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Scope and limitation of intramolecular Pauson–Khand reaction of fluorine-containing enynes

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Abstract

Intramolecular Pauson–Khand reaction of various fluorine-containing enynes was investigated under various conditions. The reaction of the substrates, which have fluorine atom(s) or fluorine-containing group(s) attached to alkenyl moiety, gave the corresponding cyclopentenones in low to moderate yield, while that of the substrates bearing fluorine-containing groups attached to alkynyl moiety afforded the corresponding cyclopentenones in low to high yield. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Pauson–Khand reaction; Fluorine-containing cyclopentenone; Fluroalkene; Fluoroalkyne

1. Introduction

The introduction of fluorine atom(s) into organic molecules strongly effected their chemical, biological, and physical properties by steric factor, high electoronegativity, and lipophilicity [1–8]. Many new fluorinated materials such as drugs [3,4] and agrochemicals [5] take advantage of these effective changes. Additionally, applications in material sciences such as dyes [6], polymers [7], and liquid crystals [8] have attracted organic chemists' attention. Since first report [9] of Pauson–Khand reaction in 1971, the reaction has been used as powerful tool for construction of cyclopentenone derivatives [10–14]. However, application of the reaction to fluorine-containing substrates has appeared very little [15] and no systematic studies have been done. Here, we wish to describe systematic studies on intramolecular Pauson–Khand reaction of various fluorine-containing enynes (Scheme 1).

2. Results and discussion

2.1. Synthesis of fluorine-containing substrates

Various enynes (**1**–**16**) bearing fluorine atom(s) or fluorine-containing groups on alkenyl or alkynyl moiety were prepared as depicted in Schemes 2 and 3, respectively. Thus, difluoromethylenation [16] of aldehyde (**34**) [17] afforded difluoroalkene (**1**) in 50% yield. Reduction [16] of **1** with Vitride® furnished monofluoroalkene (**2**) as 1:1 mixture of regioisomers in 34% yield. Aldehyde (**34**) was also converted to **3** as 71:29 mixture of regioisomers by chlorotrifluoroethylenation [18]. Unfortunately, attempts for reductive dechlorination of **3** with $LiAlH_4$ in THF or $NaBH_4$ in diglyme [19] failed. Enyne (**4**) containing a fluorophenyl group was obtained by Wittig olefination of 4-fluorobenzaldehyde with **35** [20]. Trifluoromethyl alcohols (**5**, **6**) were synthesized from **34** via Honor–Emmons type olefination, reduction and trifluoromethylation [21] (during trifluoromethylation of carbonyl compounds (**37**, **38**), we found convenient trimethylsilylation of terminal alkynes) see [22].

Formylation of **39** [23] followed by trifluoromethylation [24] furnished trifluoromethyl alcohol (**16**), oxidation of which with Dess–Martin periodinane produced trifluoromethyl ketone (**10**).[2] Fluoro-containing arylalkynes (**7**–**9**,

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[2] All attempts for direct synthesis of **10** from **39** with BuLi followed by the treatment with $(CF_3CO)_2O$ or CF_3CO_2Et failed.

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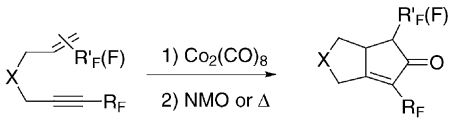
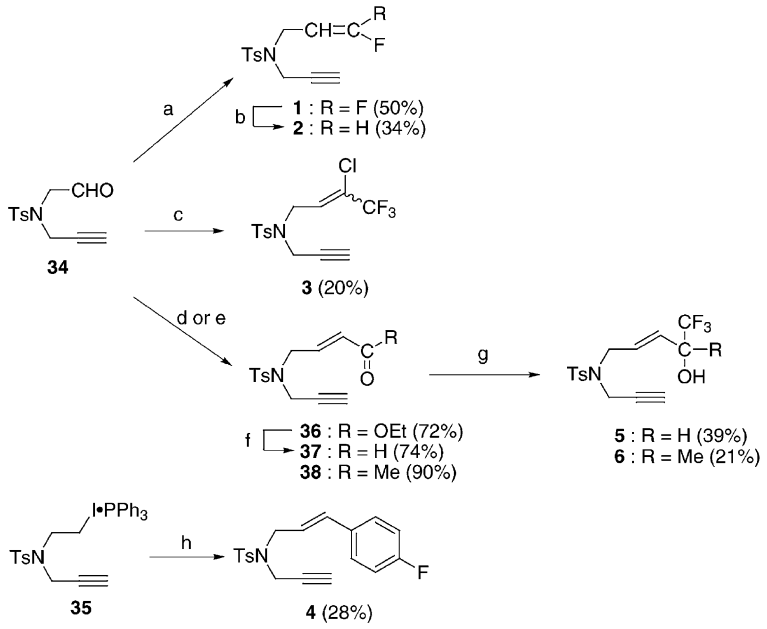
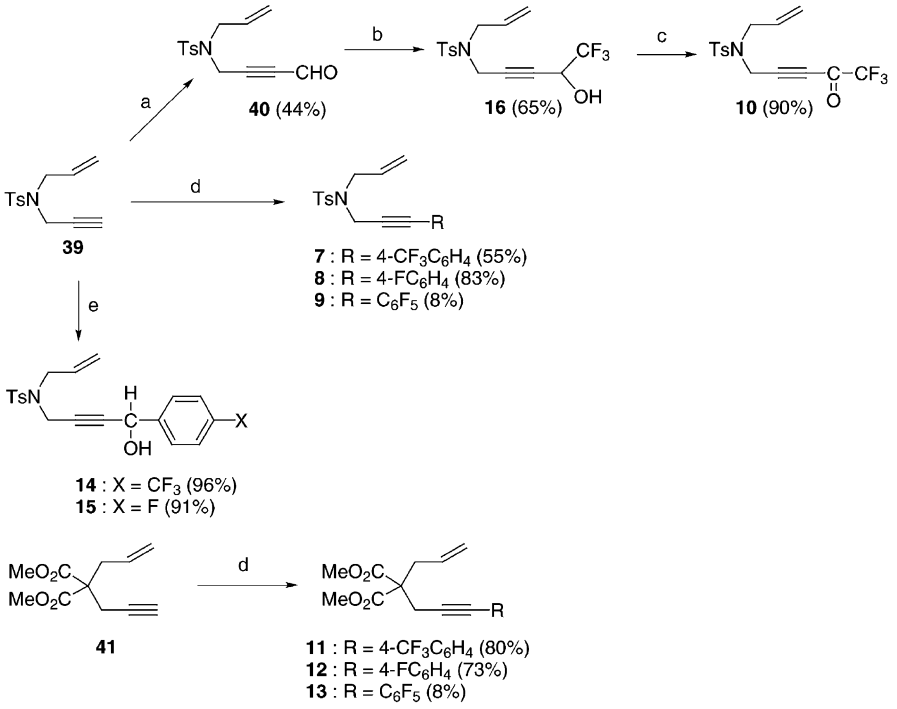


Scheme 1.

11–13) were obtained by palladium catalyzed coupling [25] of **39** or **41** [26] with corresponding fluoroiodobenzenes. Enynes (**14**, **15**) containing fluoroaryl alcohols were synthesized from **39** by the reaction of BuLi and appropriate fluoroaldehydes.



Scheme 2. (a) Zn, CF_2Br_2, PPh_3, $MeCONMe_2$, 100°C, 2 h; (b) Vitride®, benzene, *Δ*, 3 h; (c) CF_3CCl_3, PPh_3, CH_3CN, rt, 1.5 h; (d) $(EtO)_2POCH_2CO_2Et$, NaH, THF, rt, 1 h; (e) $MeC(=O)CHPPh_3$, benzene, *Δ*, 1 h; (f) DIBAH, toluene, −78°C, 0.5 h, Dess–Martin periodinane, CH_2Cl_2, rt, 0.5 h; (g) CF_3TMS, CsF, DME, rt, 0.5–3 h; (h) 4-FC_6H_4CHO, *t*-BuOK, THF, rt, 3 h.



Scheme 3. (a) BuLi, THF then DMF, −78°C, 20 min; (b) CF_3TMS, TBAF, THF, 0°C, 10 min; (c) Dess–Martin periodinane, CH_2Cl_2, rt, 0.5 h; (d) 4-$CF_3C_6H_4I$ or 4-FC_6H_4I or C_6F_5I, $PdCl_2(PPh_3)_2$, CuI, Et_3N, CH_2Cl_2, rt or 40°C, 0.5–3 h; (e) BuLi, THF then 4-$CF_3C_6H_4CHO$ or 4-FC_6H_4CHO, −78°C, 1 h.

Table 1
Pauson–Khand reaction of various fluorine-containing enynes

Entry	Substrate	Method[a]	Time (h)	Product	Yield (%)
1	**2**	A	1	**19**	37
2	**2**	B	2	**18** or **19**	0
3[b]	**3**	A	1	**20**	14
4	**3**	B	3	**20**	0
5	**4**	A	1	**21**	23 (18)[c]
6	**4**	B	3	**21**	2
7	**5**	A	1	**22**	31[d] (4)[c]
8	**5**	B	5	**22**	4[d] (12)[c]
9	**6**	A	1	**23**	34[d] (5)[c]
10	**6**	B	3	**23**	12[d] (20)[c]
11	**7**	A	0.5	**24**	42
12	**7**	B	7	**24**	55
13	**8**	A	0.5	**25**	14
14	**8**	B	7	**25**	52
15	**9**	A	0.5	**26**	15
16	**9**	B	1	**26**	33
17	**11**	A	0.5	**28**	92
18	**11**	B	1	**28**	62
19	**12**	A	0.5	**29**	85
20	**12**	B	1	**29**	67
21	**13**	A	0.5	**30**	87
22	**13**	B	1	**30**	49
23	**14**	A	0.5	**31L** + **31H**[e]	42 + 25
24	**14**	B	2	**31**	0
25	**15**	A	0.5	**32L** + **32H**[e]	41 + 25
26	**15**	B	2	**32**	0
27	**16**	A	0.5	**33**	85[f]

[a] See text.
[b] The reaction was performed at 0°C.
[c] Value in parenthesis was recovery of starting material.
[d] Obtained as an inseparable mixture of diastereomers, although the ratio was not determined.
[e] Stereochemistry of each product was not determined. **L** and **H** mean low and high polar products on TLC.
[f] An inseparable 1:1 mixture of diastereomers.

2.2. Pauson–Khand reaction of fluorine-containing substrates

With fluorine-containing enynes (**1**–**16**) in hand, intramolecular Pauson–Khand reaction was performed by following methods; treatment with NMO (*N*-methylmorpholine *N*-oxide) [27] in CH_2Cl_2 at rt (method A) or refluxing in toluene (method B).

At first, we investigated the reaction of enynes (**1**–**6**), which have fluorine group(s) attached to alkenyl moiety (Table 1 and Fig. 1). In the reaction of difluoroolefin (**1**), decomposition was observed in both methods A and B to give no cyclized product. This findings appeared to imply poor reactivity of olefin due to high electoronegativity of fluorine atom (for the successful report of Pauson–Khand reaction of activated olefins, see [28–30]). With monofluoroolefin (**2**), the reaction proceeded with defluorization to afford defluorized cyclopentenone (**19**) [31] instead of **18** (entry 1) (similar dehalogenation was reportedin the Pauson–Khand reaction of haloalkenes [32]). Furthermore, the reaction of trifluoromethyl-substituted olefin (**3**) underwent dechlorination [32] to furnish **20** as a single diastereomer in 14% yield (entry 3), while that using method B did not at all produce **20**. Stereochemistry of **20** was confirmed by NOE experiment. Similarly, 4-fluoroarylolefin (**4**) produced stereoselectively *trans*-oriented arylcyclopentenone (**21**) [33] in 23% yield by method A (entry 5). The reaction of trifluoromethyl-substituted allylic alcohols (**5**, **6**) using method A afforded in moderate yield (31–34%) corresponding cyclized products (**22**, **23**) as an inseparable diastereomeric mixture together with starting materials (**5**, **6**), however, in low yield (4–12%) by method B (entries 7–10). When enynes having fluorine atom(s) or fluorine-containing groups attached to olefin moiety was employed, method A was found to be superior to method B, although the yield of desired products was unsatisfactory.

Next, we investigated the reaction of enynes (**7**–**16**) bearing fluorine groups on alkynyl moiety. In the reaction of fluoroaromatic enynes (**7**–**9**), corresponding cyclized products (**24**–**26**) were obtained in 14–55% yields (entries 11–16). Contrary to the reaction of enynes (**3**–**5**) having fluorine-containing groups on alkene moiety, method B was superior to method A in these reactions, although the reason was uncertain. On the other hand,

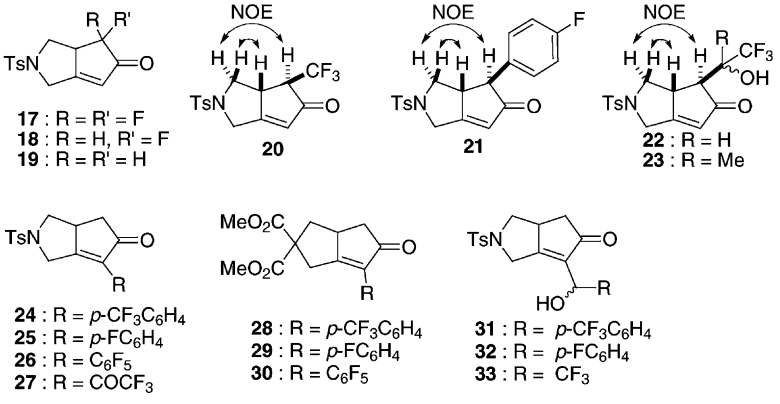


Fig. 1. Products in Pauson-Khand reaction of fluorine-containing enzymes.

the reaction of fluoroaromatic enynes (**11–13**) derived from dimethyl malonate produced corresponding cyclopentenones (**28–30**) in high yield (85–92%) by method A. Surprisingly, no desired products were obtained from trifluoromethyl ketone (**10**) in both methods A and B.[2] For the successful reports of Pauson–Khand reaction of electron deficient alkynes (see [34,35]). The reaction of markedly electron deficient alkyne recovered cobalt–alkyne complex (see [36]). Fluorine substituted propargyl alcohols (**14–16**) furnished a mixture of diastereomers of corresponding cyclopentenones (**31–33**) in good yield (67–85%) by method A (entries 23, 25, 27). Thus, the reaction of enynes having fluorine atom(s) attached to alkyne moiety was found to give corresponding cyclized products in moderate to high yield except for enyne (**10**) bearing marked electron withdrawing groups.

3. Conclusion

We have investigated Pauson–Khand reaction of various fluorine-containing enynes. Feature of the present reaction was as follows. (1) In the reaction of enynes, which have fluoro-functional groups on alkene moieties, desired cyclopentenones were obtained in low to moderate yields. (2) In the reaction of enynes bearing fluoro-functional groups on alkynyl moiety, the corresponding cyclized products were formed in moderate to high yields. (3) In each case, method A was found to superior to method B except for **7–9**.

The present study offers alternative approach to fluoro-containing cyclopentenone derivatives.

4. Experimental

4.1. General

All melting points were measured on a Büchi or a Yanagimoto (hot plate) melting point apparatus and are uncorrected. IR spectra were performed with a Hitachi 260-10 spectrophotometer in $CHCl_3$ solution, and ^1H NMR spectra were taken with a JEOL EX-270 (270 MHz) spectrometer in $CDCl_3$ solution with tetramethylsilane as an internal standard. Mass spectra were measured on a Hitachi M-80 or a JEOL JMS D-300 spectrometer. Column chromatography was performed over silica gel (Merck Kiegelsel 60). Preparative TLCs were run on Merck 7730 plates. Organic extracts were dried over $MgSO_4$, unless otherwise indicated.

[2] The reaction of **10** in refluxing CH_3CN [34] also did not give desired product (**27**).

4.2. N-(3,3-difluoro-2-propenyl)-N-(2-propynyl)tosylamide (*1*)

To a solution of **34** (1.845 g, 7.18 mmol), PPh_3 (3.930 g, 15 mmol), and CBr_2F_2 (3.147 g, 15 mmol) in dimethylacetamide (15 ml) was added Zn dust (0.980 g, 15 mmol). After the mixture was heated at 100°C for 2 h, the reaction was quenched with water. The mixture was extracted with Et_2O. The organic extracts were washed with brine, dried, and evaporated under reduced pressure to give an oily residue, which was purified by column chromatography (AcOEt:hexane = 1:10) to afford 1 (1.021 g, 50%) as crystals; mp 49–50°C; ^1H NMR δ 7.73, 7.31 (each 2H, d, $J = 8.3$ Hz), 4.21–4.37 (1H, m), 4.10 (2H, d, $J = 2.3$ Hz), 3.89 (2H, d, $J = 7.9$ Hz), 2.43 (3H, s), 2.07 (1H, t, $J = 2.3$ Hz); IR 3261, 2119, 1595 cm^{-1}; MS *m/z* 285 (M^+); high-resolution mass *m/z* calcd for $C_{13}H_{13}F_2NO_2S$ (M^+) 285.0634, found: 285.0625.

4.3. N-(3-fluoro-2-propenyl)-N-(2-propynyl)tosylamide (*2*)

A mixture of **1** (1.12 g, 3.94 mmol) and Vitride® (2.0 ml, 65% in toluene) in benzene (8 ml) was refluxed for 3 h. Usual work-up gave an oily residue, which was purified by column chromatography (AcOEt:hexane = 1:8) to afford **2** (0.360 g, 34%) as crystals; mp 50–51°C; ^1H NMR δ 7.74, 7.31 (each 2H, d, $J = 8.6$ Hz), 6.82, 6.51 (each 0.5H, d, $J = 11.2$ Hz), 5.24–5.40 (1H, m), 4.10 (2H, d, $J = 2.3$ Hz), 3.77 (2H, d, $J = 7.9$ Hz), 2.43 (3H, s), 2.05 (1H, t, $J = 2.3$ Hz); IR 3259, 2118, 1596 cm^{-1}; MS *m/z* 267 (M^+); high-resolution mass *m/z* calcd for $C_{13}H_{14}FNO_2S$ (M^+) 267.0719, found: 267.0728.

4.4. N-(3-chloro-4,4,4-trifluoro-2-butenyl)-N-(2-propynyl)tosylamide (*3*)

To a mixture of **34** (2.57 g, 10.0 mmol) and PPh_3 (14.1 g, 53.9 mmol) in CH_3CN (60 ml) was added at 0°C under argon CF_3CCl_3 (3.2 ml, 27 mmol) in one portion. After being stirred for 1.5 h, the solvent was evaporated under reduced pressure to give a residue, to which was added Et_2O. The precipitate was removed by suction and the filtrate was evaporated under reduced pressure to give a residue, which was purified by column chromatography (AcOEt:hexane = 1:10) to afford **3** (0.687 g, 20%) as a pale yellow oil; ^1H NMR δ 7.72, 7.32 (each 2H, d, $J = 8.3$ Hz), 6.51 (0.71H, t, $J = 6.3$ Hz), 6.24 (0.29H, t, $J = 6.6$ Hz), 4.09 (2H, d, $J = 2.5$ Hz), 4.05–4.13 (2H, m), 2.43 (3H, s), 2.12 (1H, t, $J = 2.5$ Hz); IR 2926, 2118, 1655, 1598 cm^{-1}; MS *m/z* 351 (M^+); high-resolution mass *m/z* calcd for $C_{14}H_{13}ClF_3NO_2S$ (M^+) 351.0308, found: 351.0317.

4.5. (2E)-N-[3-(4-fluorophenyl)-2-propenyl]-N-(2-propynyl)tosylamide (*4*)

To a mixture of 4-fluorobenzaldehyde (0.296 g, 2.38 mmol) and Wittig reagent (**35**, 1.25 g, 2.0 mmol) in THF

(20 ml) was added at rt *t*-BuOK (0.288 g, 2.36 mmol) in one portion. After being stirred for 3 h, the reaction was quenched with water. Work-up similar to that noted for **1** gave an oily residue, which was purified by column chromatography (AcOEt:hexane = 1:5) to afford **4** (0.189 g, 28%) as a colorless oil; ^{1}H NMR δ 7.70, 7.28 (each 2H, d, J = 8.3 Hz), 7.19 (2H, dd, J = 5.6, 8.6 Hz), 7.01 (2H, t, J = 8.6 Hz), 6.63 (1H, d, J = 11.7 Hz), 5.63 (1H, dt, J = 5.8, 11.7 Hz), 4.09 (2H, d, J = 2.3 Hz), 4.08 (2H, d, J = 5.8 Hz), 2.42 (3H, s), 1.86 (1H, t, J = 2.3 Hz); MS *m/z* 343 (M^+); high-resolution mass *m/z* calcd for $C_{19}H_{18}FNO_2S$ (M^+) 343.1042, found: 343.1040.

4.6. (2E)-N-(3-ethoxycarbonyl-2-propenyl)-N-(2-propynyl)tosylamide (**36**)

After a mixture of NaH (0.142 g, 3.55 mmol) and ethyl diethylphosphonoacetate (0.807 g, 3.6 mmol) in THF (10 ml) was stirred at rt for 10 min, a solution of **34** (0.767 g, 3 mmol) in THF (10 ml) was added. Then the mixture was stirred for 1 h. The reaction was quenched with 3 M HCl. Work-up similar to that noted for **1** gave an oily residue, which was purified by column chromatography (AcOEt:hexane = 1:2) to afford **36** (0.692 g, 72%) as a colorless oil; ^{1}H NMR δ 7.73, 7.30 (each 2H, d, J = 8.3 Hz), 6.79 (1H, dt, J = 5.8, 15.5 Hz), 6.02 (1H, d, J = 15.5 Hz), 4.19 (2H, q, J = 7.1 Hz), 4.09 (2H, d, J = 2.6 Hz), 3.97 (2H, d, J = 5.8 Hz), 2.42 (3H, s), 2.05 (1H, t, J = 2.6 Hz), 1.28 (3H, t, J = 7.1 Hz); IR 2120,1685, 1635 cm^{-1}; MS *m/z* 321 (M^+); high-resolution mass *m/z* calcd for $C_{16}H_{19}NO_4S$ (M^+) 321.1035, found: 321.1030.

4.7. (2E)-N-(3-formyl-2-propenyl)-N-(2-propynyl)tosylamide (**37**)

To a solution of **36** (0.647 g, 2.0 mmol) in toluene (10 ml) was added at −78°C DIBAH (6.5 ml, 6.5 mmol) over a period of 10 min. After being stirred for 0.5 h, the reaction was quenched with MeOH and water. The mixture was extracted with Et_2O. The organic layer was washed with brine, dried, and evaporated under reduced pressure to give alcohol (0.54 g, 96.0%) as an oil. The alcohol in CH_2Cl_2 (20 ml) was treated with Dess–Martin periodinane (0.848 g, 2.0 mmol) at rt for 0.5 h. The reaction was quenched with saturated aqueous $NaHCO_3$. The mixture was extracted with CH_2Cl_2. Work-up similar to that noted for **1** gave a residue, which was purified by column chromatography (AcOEt:hexane = 1:2) to afford **37** (0.414 g, 77%) as crystals; mp 68–70°C; ^{1}H NMR δ 9.58 (1H, d, J = 7.6 Hz), 7.75, 7.34 (each 2H, d, J = 8.3 Hz), 6.69 (1H, dt, J = 5.6, 15.8 Hz), 6.28 (1H, dd, J = 7.6, 15.8 Hz), 4.12 (2H, d, J = 2.3 Hz), 4.11 (2H, d, J = 5.6 Hz), 2.45 (3H, s), 2.10 (1H, t, J = 2.3 Hz); MS *m/z* 277 (M^+); high-resolution mass *m/z* calcd for $C_{14}H_{15}NO_3S$ (M^+) 277.0773, found: 277.0779.

4.8. (2E)-N-(4-oxo-2-pentenyl)-N-(2-propynyl)tosylamide (**38**)

A mixture of **34** (0.534 g, 2.1 mmol) and 1-(triphenylphosphanylidene)-2-propanone (0.664 g, 2.1 mmol) in benzene (10 ml) was refluxed for 1 h. The solvent was evaporated under reduced pressure to give an oily residue, which was purified by column chromatography (AcOEt:hexane = 1:2) to afford **38** (0.541 g, 90%) as a colorless oil; ^{1}H NMR δ 7.73, 7.31 (each 2H, d, J = 8.3 Hz), 6.63 (1H, dt, J = 5.8, 15.8 Hz), 6.22 (1H, d, J = 15.8 Hz), 4.09 (2H, d, J = 2.6 Hz), 3.99 (2H, d, J = 5.8 Hz), 2.43, 2.25 (each 3H, s), 2.07 (1H, t, J = 2.6 Hz); IR 2924, 2118, 1734, 1680, 1598 cm^{-1}; MS *m/z* 291 (M^+); high-resolution mass *m/z* calcd for $C_{15}H_{17}NO_3S$ (M^+) 291.0929, found: 291.0933.

4.9. (2E)-N-(5,5,5-trifluoro-4-hydroxy-2-pentenyl)-N-(2-propynyl)tosylamide (**5**)

To a solution of **37** (0.277 g, 1.0 mmol) and CsF (0.007 g, 0.05 mmol) in DME (1 ml) was added at rt under argon CF_3TMS (2.4 ml, 1.2 mmol) over a period of 5 min. After being stirred for 0.5 h, the reaction was quenched with 3 M HCl. Work-up similar to that noted for **1** gave an oily residue, which was purified by preparative TLC (AcOEt:hexane = 2:3) to afford **5** (0.134 g, 39%) as a colorless oil; ^{1}H NMR δ 7.69, 7.28 (each 2H, d, J = 8.3 Hz), 5.91 (1H, dt, J = 6.3, 15.7 Hz), 5.75 (1H, dd, J = 5.7, 15.7 Hz), 4.40–4.52 (1H, m), 4.04 (2H, d, J = 2.5 Hz), 3.85 (2H, d, J = 6.3 Hz), 3.17–3.30 (1H, m), 2.40 (3H, s), 2.03 (1H, t, J = 2.5 Hz); IR 3276, 2925, 2118, 1680 cm^{-1}; MS *m/z* 347 (M^+); high-resolution mass *m/z* calcd for $C_{15}H_{16}F_3NO_3S$ (M^+) 347.0803, found: 347.0803.

4.10. (2E)-N-(5,5,5-trifluoro-4-hydroxy-4-methyl-2-pentenyl)-N-(2-propynyl)tosylamide (**6**)

To a solution of **38** (0.292 g, 1.0 mmol) and CsF (0.007 g, 0.05 mmol) in DME (1 ml) was added at rt under argon CF_3TMS (2.4 ml, 1.2 mmol) over a period of 5 min. After being stirred for 3 h, the reaction was quenched with 3 M HCl. Work-up similar to that noted for **1** gave an oily residue, which was purified by preparative TLC (AcOEt:hexane = 2:3) to afford **6** (0.075 g, 21%) as a colorless oil; ^{1}H NMR δ 7.71, 7.31 (each 2H, d, J = 8.3 Hz), 5.90 (1H, dd, J = 5.6, 15.9 Hz), 5.83 (1H, d, J = 15.9 Hz), 4.05 (2H, d, J = 2.6 Hz), 3.87 (2H, d, J = 5.6 Hz), 2.42 (3H, s), 2.03 (1H, t, J = 2.6 Hz), 1.43 (3H, s); IR 3475, 2925, 2124, 1598 cm^{-1}; MS *m/z* 361 (M^+); high-resolution mass *m/z* calcd for $C_{16}H_{18}F_3NO_3S$ (M^+) 361.0966, found: 361.0959.

4.11. N-allyl-N-(4-oxo-2-butynyl)tosylamide (**40**)

To a solution of **39** (7.47 g, 30 mmol) in THF (90 ml) was added at −78°C under argon BuLi (22 ml, 33 mmol) over a

period of 5 min. After being stirred for 5 min, DMF (4.5 ml) was added. Then, the mixture was stirred for 20 min and poured into a vigorous stirred mixture of Et_2O (20 ml) and 10% aqueous NaH_2PO_3 (80 ml). The mixture was extracted with Et_2O. Work-up similar to that noted for **1** gave an oily residue, which was purified by column chromatography (AcOEt:hexane = 1:3) to afford **40** (3.67 g, 44%) as a pale yellow oil; ^{1}H NMR δ 8.91 (1H, s), 7.73, 7.32 (each 2H, d, J = 8.3 Hz), 5.66–5.81 (1H, m), 5.26–2.30 (2H, m), 4.27 (2H, s), 3.83 (2H, d, J = 6.3 Hz), 2.43 (3H, s); MS m/z 277 (M^+); high-resolution mass m/z calcd for $C_{14}H_{15}NO_3S$ (M^+) 277.0773, found: 277.0777.

4.12. N-allyl-N-(5,5,5-trifluoro-4-hydroxy-2-pentynyl)tosylamide (16)

To a solution of **40** (0.278 g, 1.0 mmol) and TBAF (50 ml, 0.05 mmol) in THF (3 ml) was added at 0°C under argon CF_3TMS (2.5 ml, 1.25 mmol) over a period of 5 min. After being stirred for 10 min, the reaction was quenched with 1 M HCl (3 ml). Work-up similar to that noted for **1** gave an oily residue, which was purified by preparative TLC (AcOEt:hexane = 1:2) to afford **16** (0.226 g, 65%) as crystals; mp 67–68°C; ^{1}H NMR δ 7.73, 7.33 (each 2H, d, J = 8.3 Hz), 5.65–5.78 (1H, m), 5.24–5.31 (2H, m), 4.35–4.48 (1H, m), 4.14 (2H, s), 3.79–3.87 (2H, m), 2.43 (3H, s); IR 3500, 2241 cm^{-1}; MS m/z 347 (M^+); high-resolution mass m/z calcd for $C_{15}H_{16}F_3NO_3S$ (M^+) 347.0803, found: 347.0813.

4.13. N-allyl-N-(5,5,5-trifluoro-4-oxo-2-pentynyl)tosylamide (10)

To a solution of 16 (0.226 g, 0.65 mmol) in CH_2Cl_2 (10 ml) was added Dess–Martin periodinane (0.347 g, 0.82 mmol). After being stirred for 0.5 h, the reaction was quenched with 10% aqueous $Na_2S_2O_3$. The mixture was extracted with CH_2Cl_2. Work-up similar to that noted for **1** gave a residue, which was purified by column chromatography (AcOEt:hexane = 1:3) to afford **10** (0.201 g, 90%) as a colorless oil; ^{1}H NMR δ 7.71, 7.32 (each 2H, d, J = 8.3 Hz), 5.70–5.80 (1H, m), 5.27–5.34 (2H, m), 4.35 (2H, s), 3.84 (2H, d, J = 6.6 Hz), 2.41(3H, s); IR 3500, 2241 cm^{-1}; MS m/z 345 (M^+); high-resolution mass m/z calcd for $C_{15}H_{14}F_3NO_3S$ (M^+) 345.0643, found: 345.0645.

4.14. General procedure for palladium-catalyzed coupling of alkynes with fluoroiodobenzenes (7–9, 11–13)

A mixture of acetylene (**39** or **41**), fluoroiodobenzene, Et_3N, CuI, and $PdCl_2(PPh_3)_2$ in CH_2Cl_2 was stirred under argon. After the precipitate was filtered, the filtrate was evaporated under reduced to give a residue, which was purified by column chromatography (AcOEt:hexane = 1:5) to afford fluoro-containing acetylenes.

4.15. N-allyl-N-[3-(4-trifluoromethylphenyl)-2-propynyl]tosylamide (7)

From **39** (1.24 g, 5.0 mmol), 4-iodobenzotrifluoride (1.0 g, 3.6 mmol), Et_3N (2.8 ml, 20.2 mmol), CuI (0.024 g, 0.12 mmol), $PdCl_2(PPh_3)_2$ (0.087 g, 0.12 mmol) in CH_2Cl_2 (11 ml) [reaction time 2.5 h (rt)], **7** (0.777 g, 55%) was obtained as crystals; mp 50–51°C; ^{1}H NMR δ 7.77, 7.50, 7.27, 7.17 (each 2H, d, J = 8.3 Hz), 5.72–5.78 (1H, m), 5.26–5.30 (2H, m), 4.32 (2H, s), 3.89 (2H, d, J = 6.6 Hz), 2.34 (3H, s); IR 2925, 1614 cm^{-1}; MS m/z 393 (M^+); high-resolution mass m/z calcd for $C_{20}H_{18}F_3NO_2S$ (M^+) 393.1010, found: 393.1007.

4.16. N-allyl-N-[3-(4-fluorophenyl)-2-propynyl]tosylamide (8)

From **39** (1.24 g, 5.0 mmol), 1-fluoro-4-iodobenzene (0.6 ml, 5.0 mmol), Et_3N (2.8 ml, 20.2 mmol), CuI (0.024 g, 0.12 mmol), $PdCl_2(PPh_3)_2$ (0.087 g, 0.12 mmol) in CH_2Cl_2 (11 ml) [reaction time 3 h (rt)], **8** (1.422 g, 83%) was obtained as crystals; mp 49–50°C; ^{1}H NMR δ 7.77, 7.25 (each 2H, d, J = 8.3 Hz), 7.05 (2H, dd, J = 5.4, 8.9 Hz), 6.93 (2H, t, J = 8.9 Hz), 5.72–5.87 (1H, m), 5.24–5.28 (2H, m), 4.29 (2H, s), 3.88 (2H, d, J = 6.6 Hz), 2.35 (3H, s); IR 2961, 2242, 1648, 1600 cm^{-1}; MS m/z 343 (M^+); high-resolution mass m/z calcd for $C_{19}H_{18}FNO_2S$ (M^+) 343.1043, found: 343.1045.

4.17. N-allyl-N-[3-(pentafluorophenyl)-2-propynyl]tosylamide (9)

From **39** (0.746 g, 3.0 mmol), pentafluoroiodobenzene (0.882 g, 3.0 mmol), Et_3N (3 ml, 21.6 mmol), CuI (0.015 g, 0.077 mmol), $PdCl_2(PPh_3)_2$ (0.060 g, 0.085 mmol) in CH_2Cl_2 (3 ml) [reaction time 1 h (40°C)], **9** (0.093 g, 8%) was obtained as crystals; mp 74–75°C; ^{1}H NMR δ 7.73, 7.24 (each 2H, d, J = 8.3 Hz), 5.70–5.85 (1H, m), 5.25–5.36 (2H, m), 4.37 (2H, s), 3.86 (2H, d, J = 6.3 Hz), 2.32 (3H, s); IR 2247, 1597, 1502 cm^{-1}; MS m/z 415 (M^+); high-resolution mass m/z calcd for $C_{19}H_{14}F_5NO_2S$ (M^+) 415.0665, found: 415.0657.

4.18. Dimethyl 2-allyl-2-[3-(4-trifluoromethylphenyl)-2-propynyl]malonate (11)

From **41** (0.630 g, 3.0 mmol), 4-iodobenzotrifluoride (0.845 g, 3.0 mmol), Et_3N (1.6 ml, 11.5 mmol), CuI (0.014 g, 0.076 mmol), $PdCl_2(PPh_3)_2$ (0.052 g, 0.075 mmol) in CH_2Cl_2 (8 ml) [reaction time 0.5 h (rt)], **11** (0.847 g, 80%) was obtained as a colorless oil; ^{1}H NMR δ 7.53, 7.46 (each 2H, d, J = 8.2 Hz), 5.59–5.74 (1H, m), 5.14–5.23 (2H, m), 3.76 (6H, s), 3.03 (2H, s), 2.86 (2H, d, J = 7.3 Hz); IR 2955, 1739, 1616, 1438 cm^{-1}; MS m/z 354 (M^+); high-resolution mass m/z calcd for $C_{18}H_{17}F_3O_4$ (M^+) 354.1079, found: 354.1083.

*4.19. Dimethyl 2-allyl-2-[3-(4-fluorophenyl)-2-propynyl]malonate (**12**)*

From **41** (0.630 g, 3.0 mmol), 1-fluoro-4-iodobenzene (0.678 g, 3.0 mmol), Et_3N (1.6 ml, 11.5 mmol), CuI (0.014 g, 0.076 mmol), $PdCl_2(PPh_3)_2$ (0.052 g, 0.075 mmol) in CH_2Cl_2 (8 ml) [reaction time 0.5 h (rt)], **12** (0.664 g, 73%) was obtained as a colorless oil; ^{1}H NMR δ 7.33 (2H, dd, J = 5.4, 8.7 Hz), 6.96 (2H, t, J = 8.7 Hz), 5.59–5.75 (1H, m), 5.12–5.22 (2H, m), 3.74 (6H, s), 2.99 (2H, s), 2.85 (2H, d, J = 7.3 Hz); IR 2954, 1738, 1602, 1508 cm^{-1}; MS *m/z* 304 (M^+); high-resolution mass *m/z* calcd for $C_{17}H_{17}FO_4$ (M^+) 304.1111, found: 304.1095.

*4.20. Dimethyl 2-allyl-2-[3-(pentafluorophenyl)-2-propynyl]malonate (**13**)*

From **41** (0.745 g, 3.0 mmol), pentafluoroiodobenene (0.452 g, 1.54 mmol), Et_3N (1.5 ml, 10.8 mmol), CuI (0.007 g, 0.037 mmol), $PdCl_2(PPh_3)_2$ (0.029 g, 0.042 mmol) in CH_2Cl_2 (1.5 ml) [reaction time 1 h (40°C)], **13** (0.044 g, 8%) was obtained as a colorless oil; ^{1}H NMR δ 5.57–5.72 (1H, m), 5.15–5.24 (2H, m), 3.77 (6H, s), 3.10 (2H, s), 2.85 (2H, d, J = 7.6 Hz); IR 2957, 2252, 1741, 1521 cm^{-1}; MS *m/z* 376 (M^+); high-resolution mass *m/z* calcd for $C_{17}H_{13}F_5O_4$ (M^+) 376.0734, found: 376.0735.

*4.21. N-allyl-N-[4-(4-trifluoromethylphenyl)-4-hydroxy-2-butynyl]tosylamide (**14**)*

To a solution of **39** (1.245 g, 5.0 mmol) in THF (15 ml) was added at −78°C under argon BuLi (3.6 ml, 5.4 mmol) over a period of 5 min. After being stirred for 5 min, 4-trifluoromethylbenzaldehyde (0.9 ml, 6.6 mmol) was added and the mixture was stirred for 1 h. The reaction was quenched with water. Work-up similar to that noted for **1** gave an oily residue, which was purified by column chromatography (AcOEt:hexane = 1:3 then 1:1) to afford **14** (2.030 g, 96%) as crystals; mp 59–60°C; ^{1}H NMR δ 7.69, 7.57, 7.41, 7.20 (each 2H, d, J = 8.3 Hz), 5.58–5.77 (1H, m), 5.19–5.25 (3H, m), 4.15 (2H, d, J = 1.7 Hz), 3.79 (2H, d, J = 6.6 Hz), 2.64 (1H, brs), 2.33 (3H, s); IR 3491, 1603, 1508 cm^{-1}; MS *m/z* 423 (M^+); high-resolution mass *m/z* calcd for $C_{21}H_{20}F_3NO_3S$ (M^+) 423.1116, found: 423.1109.

*4.22. N-allyl-N-[4-(4-fluorophenyl)-4-hydroxy-2-butynyl]tosylamide (**15**)*

To a solution of **39** (1.245 g, 5.0 mmol) in THF (15 ml) was added at −78°C under argon BuLi (3.6 ml, 5.4 mmol) over a period of 5 min. After being stirred for 5 min, 4-fluorobenzaldehyde (0.7 ml, 6.5 mmol) was added and the mixture was stirred for 1 h. Similar work-up as described above gave an oily residue, which was purified by column chromatography (AcOEt:hexane = 1:3 then 1:1) to afford **15** (1.687 g, 91%) as a colorless oil; ^{1}H NMR δ 7.58, 7.19 (each 2H, d, J = 8.3 Hz), 7.24 (2H, dd, J = 5.9, 8.7 Hz), 6.98 (2H, t, J = 8.7 Hz), 5.62–5.70 (1H, m), 5.15–5.25 (3H, m), 4.13 (2H, s), 3.78 (2H, d, J = 6.3 Hz), 2.53 (1H, brs), 2.33 (3H, s); IR 3501, 1647, 1619 cm^{-1}; MS *m/z* 373 (M^+); high-resolution mass *m/z* calcd for $C_{20}H_{20}FNO_3S$ (M^+) 373.1111, found: 373.1129.

4.23. General procedures for Pauson–Khand reaction

A mixture of enyne (1 eq) and $Co_2(CO)_8$ (1.1 eq) in CH_2Cl_2, toluene or CH_3CN was stirred at rt for 1 h. Method A: NMO (6–12 eq) was added to the reaction mixture. After the mixture was stirred for 0.5–1 h, the precipitate was removed by suction filtration through Celite 545 short pad. Method B: the mixture was refluxed in toluene for 1–7 h. Purification of the products obtained by both methods A and B was carried out on preparative TLC.

*4.24. 2-Tosyl-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (**19**)*

Mp 142–144°C ([31] 142–145°C); ^{1}H NMR δ 7.73, 7.35 (each 2H, d, J = 7.9 Hz), 5.99 (1H, s), 4.34, 4.03 (each 1H, d, J = 16.5 Hz), 4.04 (1H, t, J = 8.4 Hz), 3.09–3.19 (1H, m), 2.55–2.66 (2H, m), 2.44 (3H, s), 2.06 (1H, dd, J = 3.6, 17.8 Hz); ^{13}C NMR δ 207.8, 179.1, 144.4, 133.6, 130.3, 127.6, 126.3, 52.6, 47.9, 44.1, 40.0, 21.7; IR 1711, 1650, 1597 cm^{-1}; MS *m/z* 277 (M^+); high-resolution mass *m/z* calcd for $C_{14}H_{15}NO_3S$ (M^+) 277.0773, found: 277.0770.

4.25. (3aR, 4R*)-4-trifluoromethyl-2-tosyl-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (**20**)*

Mp 145–146°C; ^{1}H NMR δ 7.74, 7.37 (each 2H, d, J = 8.3 Hz), 6.07 (1H, s), 4.40, 4.08 (each 1H, d, J = 17.2 Hz), 4.10 (1H, dd, J = 10.8, 18.3 Hz), 3.25–2.40 (1H, m), 2.85 (1H, dq, J = 4.8, 9.4 Hz), 2.76 (1H, dd, J = 9.6, 10.8 Hz), 2.45 (3H, s); ^{13}C NMR δ 197.2, 176.7, 144.5, 133.2, 130.1, 127.5, 125.4, 53.8, 51.3, 47.5, 45.1, 45.0, 21.6; IR 1715, 1644, 1597 cm^{-1}; MS *m/z* 345 (M^+); high-resolution mass *m/z* calcd for $C_{15}H_{14}F_3NO_3S$ (M^+) 345.0646, found: 345.0643.

4.26. (3aR, 4S*)-4-(4-fluorophenyl)-2-tosyl-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (**21**)*

Mp 178–180°C; ^{1}H NMR δ 7.74, 7.36 (each 2H, d, J = 8.3 Hz), 7.02–7.11 (4H, m), 6.08 (1H, s), 4.41, 4.09 (each 1H, d, J = 17 Hz), 4.07 (1H, t, J = 9 Hz), 3.23–3.37 (1H, m), 3.23 (1H, d, J = 4.3 Hz), 2.80 (1H, dd, J = 9, 10.7 Hz), 2.45 (3H, s); ^{13}C NMR δ 176.5, 144.3, 132.2, 130.0, 129.8, 129.7, 127.5, 124.7, 116.0, 115.7, 57.4, 52.5, 52.1, 50.9, 47.7, 21.6; IR 1704, 1650, 1598 cm^{-1}; MS *m/z* 371 (M^+); high-resolution mass *m/z* calcd for $C_{20}H_{18}FNO_3S$ (M^+) 371.0992, found: 371.0997.

*4.27. 4-(2,2,2-Trifluoro-1-hydroxyethyl)-2-tosyl-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (**22**)*

Obtained as an inseparable mixture of diastereomers; mp 118–127°C; ^{1}H NMR δ 7.72, 7.36 (each 2H, d, $J = 8.3$ Hz), 6.01 (1H, s), 4.51–4.60 (1H, m), 4.32, 4.07 (each 1H, d, $J = 16.8$ Hz), 3.97 (1H, t, $J = 9.3$ Hz), 3.45–3.55 (1H, m), 2.68–2.75 (1H, m), 2.42 (3H, s), 2.33 (1H, dd, $J = 1.3$, 3 Hz); ^{13}C NMR δ 205.5, 180.0, 144.2, 133.3, 130.0, 127.4, 124.4, 122.9, 66.1, 52.5, 51.6, 47.8, 43.6, 21.5; IR 3432, 1712, 1649, 1597 cm^{-1}; MS *m/z* 375 (M^+); high-resolution mass *m/z* calcd for $C_{16}H_{16}F_3NO_4S$ (M^+) 375.0752, found: 375.0742.

*4.28. 4-(2,2,2-Trifluoro-1-hydroxy-1-methylethyl)-2-tosyl-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (**23**)*

Obtained as an inseparable mixture of diastereomers; mp 104–112°C; ^{1}H NMR δ 7.73, 7.36 (each 2H, d, $J = 8.3$ Hz), 6.02 (1H, s), 4.36, 4.07 (each 1H, d, $J = 17.2$ Hz), 3.20–3.35 (2H, m), 2.63–2.76 (1H, m), 2.44 (3H, s), 2.27 (1H, d, $J = 2.3$ Hz), 1.53 (3H, s); ^{13}C NMR δ 206.3, 178.2, 144.4, 133.3, 130.0, 127.5, 127.4, 125.1, 74.0, 56.0, 52.2, 47.6, 46.0, 45.4, 21.6; IR 3504, 1692, 1653, 1597 cm^{-1}; MS *m/z* 389 (M^+); high-resolution mass *m/z* calcd for $C_{17}H_{18}F_3O_4S$ (M^+) 389.0908, found: 389.0907.

*4.29. 6-(4-Trifluoromethylphenyl)-2-tosyl-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (**24**)*

Mp 183–184°C; ^{1}H NMR δ 7.74, 7.33 (each 2H, d, $J = 8.3$ Hz), 7.67, 7.60 (each 2H, d, $J = 8.2$ Hz), 4.68, 4.09 (each 1H, d, $J = 15.2$ Hz), 4.11 (1H, dd, $J = 6.5$, 10.9 Hz), 3.18–3.32 (1H, m), 2.84 (1H, dd, $J = 6.6$, 17.9 Hz), 2.67 (1H, dd, $J = 9.6$, 10.9 Hz), 2.42 (3H, s), 2.30 (1H, dd, $J = 3.6$, 17.9 Hz); ^{13}C NMR δ 204.8, 174.1, 144.1, 134.8, 133.5, 133.3, 130.3, 130.0, 128.4, 127.3, 125.7, 125.5, 51.8, 48.2, 42.1, 40.5, 21.4; IR 1701, 1638, 1617, 1600 cm^{-1}; MS *m/z* 421 (M^+); high-resolution mass *m/z* calcd for $C_{21}H_{18}F_3NO_3S$ (M^+) 421.0960, found: 421.0966.

*4.30. 6-(4-Fluorophenyl)-2-tosyl-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (**25**)*

Mp 188–189°C; ^{1}H NMR δ 7.73, 7.32 (each 2H, d, $J = 8.3$ Hz), 7.47 (2H, dd, $J = 5.4$, 8.6 Hz), 7.10 (2H, t, $J = 8.6$ Hz), 4.61, 4.06 (each 1H, d, $J = 16.8$ Hz), 4.09 (1H, dd, $J = 6.4$, 11.1 Hz), 3.12–3.27 (1H, m), 2.79 (1H, dd, $J = 6.4$, 18 Hz), 2.62 (1H, dd, $J = 9.4$, 11.1 Hz), 2.41 (3H, s), 2.25 (1H, dd, $J = 3.6$, 18 Hz); ^{13}C NMR δ 205.3, 171.6, 144.0, 134.9, 133.6, 130.1, 130.0, 127.3, 115.8, 115.5, 51.9, 48.2, 41.8, 40.5, 21.5; IR 1700, 1638, 1594, 1508 cm^{-1}; MS *m/z* 371 (M^+); high-resolution mass *m/z* calcd for $C_{20}H_{18}FNO_3S$ (M^+) 371.0991, found: 371.0985.

*4.31. 6-(Pentafluorophenyl)-2-tosyl-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (**26**)*

Mp 64–65°C; ^{1}H NMR δ 7.71, 7.34 (each 2H, d, $J = 8.1$ Hz), 4.36, 4.02 (each 1H, d, $J = 17.2$ Hz), 4.12 (1H, t, $J = 8.6$ Hz), 3.22–3.40 (1H, m), 2.68–2.89 (2H, m), 2.43 (3H, s), 2.30 (1H, dd, $J = 3.3$, 18.2 Hz); ^{13}C NMR δ 201.9, 178.3, 146.1, 144.4, 143.8, 139.7, 135.4, 133.5, 130.1, 127.4, 125.0, 52.3, 47.8, 43.1, 39.9, 21.6; IR 1726, 1686, 1652, 1597 cm^{-1}; MS *m/z* 443 (M^+); high-resolution mass *m/z* calcd for $C_{20}H_{14}F_5NO_3S$ (M^+) 443.0615, found: 443.0623.

*4.32. Dimethyl 6-(4-trifluoromethylphenyl)-5-oxo-3,3a,4,5-tetrahydro-1H-pentalene-2,2-dicarboxylate (**28**)*

Oil; ^{1}H NMR δ 7.69, 7.65 (each 2H, d, $J = 8.9$ Hz), 3.84, 3.73 (each 3H, s), 3.69, 3.31 (each 1H, d, $J = 19.5$ Hz), 3.08–3.25 (1H, m), 2.81–2.93 (2H, m), 2.33 (1H, dd, $J = 3.5$, 18 Hz), 1.73 (1H, t, $J = 12.6$ Hz); ^{13}C NMR δ 206.3, 180.6, 171.8, 170.9, 134.3, 129.9, 128.6, 125.3, 61.0, 53.3, 53.1, 43.1, 42.4, 38.6, 35.9; IR 2957, 1735, 1698, 1636 cm^{-1}; MS *m/z* 382 (M^+); high-resolution mass *m/z* calcd for $C_{19}H_{17}F_3O_5$ (M^+) 382.1028, found: 382.1018.

*4.33. Dimethyl 6-(4-fluorophenyl)-5-oxo-3,3a,4,5-tetrahydro-1H-pentalene-2,2-dicarboxylate (**29**)*

Mp 124–125°C; ^{1}H NMR δ 7.53 (2H, dd, $J = 5.4$, 8.7 Hz), 7.06 (2H, d, $J = 8.7$ Hz), 3.80, 3.69 (each 3H, s), 3.61, 3.25 (each 1H, d, $J = 19.1$ Hz), 3.06–3.20 (1H, m), 2.74–2.87 (2H, m), 2.26 (1H, dd, $J = 3.2$, 18.2 Hz), 1.73 (1H, t, $J = 12.7$ Hz); ^{13}C NMR δ 206.8, 178.3, 171.8, 171.0, 164.2, 160.6, 134.4, 130.1, 129.6, 115.5, 115.2, 61.1, 53.3, 53.0, 42.8, 42.2, 38.7, 35.9; IR 1742, 1703, 1633, 1601, 1508 cm^{-1}; MS *m/z* 332 (M^+); high-resolution mass *m/z* calcd for $C_{18}H_{17}FO_5$ (M^+) 332.1060, found: 332.1053.

*4.34. Dimethyl 6-(pentafluorophenyl)-5-oxo-3,3a,4,5-tetrahydro-1H-pentalene-2,2-dicarboxylate (**30**)*

Mp 114°C; ^{1}H NMR δ 3.80, 3.73 (each 3H, s), 3.38, 3.16 (each 1H, d, $J = 19.4$ Hz), 3.20–3.37 (1H, m), 2.93 (1H, dd, $J = 8$, 12.8 Hz), 2.83 (1H, dd, $J = 6.3$, 18 Hz), 2.34 (1H, dd, $J = 3.2$, 18 Hz), 1.83 (1H, t, $J = 12.8$ Hz); ^{13}C NMR δ 203.6, 184.9, 171.5, 170.7, 142.5, 139.5, 135.9, 124.4, 60.4, 53.4, 53.2, 41.9, 39.0, 35.4; IR 1746, 1719, 1672, 1653, 1523, 1501 cm^{-1}; MS *m/z* 404 (M^+); high-resolution mass *m/z* calcd for $C_{18}H_{13}F_5O_5$ (M^+) 404.0683, found: 404.0696.

*4.35. 6-[(4-Trifluoromethylphenyl)-a-hydroxymethyl]-2-tosyl-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (**31L, H**)*

31L; mp 146–148°C; ^{1}H NMR δ 7.69, 7.35 (each 2H, d, $J = 8.3$ Hz), 7.57, 7.48 (each 2H, d, $J = 7.9$ Hz), 5.56 (1H,

s), 4.26, 4.16 (each 1H, d, $J = 17.6$ Hz), 3.97 (1H, t, $J = 8.6$ Hz), 2.97–3.20 (2H, m), 2.52–2.62 (2H, m), 2.44 (3H, s), 2.10 (1H, dd, $J = 3.5$, 18 Hz); ^{13}C NMR δ 206.8, 173.7, 146.1, 144.4, 138.9, 133.4, 130.1, 129.9, 127.5, 126.4, 125.5, 68.2, 52.0, 49.2, 48.7, 42.9, 39.4, 21.6; IR 3468, 1704, 1672, 1619 cm^{-1}; MS *m/z* 451 (M^+); high-resolution mass *m/z* calcd for $C_{22}H_{20}F_3NO_4S$ (M^+) 451.1065, found: 451.1071. **31H**; mp 188–190°C; ^{1}H NMR δ 7.64, 7.34 (each 2H, d, $J = 8.2$ Hz), 7.50, 7.36 (each 2H, d, $J = 7.9$ Hz), 5.55 (1H, s), 4.29, 3.83 (each 1H, d, $J = 17.5$ Hz), 3.96 (1H, t, $J = 8.7$ Hz), 3.30–3.42 (1H, m), 3.05–3.10 (1H, m), 2.61 (1H, dd, $J = 6.4$, 18 Hz), 2.45 (3H, s), 2.42 (1H, dd, $J = 8.7$, 11.2 Hz), 2.01 (1H, dd, $J = 3.5$, 18 Hz); ^{13}C NMR δ 206.6, 173.3, 145.6, 144.5, 139.7, 132.7, 130.2, 130.1, 127.6, 126.4, 125.6, 67.7, 52.2, 49.2, 47.6, 42.5, 39.7, 21.5; IR 3422, 1704, 1674, 1618, 1598 cm^{-1}; MS *m/z* 451 (M^+); high-resolution mass *m/z* calcd for $C_{22}H_{20}F_3NO_4S$ (M^+) 451.1065, found: 451.1053.

*4.36. 6-[(4-Fluorophenyl)-a-hydroxymethyl]-2-tosyl-2,3,3a,4-tetrahydro-1H-cyclopenta[c]pyrrol-5-one (**32L, H**)*

32L; mp 189°C; ^{1}H NMR δ 7.73, 7.38 (each 2H, d, $J = 8.3$ Hz), 7.33 (2H, dd, $J = 5.5$, 8.7 Hz), 7.01 (2H, t, $J = 8.7$ Hz), 5.47 (1H, s), 4.32, 4.21 (each 1H, d, $J = 17.3$ Hz), 3.99 (1H, t, $J = 8.6$ Hz), 3.00–3.13 (1H, m), 2.58 (1H, t, $J = 8.6$ Hz), 2.56 (1H, dd, $J = 6.3$, 18 Hz), 2.46 (3H, s), 2.11 (1H, dd, $J = 3.5$, 18 Hz); ^{13}C NMR δ 206.4, 172.9, 144.0, 139.1, 137.7, 132.8, 129.7, 127.6, 127.4, 127.1, 115.0, 114.7, 67.2, 51.6, 42.4, 39.0, 21.0; IR 3496, 1711, 1684, 1602, 1507 cm^{-1}; MS *m/z* 401 (M^+); high-resolution mass *m/z* calcd for $C_{21}H_{20}FNO_4S$ (M^+) 401.1097, found: 401.1098. **32H**; mp 165–167°C; ^{1}H NMR δ 7.63, 7.33 (each 2H, d, $J = 8.3$ Hz), 7.20 (2H, dd, $J = 5.4$, 8.7 Hz), 6.98 (2H, t, $J = 8.7$ Hz), 5.47 (1H, s), 4.05, 3.66 (each 1H, d, $J = 17.3$ Hz), 3.97 (1H, t, $J = 8.6$ Hz), 3.10–3.15 (1H, m), 2.61 (1H, dd, $J = 6.2$, 18.1 Hz), 2.47 (1H, dd, $J = 8.6$, 12.2 Hz), 2.46 (3H, s), 2.04 (1H, dd, $J = 3.5$, 18.1 Hz); ^{13}C NMR δ 206.8, 172.6, 144.1, 138.9, 136.6, 133.0, 130.0, 127.9, 127.4, 115.8, 115.4, 68.7, 52.0, 47.1, 42.4, 39.5, 21.6; IR 3382, 1697, 1659, 1600, 1508 cm^{-1}; MS *m/z* 401 (M^+); high-resolution mass *m/z* calcd for $C_{21}H_{20}FNO_4S$ (M^+) 401.1097, found: 401.1098.

*4.37. 6-(2,2,2-Trifluoro-1-hydroxyethyl)-2-tosyl-2,3,3a,4-tetrahydro-1H-cyclopenta-[c]pyrrol-5-one (**33**)*

Obtained as an inseparable 1:1 mixture of diastereomers; mp 170–178°C; ^{1}H NMR δ 7.75, 7.74 (each 1H, d, $J = 8.2$ Hz), 7.39 (2H, d, $J = 8.2$ Hz), 4.79 (1H, q, $J = 6.6$ Hz), 4.49, 4.20 (together 1H, each d, $J = 18.1$ Hz), 4.44, 4.40 (together 1H, each d, $J = 17.2$ Hz), 4.00–4.08 (1H, m), 3.11–3,27 (1H, m), 2.60–2.72 (2H, m), 2.45 (3H, s), 2.12–2.21 (1H, m); ^{13}C NMR δ 205.2, 205.0, 179.3, 178.2, 144.2, 144.1, 132.9, 132.5, 132.4, 131.4, 129.8, 127.1, 64.0, 51.8, 51.5, 42.8, 42.6, 39.4, 38.7, 21.1; IR 3447, 1713, 1680, 1596 cm^{-1}; MS *m/z* 375 (M^+); high-resolution mass *m/z* calcd for $C_{16}H_{16}F_3NO_4S$ (M^+) 375.0752, found: 375.0747.

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