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The synthesis of fluorinated endcaps: Part 2. Preserving the *endo,endo* configuration in the monohydrolysis of 7-fluorinated nadic diesters

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ABSTRACT

Fluorination should impart greater thermal-oxidative stability to the versatile norbonenyl system. *Anti*-7-Fluoronadic and 7,7-difluoro nadic acid esters (5-norbornenyl-2-*endo*,3-*endo*-acid esters) **5c** and **5d** were synthesized as precursors for a variety of uses including the manufacture of high temperature aerospace polyimides (**7c** and **7d**). Acid ester **5c** and **5d** cannot be simply prepared by the saponification of symmetrical diesters **3c** and **3d** because of concomitant epimerization. We have developed an alternative approach, involving the preparation and monohydrolysis of the mixed *t*-butyl methyl diesters **8c** and **8d** – while maintaining the *cis-endo,endo* configuration around the C_2 and C_3 linkage. Selective ester hydrolysis of the mixed esters mediated by formic acid produced the desired acid ester **5c** and **5d**.

1. Introduction

The strained norbornene ring has found broad application in assorted fields [1–10] but most famously in the development of high-temperature aerospace polyimides [11–17]. Research has surprisingly shown, however, that the C_7-bridge of norbornene in these polyimides is the site of much of the oxidative degradation observed on thermal cycling [15,16,18–20]. In the search for improved thermal oxidative stability (TOS), several polymers have been prepared which incorporate fluorinated monomers [21–26]. Nevertheless, the number and variety of fluorinated norbornenes has been limited. To this end we have devoted our recent efforts to the synthesis of 7,7-difluoro and 7-fluoronadic acid esters **5c** and **5d**, as precursors in the preparation of aerospace polyimides (oligomers **7c** and **7d**, Scheme 1).

Our previous work in this field [27,28] has taught us how to conveniently insert one or two fluorines into the C_7 position of the norbornene system, beginning with 7-ketoanhydride **1a**. Treating the corresponding symmetrical dimethylester **3a** (R = CH_3) with DAST (diethylaminosulfur trifluoride) [28–33] generates the corresponding 7,7-difluoro analog **3c**. The reduced 7-hydroxydiester **3b** (R = CH_3), on the other hand, gives us convenient *entrée* to the corresponding 7-fluoro system **3d** (R = CH_3). We note that both carboxylic acids and anhydrides are reported to react with DAST to yield acyl fluorides and/or CF_3 derivatives [32,33]. Hence, we used diesters **3** – not diacids **2** – as the starting material for these fluorinations.

A second consideration in planning an effective synthetic strategy of 2,3-nadic monoacid monoesters **5** is the requirement to generate them specifically in the *cis*-2,3-*endo,endo* configuration, rather than the epimeric *trans-exo,endo* analogs **6**. Only the former can cyclize, undergoing imidization to polyimides **7c** and **7d** [34]. We have previously shown [27] that 7-oxodiacid **2a** and its 7-hydroxy analog **2b** undergo esterification via diazotization or ultrasonic methylation yielding the respective symmetrical diesters **3a** and **3b** (R = CH_3) in the *endo,endo* configuration exclusively. Similarly, no inversion of configuration is observed on the treatment of ketones **3a** or alcohols **3b** with DAST. Thus, only *cis-endo,endo* symmetrical diesters **3c** and **3d** are formed, while none of the *trans-endo,exo* analogs **4c** and **4d** are observed. However, under the strongly basic conditions required for the subsequent monohydrolysis, the symmetrical dimethyl esters **3c** and **3d** (R = CH_3) undergo partial epimerization. As a result, the nadic monoacid monomethyl esters are obtained as a mixture of both the *cis-endo,endo* (**5c** and **5d**) and the *trans-endo,exo* (**6c** and **6d**) configurations [27]. As just noted, the latter resists imide **7** formation.

We describe herein our development of an alternate synthetic strategy which successfully allows for the convenient preparation

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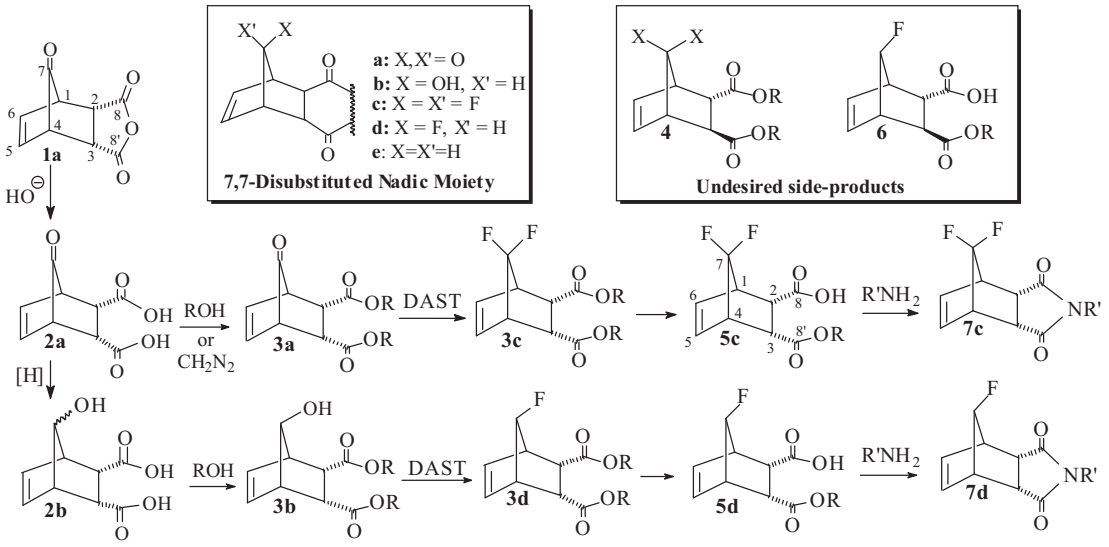


Scheme 1. Proposed scheme for the preparation of 7,7-difluoronadic and 7-fluoronadic acid esters **5c** and **5d**. Undesired *endo,exo* side-products **4** and **6** will not lead to imide **7**.

of *cis-endo,endo* acid esters **5c** and **5d**, stereospecifically and in relatively high yield.

2. Results and discussion

2.1. General synthetic strategy

As already noted above, the ultimate goal of this project was to synthesize two new acid esters: *anti*-7-fluoro and 7,7-difluoronadic acid esters (**5c** and **5d**, Scheme 1). As described in the our opening comments, the introduction of a fluorine at the C_7 position of the norbornene ring can be easily accomplished by reacting the corresponding 7-ketonadic diester **3a** or the 7-hydroxydiester **3b** with DAST [28–33].

The more serious challenge is to generate the 2,3-nadic monoacid monoester **5** specifically in a *cis-endo,endo* configuration; this is because the *trans-endo,exo* epimer **6** resists cyclization/imidization to a polyimide [34]. The companion paper [27] has shown in this regard that the fluorinated dimethyl esters of **3c** and **3d** do not undergo acid hydrolysis whatsoever. Under basic conditions symmetrical dimethyl esters **3** (R = CH_3) do undergo monohydrolysis generating the desired nadic acid ester; however, both the 2,3-*cis-endo,endo* and the *trans-endo,exo* configurations **5** and **6**, respectively, are formed (see Scheme 1, above). The above results led us to conclude that what was required were diesters which would undergo facile monohydrolysis under acid or neutral conditions such that inversion of configuration at carbons C_2 or C_3 would be avoided.

2.2. Benzylated diesters

To this end, we first decided to explore the potential of benzylated diesters **3** (R = Bn). Diacids **2a** and **2b** were obtained from 7-ketonadic anhydride (NAK, **1**) as previous described [35]. Dibenzylation of the carboxylic acid moieties was carried out using DMAP (dimethylaminopyridine), benzyl alcohol and EDCI (1-ethyl-3-(3-dimethylaminopropyl) carbodiimide). When **2a** was reacted, under these conditions, a 65% yield of two products in 3:1 ratio was obtained: the major product proved to be the desired *cis-endo,endo* diester **3a** (R = Bn), while the minor product was the *trans-endo,exo* analog **4a** (R = Bn). Presumably, DMAP is sufficiently basic to effect inversion of configuration at C_3. However, recrystallization did allow us to obtain a clean sample of **3a** (R = Bn). By contrast, when 7-hydroxynadic acid **2b** was dibenzylated under the same reaction conditions, **3b** (R = Bn) was formed as the primary product in an 84% yield, with NMR revealing the presence of <2% of epimer **4b** (R = Bn). The fact that 7-keto nadic systems (e.g. **2a**) undergo epimerization substantially more rapidly than the 7-hydroxy analog is consistent with that reported by us in the accompanying paper [27]. Indeed, as described therein, the facility of base mediated inversion of C_3 in these nadic systems is a function of the functional group at C_7.

When 7-keto diester **3a** (R = Bn) was reacted with DAST, 7,7-difluoro *cis-endo,endo*-diester **5c** (R = Bn) was obtained as the sole product in a 73% yield. Similarly, when the aforementioned 3:1 mixture of **3a**/**4a** (R = Bn) mixture was treated with DAST, the expected **3c**/**4c** (R = Bn) mixture was formed in the same ratio. Thus, no loss of configuration α to the ester carbonyls is observed during DAST reactions. Similarly, the DAST fluorination of 7-hydroxy diester **3b** (R = Bn) produced 7-fluoro diester **3d** (R = Bn) as the sole product in a 79% yield. When the reaction was carried out on a sample of **3b** (R = Bn) containing <2% of **4b** (R = Bn), the same ratio of **3d**:**4d** was observed by NMR analysis.

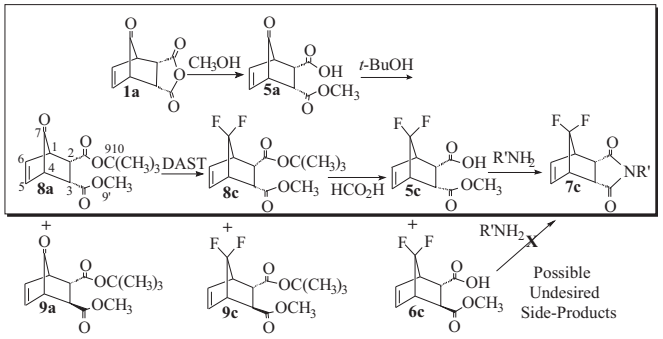
This approach was abandoned when we experienced unexpected difficulty in removing the benzyl ester groups of **3c** and **3d**. Much to our chagrin, no hydrolysis was observed under various acidic conditions (HBr [36]; HBr/HOAc [36]; p-tosic acid [37]; NO-PF_6 [38]); while hydrogenation (H_2/C-Pd) [39,40] reduced the nadic double bond as well.

2.3. t-Butylated diesters

We next attempted to convert diacids **2a** and **2b** to the corresponding *t*-butylated diesters **3a** and **3b** (R = *t*-Bu). Unfortunately, Fischer esterification [41] proved totally ineffective. When *t*-butanol was used catalyzed by DMAP and EDCI [42], NMR revealed the crude product mixture to be 90% starting material while the remaining 10% was configuration inverted product **4a** (R = *t*-Bu). The 7,7-diprotio analog *exo,endo*-**4e** (R = *t*-Bu) [3,43] is known in the literature.

2.4. t-Butyl methyl diesters

From the above experiments and those in the companion paper [27], it became clear that a new synthetic strategy was required. As before, our goal would be to prepare the monoacid monoesters **5c**



Scheme 2. Synthetic scheme for the preparation of 7,7-difluoronadic acid ester **5c** and the corresponding polyimides **7c**. The large rectangular box includes the critical precursors along this synthetic pathway, while those compounds lying outside the box are possible undesired side-products with inverted configuration at C_3.

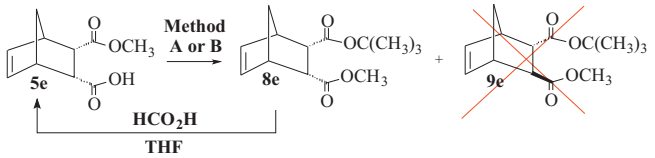
and **5d.** However, we now realized that it would be necessary to distinguish between the two nadic carboxylic groups very early on in the synthesis. To this end, we decided to convert one of the two carboxylic groups to a methyl ester which is more resistant to hydrolysis. The other would be *t*-butylated and, hence, hopefully undergo a more facile hydrolysis when required. The proposed strategy leading to acid ester **5c** is outlined in Scheme 2.

To test the facility of preparing and removing the *t*-butyl group, we began with a commercially available model nadic acid ester, methyl nadic-2,3-*endo,endo*-dicarboxylate (**5e**). As shown in Scheme 3, this 7,7-diprotio analog could be *t*-butylated using two different reaction procedures. In the first ("Method A" in Scheme 3), the carboxylic acid was converted directly to the *t*-butyl ester, in a 73% yield, with EDCI and *t*-butanol in the presence of the mild base pyridine. In the second ("Method B"), the carboxylic acid was first converted to the acyl chloride in pyridine, followed by esterification with *t*-butanol (23% yield). NMR analysis revealed that the only product formed in both procedures was the desired uninverted *cis-endo,endo* isomer **8e**, with none of the *trans-endo,exo* isomer **9e** detectable. The retention of the C_3 configuration in this 7-unsubstituted system despite the mild basic conditions, is to be contrasted with the greater sensitivities reported by us for the 7-fluoro, 7,7-difluoro, 7-hydroxy and 7-oxo systems [27].

Of the two procedures, "Method A" is clearly preferable for producing mixed diester **8e**: it is a one-step process, which does not require particularly strict dryness, and gives the desired uninverted product in a relatively decent yield. As also shown in Scheme 3, formic acid successfully mediated the selective hydrolysis of the *t*-butyl moiety of diester **8e** back to acid ester **5e** [44] leaving the methyl ester and the rest of the nadic system intact.

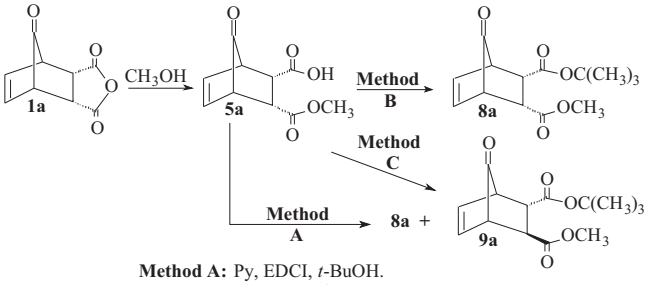
2.5. Synthesis of 7,7-difluoronadic acid ester (2-endo,3-endo; **5c**)

In the light of the above success, we turned to the synthesis of 7,7-difluoronadic acid ester **5c**. As shown in Scheme 4, the *endo*



Method A: Py, EDCI, *t*-BuOH.
Method B: (1) Py, $SOCl_2$; (2) *t*-BuOH, Py.

Scheme 3. Synthesis of *t*-butyl methyl nadic 2-*endo*,3-*endo*-dicarboxylate (**8a**).



Method A: Py, EDCI, *t*-BuOH.
Method B: (1) Py, $SOCl_2$; (2) *t*-BuOH, Py.
Method C: DMAP, EDCI, *t*-BuOH.

Scheme 4. Synthesis of 7-ketonadic diesters **8a** and **9a**.

anhydride **1a** was reacted, as previously described [27] with methanol yielding monoacid monomethyl ester **5a**. As in the case of **5e,** 7-keto analog **5a** was reacted with EDCI, pyridine and *t*-butanol ("Method A" in Schemes 3 and 4). However, much to our chagrin, only a 17% yield of product was obtained. What was worse, careful NMR analysis revealed the product to be an isomeric mixture of the desired *endo,endo* diester **8a** accompanied by *endo,exo* analog **9a** in a 3:7 ratio. Clearly, the 7-keto acid ester **5a** is highly sensitive to even a mild base like pyridine, and undergoes configuration inversion. The great sensitivity of the 7-keto nadic system to configuration inversion of C_3 has been previously described in the companion paper [27]. Indeed, when we used the even more basic dimethylaminopyridine instead of pyridine ("Method C") full inversion of the configuration at C_3 took place, yielding **9a** exclusively (24% yield).

When, however, the two-step "Method B" approach was used, the desired 7-keto diester **8a** was obtained in a 44% yield after recrystallization. X-ray analysis confirms the *endo,endo* configuration of the desired product. Interestingly, both enantiomers of **8a** (*R,S* and *S,R* around C_2 and C_3) were present in the same unit cell, as seen from the crystal structure below (Fig. 1) [45].

After the desymmetrization, diester **8a** was fluorinated by DAST in dry methylene chloride with a catalytic amount of ethanol, to yield the corresponding difluoride **8c** (45% yield). In the final step, the selective hydrolysis of the *t*-butyl ester was achieved with formic acid generating the 7,7-difluoronadic monoacid monoester (**5c**, 97% yield) in the desired *endo-endo* configuration, as shown in Scheme 5. As mentioned before, the methyl ester remains resilient under these acidic reaction conditions.

2.6. Synthesis of anti-7-fluoronadic acid ester (2-endo,3-endo; **5d**)

As seen from Scheme 1, the synthesis of the *anti*-7-fluoro analog **5d** is seriously complicated by the necessity to reduce the 7-keto moiety to the corresponding *anti*-7-hydroxyl group. One approach to latter would be to carry out a borohydride reduction of the carbonyl of the 7-keto acid ester **5a** (Scheme 6). This approach was rejected for two reasons: firstly, experience has painfully taught us that the strongly basic conditions (NaOH) used in the standard $NaBH_4$ reduction conditions could invert the configuration of C_3 adjacent to the ester. In addition, there are assorted reports of methyl esters reacting with the $NaBH_4$ [46–48]. We decided instead to convert 7-keto anhydride **1a** to the corresponding diacid and reduce the latter to *anti*-7-hydroxynadic acid (**2b**) with $NaBH_4$ in aq. NaOH, as previously described [27]. We then hoped to dehydrate diacid **2b** to anhydride **1f** with trifluoroacetic anhydride (TFAA), as shown in Scheme 6. Unfortunately, TFAA treatment acetylated the C_7-hydroxy group yielding TFA ester anhydride **1f**.

The successful route to 7-fluoro acid ester **5d** begins again with ketoanhydride **1a**, which is reduced with $NaBH_4$ in an 80% yield to give 7-hydroxy diacid **2b** (Scheme 7) [27]. The latter is actually

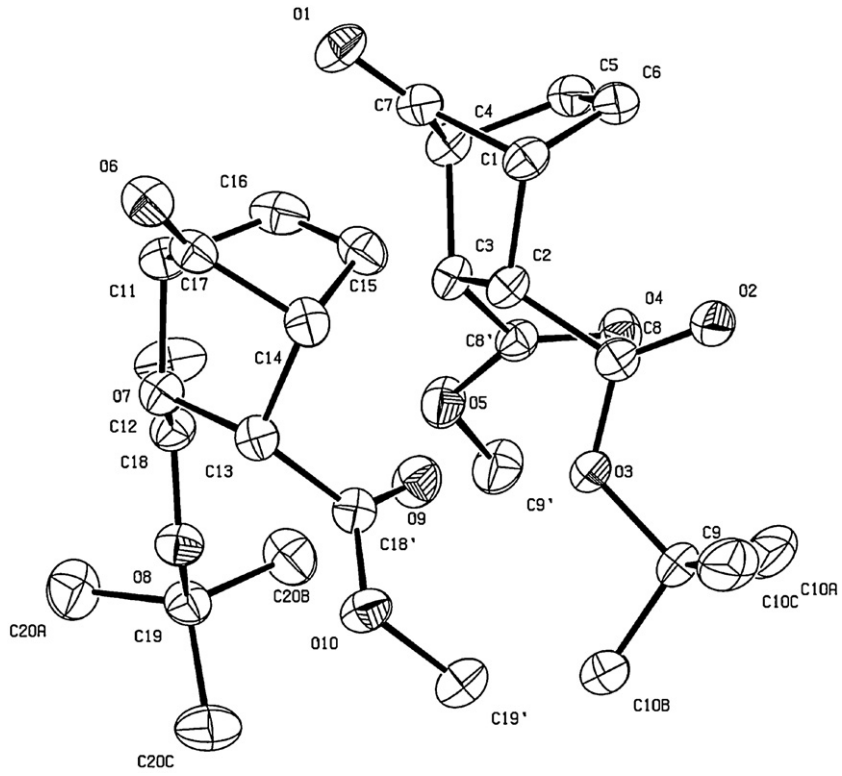
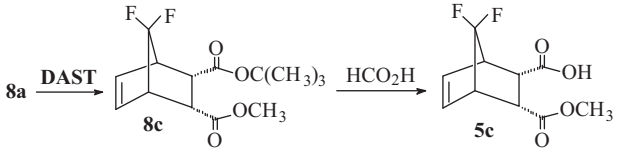


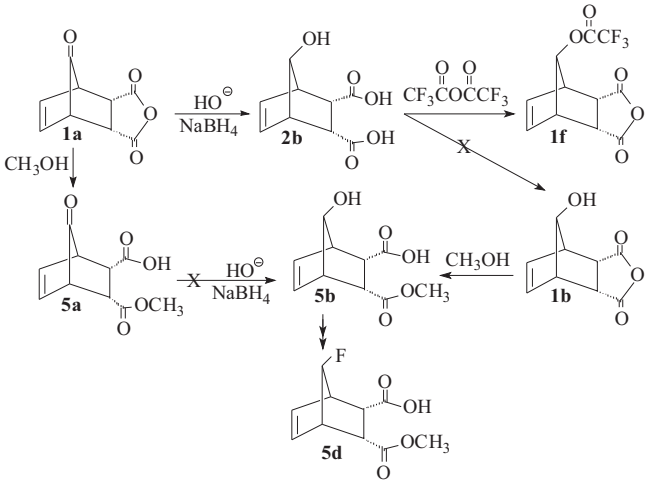
Fig. 1. X-ray structure of *t*-butyl methyl 7-oxo-5-norbornene-2-*endo*,3-*endo*-dicarboxylate (**8a)** showing both the *R,S* and *S,R* enantiomers.



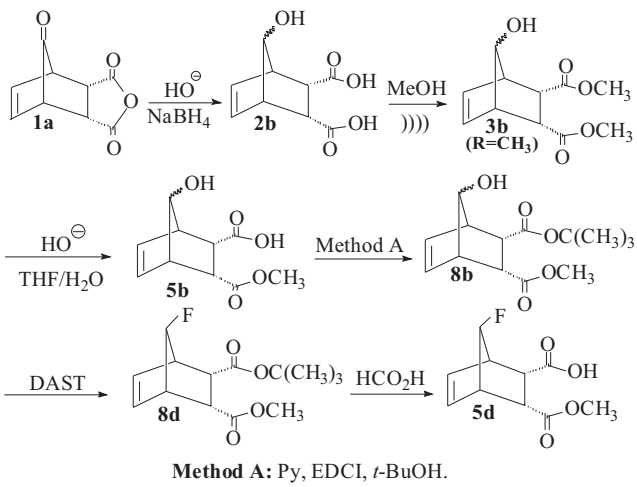
Scheme 5. Synthesis of 2-*endo*,3-*endo* 7,7-difluoronadic acid ester **5c**.

formed in an *anti* to *syn* ratio (with respect to the olefin linkage) of 93:7. These isomers were identified and fully characterized by NMR spectral analysis, as previously described [35]. The *anti/syn* mixture **2b** was converted to diester **3b** (R = CH_3) in a 78% yield via sonication in methanol with catalytic amount of sulfuric acid [28]. Half-hydrolysis of diester **3b** in cold aq. THF gave an 83% yield of the uninverted 7-hydroxy acid ester **5b** (93:7 *anti/syn* mixture) [27]. With acid ester **5b** in hand, "Method A" was used to *t*-butylate the acidic carboxylate yielding mixed diester **8b** in a 48% yield (still 93:7 *anti/syn* mixture). Fortunately, the mild basic condition of the "Method A" did not epimerize C_3 of **8b**, yielding the *endo,endo* configuration exclusively.

The reaction of **8b** with DAST [28] yields the desired *anti*-7-fluoro diester **8d** in an 87% yield. The formation of the exclusively *anti*-7-fluoro isomer from a 93:7 *anti/syn* mixture of the 7-hydroxy precursor **8b** is consistent with the previously reported mechanism [28]. Finally the 7-fluoronadic *endo-endo* monomethyl nadic ester **5d** was generated via the selective hydrolysis of the *t*-butyl ester with formic acid (91% yield). As



Scheme 6. Initial strategies for the synthesis of 7-fluoronadic acid ester **5d**.



Scheme 7. Synthesis of 7-fluoronadic acid ester **5d**.

noted before, the methyl ester does not undergo hydrolysis under these reaction conditions.

3. Conclusion

The novel *anti*-7-fluoronadic and 7,7-difluoronadic acid esters **5c** and **5d** were synthesized in good yield for the manufacture of high temperature polyimides (**7c** and **7d**). The crucial step of this approach is the preparation of the 7-keto and 7-hydroxy *mixed t*-butyl methyl diesters **8a** and **8b**, respectively – while maintaining the cis-*endo,endo* configuration around the C_2 and C_3 linkage. Fluorination of **8a** and **8b** with DAST yields the 7-fluorinated mixed esters **8c** and **8d**. The latter could then be converted to the desired acid esters **5c** and **5d** by selectively deprotecting the *t*-butyl moiety with formic acid. Pathways involving dimethyl, di-*t*-butyl or dibenzyl esters have proved ineffective. We are presently studying the utility of these fluorinated norbornenes in the preparation of TOS polyimides.

4. Experimental

4.1. General

NMR spectra were recorded on a DRX 200, DRX 300, DMX 600, and DMX 700 MHz Fourier transform spectrometers. For 1D NMR spectra, a QNP probe was used. All 2D experiments (COSY, HMQC, HMBC, and NOSEY) were run and processed by Bruker software. NMR spectra were generally run at 25 ± 1 °C and recorded while locked on the deuterium signals of the sample solvent. ^1H and ^{13}C NMR chemical shifts are expressed in δ (ppm) relative to TMS or a solvent peak (DMSO-d_6, acetone-d_6 or $CDCl_3$) as reported by Gottlieb et al. [49]. The ^{19}F NMR chemical shifts are also expressed in δ (ppm) relative to $CFCl_3$. MS and HRMS were determined in an AutoSpec Premier manufactured by Waters (UK) in DCI/CH_4 mode. TLC was performed using Merck silica gel 60 F_{254} microcards. The TLC plate was developed with a UV lamp (365, 254 nm) or by brief immersion into a $KMnO_4$ solution, drained and dried with a heating fan. Column chromatography separation was carried out using Merck silica gel 60 (230–400 mesh) applying positive nitrogen pressure. Melting points were determined on one of the following capillary melting point apparatus: Electrothermal Digital Melting Point Apparatus or Buchi 510. X-ray spectroscopy was carried out on a single crystal of the sample in a Bruker Smart Apex CCD X-ray diffractometer system controlled by a Pentium-based PC using the Smart-NT V5.6 (Bruker) software package, as described previously [20].

Unless otherwise indicated, all solvents and reagents were obtained from Sigma Aldrich and used as received. 7-Ketonadic anhydride (NAK, **1a**) [35], 7-hydroxynadic acid **(2b)** [35], methyl 7-oxonadic acid ester (**5a**; R = CH_3) [27] and dimethyl 7-hydroxynadic diester (**3b**, R = CH_3) [28] were synthesized as previous described.

4.2. Anti 7-trifluoroacetoxynadic anhydride (*1f*)

7-Hydroxynadic acid **2b** [35] (0.50 g, 2.52 mmol) was suspended in 5 mL of trifluoroacetic anhydride in a 50 mL round bottom flask equipped with a magnetic stirrer and reflux condenser topped with a drying tube ($CaCl_2$). The resulting mixture was stirred at r.t. for 3 days, at which time the volatiles were removed by rotary evaporation to yield ester anhydride **1f** (0.68 g, 2.46 mmol, 89% yield) as a yellowish oil.

1f: **^1H NMR** (300 MHz, $CDCl_3$) δ 6.355 ("t", J = 2.1 Hz, 2H, H_5 and H_6), 4.915 (bs, 1H, H_7), 3.772 (m, 2H, H_2 and H_3), 3.592 (m, 2H, H_1 and H_4). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 177.47 (C_9), 170.29 (C_8 and $C_{8'}$), 133.59 (C_5 and C_6), 114.04 (q, J = 79.3 Hz, C_{10}), 87.80 (C_7), 47.05 (C_1 and C_4), 44.64 (C_2 and C_3). **^{19}F NMR** (188 MHz, $CDCl_3$): δ −75.52 (s). **MS** (DCI–CH_4) m/z: 277 (MH^+, 94%), 281 (MH_2^+–$COCF_3$, 100%), 163 (MH^+–$COCF_3$–OH, 63%). **HRMS** (DCI–CH_4) m/z: calcd for $C_{11}H_8F_3O_5$ (MH^+), 277.0324; found, 277.0311.

4.3. Preparation of dibenzyl esters (*3* and *4*)

Dibenzyl 7-Oxo-5-norbornene-2-endo,3-endo-dicarboxylate (3a, R = Bn) **and Dibenzyl 7-Oxo-5-norbornene-2-endo,3-exo-dicarboxylate (4a,** R = Bn). This procedure was based on that of Dhaon et al. [42] with several changes. 7-Ketonadic acid (**2a**) (1.27 g, 6.47 mmol) was suspended in 65 mL of CH_2Cl_2 in a 250 mL round bottom flask equipped with a magnetic stirrer and a reflux condenser topped by a drying tube ($CaCl_2$). DMAP (dimethylaminopyridine, 1.68 g, 13.4 mmole), benzyl alcohol (2.0 mL) and EDCI (2.6 g, 13.5 mmol) were added to the reaction flask [upon addition of the benzyl alcohol, the suspension dissolves]. The resulting mixture was stirred 3 days at 60 °C in an oil bath and monitored by TLC. The reaction mixture was extracted with saturated $NaHCO_3$ (2× 60 mL), water (1× 60 mL), 3% HCl (2× 60 mL) and finally with saturated NaCl solution (1× 60 mL). The organic layer was dried over $MgSO_4$ and rotary evaporated, leaving a yellowish oil. The crude product (ca. 3.4 g) was purified by flash chromatography (EtOAc/Hex, 1:2) yielding white crystals (1.58 g, 4.20 mmol, 65% yield) of a mixture of *endo,endo*-**3a** (R = Bn) and *endo,exo* **4a** (R = Bn) in a 3:1 ratio. A pure sample of the major product **3a** (R = Bn) was obtained by recrystallization (Et_2O/Hex).

3a (R = Bn): **mp**: 78 °C. R_f (Hex/EtOAc, 2:1): 0.51, R_f (Et_2O/Hex, 1:1): 0.60. **^1H NMR** (300 MHz, $CDCl_3$): δ 7.299 (AA′BB′Cm, 10H, H_{11}, H_{12} and H_{13}), 6.593 ("t", J = 2.4 Hz, 2H, H_5 and H_6), 5.063 and 4.905 (ABq, J = 12 Hz, 4H, H_9 and $H_{9'}$), 3.530 (bt, J = 1.5 Hz, 2H, H_2 and H_3), 3.271 (m, 2H, H_1 and H_4). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 198.03 (C_7), 170.13 (C_8 and $C_{8'}$), 135.47 (C_{10} and $C_{10'}$), 131.24 (C_5 and C_6), 128.62 (C_{12} and $C_{12'}$), 128.53 (C_{11} and $C_{11'}$), 128.46 (C_{13} and $C_{13'}$), 67.19 (C_9 and $C_{9'}$), 49.56 (C_1 and C_4), 43.78 (C_2 and C_3). **MS** (DCI–CH_4) m/z: 377 (MH^+, 32%), 181 (MH^+ –Ph, –Bn, –CO, 53%), 91 (Bn^+, 100%). **HRMS** (DCI–CH_4) m/z: calcd for $C_{23}H_{21}O_5$ (MH^+), 377.1389; found, 377.1386.

4a (R = Bn): R_f (Hex/EtOAc, 2:1): 0.51. **^1H NMR** (300 MHz, $CDCl_3$): δ 7.299 (AA′BB′Cm, 10H, H_{11}, H_{12} and H_{13}), 6.618 (m, 1H, H_5), 6.384 (m, 1H, H_6), 5.166 (s, 2H, $H_{9'}$), 5.164 and 5.098 (ABq, J = 12 Hz, 1H, H_9), 3.609 (bt, J = 4.2 Hz, 1H, H_2), 3.366 (m, 1H, H_1), 3.231 (dm, J = 2.4 Hz, 1H, H_4), 2.952 (dd, J = 5.3, 0.5 Hz, 1H, H_3). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 198.03 (C_7), 171.801 and 170.80(C_8 and $C_{8'}$), 135.39 (C_{10} and $C_{10'}$), 133.50 and 131.79 (C_5 and C_6), 128.54 (C_{12} and $C_{12'}$), 128.46 (C_{11} and $C_{11'}$), 128.21 (C_{13} and $C_{13'}$), 67.32 (C_9), 67.12 ($C_{9'}$), 50.13 (C_1), 48.67 (C_4), 44.59 (C_3), 43.22 (C_2).

4.4. *Dibenzyl 7-hydroxy*-5-norbornene-*2*-endo,*3*-endo-*dicarboxylate (3b, R = Bn)*

7-Hydroxynadic diacid **2b** (2.88 g, 14.69 mmol) was reacted according to the benzyl esterification procedure used for **3a**. Following work-up the crude product mixture contained traces of DMAP, which were removed by passing the mixture over a short SiO_2 column (eluting with 1:1 Et_2O/Hex) to yield the desired dibenzyl ester **3b** (4.68 g, 12.36 mmol, 84%). NMR analysis revealed the presence of <2% of epimer **4b**. A sample of the crude product mixture (ca. 100 mg) was purified by preparative TLC (Et_2O/Hex, 1:1) to yield an analytically pure sample of **3b** (21 mg) as a yellowish oil.

3b (R = Bn): R_f (Et_2O/Hex, 1:1): 0.30. **^1H NMR** (300 MHz, $CDCl_3$): δ 7.302 (AA′BB′Cm, 10H, H_{11}, H_{12} and H_{13}), 6.133 ("t", J = 2.1 Hz, 2H, H_5 and H_6), 5.048 and 4.893 (ABq, J = 12.3 Hz, 4H, H_9 and $H_{9'}$), 3.660 ("t", J = 2.1 Hz, 1H, H_7), 3.616 (m, 2H, H_2 and H_3), 2.933 (m, 2H, H_1 and H_4), 2.023 (bs, 1H, O<u>H</u>). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 172.77 (C_8 and $C_{8'}$), 136.13 (C_{10} and $C_{10'}$), 133.49 (C_5 and C_6), 128.58 (C_{12} and $C_{12'}$), 128.42 (C_{11} and $C_{11'}$), 128.22 (C_{13} and $C_{13'}$), 82.39 (C_7), 66.47

(C_9 and $C_{9'}$), 50.38 (C_1 and C_4), 45.81 (C_2 and C_3). **MS** (DCI–CH_4) *m/z*: 379 (MH^+, 13%), 361 (M^+–OH, 25%), 287 (M^+–Bn, 19%), 271 (M^+–OBn, 7%), 91 (Bn^+, 100%). **HRMS** (DCI–CH_4) *m/z*: calcd for $C_{23}H_{23}O_5$ (MH^+), 379.1545; found, 379.1555.

4.5. *Dibenzyl 7,7-difluoro*-5-norbornene-*2*-endo,*3*-endo-*dicarboxylate (**3c**, R = Bn) and dibenzyl 7,7 difluoro*-5-norbornene-*2-endo,3-exo-dicarboxylate (**4c**, R = Bn)*

7-Oxonadic diester **3a** (R = Bn) (1.54 g, 4.09 mmol) was reacted with DAST according to the previously published procedure [28], to yield the corresponding 7,7-difluorodiester **3c** (1.54 g, 3.87 mmol, 95% yield) as a viscous colorless liquid. The crude was purified by flash chromatography (Hex/Et_2O 2:1) to yield pure **3c** (1.19 g, 2.99 mmol, 73%). When a 3:1 mixture of epimeric diesters **3a** and **4a** (R = Bn) was treated with DAST under in the same reaction conditions, the expected mixture of difluoro epimers **3c/4c** (R = Bn) was obtained in the same 3:1 ratio. Partial spectroscopic data for **4c** was obtained from the **3c/4c** mixture.

3c (R = Bn): R_f (Et_2O/Hex, 1:1): 0.47, R_f (Et_2O): 0.71. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.314 (AA′BB′Cm, 10H, H_{11}, H_{12} and H_{13}), 6.274 (bs, 2H, H_5 and H_6), 5.054 and 4.888 (ABq, J = 12 Hz, 4H, H_9 and $H_{9'}$), 3.596 (m, 2H, H_2 and H_3), 3.226 (m, 2H, H_1 and H_4). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 170.30 (C_8), 135.57 (C_{10}), 131.92 (d, $^3J_{CF}$ = 5.4 Hz, C_5 and C_6), 128.61 (C_{12}), 128.52 (C_{11}), 128.42 (C_{13}), 66.86 (C_9), 48.82 (d, $^2J_{CF}$ = 20 Hz, C_1 and C_4), 45.11 (d, $^2J_{CF}$ = 2 Hz, C_2 and C_3). **^{19}F NMR** (188 MHz, $CDCl_3$): δ −117.13 (d, $^2J_{FF}$ = 188 Hz), −138.34 (d, $^2J_{FF}$ = 188 Hz). **MS** (DCI–CH_4) *m/z*: 399 (MH^+, 38%), 271 (M^+–CF_2–Bn, 26%), 181 (MH^+–CF_2–Bn–Ph, 100%), 119 (M^+, 20%), 91 (Bn^+, 100%, 100%). **HRMS** (DCI–CH_4) *m/z*: calcd for $C_{23}H_{21}F_2O_4$ (MH^+), 399.1408; found, 399.1407.

4c (R = Bn): **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.284 (AA′BB′Cm, 10H, H_{11}, H_{12} and H_{13}), 6.584 (bs, 2H, H_5 and H_6), 3.514 (m, 2H, H_2 and H_3), 3.255 (m, 2H, H_1 and H_4); **^{19}F NMR** (188 MHz, $CDCl_3$): δ −117.30 (d, $^2J_{FF}$ = 187.5 Hz), −135.98 (d, $^2J_{FF}$ = 187.5 Hz).

4.6. *Dibenzyl 7-fluoro*-5-norbornene-*2-endo,3-endo-dicarboxylate (**3d**, R = Bn)*

7-Hydroxynadic dibenzyl diester **3b** (R = Bn) (0.49 g, 1.30 mmol) was reacted with DAST as previously described [28], yielding the desired product 7-fluoronadic diester **3d** (R = Bn) (0.389 g, 1.02 mmol, 79% yield) as a viscous yellowish liquid. Quite often, the product proves to be essentially pure; when this is not the case, however, the product can be purified by flash chromatography (Hex/Et_2O, 2:1).

3d (R = Bn): R_f (Et_2O): 0.62, R_f (Et_2O/Hex, 1:1): 0.42. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.282 (AA′BB′Cm, 10H, H_{11}, H_{12} and H_{13}), 6.104 (m, 2H, H_5 and H_6), 5.044 and 4.888 (ABq, J = 12.3 Hz, 4H, H_9 and $H_{9'}$), 4.260 (dt, J = 58.8, 2.1 Hz, 1H, H_7), 3.541 (q, J = 1.5 Hz, 2H, H_2 and H_3), 3.105 (m, 2H, H_1 and H_4). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 171.63 (C_8 and $C_{8'}$), 135.78 (C_{10} and $C_{10'}$), 131.96 (d, $^3J_{CF}$ = 75.6 Hz, C_5 and C_6), 128.44 (C_{12} and $C_{12'}$), 128.33 (C_{11} and $C_{11'}$), 128.15 (C_{13} and $C_{13'}$), 96.78 (d, $^3J_{CF}$ = 215.0 Hz, C_7), 66.47 (C_9 and $C_{9'}$), 48.24 (d, $^3J_{CF}$ = 16.3 Hz, C_1 and C_4), 45.31 (C_2 and C_3). **^{19}F NMR** (188 MHz, $CDCl_3$): δ −177.79 (d $^2J_{HF}$ = 58.8 Hz). **MS** (DCI–CH_4) *m/z*: 381 (MH^+, 52%), 273 (M^+–OBn, 15%), 107 (OBn^+, 26%), 91 (Bn^+, 100%). **HRMS** (DCI–CH_4) *m/z*: calcd for $C_{23}H_{22}FO_4$ (MH^+), 381.1502; found, 381.1497.

4.7. *General procedures for* t-*butyl methyl nadic diester formation (**8** and **9**)*

4.7.1. *Method A*

This one-step procedure was based on that of Dhaon et al. [42] with several modifications. A 50 mL round bottom flask equipped with a magnetic stirrer and a reflux condenser topped by a drying tube ($CaCl_2$) was charged with the monomethyl ester of nadic diacid **5** (1.0 mmol) and *t*-butanol (8 mL). Pyridine (0.15 mL, 1.86 mmol) or 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDCI) (0.23 g, 1.20 mmol) were then added to the reaction mixture. The resulting reaction solution was stirred at 40–70 °C for 5 days and the progress of the reaction (disappearance of starting material and appearance of product) was monitored by TLC (Et_2O or EtOAc). All the volatiles were then removed by rotary evaporation. The remaining brown oil was dissolved in CH_2Cl_2 (20 mL) and washed once with water (10 mL), twice with saturated $NaHCO_3$ (10 mL each), twice with 3% HCl (10 mL each) and once with saturated NaCl solution (10 mL). The organic layer was dried over $MgSO_4$ and rotary evaporated to yield the *t*-butyl methyl diester.

4.7.2. *Method B*

In this two-step procedure, the monoacid is first converted to the corresponding acid chloride (“chlorination step”). A 50 mL two-neck round bottom flask equipped with magnetic stirrer, a septum and a reflux condenser topped by an argon atmosphere inlet tube, was charged with the starting monomethyl ester of nadic diacid **5** (2.0 mmol) dissolved in CH_2Cl_2 (8 mL). Pyridine (0.040 mL, 0.495 mmol) and thionyl chloride (0.73 mL, 10.0 mmol) were syringed in through the septum to the reaction mixture and the resulting solution was stirred overnight at 40 °C. All the volatiles were then removed under vacuum leaving the crude acyl chloride under dry argon. *t*-Butanol (8 mL) and pyridine (0.25 mL, 3.00 mmol) were then added to the reaction vessel and the resulting solution was stirred at 40–60 °C. The progress of the reaction (disappearance of starting material and appearance of product) was monitored by TLC (Et_2O or EtOAc) and, depending on the compound, completion was attained in 4–7 days. The volatiles were removed by rotary evaporation. The remaining brown oil was dissolved in CH_2Cl_2 (20 mL) and washed twice with saturated $NaHCO_3$ (10 mL each), once with water (10 mL), twice with 3% HCl (10 mL each) and finally with saturated NaCl solution (10 mL). The organic layer was dried over $MgSO_4$ and rotary evaporated to yield the *t*-butyl methyl diester.

4.8. t-*Butyl methyl 7-oxo*-5-norbornene-*2*-endo,*3*-endo-*dicarboxylate (**8a**)*

Monomethyl nadic acid ester **5a** (1 g, 4.76 mmol) was *t*-butylated according to “Method B” but with several modifications. Thus, in the chlorination step, in addition to pyridine and $SOCl_2$, DMF (0.5 mL) was added to give a homogeneous solution. The second esterification step was run for over a week at 55–60 °C. After work-up, a crude brown oil was isolated. The latter was treated with charcoal, followed by recrystallization from Et_2O in the freezer. Colorless crystals of the desired product **8a** were obtained (0.56 g, 0.21 mmol, 44% yield).

8a: mp: 48 °C. R_f (EtOAc): 0.72. R_f (Et_2O): 0.87. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 6.695 (m, 1H, H_5), 6.556 (m, 1H, H_6), 3.657 (s, 3H, $H_{9'}$), 3.442 (dd, J = 10.8, 3.5 Hz, 1H, H_2), 3.405 (dd, J = 10.8, 3.5 Hz, 1H, H_3), 3.231 (m, 1H, H_1), 3.226 (m, 1H, H_4), 1.420 (s, 9H, H_{10}). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 198.49 (C_7), 170.89 ($C_{8'}$), 169.12 (C_8), 131.64 (C_5), 130.28 (C_6), 81.79 (C_9), 51.81 ($C_{9'}$), 50.08 (C_1), 49.80 (C_4), 44.74 (C_2), 43.45 (C_3), 27.98 (C_{10}). **MS** (DCI–CH_4) *m/z*: 267 (MH^+, 83%), 210 (MH^+–C_4H_9, 100%), 193 (M^+–OC_4H_9, 89%), 182 (MH^+–C_4H_9–CO, 21%), 164 (MH_2^+–OC_4H_9–OCH_3, 27%), **HRMS** (DCI–CH_4) *m/z*: calcd for $C_{14}H_{19}O_5$ (MH^+), 267.1232; found, 267.1196. Calcd for $C_{10}H_{10}O_5$ (MH^+–C_4H_9), 210.0528; found, 210.0529.

Crystal data for 8a: $C_{14}H_{18}O_5$, Fw = 266.28, monoclinic, space group $P2(1)/c$, a = 10.18660(10) Å, b = 15.7704(2) Å, c = 17.1743(2) Å, α = 90°, β = 96.7327(6)°, γ = 90°, volume = 2739.96(5) Å^3, F(0 0 0) = 1136, Z = 8,

D_c = 1.291 mg/m^3, μ = 0.098 mm^{-1}. The crystallographic data for **8a** have been deposited in the Cambridge Crystallographic Data Center: CCDC 873358 [45].

4.9. t-*Butyl methyl anti-7-hydroxy*-5-norbornene-*2*-endo,*3*-endo-*dicarboxylate* (***8b***)

The title diester **8b** was prepared by *t*-butylating 7-hydroxynadic monoacid monoester **5b** (0.60 g, 2.83 mmol) according to "Method A" (with pyridine). The reaction mixture was stirred for 5 days at 55–60 °C, and after the work up, the mixed ester **8b** (0.37 g, 1.37 mmol, 48% yield) was isolated as a yellowish oil.

8b: R_f (EtOAc): 0.62. R_f (Et_2O): 0.68. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 6.225 (dd, J = 3.5, 5.6 Hz,1H, H_6), 6.063 (dd, J = 3.5, 5.6 Hz,1H, H_5), 3.646 (s, 1H, H_7), 3.620 (s, 3H, $H_{9'}$), 3.490 (s, 1H, H_2), 3.480 (s, 1H, H_3), 2.890 (s, 1H, H_1), 2.880 (s, 1H, H_4), 2.515 (bs, 1H, OH), 1.403 (s, 9H, H_{10}). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 173.60 ($C_{8'}$), 171.97 (C_8), 133.96 (C_6), 132.47 (C_5), 82.29 (C_7), 80.53 (C_9), 51.38 ($C_{9'}$), 50.54 (C_1), 49.94 (C_4), 46.80 (C_2), 45.47 (C_3), 28.04 (C_{10}). **MS** (DCI–CH_4) m/z: 269 (MH^+, 6%), 213 (MH_2^+, –C_4H_9, 53%), 195 (M^+, –OC_4H_9, 96%), 181 (MH^+–C_4H_9–OCH_3, 100%), 113 (MH^+–OC_4H_9–C_5H_6–OH, 35%). **HRMS** (DCI–CH_4) m/z: calcd for $C_{14}H_{21}O_5$ (MH^+), 269.1389; found, 269.1409.

4.10. t-*Butyl methyl 7,7-fluoro*-5-norbornene-*2*-endo,*3*-endo-*dicarboxylate* (***8c***)

7-Oxonadic **8a** (1.268 g, 4.76 mmol) was reacted with DAST, as previously described [28] to yield a crude mixture (1.320 g, 96% yield) of mixed diester **8c** and the starting material in a 2:1 ratio, as a viscous brown liquid. The product mixture was purified by flash chromatography (Hex/Et_2O, 2:1) to yield pure diester **8c** (0.615 g, 2.13 mmol, 45%) as a viscous yellowish liquid.

8c: R_f (Hex/Et_2O 2:1): 0.49. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.393 (m, 1H, H_5), 6.232 (m, 1H, H_6), 3.640 (s, 3H, $H_{9'}$), 3.495 (m, 2H, H_2 and H_3), 3.196 (bd, J = 3.6 Hz, 2H, H_1 and H_4), 1.410 (s, 9H, H_{10}). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.25 ($C_{8'}$), 169.46 (C_8), 132.52 (d, J = 5.2 Hz, C_5), 132.02(t, J = 267.4 Hz, C_7), 130.93 (d, J = 5.4 Hz, C_6), 81.54 (C_9), 51.74 ($C_{9'}$), 49.33 (t, J = 20.4 Hz, C_1), 48.98 (t, J = 20.2 Hz, C_4), 46.27 (d, J = 2.0 Hz, C_2), 44.82 (d, J = 2.6 Hz, C_3), 28.04 (C_{10}). **^{19}F NMR** (188 MHz, $CDCl_3$): δ −117.36 (d, $^2J_{FF}$ = 187.2 Hz), −138.42 (d, $^2J_{FF}$ = 187.2 Hz). **MS** (TOF–MS-ES+) m/z: 313 (M+Na^+, 100%). **HRMS** (DCI–CH_4) m/z: calcd for $C_{10}H_{10}O_4F_2$ (MH^+–C_4H_9), 232.0547; found, 232.0556.

4.11. t-*Butyl methyl anti-7-fluoro*-5-norbornene-*2*-endo,*3*-endo-*dicarboxylate* (***8d***)

7-Hydroxynadic mixed diester **8b** (0.360 g, 1.34 mmol) was reacted with DAST as previously described [28], to yield the desired 7-fluoro analog **8d** (0.315 g, 1.17 mmol, 87% yield) as a viscous colorless liquid. Generally speaking, the product did not require further purification; however, when required, the product was purified by flash chromatography (eluting with a 2:1 mixture of Hex/Et_2O).

8d: R_f (Et_2O): 0.71, R_f (Et_2O/Hex, 1:1): 0.37. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.218 (m, 1H, H_5), 6.062 (m, 1H, H_6), 4.280 (dt, J = 59.1, 2.1 Hz, 1H, H_7), 3.638 (s, 3H, $H_{9'}$), 3.452 (dq, J = 10.5, 1.4 Hz, 1H, H_2), 3.426 (dq, J = 10.5, 1.4 Hz, 1H, H_3), 3.090 (m, 2H, H_1 and H_4), 1.409 (s, 9H, H_{10}). **^{13}C NMR** (75 MHz, acetone-d_6) δ 172.57 (C_8), 170.94 ($C_{8'}$), 132.56 (d, $^3J_{CF}$ = 7.4 Hz, C_5), 131.12 (d, $^3J_{CF}$ = 7.9 Hz, C_6), 96.92 (d, $^1J_{CF}$ = 214.7 Hz, C_7), 80.86 (C_9), 51.49 ($C_{9'}$), 48.54 (d, $^2J_{CF}$ = 16.7 Hz, C_1), 48.05 (d, $^2J_{CF}$ = 16.0 Hz, C_4), 46.43 (C_2), 45.15 (C_3), 28.02 (C_{10}). **^{19}F NMR** (188 MHz, $CDCl_3$): δ –178.25 (d $^2J_{HF}$ = 58.8 Hz). **MS** (DCI–CH_4) m/z: 271 (M^+, 12%), 214 (MH^+–C_4H_9, 38%), 197 (M^+–OC_4H_9, 40%), 195 (M^+–C_4H_9–F, 100%). **HRMS** (DCI–CH_4) m/z: calcd for $C_{14}H_{20}FO_4$ (MH^+), 271.1346; found, 271.1307.

4.12. t-*Butyl methyl* 5-norbornene-*2*-endo,*3*-endo-*dicarboxylate* (***8e***)

The title compound was obtained via both procedures for *t*-butyl methyl nadic diester formation. Following "Method A," monomethyl ester **5e** (0.20 g, 1.02 mmol) was reacted at 40 °C for 5 days (with pyridine), and the desired mixed diester **8e** (0.18 g, 0.74 mmol,) was obtained as a yellowish oil in a 73% yield. NMR revealed that the product was essentially clean and could be used without further purification. Following "Method B," monomethyl ester **5e** (0.40 g, 2.04 mmol) was converted to the acid chloride, which was then stirred with *t*-butanol for 4 days at 40 °C. Work-up yielded the desired product **8e** (0.11 g, 0.45 mmol) as a yellowish oil in only 23% yield. NMR revealed the compound to be essentially pure and it was used without further purification.

8e: R_f (Et_2O): 0.72. R_f (Et_2O/Hex 3:1): 0.60. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 6.343 (dd, J = 2.8, 5.6 Hz,1H, H_6), 6.164 (dd, J = 2.8, 5.6 Hz, 1H, H_5), 3.604 (s, 3H, $H_{9'}$), 3.246 (dd, J = 3.5, 10.5 Hz, 1H, H_2), 3.192 (dd, J = 3.5, 10.5 Hz, 1H, H_3), 3.125 (m, 1H, H_4), 3.115 (m, 1H, H_1), 1.44 (td, J = 1.4, 8.4, Hz, 1H, H_7), 1.400 (s, 9H, H_{10}), 1.296 (d, J = 8.4, Hz, 1H, $H_{7'}$). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 173.16 ($C_{8'}$), 171.52 (C_8), 135.46 (C_6), 134.07 (C_5), 80.39 (C_9), 51.26 ($C_{9'}$), 49.30 (C_2), 48.69 (C_7), 48.15 (C_3), 46.71 (C_4), 46.05 (C_1), 28.03 (C_{10}). **MS** (DCI–CH_4) m/z: 196 (MH^+, –C_4H_9, 59%), 179 (M^+–OC_4H_9, 38%), 165 (MH^+–C_4H_9, –OCH_3, 34%), 131 ($C_5H_6^+$, 97%), 113 (M^+–OC_4H_9, –C_5H_6, 42%), 66 ($C_5H_6^+$, 100%). **HRMS** (DCI–CH_4) m/z: calcd for $C_{10}H_{11}O_3$ (M^+–OC_4H_9,), 179.0708; found, 179.0706.

4.13. t-*Butyl methyl 7-oxo*-5-norbornene-*2*-endo,*3*-exo-*dicarboxylate* (***9a***)

The title compound was obtained in two different ways. In the first approach, monoester **5a** (0.50 g, 2.38 mmol) was reacted according to the "Method A" using pyridine as the base. The reaction mixture was stirred at 70 °C for 5 days, and, after work-up, a yellowish oil (0.11 g, 0.41 mmol, 17% yield) was obtained. Careful NMR analysis reveals the product to be a mixture of two isomers, *endo,endo*-**8a** and *endo,exo*-**9a**, in a 3:7 ratio. The reaction was repeated, but this time the stronger base DMAP (0.29 g, 2.38 mmol) was used, instead of pyridine (dubbed "Method C"). The reaction mixture was stirred for 5 days at 70 °C as before and, after work-up, mixed diester **9a** (0.15 g, 0.56 mmol, 24% yield) was obtained as a yellowish oil. NMR analysis revealed that this product was *not* contaminated with the *endo,endo* epimer **8a**.

9a: R_f (EtOAc): 0.72. R_f (Et_2O): 0.87. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 6.647 (m, 1H, H_5), 6.475 (m, 1H, H_6), 3.707 (s, 3H, $H_{9'}$), 3.493 (t, J = 2.5 Hz, 1H, H_2), 3.323 (m, 1H, H_1), 3.163 (d, J = 3.5 Hz, 1H, H_4), 2.766 (d, J = 4.9 Hz, 1H, H_3), 1.463 (s, 9H, H_{10}). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 198.58(C_7), 171.80 ($C_{8'}$), 171.12 (C_8), 133.57 (C_5), 131.73 (C_6), 82.12 (C_9), 52.40 ($C_{9'}$), 50.50 (C_4), 48.76 (C_1), 45.72 (C_3), 43.06 (C_2), 27.98 (C_{10}). **MS** (DCI–CH_4) m/z: 210 (MH^+–C_4H_9, 83%), 193 (M^+–OC_4H_9, 100%), 164 (MH_2^+–OC_4H_9–OCH_3, 63%). **HRMS** (DCI–CH_4) m/z: calcd for $C_{10}H_{10}O_5$ (MH^+–C_4H_9), 210.0528; found, 210.0524. Calcd for $C_{10}H_9O_4$ (M^+–OC_4H_9), 193.0501; found, 193.0534.

4.14. *General procedure for* t-*butyl ester hydrolysis of diester* ***8*** *to acid esters* ***5***

This procedure selectively hydrolyzes a *t*-butyl ester in the presence of a methyl ester and is based on the work of Chandrasekaran et al. [44]. A 100 mL round bottom flask, equipped with a magnetic stirrer and a reflux condenser (open to the air) was charged with the *t*-butyl methyl diester **8** (3.30 mmol) dissolved in

THF (4.5 mL). Formic acid (22 mL) was added to the solution and the resulting mixture was stirred for 10 days at room temperature (15–20 °C) and monitored by TLC. All the volatiles were removed by rotary evaporation to yield the respective monomethyl ester of nadic diacid, **5**.

4.15. Methyl 7,7-difluoro-5-norbornene-*2*-endo,*3*-endo-*dicarboxylate (**5c**)*

Diester **8c** (0.538 g, 1.866 mmol) was hydrolyzed according to the "General Procedure for *t*-Butyl Ester Hydrolysis" to yield the desired monoacid monomethyl ester **5c** (0.420 g, 1.809 mmol, 97% yield) as a yellowish oil. The NMR data correspond well to that previously reported [27]. We note that in the latter case the data for **5c** was extracted from a mixture, while here the compound was obtained pure (see Supporting Information for spectra).

5c: MS (TOF–MS-ES+) *m/z*: 233 (MH^+, 86%), 215 (M^+–OH, 100%). **HRMS** (DCI–CH_4) *m/z*: calcd for $C_{10}H_{11}O_4F_2$ (MH^+), 233.0625; found, 233.0646. Calcd for $C_{10}H_9O_3F_2$ (MH^+–OH), 215.0520; found, 215.0553.

4.16. Methyl anti 7-fluoro-5-norbornene-*2*-endo,*3*-endo-*dicarboxylate (**5d**)*

Diester **8d** (0.893 g, 3.302 mmol) was hydrolyzed according to the "General Procedure for *t*-Butyl Ester Hydrolysis" to yield the desired monoacid monomethyl ester **5d** (0.645 g, 3.013 mmol, 91% yield) as a yellowish oil. The NMR data correspond well to that previously described [27]. We note that in the latter case the data for **5d** was extracted from a mixture, while here the compound was obtained pure (see Supporting Information for spectra).

5d: MS (DCI–CH_4) *m/z*: 214 (M^+, 16%), 183 (M^+–OCH_3, 19%), 169 (M^+–CO_2H, 18%), 155 (M^+–CO_2CH_3, 26%), 138 (M^+–OH–OCH_3–CO, 18%), 109 (M^+–CO_2H–CO_2CH_3–H, 51%), 84 ($C_5H_5F^+$, 100%). **HRMS** (DCI–CH_4) *m/z*: calcd for $C_{10}H_{11}FO_4$ (M^+), 214.0641; found, 214.0618.

4.17. Methyl 5-norbornene-*2*-endo,*3*-endo-*dicarboxylate (**5e**)*

Diester **8e** (0.18 g, 0.74 mmol) was hydrolyzed according to the "General Procedure for *t*-Butyl Ester Hydrolysis" to give a quantitative yield of the desired nadic monoacid monomethyl ester **5e** (0.15 g, 0.74 mmol) as a yellowish oil. The spectroscopic data corresponded well with the previously published data [50–53].

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jfluchem.2013.01.030.

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