan mode] and corrected for absorption using the SADABS program.[20] The data were indexed and integrated using the SAINT program.[21] The structure was determined by direct methods[22] and refined by full-matrix least squares technique on F^2 with anisotropic displacement parameters for non-hydrogen atoms. The hydrogen atom of the hydroxy group was objectively localized in the difference-Fourier map and refined isotropically with fixed isotropic displacement parameters [U_{iso}(H) = 1.5U_{eq}(O)]. The other hydrogen atoms were placed in calculated positions and refined within riding model with fixed isotropic displacement parameters [U_{iso}(H) = 1.5U_{eq}(C) for the methyl groups and 1.2U_{eq}(C) for the other groups]. The calculations were carried out using the SHELXTL program.[23]

CCDC 2189233 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

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