A New Regio- and Chemoselective Approach to β-Keto Amides and β-Enamino Carboxamides via 1,3,2-Dioxaborinanes

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Abstract: Surprisingly, 5,6-disubstituted 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes, which can be easily obtained from β-keto esters, reacted regio- and chemoselectively with amines under mild reaction conditions to form 2,2-difluoro-4-alkylamino-1,3,2-dioxaborinanes in almost quantitative yields. The latter compounds can be easily deprotected, yielding β-keto amides, or directly transformed into β-enamino carboxamides. This procedure was also applied to the reaction of 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes with arylhydrazines which selectively afforded β-hydrazono esters, in some cases without further cyclization to pyrazolones.

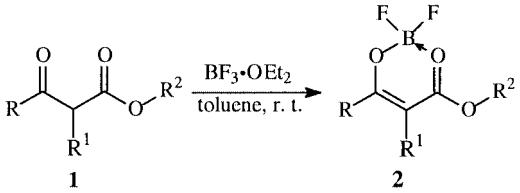
Key words: keto amides, enamino carboxamines, dioxaborinanes, chemoselectivity.

β-Keto amides and β-enamino carboxamides are important intermediates in the synthesis of natural products,[1] heterocycles,[2] and γ-aminols.[3] Additionally, β-*N*-alkenylenamino carboxamides have been utilized in the asymmetric synthesis of spirolactams[4] and some of them are also known to act as acyl-CoA: cholesterol acyltransferase inhibitors.[5] For these reasons it is of interest to find new, efficient, and simple procedures for the preparation of these compounds.

Generally, β-keto esters react with primary amines at room or elevated temperatures, to form β-enamino esters. Only in a few cases selective preparation of the corresponding β-keto amides starting from β-keto esters has been achieved. For example, by using 4-dimethyl-aminopyridine as a catalyst, it is possible to prepare β-keto amides directly from β-keto esters if secondary amines are used.[6] An alternative approach to β-keto amides is the room temperature aminolysis of β-ketothio ester derivatives,[7] but these compounds are not so readily available.[8]

In a previous communication,[9] we described the regioselective synthesis of β-enaminones and pyrazoles, starting from 1,3-diketonatoboron difluorides. Here we report that 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes, easily available from the corresponding β-keto esters and $BF_3{\cdot}OEt_2$ (Scheme 1, Table 1),[10] react with various amines to give 2,2-difluoro-4-alkylamino-1,3,2-dioxaborinanes.

Furthermore, we wish to describe the specific reactivity of 5,6-disubstituted 2,2-difluoro-4-alkoxy-1,3,2-dioxa-borinanes (**2a**–**e**) towards a series of amino and hydrazino compounds, which, despite the common use of difluoride complexes as intermediates in organic synthesis,[11] have never been studied before. To the best of our knowledge these reactions represent the first examples of the direct transformation of 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes to 2,2-difluoro-4-alkyl-amino-1,3,2-dioxaborinanes.



Scheme 1

Table 1 Preparation of Dioxaborinanes **2**

Entry	R	R^1	R^2	Product	Yield (%)[a]
1	Me	H	Et	**2a**	90
2	Ph	H	Et	**2b**[12]	88
3	$-(CH_2)_4-$		Et	**2c**	99
4	Me	MeO_2CCH_2	Me	**2d**	99
5	Me	$-(CH_2)_2-$		**2e**	99

[a] Isolated yields after reaction in toluene at r.t. for 16 h.

Treatment of **2a**–**e** with various amines led to the corresponding 2,2-difluoro-4-alkylamino-1,3,2-dioxaborinanes (**3**, Scheme 2).

The reaction appeared to be highly solvent dependent. The best conversions and yields of compounds **3** were obtained in acetonitrile.[13] Conversions were significantly lower in other solvents (ethyl acetate, diethyl ether, THF, dichloromethane, and nitromethane). In those solvents, which might act as good nucleophiles (alcohols) the reaction did not occur and β-keto esters were isolated as the only products. We also varied the amount of amine, i.e. 1–3 equivalents, and the temperature of the reaction. The best results were obtained by treating 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes (**2a**–**e**) with 1.3 equivalents of the corresponding amine in acetonitrile at 25 °C

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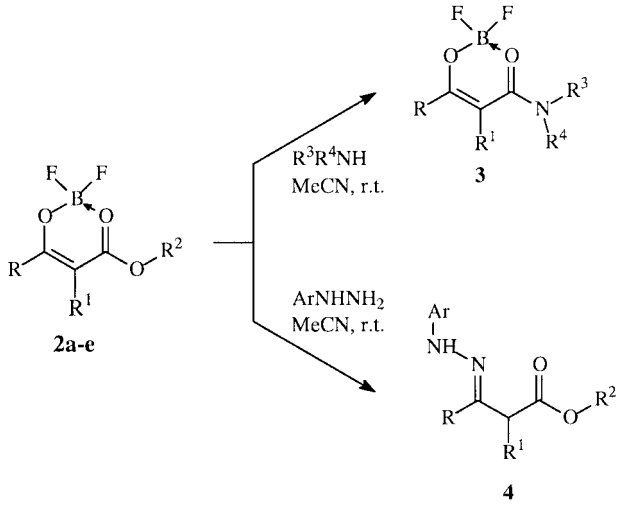


Scheme 2

(Table 2). Moreover, many attempts to form the 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes in situ, which could then react with amines to derive the desired products, failed.

The reaction seems to be initiated by the attack of an amino group to the ester carbonyl moiety yielding an α-alkoxy-α-alkylamino-1,3,2-dioxaborinane intermediate which in turn eliminates an α-alkoxy group, thus forming a more stable amido product of type **3**.

The reaction has been applied to a series of amines. As shown in Table 2, yields are generally good. The reaction works well with primary amines (including *t*-butylamine) and secondary amines. In order to extend the scope of this methodology, we decided to study the chemo- and regioselectivity of the reaction. For this reason the dimethyl 2-acetylsuccinate analog, **2d** (Table 1), was prepared. The latter compound reacted with different types of amines by addition only to the ester group at the β-position to the carbonyl group. In such a manner we were able to carry out selective introduction of an amido group to a multi functional system. Even more, in the case of cystine amine (entry 13, Table 2) the amino group reacted exclusively, leading to a single product. Subsequently, having demonstrated that **2d** can be selectively transformed, we briefly investigated the reactivity of 2-acetylbutyrolactone boron complex **2e** with various amines. Thus, as outlined in Table 2, the reaction of **2e** with amines led, as expected, to lactone opening and so deriving 5-(2-hydroxyethyl) substituted products **3o** and **3p**. Identification of **3** was confirmed by X-ray structure analysis and NMR spectroscopy. One can observe in ^{13}C NMR spectra ^{19}F–^{13}C coupling of 2.5 Hz for =*C*–*O*–B*F*$_2$ and 2 Hz for –*C*=O→B*F*$_2$.

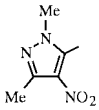
Different reactivities for alkyl and aryl hydrazines were also found. Alkylhydrazines reacted with **2a** similar to amino compounds, deriving hydrazido analogs **3e** and **3f**, whereas arylhydrazines led to hydrazono derivatives[14] **4a**–**e** (Table 3). It is noteworthy that methylhydrazine

Table 2 Preparation of 2,2-Difluoro-4-alkylamino-1,3,2-dioxaborinanes

Entry	R	R^1	R^3	R^4	Product **3**	Time (h)	Yield (%)[a]
1	Ph	H	–(CH$_2$)$_5$–		**a**	0.5	96
2	Ph	H	*t*-Bu	H	**b**	0.5	71
3	Ph	H	CH$_2$=CHCH$_2$	H	**c**	0.5	89
4	Ph	H	H$_2$NCH$_2$CH$_2$	H	**d**	0.5	89
5	Ph	H	(Me)$_2$N	H	**e**	4	81
6	Ph	H	Me	NH$_2$	**f**	0.5	80
7	–(CH$_2$)$_4$–		*i*-Pr	H	**g**	0.5	99
8	–(CH$_2$)$_4$–		PhCH$_2$	H	**h**	0.5	78
9	Me	H	*i*-Pr	H	**i**	0.5	92
10	Me	H	3-PyCH$_2$	H	**j**	0.5	95
11	Me	MeO$_2$CCH$_2$	H	H	**k**	0.5	99
12	Me	MeO$_2$CCH$_2$	–(CH$_2$)$_4$–		**l**	0.5	97
13	Me	MeO$_2$CCH$_2$	HSCH$_2$CH$_2$	H	**m**	1	71
14	Me	MeO$_2$CCH$_2$	CH$_2$=CHCH$_2$	H	**n**	0.5	90
15	Me	HO(CH$_2$)$_2$	*i*-Pr	H	**o**	0.5	45
16	Me	HO(CH$_2$)$_2$	(MeO)$_2$CHCH$_2$	H	**p**	0.5	53

[a] Isolated yields.

Table 3 Preparation of Hydrazono Derivatives

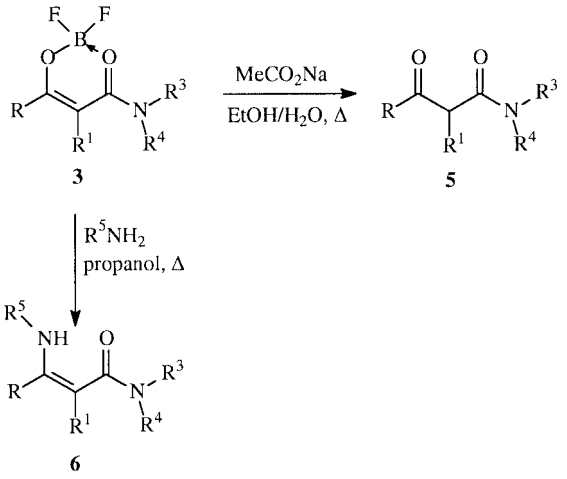
4	Ar	R	R^1	R^2	Time (h)	Yield (%)[a]
a[15]	2,4-$NO_2C_6H_3$	Ph	H	Et	12	91
b	2-NO_2,4-CNC_6H_3	Ph	H	Et	12	93
c		Ph	H	Et	12	95
d	2-NO_2,4-CNC_6H_3	Me	H	Et	8	89
e	2-NO_2,4-CNC_6H_3	Me	MeO_2CCH_2	Me	5	87

[a] Isolated yields.

reacted selectively with N–1, deriving a single product, illustrating once again the high chemoselectivity of the transformation.

Deprotection of **3** with sodium acetate (5 equiv) in a refluxing mixture of solvents ethanol/water 1/1 v/v, afforded β-keto amides **5** in good yields (Scheme 3, Table 4).

On the basis of these results, we then designed an experimentally convenient one-pot synthesis of β-enamino carboxamides from dioxaborinanes.[19] Reaction of **3** and amine (5 equiv) in propanol at 130 °C in an Ace pressure tube, gave high yields of β-enamino carboxamides **6**. As illustrated in Table 4, selective introduction of an amino moiety can be applied either on the enamino or amido part of the molecule (Table 4, entry 8–11) simply by changing the sequence of the reactions. Despite the rather high instability of the *N*-allylenamines **6c** and **6e**, they could be stored in the refrigerator for a couple of days.



Scheme 3

Table 4 Preparation of β-Keto Amides and β-Enamino Carboxamides

Entry	Product	R	R^1	R^3	R^4	R^5	Time (h)	Yield[a] (%)
1	**5a**	Ph	H	*i*-Pr	H	–	15	88
2	**5b**	Ph	H	3-$PyCH_2$	H	–	2	97
3	**5c**[16]	Ph	H	CH_2=$CHCH_2$	H	–	3	91
4	**5d**[17]	Me	H	*i*-Pr	H	–	10	98
5	**5e**[6a]	–$(CH_2)_4$–		*i*-Pr	H	–	16	95
6	**5f**[18]	–$(CH_2)_4$–		$PhCH_2$	H	–	16	93
7	**5g**	Me	MeO_2CCH_2	–$(CH_2)_4$–		–	2	97
8	**6a**	Ph	H	3-$PyCH_2$	H	*i*-Pr	5	96
9	**6b**	Ph	H	*i*-Pr	H	3-$PyCH_2$	12	90
10	**6c**	Ph	H	3-$PyCH_2$	H	CH_2CH=CH_2	8	87
11	**6d**	Ph	H	CH_2=$CHCH_2$	H	*i*-Pr	5	89
12	**6e**	Ph	H	–$(CH_2)_5$–		CH_2CH=CH_2	5	93
13	**6f**	–$(CH_2)_4$–		*i*-Pr	H	PhNH	5	90

[a] Isolated yields.

In summary, we have explored the previously unknown direct conversion of 5,6-disubstituted 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes to 2,2-difluoro-4-alkyl-amino analogues with a variety of amines. As well, we have demonstrated a preparatively useful method for the synthesis of β-keto amides and β-enamino carboxamides in two overall steps and good yields starting from easily accessible starting materials. This chemo- and regioselective approach could be the method of choice for the preparation of such systems.

Acknowledgment

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(10) **General Procedure for the Preparation of 2,2-Difluoro-4-alkoxy-1,3,2-dioxaborinanes (2a–e)**. To a solution of the corresponding 1,3-ketoester (1 mmol) in toluene (5 mL) $BF_3{\cdot}Et_2O$ (3 equiv) was added at r.t. After being stirred at r.t. for 16 h, the reaction mixture was concentrated to 1/3 of volume (in the case of ethyl acetoacetate, ethyl benzoylacetate, and ethyl cyclohexanone-2-carboxylate) and than cooled to –10 °C. Precipitated material was filtered off and washed with mixture of solvents petroleum ether/EtOAc = 5/1 (5 mL), yielding pure product. In the case of dimethyl 2-acetylsuccinate and 2-acetylbutyrolactone the reaction mixture was evaporated to dryness yielding yellowish oil, which was used in the next step without further purification. Compound **2a**: mp 28–31 °C (from hexane). IR (NaCl-plates): ν = 2980, 1590, 1540, 1380, 1330, 1185, 1040, 790 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.42 (t, 3 H, *J* = 7.2 Hz), 2.18 (s, 3 H), 4.51 (q, 2 H, *J* = 7.2 Hz), 5.41 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8, 23.1, 66.3, 87.1, 175.0 (t, *J* = 2.3 Hz), 186.4 (t, *J* = 1.4 Hz). MS (EI, 70 eV): *m/z* (%) = 178 (52) [M^+], 135 (42), 84 (100), 69 (97). HRMS (EI): *m/z* calcd for $C_6H_9BF_2O_3$: 178.0613; found: 178.0618. Compound **2d**: yellowish oil. IR (NaCl-plates): ν = 2963, 1719, 1609, 1509, 1337, 1053 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.22 (s, 3 H), 3.35 (s, 2 H), 3.77 (s, 3 H), 4.10 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2, 29.6, 53.1, 56.6, 92.1, 172.7, 174.2, 185.4. MS (EI, 70 eV): *m/z* (%) = 236(16) [M^+], 217(89), 177(68), 97(100), 55(75). HRMS (EI): *m/z* calcd for $C_8H_{11}BF_2O_5$: 236.0668; found: 236.0674.

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(13) **General Procedure for the Reaction of 2,2-Difluoro-4-alkoxy-1,3,2-dioxaborinanes (2a–e) with Amines**. To a solution of the corresponding amine (1.3 mmol) in MeCN (5 mL) 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinane (1 mmol) was added at r.t. The reaction mixture was stirred at r.t. for the period of time noted in Table 2. In the case where product precipitated from the reaction mixture, it was filtered off and washed with cold MeCN (3 mL), otherwise the reaction solvent was evaporated in vacuo and the residue dissolved in CH_2Cl_2 or EtOAc (30 mL), washed with H_2O (2 × 10 mL), dried over $MgSO_4$ and evaporated in vacuo. In some cases products were purified by flash chromatography. Selected spectroscopic data for compound of type **3**. Compound **3f**: mp 151–153 °C (from MeCN). IR (KBr): ν = 3445, 3350, 1677, 1605, 1503, 1407, 1355, 1230, 911, 778, 693 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 3.32 (s, 3 H), 5.54 (br s, 2 H), 6.78 (s, 1 H), 7.50–7.62 (m, 3 H), 7.88–7.91 (m, 2 H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 40.0, 84.2, 127.5, 129.9, 133.2, 134.1, 169.0 (t, *J* = 2.6 Hz), 170.9 (t, *J* = 2.0 Hz). MS (EI, 70 eV): *m/z* (%) = 240 (41) [M^+], 195(46), 105 (100), 94 (34), 77 (45). HRMS (EI): *m/z* calcd for $C_{10}H_{11}BF_2N_2O_2$: 240.0882; found: 240.0891. Compound **3h**: mp 135–137 °C (from Et_2O–EtOAc). IR (KBr): ν = 3399, 2955, 1612, 1528, 1339, 1263, 1197, 1038, 978, 743, 698 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 1.64–1.66 (m, 4 H), 2.19–2.26 (m, 4 H), 4.52 (s, 2 H), 7.27–7.40 (m, 5 H), 9.49 (br s, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 21.8, 22.0, 22.3, 31.0, 44.6, 95.7, 128.3, 128.4, 129.5, 137.9, 168.0 (t, *J* = 2.6 Hz), 174.2 (t, *J* = 2.2 Hz). MS (EI, 70 eV): *m/z* (%) = 279 (24) [M^+], 91 (100). HRMS (EI): *m/z* calcd for $C_{14}H_{16}BF_2NO_2$: 279.1242; found: 279.1249. Compound **3k**: mp 108–109 °C (from light petroleum ether–EtOAc). IR (KBr): ν = 3458, 3370, 3284, 2996, 2961, 1744, 1663, 1597, 1356, 1179, 954, 784, 578 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 2.00 (s, 3 H), 3.38 (s, 2 H), 3.59 (s, 3 H), 8.72 (br s, 1 H), 9.09 (bs, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 20.4, 29.8, 51.8, 91.6, 169.5 (t, *J* = 2.3 Hz), 170.7, 176.3 (t, *J* = 2.3 Hz). MS (EI, 70 eV): *m/z* (%) = 221 (27) [M^+], 162 (100), 97 (94). HRMS (EI): *m/z* calcd for $C_7H_{10}BF_2NO_4$: 221.0671; found: 221.0677. Compound **3p**: The colorless oil obtained on work-up was subjected to flash chromatography (1:10 MeOH–$CHCl_3$ elution). IR (NaCl-plates): ν = 3564, 3401, 2945, 1605, 1523, 1458, 1300, 1200, 1128, 1047 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.07 (s, 3 H), 2.44 (t, 2 H, *J* = 5.4 Hz), 3.16 (bs, 1 H), 3.37 (s, 6 H), 3.51 (t, 2 H, *J* = 5.4 Hz), 3.74 (dd, 2 H, J_1 = 4.8 Hz, J_2 = 5.4 Hz), 4.46 (t, 1 H, *J* = 5.4 Hz), 8.22 (t, 1 H *J* = 4.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.4, 28.3, 42.2, 54.3, 62.5, 96.7, 101.5, 169.3 (t, *J* = 2.5 Hz), 174.7 (t, *J* = 1.7 Hz). MS (EI, 70 eV): *m/z* (%) = 281 (0.3) [M$^+$], 111(81), 84(100).

(14) **General Procedure for the Preparation of Hydrazones 4.** To a stirred solution of 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinane (1 mmol) in MeCN (5 mL) the corresponding arylhydrazine (1.05 mmol) was added, which promptly dissolved. The reaction mixture was stirred at r.t. for 5–12 h. The precipitated material was filtered off and washed with cold MeCN (3 mL) and then recrystallized. Compound **4c**: mp 100–102 °C (from EtOH). IR (KBr): ν = 3215, 1724, 1605, 1443, 1301, 764 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29 (t, 3 H, *J* = 7.2 Hz), 2.52 (s, 3 H), 3.91 (s, 2 H), 4.13 (s, 3 H), 4.28 (q, 2 H, *J* = 7.2 Hz), 7.43–7.46 (m, 3 H), 7.77–7.81 (m, 2 H), 10.76 (br s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (2 C), 33.6, 40.0, 61.5, 117.4, 126.2, 128.8, 129.8, 136.4, 142.6, 143.7, 147.5, 167.7. MS (EI, 70 eV): *m/z* (%) = 345 (100) [M$^+$], 225 (35), 103 (91), 77 (68). HRMS (EI): *m/z* calcd for $C_{16}H_{19}N_5O_4$: 345.1437; found: 345.1449. Compound **4e**: mp 102–103 °C (from light petroleum ether–EtOAc). IR (KBr): ν = 3318, 2954, 2226, 1734, 1624, 1567, 1524, 1283, 1157, 998, 918, 762 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.11 (s, 3 H), 2.93 (d, 2 H, *J* = 6.9 Hz), 3.62 (s, 3 H), 3.69 (s, 3 H), 3.94 (t, 1 H, *J* = 6.9 Hz), 7.72 (d, 1 H, *J* = 9.0 Hz), 7.97 (dd, 1 H, J_1 = 1.8 Hz, J_2 = 9.0 Hz), 8.57 (d, 1 H, *J* = 1.8 Hz), 10.63 (bs, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 15.4, 33.0, 49.4, 51.6, 52.3, 99.8, 116.1, 117.8, 130.6, 131.3, 138.1, 143.3, 152.6, 170.7, 171.4. MS (EI, 70 eV): *m/z* (%) = 348 (30) [M$^+$], 317 (30), 256 (100), 210(23). HRMS (EI): *m/z* calcd for $C_{15}H_{16}N_4O_6$: 348.1070; found: 348.1081.

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(19) **General Procedure for the Preparation of β-Carboxamido Enamines 6**. In a typical experiment the solution of 2,2-difluoro-4-alkylamino-1,3,2-dioxaborinane (1 mmol) and corresponding amine (5 equiv) in PrOH (5 mL) was heated with stirring in an Ace pressure tube at 130–140 °C. After heating for 5–12 h, the reaction mixture was evaporated under reduced pressure and the residue purified by flash chromatography. Spectroscopic data for compound of type **6**. Compound **6a**: The colorless oil obtained on work-up was subjected to flash chromatography (5:3 light petroleum ether–EtOAc elution). Mp 117–120 °C (from Et_2O). IR (KBr): ν = 3213, 2963, 1624, 1593, 1428, 1303, 1212, 1171, 1124, 1035, 768, 708 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (d, 6 H, *J* = 6.9 Hz), 3.36–3.48 (m, 1 H), 4.41 (s, 1 H), 4.48 (d, 2 H, *J* = 6.0 Hz), 5.45 (br s, 1 H), 7.23 (dd, 1 H, J_1 = 4.6 Hz, J_2 = 7.8 Hz), 7.34–7.39 (m, 5 H), 7.64–7.67 (m, 1 H), 8.48 (dd, 1 H, J_1 = 1.8 Hz, J_2 = 4.6 Hz), 8.54 (d, 1 H, *J* = 2.1 Hz), 8.86 (br s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.2, 40.3, 45.6, 87.8, 123.4, 127.7, 128.2, 128.8, 135.0, 135.3, 137.1, 148.5, 149.0, 162.1, 170.2. MS (EI, 70 eV): *m/z* (%) = 295 (31) [M$^+$], 252 (49), 188 (56), 160 (100), 146 (85), 104 (83), 92 (47). HRMS (EI): *m/z* calcd for $C_{18}H_{21}N_3O$: 295.1685; found: 295.1690. Compound **6b**: The colorless oil obtained on work-up was subjected to flash chromatography (1:1 light petroleum ether–EtOAc elution). Mp 114–116 °C (from Et_2O). IR (KBr): ν = 3227, 2961, 1620, 1545, 1324, 1215, 1017, 922, 791, 768, 733, 702 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16 (d, 6 H, *J* = 6.8 Hz), 4.07–4.14 (m, 1 H), 4.19 (d, 2 H, *J* = 6.6 Hz), 4.50 (s, 1 H), 4.98 (br s, 1 H), 7.20 (ddd, 1 H, J_1 = 0.8 Hz, J_2 = 4.7 Hz, J_3 = 7.7 Hz), 7.27–7.37 (m, 5 H), 7.56 (ddd, 1 H, J_1 = J_2 = 2.0 Hz, J_3 = 7.7 Hz), 8.32 (d, 1 H, *J* = 2.0 Hz), 8.45 (dd, 1 H, J_1 = 1.5 Hz, J_2 = 4.7 Hz), 9.40 (bs, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.1, 40.6, 45.7, 90.8, 123.4, 127.8, 128.4, 129.0, 134.7, 135.3, 136.3, 148.4, 148.7, 161.4, 169.4. MS (EI, 70 eV): *m/z* (%) = 295 (64) [M$^+$] 237 (69), 209 (100), 92 (98). HRMS (EI): *m/z* calcd for $C_{18}H_{21}N_3O$: 295.1685; found: 295.1694. Compound **6d**: The colorless oil obtained on work-up was subjected to flash chromatography (1:10 MeOH–$CHCl_3$ elution). Colorless oil. IR (NaCl-plates): ν = 3300, 2969, 1614, 1540, 1496, 1299, 1213, 1168, 770, 702 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.07 (d, 6 H, *J* = 6.6 Hz), 3.33–3.43 (m, 1 H), 3.88–3.92 (m, 2 H), 4.41 (s, 1 H), 5.07–5.22 (m, 2 H), 5.17 (br s, 1 H), 5.83–5.92 (m, 1 H), 7.33–7.38 (m, 5 H), 8.81 (bs, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.1, 41.2, 45.4, 88.4, 115.5, 127.6, 128.1, 128.6, 135.3, 137.3, 161.5, 170.1. MS (EI, 70 eV): *m/z* (%) = 244 (53) [M$^+$], 188 (100), 160 (71), 146 (84), 104 (95). HRMS (EI): *m/z* calcd for $C_{15}H_{20}N_2O$: 244.1576; found: 244.1580. Compound **6e**: The colorless oil obtained on work-up was subjected to flash chromatography (10:1 light petroleum ether–EtOAc elution). Colorless oil. IR (NaCl-plates): ν = 2933, 1853, 1609, 1596, 1573, 1481, 1408, 1219, 1123, 1022, 775, 702 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.50–1.63 (m, 6 H), 3.33–3.48 (m, 4 H), 3.58–3.62 (m, 2 H), 4.77 (s, 1 H), 5.03–5.21 (m, 2 H), 5.72–5.81 (m, 1 H), 7.33–7.39 (m, 5 H), 9.52 (br s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.7, 25.9, 46.6, 85.1, 115.3, 127.7, 128.0, 128.5, 128.6, 135.7, 137.2, 162.7, 169.1. MS (EI, 70 eV): *m/z* (%) = 270 (42) [M$^+$], 186 (100), 159 (65), 84 (66). HRMS (EI): *m/z* calcd for $C_{17}H_{22}N_2O$: 270.1732; found: 270.1739. Compound **6f**: The colorless oil obtained on work-up was subjected to flash chromatography (5:1 light petroleum ether–EtOAc elution). Mp 114–117 °C. IR (KBr): ν = 3296, 2968, 2937, 1646, 1599, 1531, 1456, 1167, 752 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (d, 3 H, *J* = 6.6 Hz), 1.18 (d, 3 H, *J* = 6.6 Hz), 1.61–1.70 (m, 2 H), 1.70–1.92 (m, 3 H), 2.12–2.45 (m, 3 H), 3.21 (t, 1 H, *J* = 4.9 Hz), 4.05–4.16 (m, 1 H), 6.31 (br s, 1 H), 6.85–6.90 (m, 1 H), 7.04–7.07 (m, 2 H), 7.24–7.30 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.7, 22.8, 23.3, 24.3, 25.0, 29.0, 41.3, 49.9, 112.9, 119.2, 145.4, 148.2, 170.6. MS (EI, 70 eV): *m/z* (%) = 273 (25) [M$^+$], 214 (100), 93 (32). Anal. Calcd for $C_{16}H_{23}N_3O$: C, 70.30; H, 8.48; N, 15.37. Found: C, 70.01; H, 8.32; N, 15.63.