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Synthesis of fluoro- and polyfluoro-veratraldehydes by electrophilic fluorination

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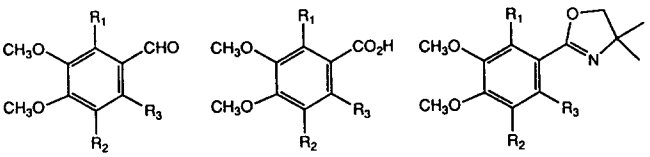
Abstract

Lithiation of oxazolines derived from fluorinated veratric acid, followed by electrophilic fluorination and subsequent reductive oxazoline cleavage, provides a convenient route to di- and tri-fluoroveratraldehydes. Similarly, 4-fluoroveratrol was converted by lithiation and fluorination to 3,4-difluoroveratrol, which can be used to prepare 5,6-difluoroveratraldehyde.

Keywords: Fluoroveratraldehydes; Polyfluoroveratraldehydes; Electrophilic fluorination; NMR spectroscopy; Mass spectrometry

1. Introduction

We have studied ring-fluorinated analogues of dopamine, norepinephrine and epinephrine extensively as selective receptor agonists and as probes for studying enzyme mechanisms [1]. In many of our syntheses of these analogues, as well as of fluorinated analogues of the catecholamino acids, 3,4-dihydroxyphenylalanine and 3,4-dihydroxyphenylserine, 2-, 5- and 6-fluoroveratraldehydes (**1b–d**) were important starting materials. As part of our studies of fluorine-induced adrenergic selectivities, we also prepared 2,5- and 2,6-difluoronorepinephrine, and 2,5-difluoroepinephrine [2]. Whereas 2,5-difluoro-3,4-dibenzyloxybenzaldehyde, the key intermediate in the 2,5-difluoro series, was conveniently prepared from 2,5-difluorophenol, the substitution pattern in the 2,6-difluoro series presented several tactical difficulties. After much effort, we were able to prepare 2,6-difluoroveratraldehyde (**1e**) from 2,4-difluorophenol in eight steps, with an overall yield of 15% [2]. This route provided sufficient material for the synthesis of 2,6-difluoronorepinephrine, but it became clear that extended work in this series would mandate a more convenient source of **1e**. Although we earlier had explored electrophilic fluorination of monofluoro substrates, or anions derived therefrom, as an alternative strategy, we had met with no success. We report herein the successful realization of this latter strategy.



Series **a**: $R_1 = R_2 = R_3 = H$
b: $R_1 = F, R_2 = R_3 = H$
c: $R_1 = R_3 = H, R_2 = F$
d: $R_1 = R_2 = H, R_3 = F$
e: $R_1 = R_3 = F, R_2 = H$
f: $R_1 = H, R_2 = R_3 = F$
g: $R_1 = R_2 = R_3 = F$

2. Results and discussion

We were encouraged to reinvestigate this strategy, based on the recent report of Snieckus and coworkers on the facile fluorination of aryl-lithium intermediates using *N*-fluorobenzenesulfonimide (NFSi) or *N*-fluoro-*O*-benzenedisulfonimide [3]. We applied this sequence (n-butyl-lithium, NFSi) to oxazolines derived from veratric acid and its fluorinated analogues and, through reductive hydrolysis of the derived products, have achieved facile preparations of **1e**, as well as of the previously unreported 5,6-difluoroveratraldehyde (**1f**) and 2,5,6-trifluoroveratraldehyde (**1g**). Fluorination yields are moderate to good. Competing nucleophilic displacement

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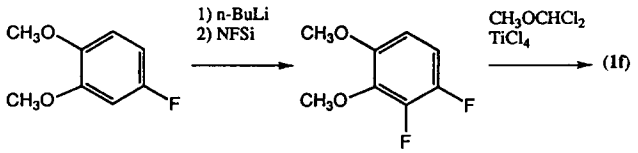
of fluorine by butyl-lithium [4,5] becomes significant in the present series only during lithiation of **3e**.

6-Fluoroveratraldehyde (**1d**) is conveniently prepared in one step from commercially available 4-fluoroveratrol. Permanganate oxidation of **1d** gave 6-fluoroveratric acid (**2d**) which was converted to the oxazoline **3d** (isolated as an oil) [5]. Snieckus and coworkers reported that 2-(4-methoxyphenyl)-4,4-dimethyl-2-oxazoline is selectively lithiated and fluorinated *ortho* to the oxazoline ring, demonstrating that the oxazoline function is a better *ortho*-directing group for lithiation than is the methoxy group. The oxazoline **3d** is doubly activated at both available positions, at position-2 by methoxy and oxazoline and at position-5 by fluorine and methoxy. Since oxazoline is a better *ortho*-directing group than methoxy, and methoxy is a better *ortho*-directing group than fluorine [6], we felt the double activation at position-2 should lead to highly selective lithiation at this position. Lithiation (*n*-butyl-lithium, −78 °C) of **3d**, followed by reaction with NFSi, gave a 3:1 mixture of difluorooxazolines, which were assigned structures **3e** and **3f**, respectively, based on NMR spectral data.

The oxazolines **3e** and **3f** were very difficult to separate by chromatography. Accordingly, the mixture was subjected to methylation with methyl trifluoromethanesulfonate, sodium borohydride reduction and acid hydrolysis to give **1e** and **1f**, readily separable by silica gel chromatography. The former product was identical (NMR, m.p.) with **1e** prepared previously. By the isolation of **1f** from this reaction sequence, we now have available a new starting material for catecholamines and amino acids having a previously unknown fluorine substitution pattern. We are currently preparing 5,6-difluorocatecholamines and amino acids, with the goal of determining the effects of this substitution pattern on receptor selectivities and behavior towards biosynthetic and metabolic enzymes.

Based on the results of Snieckus and coworkers, the oxazoline **3b** derived from 2-fluoroveratric acid (**2b**) could be expected to show high selectivity for lithiation in the single position *ortho* to the oxazoline functionality. Rather than prepare precursor **2b** from 2-fluoroveratraldehyde (available in three steps from 3-fluoroanisole), we chose to prepare **3b** directly by electrophilic fluorination of the oxazoline **3a** prepared from veratric acid. The lithiation–fluorination sequence with **3a** was directed exclusively to the doubly activated 2-position to give **3b** in 65% yield. After purification of **3b** by flash chromatography, it was subjected to a second lithiation–fluorination procedure to give **3e** in 57% yield, identical in all respects with the sample prepared from **3d**. Based on higher yields and regioselectivities, the route starting from veratric acid becomes the method of choice. It may be noted that our previous synthesis of **1e** from 2,4-difluorophenol required several weeks, while the present procedure can be carried out conveniently (from veratric acid) in 2–3 d. This has made available quantities of **1e** adequate to prepare additional 2,6-difluoro analogues of biogenic amines and amino acids.

With the synthesis of 5,6-difluoroveratraldehyde (**1f**) described above, we have the three isomers of difluoroveratraldehyde now in hand. In order to have access to substantial quantities of **1f**, however, we desired an alternative synthesis that would provide this compound as the main product. Lithiation of 4-fluoroveratrol occurs exclusively at the doubly activated 3-position. Reaction of the 3-lithio intermediate with NFSi gave 3,4-difluoroveratrol (**4**) in 57% yield. Formylation of **4** (CH_3OCHCl_2, $TiCl_4$) gave **1f** in 28% yield.



(4)

The remaining fluoro derivative is 2,5,6-trifluoroveratraldehyde (**1g**), which would represent a starting material for the synthesis of the corresponding catecholamines and amino acids, analogues that could be expected to have dramatic alterations in lipophilicities and phenol acidities, alterations likely to modify biological activities. We were pleased to find that lithiation–fluorination of **3e** gave the trifluorooxazoline **3g**, although this material was contaminated with significant amounts of impurities, tentatively identified by GC/MS as monofluoro, mono-n-butyl-substituted oxazolines. These impurities were difficult to remove, so the mixture was converted to aldehyde, and trifluoroveratraldehyde was isolated in 38% yield from crude **3g** after purification by preparative thin layer chromatography.

In summary, the procedure developed by Snieckus and coworkers provides an efficient route to fluoroveratraldehydes, including di- and tri-fluoro analogues. We are currently using these intermediates in the syntheses of several di- and tri-fluoro analogues of catecholamines and amino acids.

3. Experimental details

3.1. General

All moisture-sensitive reactions were carried out using anhydrous solvents in an inert atmosphere of dry nitrogen or argon. NMR spectra were recorded on a Varian Gemini 300 MHz spectrometer. CI mass spectra were measured on a Finnigan 1015 mass spectrometer by the staff of the Laboratory of Analytical Chemistry, NIDDK. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

3.2. 2-Fluoro-4,5-dimethoxybenzoic acid (1d)

A suspension of 6-fluoroveratraldehyde (8.22 g, 45 mmol) in 160 ml of water was heated to 100 °C with efficient stirring. A solution of 10.6 g (67 mmol) of potassium permanganate

in 150 ml of hot water was added slowly to the suspension of aldehyde. Stirring and reflux were continued for an additional 1 h. The solution was made basic with 10% NaOH and the dark precipitate of manganese dioxide was removed from the hot solution by filtration and washed with hot water. The combined filtrate and washings were cooled and acidified with hydrochloric acid. The solution was cooled and the resulting white precipitate was filtered and washed with cold water until free of salt. The precipitate was dried under vacuum to give 7.3 g (46.5 mmol, 87%) of white solid, m.p. 198–200 °C. MS (CI NH_3) m/z: 235 ($M^+ + 35$, $N_2H_7^+$); 218 ($M^+ + 18$, NH_4^+).

3.3. 2-(2-Fluoro-4,5-dimethoxybenzoyl)amino-2-methyl-1-propanol

A mixture of 7.26 g (36.3 mmol) of 6-fluoroveratric acid and 50 ml of thionyl chloride was stirred at reflux for 2 h. The excess thionyl chloride was removed from the green solution by vacuum rotary evaporation to give 2-fluoro-4,5-dimethoxybenzoyl chloride as white crystals. This product was dissolved in 150 ml of methylene chloride and the solution was added dropwise to an ice-cold solution of 6.46 g (72.6 mmol) of 2-amino-2-methyl-1-propanol in 150 ml of methylene chloride to give a pale yellow solution containing a white precipitate. The mixture was stirred for 2 h at room temperature, then evaporated to give a yellow solid. This solid was taken up in ethyl acetate, the solution filtered and the residual white solid washed with a small amount of ethyl acetate. The combined filtrate and washings were washed with 10% HCl, water and brine, and dried over Na_2SO_4. Evaporation of solvent gave 12.5 g of a yellow oil that was purified by flash chromatography (silica gel, 5% MeOH in $CHCl_3$) to give 9.0 g (33 mmol, 92%) of white solid, m.p. 83–85 °C. MS (CI NH_3) m/z: 272 ($M^+ + 1$). ^{1}H NMR ($CDCl_3$) δ: 1.41 (s, 6H, 2 CH_3); 3.71–3.69 (d, 6H, $J = 7.4$ Hz, CH_2); 3.92 (s, 6H, 2 ArOCH_3); 6.64–6.60 (d, 1H, $J^o_{HF} = 13.5$ Hz, ArH_3); 7.54–7.52 (d, 1H, $J^m_{HF} = 7.6$ Hz, ArH_6) ppm. Analysis: Calc. for $C_{13}H_{18}O_4FN$: C, 57.56; H, 6.69; F, 7.00; N, 5.16%. Found: C, 57.54; H, 6.63; F, 6.79; N, 5.06%.

3.4. 1-(4,5-Dimethoxy-2-fluorophenyl)-4,4-dimethyl-2-oxazoline (3d)

Thionyl chloride (15 ml) was added dropwise to 6.1 g (23 mmol) of 2-(2-fluoro-4,5-dimethoxybenzoyl) amino-2-methyl-1-propanol while stirring. After the addition, a homogeneous yellow solution was formed. This solution was concentrated to about 5 ml and poured into 40 ml of dry ether. The white crystals of the hydrochloride salt that formed were collected by filtration. The solid was taken up in cold 10% NaOH and the solution adjusted to neutrality with dilute HCl. The free base was extracted with ether, the ether extracts washed with water and brine, and dried over Na_2SO_4. Evaporation gave a yellow oil which solidified. Recrystallization from hexanes gave 4.93 g (19.5 mmol, 87%) of oxazoline **3d** as white crystals, m.p. 74–75 °C. MS (CI NH_3) m/z: 254 ($M^+ + 1$). ^{1}H NMR ($CDCl_3$) δ: 1.39 (s, 6H, 2CH_3); 3.90 (s, 6H, 2 Ar–OCH_3); 4.09 (s, 2H, CH_2); 6.68–6.64 (d, 1H, $J^o_{HF} = 11.8$ Hz, ArH_5); 7.33–7.31 (d, 1H, $J^m_{HF} = 6.6$ Hz, ArH_2) ppm. Analysis: Calc. for $C_{13}H_{16}O_3FN$: C, 61.65; H, 6.37; F, 7.50; N, 5.53%. Found: C, 61.71; H, 6.51; F, 7.07; N, 5.43%.

3.5. 1-(3,4-Dimethoxyphenyl)-4,4-dimethyl-2-oxazoline (3a)

A solution of veratric acid (9.1 g, 0.05 mol) in thionyl chloride was refluxed as described above to give the acid chloride. This material was dissolved in 20 ml of methylene chloride and the solution added slowly to a solution of 8 g of 2-amino-2-methyl-1-propanol in 20 ml of methylene chloride which had been chilled to −10 °C. The solution was allowed to warm to room temperature and stirred overnight. Water was added, most of the methylene chloride removed by rotary evaporation and the aqueous solution extracted with ethyl acetate until TLC showed no product remaining in the aqueous phase. The ethyl acetate layer was washed successively with water, dilute sodium carbonate, water, dilute HCl, water and brine. After being dried over Na_2SO_4, the solvent was removed to afford 13.6 g of amide.

The amide was cyclized as above by dropwise addition of 20 g of thionyl chloride with stirring. Work-up as described above gave 10.95 g of oxazoline **3a** as an oil. ^{1}H NMR ($CDCl_3$) δ: 1.38 (s, 6H, 2CH_3); 3.92 (s, 3H, ArOCH_3); 3.94 (s, 3H, ArOCH_3); 6.87 (d, 1H, $J^o_{HH} = 8.6$ Hz, ArH_5); 7.47 (d, 1H, $J^m_{HH} = 1.9$ Hz, ArH_2); 7.53 (q, 1H, $J^m_{HH} = 2.0$ Hz, $J^o_{HH} = 8.8$ Hz, ArH_6) ppm.

3.6. General fluorination procedure

The procedure followed was similar to that described by Snieckus et al. [3]. Lithiations with n-butyl-lithium in THF were carried out for 1 h at −78 °C. After dropwise addition of 1.0–1.5 mol of NFSi [1] in THF, the mixture was kept at −78 °C for 15 min, then allowed to come to room temperature and stirred for 1 h. Water was added and the product was extracted with ether. After being washed with water and brine, the ether solution was dried (Na_2SO_4) and evaporated. The product was separated from unreacted oxazoline, NFSi and side-products by silica gel chromatography.

3.6.1. 1-(2,6-Difluoro-3,4-dimethoxyphenyl)-4,4-dimethyl-2-oxazoline (3e) and 5,6-difluoro-3,4-dimethoxyphenyl)-4,4-dimethyl-2-oxazoline (3f)

Lithiation of **3d** (2.0 g, 7.9 mmol) in 50 ml of THF with 5 ml of 1.6 M n-butyl-lithium in hexane (7.9 mmol), followed by addition of a solution of 2.74 g (8.7 mmol) of NFSi in 20 ml of THF was carried out according to the general procedure. Work-up as described gave 3.0 g of a yellow oil.

[1] Commercial quantities of *N*-fluorobenzenesulfonimide (NFSi) are available from Allied Signal Inc., 20 Peabody St., Buffalo, NY.

Flash chromatography (5:1 petroleum ether/ethyl acetate) gave 706 mg of a 3:1 mixture of **3e** and **3f** (2.6 mmol, 33%) along with 740 mg (2.9 mmol) of starting material.

3.6.2. 1-(2-Fluoro-3,4-dimethoxy)-4,4-dimethyl-2-oxazoline (3b)

Addition of 7.5 ml of 1.6 M n-butyl-lithium (12 mmol) to **3a** (2.7 g, 12 mmol) in 75 ml of THF was followed by addition of 4.1 g of NFSi (13 mmol) in 25 ml of THF; work-up was carried out according to the general procedure. The crude product was purified by flash chromatography (2:1 petroleum ether/ethyl acetate) to give 1.89 g (65%) of **3b** as a yellow oil. MS (CI NH_3) m/z: 254 ($M^+ + 1$). ^1H NMR ($CDCl_3$) δ: 1.39 (s, 6H, 2 CH_3); 3.91–3.83 (2s, 6H, 2 CH_3O); 6.69–6.72 (d, $J^o_{HH} = 8.4$ Hz, 1H, ArH_5); 7.53–7.58 (t, $J^o_{HH} = 8.4$ Hz, $J^m_{HF} = 8.3$ Hz, 1H, ArH_6) ppm.

3.6.3. 1-(2,6-Difluoro-3,4-dimethoxyphenyl)-4,4-dimethyl-2-oxazoline (3e)

Using the general procedure, 4.08 g (16.1 mmol) of **3b** gave, following flash chromatography of the crude product (8:1 petroleum ether/ethyl acetate), 2.46 g (9.1 mmol, 57%) of **3e** as a yellow oil. MS (CI NH_3) m/z: 272 ($M^+ + 1$). ^1H NMR ($CDCl_3$) δ: 1.41 (s, 6H, 2 CH_3); 3.87 (s, 6H, CH_3O); 4.10 (s, 2H, CH_2); 6.49–6.52 (dd, 1H, $J^o_{HF} = 11.3$ Hz, $J^p_{HF} = 2.3$ Hz, ArH_5) ppm.

3.6.4. 1-(3,4-Dimethoxy-2,5,6-trifluorophenyl)-4,4-dimethyl-2-oxazoline (3g)

From 2.62 g (9.7 mmol) of **3e**, there was obtained, following flash chromatography, 1.72 g (5.95 mmol) of **3g**. MS (CI NH_3) m/z: 290 ($M^+ + 1$). ^1H NMR ($CDCl_3$) δ: 1.41 (s, 6H, 2 CH_3); 3.91 (s, 3H, CH_3O); 4.07 (s, 3H, CH_3O); 4.12 (s, 2H, CH_2) ppm. The product **3g** was contaminated by 8%–10% of compounds that from MS and NMR appear to be products of the displacement of fluorine in **3e** by the n-butyl carbanion. From GC, the yield of **3g** was estimated to be 57%. Since purification is much more convenient at the aldehyde stage, the impure product was carried through the next step.

3.7. General procedure for conversion of oxazoline to aldehyde

Following the procedure described in Ref. [5], the oxazoline was treated with methyl trifluoromethanesulfonate in methylene chloride. Reduction with $NaBH_4$ and hydrolysis with aqueous oxalic acid gave the aldehyde. This sequence is illustrated for the preparation of **1e** and **1f** from the mixture containing **3e** and **3f**.

3.7.1. 2,6-Difluoroveratraldehyde (1e) and 5,6-difluoroveratraldehyde (1f)

To a solution of 862 mg (3.18 mmol) of the mixture of **3e** and **3f** in 20 ml of anhydrous dichloromethane was added 642 mg (3.91 mmol) of methyl trifluoromethanesulfonate, and the reaction was stirred for 3 h at room temperature. The reaction mixture was chilled to 0 °C and added dropwise to a suspension of 363 mg (9.45 mg) of sodium borohydride in 12 ml of ethanol. After the reaction mixture had been stirred for 45 min at ice-bath temperature, the solvent was removed by evaporation and the residual white solid dissolved in 30 ml of 4:1 THF/H_2O. To this solution was added 1.59 g of oxalic acid in portions, causing an exothermic reaction. The reaction mixture was stirred overnight at room temperature, the THF solvent evaporated and the aqueous solution extracted with ethyl acetate. The ethyl acetate solution was washed with 10% Na_2CO_3, water and brine, and dried over Na_2SO_4. Removal of Na_2SO_4 and evaporation of the solvent gave 779 mg of a yellow solid. Purification of the crude product on a preparative TLC plate (silica gel, 5:1 petroleum ether/ethyl acetate) gave, as the second dinitrophenylhydrazine (DNP)-positive band, 348 mg (1.72 mmol, 54%) of 2,6-difluoro-3,4-dimethoxybenzaldehyde (**1e**) as a white solid, m.p. 80–83 °C (lit. value [2] m.p. 78–80 °C). MS (CI NH_3) m/z: 235 ($M^+ + 35$, $N_2H_7^{2+}$); 220 ($M^+ + 18$, NH_4^+); 203 (M^+). ^1H NMR ($CDCl_3$) δ: 3.90 (s, 3H, CH_3O); 3.95 (s, 3H, CH_3O); 6.55–6.50 (dd, 1H, $J^o_{HF} = 11.7$ Hz, $J^p_{HF} = 1.9$ Hz, ArH); 10.2 (s, 1H, CHO) ppm. Analysis: Calc. for $C_9H_8O_3F_2$: C, 53.47; H, 3.99; F, 18.80%. Found: C, 53.50; H, 4.07; F, 18.41%.

5,6-Difluoroveratraldehyde (**1f**), 87 mg (0.43 mmol, 14%), was obtained as the first DNP-positive band, m.p. 61–64 °C. ^1H NMR ($CDCl_3$) δ: 3.90 (s, 3H, CH_3O); 4.01 (s, 3H, CH_3O); 7.12–7.11 (d, 1H, $J = 2.6$ Hz, ArH); 10.26 (s, 1H, CHO) ppm.

3.7.2. 2,5,6-Trifluoroveratraldehyde (1g)

From 1.7 g (5.9 mmol) of **3g** there was obtained, following chromatographic purification, 740 mg (55%) of **1g** as an oil. MS (CI NH_3) m/z: 221 (M^+). ^1H NMR ($CDCl_3$) δ: 3.90 (s, 3H, CH_3O); 4.16–4.17 (d, 3H, $J = 2.7$ Hz, CH_3O); 10.2 (s, 1H, CHO) ppm.

3.8. 3,4-Difluoroveratrol (4)

To a solution of 3.12 g (20 mmol) of 4-fluoroveratrol in 75 ml of THF, cooled to −78 °C, was added dropwise 15.6 ml (25 mmol) of 1.6 M n-butyl-lithium. After the solution had stirred for 1 h at −78 °C, 8.00 g (25 mmol) of NFSi in 25 ml of THF was added. The solution was stirred for an additional 1 h at −78 °C and was allowed to warm to room temperature. Saturated aqueous NaH_2PO_4 was added and the solution extracted with ethyl acetate. The ethyl acetate layer was washed with water and brine, dried with Na_2SO_4 and evaporated to give, after chromatography (silica gel, 8:1 petroleum ether/ethyl acetate) 2.1 g (57%) of **4**. ^1H NMR ($CDCl_3$) δ: 3.84, 3.95 (2s, 6H, CH_3O); 6.53–6.60 (m [dq], 1H, ArH); 6.76–6.85 (m [q], 1H, ArH) ppm.

3.9. 5,6-Difluoroveratraldehyde (1f) from 4

To an ice-bath cooled solution of 2 g (11.5 mmol) of 5,6-difluoroveratraldehyde (**4**) in 12 ml of methylene chloride was added dropwise a solution of 2.02 ml of $TiCl_4$ in 5 ml of methylene chloride. To this mixture was added dropwise 1.53 ml of Cl_2CHOCH_3 in 10 ml of methylene chloride. The solution was allowed to warm to room temperature and stirred overnight. The solution was then poured into ice, the organic layer separated and the aqueous layer extracted with methylene chloride. The organic fractions were combined and washed with saturated $NaHCO_3$ and brine. After drying (Na_2CO_3), the solvent was removed and the residue purified by chromatography (silica gel, 20:1 petroleum ether/ethyl acetate) to give 642 mg (28%) of **1f** as white crystals, m.p. 61–64 °C. The NMR of this sample was identical to the NMR of the material prepared above from the oxazoline as described above. Analysis: Calc. for $C_9H_8F_2O_3$: C, 52.31; H, 4.02; F, 18.39%. Found: C, 52.34; H, 4.02; F, 18.24%.

References

[1] For a review, see K.L. Kirk, in J.T. Welch (ed.), *Selective Fluorination in Organic and Bioorganic Chemistry*, Am. Chem. Soc., Washington, DC, 1991, pp. 136–155.
[2] G.T. Chen, M. King, F. Gusovsky, C.R. Creveling, J.W. Daly, B.-H. Chen, J.-y. Nie and K.L. Kirk, *J. Med. Chem., 36* (1993) 3947.
[3] V. Snieckus, F. Beaulieu, F. Mohri, W. Han, C.K. Murphy and F.A. Davis, *Tetrahedron Lett., 35* (1994) 3465.
[4] M. Reuman and A.I. Meyers, *Tetrahedron, 41* (1985) 860.
[5] A.I. Meyers and M.E. Flanagan, *Org. Synth., 71* (1993) 117.
[6] D.C. Furlano, S.N. Calderon, G. Chen and K.L. Kirk, *J. Org. Chem., 53* (1988) 3147.