# Spiro[4*H*-chromene-4,5´-isoxazolines] and related compounds: synthesis and reactivities

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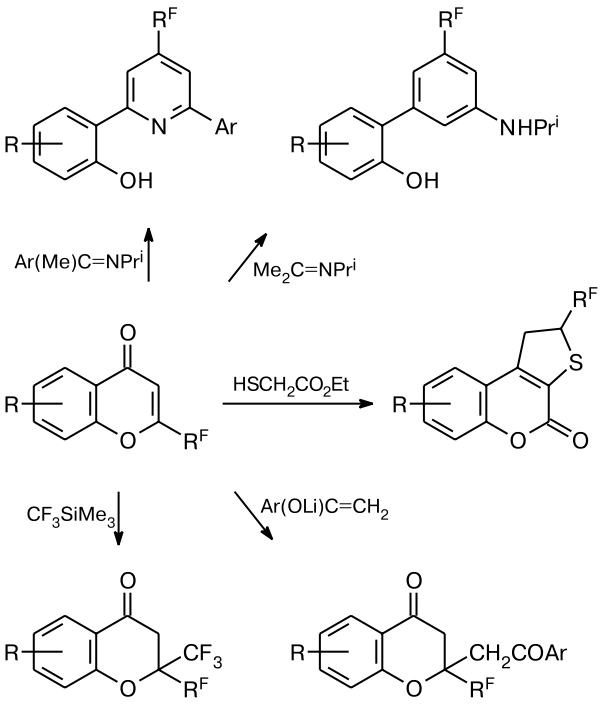
Reactions of chromones with methyl ketoximes in the presence of lithium diisopropylamide follow the nucleophilic 1,2-addition mechanism to give spiro[4*H*-chromene-4,5´-isoxazolines] in good yields. The isoxazoline ring in spiro[4*H*-chromene-4,5´-isoxazolines] undergoes opening under the action of conc. $H_2SO_4$, yielding α,β-unsaturated oximes. Their nitrosation and bromination lead to the corresponding spiroisoxazolines, while the Beckmann rearrangement, to α,β-unsaturated amides. The latter are also formed directly from spiro[4*H*-chromene-4,5´-isoxazolines] under the action of $PCl_5$. *N*-Substituted acetophenone hydrazones in the presence of lithium diisopropylamide react at the C(4) atom of 2-trifluoromethylchromone, while acetophenone anil under the same conditions, at the C(2) atom.

**Key words:** chromones, dilithio oximes and dilithio hydrazones, spiro[4*H*-chromene-4,5´-isoxazolines] and spiro[4*H*-chromone-4,5´-pyrazolines], α,β-unsaturated oximes and amides, Beckmann rearrangement, nitrosation, bromination.

Chromone (4*H*-chromen-4-one, 4*H*-1-benzopyran-4-one) is a parent structure for an important class of oxygen-containing heterocycles, in particular, flavone (2-phenylchromone) derivatives, which are widely encountered in the plant world. These compounds exhibit a variety of biological activity[1] and find application as active principles in a number of pharmaceutical preparations including antitumor[2] drugs. The chemistry of chromones has been much investigated;[1,3—5] however, data on reactions of 2-substituted chromones with C-nucleophiles are very scarce. Recently, we have demonstrated that dinucleophiles such as methyl ketone imines (1,3-C,N- and 1,3-C,C-dinucleophiles)[6,7] and alkyl mercaptoacetates (1,2-S,C-dinucleophiles)[8] react with 2-$R^F$-chromones at the C(2) atom with cleavage of the O(1)—C(2) bond followed by condensation at the carbonyl group to give $R^F$-containing aromatic and heterocyclic compounds. Reactions of 2-$R^F$-chromones with C-nucleophiles such as trimethyl(trifluoromethyl)silane (Ruppert´s reagent) and lithium enolates of aryl methyl ketones also occur at the C(2) atom, but without opening of the pyrone ring, yielding 1,4-addition products: 2,2-bis(trifluoromethyl)chroman-4-ones[9] and 2-phenacyl-2-trifluoromethylchroman-4-ones,[10] respectively (Scheme 1).

**Scheme 1**




We found that unlike reactions with Ruppert´s reagent and lithium enolates of methyl ketones, condensation of 2-trifluoromethylchromones with lithiated oximes and hydrazones of methyl ketones follows the nucleo-

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 3, pp. 516—522, March, 2006.

philic 1,2-addition mechanism, affording derivatives of spiro[4*H*-chromene-4,5′-isoxazoline] and spiro[4*H*-chromene-4,5′-pyrazoline], which are novel spiroannulated heterocyclic systems (see preliminary communication[11]).

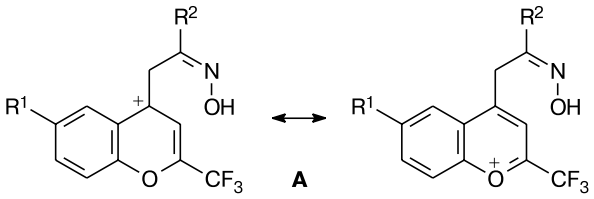
## Results and Discussion

1,4-Dianions generated from methyl ketoximes by *n*-butyllithium or lithium diisopropylamide are valuable intermediates in organic synthesis. Condensation of C,O-lithiated oximes with various electrophilic substrates such as esters,[12—15] amides,[16—18] ketones, and α,β-unsaturated ketones[19,20] ensures a regiocontrolled approach to β-oxo and β-hydroxy oximes, which easily undergo acid-catalyzed cyclodehydration into isoxazoles and 2-isoxazolines. However, reactions of dilithio oximes with chromones have not been studied hitherto.

We found that a reaction of acetophenone *E*-oxime[21] with 2.2 equiv. of lithium diisopropylamide in ether at 0 °C followed by addition of 2-trifluoromethylchromones (−20 °C→~20 °C, 2 h) and hydrolysis of the resulting mixture with water gives β-hydroxy oximes **1a,b** in good yields. In acidic media, oximes **1a,b** easily undergo cyclization (*via* dehydration) into spiroisoxazolines **2a,b**, which can also be obtained without the formation of oximes **1** if the reaction mixture is treated with dilute HCl. In the case of aliphatic oximes, unstable intermediate β-hydroxy oximes **1c,d** were not isolated: spiroisoxazolines **2c,d** were directly obtained in 64 and 26% yields, respectively (Scheme 2). This reaction is an earlier unknown transformation at the C(4) atom of the chromone system, which should be regarded as nucleophilic 1,2-addition of dilithio oxime with the formation of a new C—C bond followed by cyclodehydration into spiro[4*H*-chromene-4,5′-isoxazolines] **2**.

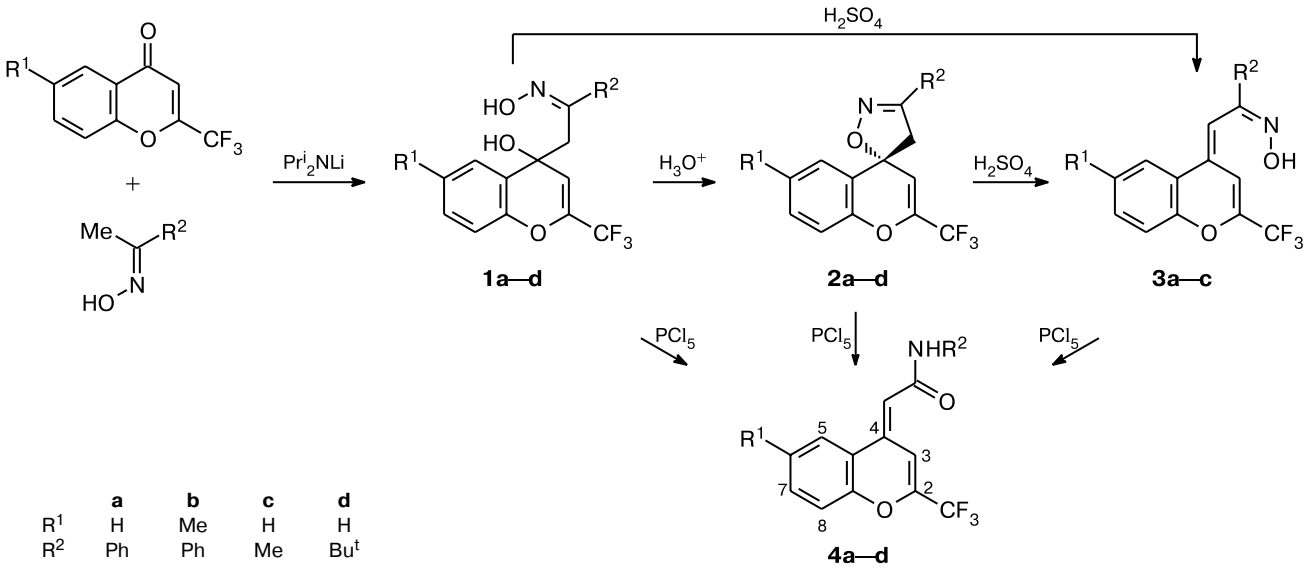
Treatment of compounds **2a—c** with conc. $H_2SO_4$ at ~20 °C for 20 min followed by hydrolysis with water gave, through opening of the isoxazoline ring, α,β-unsaturated oximes **3a—c** in 45—85% yields. This outcome was quite unexpected and is specific to the spiro[chromene-4,5′-isoxazoline] system. Earlier,[22,23] the opening of the 2-isoxazoline ring has been reported to occur only in the presence of bases.

Most likely, the driving force of the opening of the spiro node under the action of $H_2SO_4$ is the formation of intermediate aromatic benzopyrilium cation **A**, whose deprotonation gives α,β-enoximes **3**. An analogous transformation was observed in the treatment of oximes **1a,b** with $H_2SO_4$: their dehydration into compounds **3a,b** also proceeded through intermediate cation **A** undergoing subsequent deprotonation.



The *E*-configuration of the *exo*-cyclic C=C bond in oximes **3** was proved by the 2D NOESY technique. The 2D NOESY spectrum of compound **3a** shows cross-peaks between the signals for the proton of the *exo*-C=C bond (δ 6.79) and for the aromatic H(5) proton (δ 7.86). In the oxime fragments of compounds **1** and **3**, the *anti*-arrangement of the hydroxy and phenyl groups was expected

**Scheme 2**



| | a | b | c | d |
|---|---|---|---|---|
| $R^1$ | H | Me | H | H |
| $R^2$ | Ph | Ph | Me | Bu$^t$ |

since the *E*-configuration of the starting oxime is retained during the reaction.[17,24] This was confirmed by the structures of the products of the Beckmann rearrangement, which is known[25] to involve intramolecular migration of the substituent in the *anti*-position relative to the leaving OH group.

Indeed, oximes **1a,b** and **3a,b** in the presence of $PCl_5$ in ether at ~20 °C were rearranged into amides **4a,b** in high yields; therefore, in compounds **1** and **3**, the substituent $R^2$ is *anti* to the N—O bond. Interestingly, the Beckmann rearrangement easily occurs not only with oximes **1** and **3** but also with spiroisoxazolines **2a—d**, which behave like a latent oxime form under these conditions. This reaction is the first example of involvement of the isoxazoline ring in the Beckmann rearrangement without isolation of the corresponding α,β-unsaturated oxime. Note that spiroisoxazoline **2d** did not undergo opening into enoxime **3** on treatment with $H_2SO_4$, while in the presence of $PCl_5$, it immediately transformed into amide **4d**; hence, the rearrangement **2**→**4** occurs at the step of the formation of benzopyrilium cation **A**.

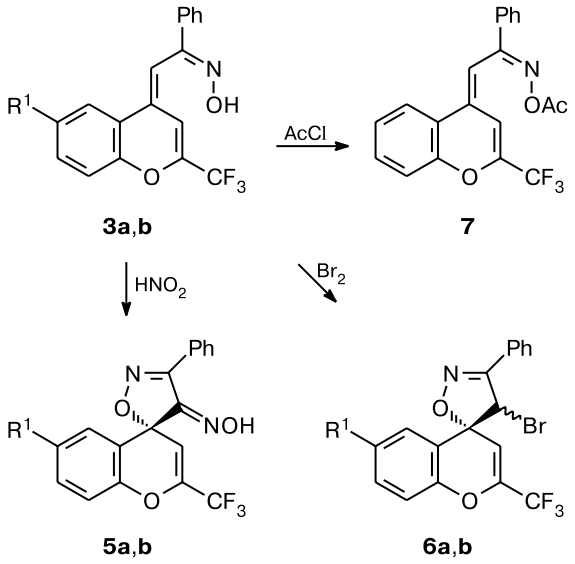
The stereochemistry of amides **4** was determined and their H(3) and =CH protons were assigned from the 2D NOESY and 2D HSQC data for amide **4c**. Its 2D NOESY spectrum shows cross-peaks between the signals for the =CH, H(5), and NH protons and no cross-peaks with the H(3) proton, which suggests the *E*-configuration of the *exo*-methylene double bond and the preferred s-*cis*-conformation. Indeed, the signal for the H(3) proton in the $^1$H NMR spectra of amides **4** appears in the unusually low field (δ 8.42—8.49) in both $CDCl_3$ and DMSO-$d_6$. Such a strong deshielding of the H(3) proton, whose signal in chromones usually appears at δ 6—7, is due to the close vicinity of the carbonyl O atom and the H(3) atom, which is possible only in the s-*cis*-conformer. In the $^{13}$C NMR spectrum of compound **4c**, the signal for the C(3) atom was easily identified from splitting at the F atoms with $^3J_{C,F}$ = 4.2 Hz. In turn, the 2D HSQC spectrum shows a cross-peak between the signal for this C atom and a singlet at δ 8.48, which allows unambiguous assignment of this singlet to the H(3) proton.

Apart from the Beckmann rearrangement, we studied other reactions of α,β-unsaturated oximes **3a,b**. We found that nitrosation of these compounds with $NaNO_2$ in dilute HCl gives hydroxyiminospiroisoxazolines **5a,b** in 78 and 59% yields, respectively; in this case, no deoximation products were detected (Scheme 3). Apparently, the transformation of enoxime **3** into spiroisoxazoline **5** involves an electrophilic attack of the nitrosonium cation at the α-position of compound **3**; the resulting cationic species, due to the presence of the hydroxy group, undergoes cyclization into 4-nitrosoisoxazoline existing in the oxime form **5**. Despite possible geometrical isomerism at the oxime group, compounds **5a,b** were isolated as only one stereoisomer. The formation of these products provides additional evidence for the *E*-configuration of the C=N bond of oximes **3**, because it has been shown earlier[26] that 4-hydroxyiminoisoxazolines are formed only from α,β-enoximes in which the OH group is *syn* to the double bond. For the *anti*-arrangement of these functions, the major products are 1-hydroxypyrazole 2-oxides resulting from an initial attack of the nitrosonium cation at the oxime N atom.[26]

It is known that halogenation of α,β-unsaturated oximes with *N*-halosuccinimides affords 4-haloisoxazolines.[27] In our case, oximes **3a,b** easily reacted with bromine in $CHCl_3$ at ~20 °C to give 4-bromoisoxazolines **6a,b** as mixtures of two diastereomers in 89—92% yields (the ratio of the diastereomers was 92 : 8 for **6a** and 96 : 4 for **6b**). Under analogous conditions, spiroisoxazoline **2a** resisted bromination, being recovered unchanged. Note that when the molar ratio of oxime **3b** to bromine was 1 : 1.5 (the same as was used in the halogenation of compound **3a**), we obtained a mixture of 4-bromo- and 4,4-dibromoisoxazolines in the ratio 62 : 38, respectively. Individual compound **6b** was obtained from an equimolar mixture of the reagents, while the use of a two- to threefold excess of bromine always gave a mixture of mono- and dibromo derivatives.

The relatively easy formation of compounds **5a,b** and **6a,b** upon an electrophilic attack on the α-C atom of the exocyclic double bond in oximes **3** can be associated with stable chromylium intermediate **A** undergoing rapid cyclization into a spiro system. Nevertheless, a reaction of oxime **3a** with such an electrophilic reagent as acetyl chloride occurred at the hydroxy group (~20 °C, 1 h), affording compound **7** in 67% yield (Scheme 3).

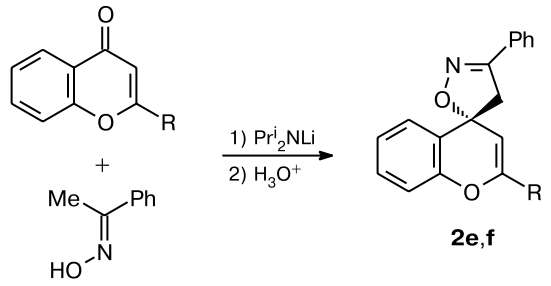
**Scheme 3**




$R^1$ = H (**a**), Me (**b**)

To determine the limits of application of the aforesaid reaction, we studied reactions of 2-methylchromone, flavone, and chromone with acetophenone oxime in the presence of lithium diisopropylamide. We found that despite the known tendency of the 2-methyl group to be deprotonated by bases,[28] 2-methylchromone under these conditions gives spiroisoxazoline **2e** in a virtually quantitative yield. An analogous reaction of flavone gave compound **2f** in 65% yield (Scheme 4). However, in the case of unsubstituted chromone, the reaction mixture almost immediately turned dark red and underwent resinification, probably because of the absence of a substituent in position 2 and the accessibility of the C(2) and H(2) atoms to an attack by a base.[29] It should also be noted that unlike spiroisoxazolines **2a—d** containing the $CF_3$ group at the C(2) atom, compounds **2e,f** did not react with conc. $H_2SO_4$, undergoing resinification under the action of $PCl_5$; this indicates a specific role of the $CF_3$ group in the aforesaid transformations.

**Scheme 4**

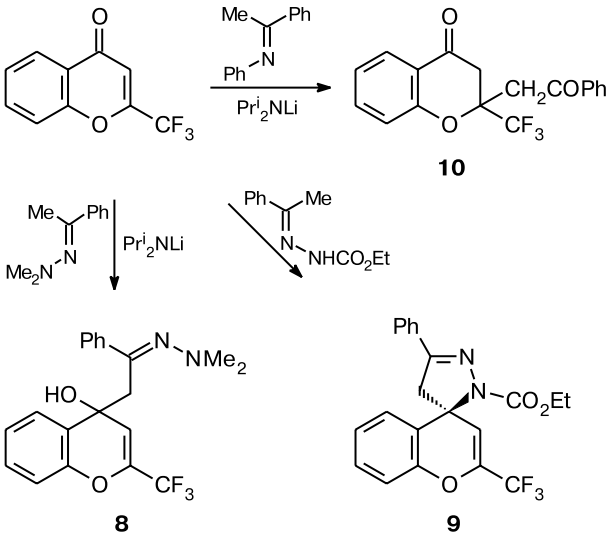



**2e,f**

R = Me (**e**), Ph (**f**)

Literature data on reactions of chromones with lithiated hydrazones and anils of methyl ketones are lacking. It is only known that the 1,4-dianion of acetophenone *N*-ethoxycarbonylhydrazone reacts with carbonyl compounds such as esters, acyl chlorides, amides, and α-halo ketones to give pyrazole and pyrazoline derivatives.[30] We found that a reaction of acetophenone dimethylhydrazone (in place of oximes) with 2-trifluoromethylchromone gives β-hydroxy hydrazone **8** in 22% yield as the result of nucleophilic addition of lithium aza enolate to the oxo group of the chromone. An analogous reaction with acetophenone *N*-ethoxycarbonylhydrazone afforded spiropyrazoline **9** in 26% yield, which is also a 1,2-adduct. However, acetophenone anil behaved differently under the same conditions, giving, *via* 1,4-addition, 2-phenacyl-2-trifluoromethylchroman-4-one (**10**) in 69% yield; earlier,[10] we have obtained this compound in 32% yield by the reaction of 2-trifluoromethylchromone with lithium enolate of acetophenone (Scheme 5). It should be noted that the $^1$H NMR spectrum of spiropyrazoline **9** shows strongly broadened signals for the protons of the ethoxycarbonyl group; this can be attributed to hindered rotation of the $CO_2Et$ group about the C—N bond.

**Scheme 5**




Thus, in contrast to lithium enolates of ketones and aza enolates of anils, lithiated oximes and hydrazones of methyl ketones react with chromones at the carbonyl C atom (1,2-addition) to give, on acidification, spiro[4*H*-chromene-4,5′-isoxazolines] and spiro[4*H*-chromene-4,5′-pyrazolines], which are of synthetic interest for further modification at position 4 of the chromone system.

## Experimental

IR spectra were recorded on IKS-29 and Perkin—Elmer Spectrum BX-II instruments (Nujol or KBr pellets). $^1$H and $^{13}$C NMR spectra were recorded on a Bruker DRX-400 spectrometer (400.1 and 100.6 MHz, respectively) in $CDCl_3$ with $Me_4Si$ as the internal standard.

**Synthesis of β-hydroxy oximes 1a,b.** Diisopropylamine (1.87 g, 18.5 mmol) was added to a solution of *n*-butyllithium prepared from metallic Li (37.0 mmol) and *n*-butyl bromide (18.5 mmol) in anhydrous diethyl ether (10 mL). The mixture was cooled with ice water and stirred for 30 min. Then a solution of methyl ketoxime (8.4 mmol) in diethyl ether (5 mL) was added to the resulting transparent solution of lithium diisopropylamide. The mixture was stirred for 40 min and cooled to –20 °C and a solution of an appropriate chromone (7.0 mmol) in anhydrous THF (6 mL) was added. The reaction mixture was stirred at ~20 °C for 2 h and hydrolyzed with water (50 mL). The product was extracted with ether (20 mL). The organic layer was separated and concentrated and the resulting oil was triturated with pentane to initiate crystallization. The solid product was filtered off, dried, and recrystallized from an appropriate solvent.

**2-(4-Hydroxy-2-trifluoromethyl-4*H*-chromen-4-yl)-1-phenylethan-1-one oxime (1a).** The yield was 72%, colorless needle-like crystals, m.p. 134—135 °C ($CCl_4$). Found (%): C, 61.70; H, 4.00; N, 3.98. $C_{18}H_{14}F_3NO_3$. Calculated (%): C, 61.89;

H, 4.04; N, 4.01. IR, ν/cm$^{-1}$: 3520 (OH), 3230 (NOH), 1695 (C=C), 1620, 1585 (arom.). $^1$H NMR ($CDCl_3$), δ: 3.32 (d, 1 H, CHH, $J$ = 13.6 Hz); 3.72 (d, 1 H, CHH, $J$ = 13.6 Hz); 4.0 (br.s, 1 H, OH); 5.67 (s, 1 H, H(3)); 7.01 (d, 1 H, H(8), $J_o$ = 8.3 Hz); 7.14 (t, 1 H, H(6), $J_o$ = 7.6 Hz); 7.22—7.40 (m, 6 H, H(7), Ph); 7.67 (d, 1 H, H(5), $J_o$ = 7.8 Hz); 9.0 (br.s, 1 H, NOH).

**2-(4-Hydroxy-6-methyl-2-trifluoromethyl-4*H*-chromen-4-yl)-1-phenylethan-1-one oxime (1b).** The yield was 62%, colorless needle-like crystals, m.p. 156—157 °C (toluene—hexane (2 : 1)). Found (%): C, 62.49; H, 4.34; N, 4.09. $C_{19}H_{16}F_3NO_3$. Calculated (%): C, 62.81; H, 4.44; N, 3.85. IR (KBr), ν/cm$^{-1}$: 3535 (OH), 3245 (NOH), 1695 (C=C), 1495 (arom.). $^1$H NMR ($CDCl_3$), δ: 2.28 (s, 3 H, Me); 3.33 (d, 1 H, CHH, $J$ = 13.5 Hz); 3.70 (d, 1 H, CHH, $J$ = 13.5 Hz); 3.85 (s, 1 H, OH); 5.65 (s, 1 H, H(3)); 6.90 (d, 1 H, H(8), $J_o$ = 8.4 Hz); 7.03 (dd, 1 H, H(7), $J_o$ = 8.4 Hz, $J_m$ = 2.1 Hz); 7.26—7.35 (m, 3 H, H(3´), H(4´), H(5´)); 7.40 (d, 1 H, H(5), $J_m$ = 1.8 Hz); 7.41—7.43 (m, 2 H, H(2´), H(6´)); 8.3 (br.s, 1 H, NOH).

**3´-Phenyl-2-trifluoromethylspiro[4*H*-chromene-4,5´,4´,5´-dihydroisoxazole] (2a).** A solution of conc. HCl (0.5 mL) in ethanol (2 mL) was added to a solution of compound **1a** (490 mg, 1.4 mmol) in ethanol (3 mL). This immediately resulted in the formation of a copious white precipitate. The mixture was stirred for 5 min and then diluted with water (5 mL). The precipitate was filtered off, washed with water, dried, and recrystallized from ethanol. The yield was 83%, colorless needle-like crystals, m.p. 124—125 °C.

Spiroisoxazoline **2a** was also obtained in 53% yield under the conditions of the synthesis of oximes **1a,b** by hydrolysis of the reaction mixture with a solution of oxalic acid. Found (%): C, 65.18; H, 3.43; N, 4.20. $C_{18}H_{12}F_3NO_2$. Calculated (%): C, 65.26; H, 3.65; N, 4.23. IR, ν/cm$^{-1}$: 1695 (C=C), 1615, 1595, 1585 (arom.). $^1$H NMR ($CDCl_3$), δ: 3.57 (d, 1 H, CHH, $J$ = 17.5 Hz); 3.78 (d, 1 H, CHH, $J$ = 17.5 Hz); 5.95 (s, 1 H, H(3)); 7.18 (dd, 1 H, H(8), $J_o$ = 8.4 Hz, $J_m$ = 1.1 Hz); 7.24 (ddd, 1 H, H(6), $J_o$ = 7.9 and 7.3 Hz, $J_m$ = 1.1 Hz); 7.39 (ddd, 1 H, H(7), $J_o$ = 8.4 and 7.3 Hz, $J_m$ = 1.6 Hz); 7.42—7.49 (m, 3 H, H(3´), H(4´), H(5´)); 7.52 (dd, 1 H, H(5), $J_o$ = 7.9 Hz, $J_m$ = 1.6 Hz); 7.68—7.73 (m, 2 H, H(2´), H(6´)).

**6-Methyl-3´-phenyl-2-trifluoromethylspiro[4*H*-chromene-4,5´,4´,5´-dihydroisoxazole] (2b)** was obtained analogously from compound **1b**. The yield was 89%, colorless needle-like crystals, m.p. 135—136 °C (ethanol). Found (%): C, 66.04; H, 4.10; N, 3.87. $C_{19}H_{14}F_3NO_2$. Calculated (%): C, 66.09; H, 4.09; N, 4.06. IR (KBr), ν/cm$^{-1}$: 1700 (C=C), 1595, 1570, 1500 (arom.). $^1$H NMR ($CDCl_3$), δ: 2.32 (s, 3 H, Me); 3.55 (d, 1 H, CHH, $J$ = 17.5 Hz); 3.78 (d, 1 H, CHH, $J$ = 17.5 Hz); 5.91 (s, 1 H, H(3)); 7.07 (d, 1 H, H(8), $J_o$ = 8.5 Hz); 7.18 (br.dd, 1 H, H(7), $J_o$ = 8.5 Hz, $J_m$ = 2.0 Hz); 7.28 (br.d, 1 H, H(5), $J_m$ = 2.0 Hz); 7.44—7.48 (m, 3 H, H(3´), H(4´), H(5´)); 7.70—7.73 (m, 2 H, H(2´), H(6´)).

**3´-Methyl-2-trifluoromethylspiro[4*H*-chromene-4,5´,4´,5´-dihydroisoxazole] (2c)** was obtained under the conditions of the synthesis of oximes **1a,b** by hydrolysis of the reaction mixture with dilute HCl (1 : 3). The yield was 64%, colorless needle-like crystals, m.p. 96—97 °C (hexane—$CHCl_3$). Found (%): C, 57.88; H, 3.97; N, 5.35. $C_{13}H_{10}F_3NO_2$. Calculated (%): C, 58.00; H, 3.74; N, 5.20. IR (KBr), ν/cm$^{-1}$: 1698 (C=C), 1636, 1617, 1588, 1493 (arom.). $^1$H NMR ($CDCl_3$), δ: 2.09 (t, 3 H, Me, $^4J$ = 1.0 Hz); 3.13 (dq, 1 H, CHH, $^2J$ = 17.9 Hz, $^4J$ = 1.0 Hz); 3.35 (dq, 1 H, CHH, $^2J$ = 17.9 Hz, $^4J$ = 1.0 Hz); 5.86 (s, 1 H, H(3)); 7.14 (dd, 1 H, H(8), $J_o$ = 8.3 Hz, $J_m$ = 1.2 Hz); 7.25 (ddd, 1 H, H(6), $J_o$ = 7.9 and 7.3 Hz, $J_m$ = 1.2 Hz); 7.37 (ddd, 1 H, H(7), $J_o$ = 8.3 and 7.3 Hz, $J_m$ = 1.6 Hz); 7.47 (dd, 1 H, H(5), $J_o$ = 7.9 Hz, $J_m$ = 1.6 Hz).

**3´-*tert*-Butyl-2-trifluoromethylspiro[4*H*-chromene-4,5´,4´,5´-dihydroisoxazole] (2d)** was obtained under the conditions of the synthesis of oximes **1a,b** by hydrolysis of the reaction mixture with dilute HCl (1 : 3). The yield was 26%, colorless crystals, m.p. 84—85 °C (hexane). Found (%): C, 61.76; H, 5.18; N, 4.33. $C_{16}H_{16}F_3NO_2$. Calculated (%): C, 61.73; H, 5.18; N, 4.50. IR (KBr), ν/cm$^{-1}$: 2975, 1703 (C=C), 1615, 1584, 1488 (arom.). $^1$H NMR ($CDCl_3$), δ: 1.28 (s, 9 H, Bu$^t$); 3.17 (d, 1 H, CHH, $J$ = 17.7 Hz); 3.38 (d, 1 H, CHH, $J$ = 17.7 Hz); 5.84 (s, 1 H, H(3)); 7.13 (dd, 1 H, H(8), $J_o$ = 8.3 Hz, $J_m$ = 1.1 Hz); 7.24 (ddd, 1 H, H(6), $J_o$ = 7.9 and 7.3 Hz, $J_m$ = 1.1 Hz); 7.36 (ddd, 1 H, H(7), $J_o$ = 8.3 and 7.3 Hz, $J_m$ = 1.6 Hz); 7.45 (dd, 1 H, H(5), $J_o$ = 7.9 Hz, $J_m$ = 1.6 Hz).

**2-Methyl-3´-phenylspiro[4*H*-chromene-4,5´,4´,5´-dihydroisoxazole] (2e)** was obtained from 2-methylchromone as described for compounds **2c,d**. The yield was 97%, colorless needles, m.p. 131—132 °C (ethanol). Found (%): C, 78.03; H, 5.31; N, 5.22. $C_{18}H_{15}NO_2$. Calculated (%): C, 77.96; H, 5.45; N, 5.05. IR (KBr), ν/cm$^{-1}$: 1695 (C=C), 1616, 1595, 1581, 1568, 1486 (arom.). $^1$H NMR ($CDCl_3$), δ: 2.06 (d, 1 H, Me, $J$ = 0.8 Hz); 3.42 (d, 1 H, CHH, $J$ = 17.4 Hz); 3.70 (d, 1 H, CHH, $J$ = 17.4 Hz); 5.12 (q, 1 H, H(3), $J$ = 0.8 Hz); 7.05 (dd, 1 H, H(8), $J_o$ = 8.4 Hz, $J_m$ = 1.1 Hz); 7.13 (ddd, 1 H, H(6), $J_o$ = 7.9 and 7.2 Hz, $J_m$ = 1.1 Hz); 7.30 (ddd, 1 H, H(7), $J_o$ = 8.4 and 7.2 Hz, $J_m$ = 1.6 Hz); 7.41—7.45 (m, 3 H, H(3´), H(4´), H(5´)); 7.46 (dd, 1 H, H(5), $J_o$ = 7.9 Hz, $J_m$ = 1.6 Hz); 7.69—7.73 (m, 2 H, H(2´), H(6´)).

**2,3´-Diphenylspiro[4*H*-chromene-4,5´,4´,5´-dihydroisoxazole] (2f)** was obtained from flavone as described for compounds **2c,d**. The yield was 65%, colorless needles, m.p. 124—125 °C (ethanol). Found (%): C, 81.28; H, 5.01; N, 4.15. $C_{23}H_{17}F_3NO_2$. Calculated (%): C, 81.40; H, 5.05; N, 4.13. IR (KBr), ν/cm$^{-1}$: 1665 (C=C), 1615, 1595, 1585, 1565, 1495 (arom.). $^1$H NMR ($CDCl_3$), δ: 3.57 (d, 1 H, CHH, $J$ = 17.4 Hz); 3.80 (d, 1 H, CHH, $J$ = 17.4 Hz); 5.84 (s, 1 H, H(3)); 7.19 (ddd, 1 H, H(6), $J_o$ = 7.9 and 7.2 Hz, $J_m$ = 1.1 Hz); 7.23 (dd, 1 H, H(8), $J_o$ = 8.4 Hz, $J_m$ = 1.1 Hz); 7.37 (ddd, 1 H, H(7), $J_o$ = 8.4 and 7.2 Hz, $J_m$ = 1.6 Hz); 7.40—7.46 (m, 6 H, arom.); 7.54 (dd, 1 H, H(5), $J_o$ = 7.9 Hz, $J_m$ = 1.6 Hz); 7.72—7.80 (m, 4 H, arom.).

**Synthesis of α,β-unsaturated oximes 3a—c.** Concentrated $H_2SO_4$ (3 mL) was added to spiroisoxazoline **2** (0.7 mmol). The reaction mixture was stirred at ~20 °C for 20 min and poured into ice water (10 mL). The precipitate that formed was filtered off, washed with water, dried, and recrystallized from toluene. Under analogous conditions, compounds **3a,b** were also obtained from oximes **1a,b**.

**1-Phenyl-2-(2-trifluoromethyl-4*H*-chromen-4-ylidene)ethan-1-one oxime (3a).** The yield was 85% (89% from **1a**), light yellow needles, m.p. 174—175 °C. Found (%): C, 65.38; H, 3.63; N, 4.22. $C_{18}H_{12}F_3NO_2$. Calculated (%): C, 65.26; H, 3.65; N, 4.23. IR, ν/cm$^{-1}$: 3200 (OH), 1675 (C=C), 1620, 1595, 1575 (arom.). $^1$H NMR ($CDCl_3$), δ: 6.03 (s, 1 H, H(3)); 6.79 (s, 1 H, =CH); 7.18 (dd, 1 H, H(8), $J_o$ = 8.3 Hz, $J_m$ = 1.2 Hz); 7.27 (ddd, 1 H, H(6), $J_o$ = 8.1 and 7.3 Hz, $J_m$ = 1.2 Hz); 7.38—7.44 (m, 4 H, H(7), H(3´), H(4´), H(5´)); 7.56—7.59 (m, 2 H, H(2´), H(6´)); 7.86 (dd, 1 H, H(5), $J_o$ = 8.1 Hz, $J_m$ = 1.6 Hz); 8.0—9.0

(br.s, 1 H, OH). $^1$H NMR (DMSO-$d_6$), δ: 6.00 (s, 1 H, H(3)); 6.92 (s, 1 H, =CH); 7.30 (dd, 1 H, H(8), $J_o$ = 8.3 Hz, $J_m$ = 1.2 Hz); 7.36 (ddd, 1 H, H(6), $J_o$ = 8.1 and 7.3 Hz, $J_m$ = 1.2 Hz); 7.41—7.44 (m, 3 H, H(3′), H(4′), H(5′)); 7.50 (ddd, 1 H, H(7), $J_o$ = 8.3 and 7.3 Hz, $J_m$ = 1.5 Hz); 7.55—7.58 (m, 2 H, H(2′), H(6′)); 8.07 (dd, 1 H, H(5), $J_o$ = 8.1 Hz, $J_m$ = 1.5 Hz); 11.70 (s, 1 H, OH).

**2-(6-Methyl-2-trifluoromethyl-4*H*-chromen-4-ylidene)-1-phenylethan-1-one oxime (3b).** The yield was 72% (71% from **1b**), light yellow needles, m.p. 170—171 °C. Found (%): C, 65.87; H, 4.14; N, 3.88. $C_{19}H_{14}F_3NO_2$. Calculated (%): C, 66.09; H, 4.09; N, 4.06. IR (KBr), ν/cm$^{-1}$: 3235 (OH), 1680 (C=C), 1605, 1490 (arom.). $^1$H NMR ($CDCl_3$), δ: 2.41 (s, 3 H, Me); 6.01 (s, 1 H, H(3)); 6.77 (s, 1 H, =CH); 7.07 (d, 1 H, H(8), $J_o$ = 8.4 Hz); 7.21 (br.dd, 1 H, H(7), $J_o$ = 8.4 Hz, $J_m$ = 1.7 Hz); 7.38—7.43 (m, 3 H, H(3′), H(4′), H(5′)); 7.56—7.59 (m, 2 H, H(2′), H(6′)); 7.65 (br.s, 1 H, H(5)); 7.9—8.8 (br.s, 1 H, OH).

**1-(2-Trifluoromethyl-4*H*-chromen-4-ylidene)acetone oxime (3c).** The yield was 45%, light yellow crystals, m.p. 160—162 °C. Found (%): C, 56.81; H, 3.86; N, 5.10. $C_{13}H_{10}F_3NO_2 \cdot 1/3H_2O$. Calculated (%): C, 56.73; H, 3.91; N, 5.09. IR (KBr), ν/cm$^{-1}$: 3181, 3118 (OH), 1668, 1634, 1609, 1589, 1575, 1483 (arom.). $^1$H NMR ($CDCl_3$), δ: 2.16 (s, 3 H, Me); 6.61 (s, 1 H, H(3)); 6.63 (s, 1 H, =CH); 7.17 (dd, 1 H, H(8), $J_o$ = 8.3 Hz, $J_m$ = 1.2 Hz); 7.23 (ddd, 1 H, H(6), $J_o$ = 8.2 and 7.1 Hz, $J_m$ = 1.2 Hz); 7.38 (ddd, 1 H, H(7), $J_o$ = 8.3 and 7.1 Hz, $J_m$ = 1.5 Hz); 7.74 (dd, 1 H, H(5), $J_o$ = 8.2 Hz, $J_m$ = 1.5 Hz); 7.0—8.0 (br.s, 1 H, OH). $^1$H NMR (DMSO-$d_6$), δ: 2.07 (s, 3 H, Me); 6.64 (s, 1 H, H(3)); 6.72 (s, 1 H, =CH); 7.29 (dd, 1 H, H(8), $J_o$ = 8.3 Hz, $J_m$ = 1.0 Hz); 7.32 (ddd, 1 H, H(6), $J_o$ = 8.1 and 7.1 Hz, $J_m$ = 1.0 Hz); 7.47 (ddd, 1 H, H(7), $J_o$ = 8.3 and 7.1 Hz, $J_m$ = 1.4 Hz); 7.87 (dd, 1 H, H(5), $J_o$ = 8.1 Hz, $J_m$ = 1.4 Hz); 10.95 (s, 1 H, OH).

***N*-Phenyl-(2-trifluoromethyl-4*H*-chromen-4-ylidene)acetamide (4a).** Phosphorus pentachloride (330 mg, 1.6 mmol) was added to a solution of oxime **3a** (265 mg, 0.8 mmol) in anhydrous diethyl ether (10 mL). The reaction mixture was stirred at ~20 °C for 30 min and poured into water (30 mL). The product was extracted with ether (20 mL). The organic layer was separated and concentrated and the solid residue was recrystallized from toluene. Under analogous conditions, amide **4a** was also obtained from oxime **1a** and spiroisoxazoline **2a**. The yield was 84 (from **3a**), 79 (from **1a**), and 80% (from **2a**), light yellow needles, m.p. 191—192 °C. Found (%): C, 65.37; H, 3.66; N, 4.11. $C_{18}H_{12}F_3NO_2$. Calculated (%): C, 65.26; H, 3.65; N, 4.23. IR (KBr), ν/cm$^{-1}$: 3420, 3300 (NH), 1670, 1640 (C=O, NH), 1595, 1540, 1530, 1500 (arom.). $^1$H NMR ($CDCl_3$), δ: 6.14 (s, 1 H, =CH); 7.12 (t, 1 H, H(4′), $J$ = 7.3 Hz); 7.25—7.29 (m, 2 H, H(6), H(8)); 7.32—7.36 (m, 3 H, H(3′), H(5′), NH); 7.48 (ddd, 1 H, H(7), $J_o$ = 8.3 and 7.3 Hz, $J_m$ = 1.0 Hz); 7.54—7.60 (m, 2 H, H(2′), H(6′)); 7.72 (br.d, 1 H, H(5), $J_o \approx$ 7.0 Hz); 8.49 (s, 1 H, H(3)). $^1$H NMR (DMSO-$d_6$), δ: 6.63 (s, 1 H, =CH); 7.07 (tt, 1 H, H(4′), $J_o$= 7.4 Hz, $J_m$ = 1.1 Hz); 7.31—7.36 (m, 2 H, H(3′), H(5′)); 7.42 (dd, 1 H, H(8), $J_o$ = 8.3 Hz, $J_m$ = 1.1 Hz); 7.46 (ddd, 1 H, H(6), $J_o$ = 8.2 and 7.3, $J_m$ = 1.1 Hz); 7.61 (ddd, 1 H, H(7), $J_o$ = 8.5 and 7.3 Hz, $J_m$ = 1.5 Hz); 7.66—7.70 (m, 2 H, H(2′), H(6′)); 7.82 (dd, 1 H, H(5), $J_o$ = 8.2 Hz, $J_m$ = 1.5 Hz); 8.48 (s, 1 H, H(3)); 10.19 (s, 1 H, NH).

***N*-Phenyl-(6-methyl-2-trifluoromethyl-4*H*-chromen-4-ylidene)acetamide (4b)** was obtained analogously from compound **3b**. The yield was 87%, light yellow needles, m.p. 201—202 °C (toluene). Found (%): C, 66.01; H, 4.08; N, 3.82. $C_{19}H_{14}F_3NO_2$. Calculated (%): C, 66.09; H, 4.09; N, 4.06. IR (KBr), ν/cm$^{-1}$: 3435, 3280 (NH), 1670, 1635 (C=O, NH), 1590, 1525, 1490 (arom.). $^1$H NMR ($CDCl_3$), δ: 2.41 (s, 3 H, Me); 6.12 (s, 1 H, =CH); 7.12 (t, 1 H, H(4′), $J_o$ = 7.4 Hz); 7.17 (d, 1 H, H(8), $J_o$ = 8.5 Hz); 7.28—7.31 (m, 2 H, H(7), NH); 7.33—7.37 (m, 2 H, H(3′), H(5′)); 7.52 (br.s, 1 H, H(5)); 7.54—7.60 (m, 2 H, H(2′), H(6′)); 8.48 (s, 1 H, H(3)). $^1$H NMR (DMSO-$d_6$), δ: 2.41 (s, 3 H, Me); 6.60 (s, 1 H, =CH); 7.07 (tt, 1 H, H(4′), $J_o$ = 7.4 Hz, $J_m$ = 1.1 Hz); 7.32 (d, 1 H, H(8), $J_o$ = 8.5 Hz); 7.31—7.35 (m, 2 H, H(3′), H(5′)); 7.43 (br.dd, 1 H, H(7), $J_o$ = 8.5 Hz, $J_m \sim$ 2.0 Hz); 7.62 (br.s, 1 H, H(5)); 7.66—7.69 (m, 2 H, H(2′), H(6′)); 8.47 (s, 1 H, H(3)); 10.16 (s, 1 H, NH).

***N*-Methyl-(2-trifluoromethyl-4*H*-chromen-4-ylidene)acetamide (4c)** was obtained analogously from compound **2c**. The yield was 89%, light yellow crystals, m.p. 191—192 °C (toluene). Found (%): C, 57.76; H, 3.93; N, 5.19. $C_{13}H_{10}F_3NO_2$. Calculated (%): C, 58.00; H, 3.74; N, 5.20. IR (KBr), ν/cm$^{-1}$: 3280 (NH), 1675, 1630 (C=O, NH), 1595, 1560 (arom.). $^1$H NMR (DMSO-$d_6$), δ: 2.70 (d, 3 H, Me, $J$ = 4.8 Hz); 6.40 (s, 1 H, =CH); 7.35—7.42 (m, 2 H, H(8), H(6)); 7.56 (ddd, 1 H, H(7), $J_o$ = 8.4 and 7.2 Hz, $J_m$ = 1.4 Hz); 7.75 (dd, 1 H, H(5), $J_o$ = 8.1 Hz, $J_m$ = 1.4 Hz); 8.08 (br.q, 1 H, NH, $J$ = 4.8 Hz); 8.48 (s, 1 H, H(3)). $^{13}$C NMR (DMSO-$d_6$), δ: 25.43 (Me), 105.45 (q, C(3), $^3J_{C,F}$ = 4.2 Hz), 109.67 (C(4′)), 118.05 (C(8)), 119.21 (q, $CF_3$, $^1J_{C,F}$ = 271.5 Hz), 119.25 (C(4a)), 122.84 (C(5)), 126.10 (C(6)), 131.22 (C(4)), 131.72 (C(7)), 139.93 (q, C(2), $^2J_{C,F}$ = 36.8 Hz), 150.30 (C(8a)), 166.13 (C=O).

***N-tert*-Butyl-(2-trifluoromethyl-4*H*-chromen-4-ylidene)acetamide (4d)** was obtained analogously from compound **2d**. The yield was 63%, light yellow crystals, m.p. 217—218 °C (toluene). Found (%): C, 61.69; H, 5.17; N, 4.21. $C_{16}H_{16}F_3NO_2$. Calculated (%): C, 61.73; H, 5.18; N, 4.50. IR (KBr), ν/cm$^{-1}$: 3285 (NH), 1670, 1635 (C=O, NH), 1600, 1555 (arom.). $^1$H NMR ($CDCl_3$), δ: 1.43 (s, 9 H, Bu$^t$); 5.43 (br.s, 1 H, NH); 5.93 (s, 1 H, =CH); 7.21—7.25 (m, 2 H, H(8), H(6)); 7.43 (ddd, 1 H, H(7), $J_o$ = 8.4 and 7.2 Hz, $J_m$ = 1.5 Hz); 7.65 (dd, 1 H, H(5), $J_o$ = 8.3 Hz, $J_m$ = 1.5 Hz); 8.42 (s, 1 H, H(3)).

**3′-Phenyl-2-trifluoromethylspiro[4*H*-chromene-4,5′,4′,5′-dihydroisoxazol]-4′(5′*H*)-one oxime (5a).** Sodium nitrite (50 mg, 0.7 mmol) was added to a solution of oxime **3a** (200 mg, 0.6 mmol) in an ethanol—water—THF mixture (1 : 2 : 2; 5 mL). Then the stirred mixture was acidified dropwise with aqueous HCl (1 : 3) to pH 1—2. The solvent was removed, the solid residue was treated with water, and the precipitate was filtered off, dried, and recrystallized from hexane—chloroform (3 : 1). The yield was 78%, colorless needles, m.p. 157—158 °C. Found (%): C, 59.99; H, 3.26; N, 7.82. $C_{18}H_{11}F_3N_2O_3$. Calculated (%): C, 60.01; H, 3.08; N, 7.77. IR (KBr), ν/cm$^{-1}$: 3250 (OH), 1695 (C=C), 1615, 1585, 1490 (arom.). $^1$H NMR ($CDCl_3$), δ: 5.80 (s, 1 H, H(3)); 7.20 (td, 1 H, H(6), $J_o$ = 7.8 Hz, $J_m$ = 1.1 Hz); 7.23 (dd, 1 H, H(8), $J_o$ = 8.3 Hz, $J_m$ = 1.1 Hz); 7.24 (dd, 1 H, H(5), $J_o$ = 8.0 Hz, $J_m$ = 1.7 Hz); 7.42 (m, 1 H, H(7)); 7.45—7.52 (m, 3 H, H(3′), H(4′), H(5′)); 7.60 (s, 1 H, OH); 8.07—8.10 (m, H(2′), H(6′)). MS (EI, 70 eV), $m/z$ ($I_{rel}$ (%)): 360 $[M]^+$ (40), 343 (100), 299 (43), 240 (27), 224 (99), 129 (22), 77 (23). Found: $m/z$ 360.0711 $[M]^+$. $C_{18}H_{11}F_3N_2O_3$. Calculated: $M$ = 360.0722.

**6-Methyl-3′-phenyl-2-trifluoromethylspiro[4*H*-chromene-4,5′,4′,5′-dihydroisoxazol]-4′(5′*H*)-one oxime (5b)** was ob-

tained analogously from compound **3b**. The yield was 59%, colorless needles, m.p. 168—169 °C. Found (%): C, 60.97; H, 3.51; N, 7.58. $C_{19}H_{13}F_3N_2O_3$. Calculated (%): C, 60.97; H, 3.50; N, 7.48. IR (KBr), ν/cm$^{-1}$: 3250 (OH), 1695 (C=C), 1500 (arom.). $^1$H NMR ($CDCl_3$), δ: 2.30 (s, 3 H, Me); 5.76 (s, 1 H, H(3)); 6.99 (br.d, 1 H, H(5), $J_m$ = 2.0 Hz); 7.11 (d, 1 H, H(8), $J_o$ = 8.5 Hz); 7.21 (ddq, 1 H, H(7), $J_o$ = 8.5 Hz, $J_m$ = 2.1 Hz, $J_{H,CH_3}$ = 0.5 Hz); 7.44—7.52 (m, 3 H, H(3′), H(4′), H(5′)); 7.64 (s, 1 H, OH); 8.08—8.11 (m, 2 H, H(2′), H(6′)).

**4′-Bromo-3′-phenyl-2-trifluoromethylspiro[4*H*-chromene-4,5′,4′,5′-dihydroisoxazole] (6a).** A solution of bromine (110 mg, 0.69 mmol) in chloroform (2 mL) was added dropwise to a solution of enoxime **3a** (150 mg, 0.45 mmol) in dry chloroform (2 mL). The mixture was stirred at ~20 °C for 10 min, whereupon the solvent was removed and the solid residue was kept in boiling ethanol (3 mL) for 5 min. On cooling, the precipitate that formed was filtered off, washed with ethanol, and dried. The yield was 89%, colorless needles, m.p. 136—137 °C. Found (%): C, 52.53; H, 2.71; N, 3.51. $C_{18}H_{11}BrF_3NO_2$. Calculated (%): C, 52.71; H, 2.70; N, 3.41. IR (KBr), ν/cm$^{-1}$: 1697 (C=C), 1615, 1585, 1564, 1485 (arom.). $^1$H NMR ($CDCl_3$), δ: 5.53 (s, 1 H, CH); 6.19 (s, 1 H, H(3)); 7.17 (ddd, 1 H, H(6), $J_o$ = 8.1 and 7.2 Hz, $J_m$ = 1.1 Hz); 7.25 (dd, 1 H, H(8), $J_o$ = 8.6 Hz, $J_m$ = 1.1 Hz); 7.33 (dd, 1 H, H(5), $J_o$ = 8.1 Hz, $J_m$ = 1.6 Hz); 7.42 (ddd, 1 H, H(7), $J_o$ = 8.6 and 7.2 Hz, $J_m$ = 1.6 Hz); 7.47—7.52 (m, 3 H, H(3′), H(4′), H(5′)); 7.83—7.87 (m, H(2′), H(6′)).

**4′-Bromo-6-methyl-3′-phenyl-2-trifluoromethylspiro[4*H*-chromene-4,5′,4′,5′-dihydroisoxazole] (6b)** was obtained analogously from compound **3b** for the equimolar ratio of **3b** to $Br_2$. The yield was 92%, colorless needles, m.p. 156—157 °C. Found (%): C, 53.83; H, 3.17; N, 3.40. $C_{19}H_{13}BrF_3NO_2$. Calculated (%): C, 53.80; H, 3.09; N, 3.30. IR (KBr), ν/cm$^{-1}$: 1697 (C=C), 1592, 1564, 1498 (arom.). $^1$H NMR ($CDCl_3$), δ: 2.26 (s, 3 H, Me); 5.54 (s, 1 H, CH); 6.14 (s, 1 H, H(3)); 7.08 (br.s, 1 H, H(5)); 7.13 (d, 1 H, H(8), $J_o$ = 8.5 Hz); 7.22 (br.dd, 1 H, H(7), $J_o$ = 8.5 Hz, $J_m$ = 1.7 Hz); 7.47—7.52 (m, 3 H, H(3′), H(4′), H(5′)); 7.83—7.87 (m, 2 H, H(2′), H(6′)).

**4-(2-Acetoxyimino-2-phenylethylidene)-2-trifluoromethyl-4*H*-chromene (7).** Acetyl chloride (55 mg, 0.7 mmol) was added to a solution of oxime **3a** (200 mg, 0.6 mmol) in diethyl ether (10 mL). The mixture was stirred at ~20 °C for 1 h and concentrated. The solid residue was recrystallized from hexane. The yield of compound **7** was 0.15 g (67%), yellowish crystals, m.p. 141—142 °C. Found (%): C, 64.43; H, 3.70; N, 3.52. $C_{20}H_{14}F_3NO_3$. Calculated (%): C, 64.34; H, 3.78; N, 3.75. IR (KBr), ν/cm$^{-1}$: 1772 (CO), 1671 (C=C), 1600, 1541 (arom.). $^1$H NMR ($CDCl_3$), δ: 2.27 (s, 3 H, Me); 5.98 (s, 1 H, H(3)); 6.75 (s, 1 H, =CH); 7.23 (dd, 1 H, H(8), $J_o$ = 8.3 Hz, $J_m$ = 1.2 Hz); 7.33 (ddd, 1 H, H(6), $J_o$ = 8.1 and 7.2 Hz, $J_m$ = 1.2 Hz); 7.41—7.52 (m, 4 H, H(7), H(3′), H(4′), H(5′)); 7.66—7.69 (m, 2 H, H(2′), H(6′)); 7.86 (dd, 1 H, H(5), $J_o$ = 8.1 Hz, $J_m$ = 1.5 Hz).

**2-(4-Hydroxy-2-trifluoromethyl-4*H*-chromen-4-yl)-1-phenylethan-1-one *N*,*N*-dimethylhydrazone (8).** A solution of diisopropylamine (0.57 g, 5.6 mmol) in anhydrous diethyl ether (3 mL) was added to a solution of *n*-butyllithium prepared from metallic Li (11.2 mmol) and *n*-butyl bromide (5.6 mmol) in anhydrous diethyl ether (10 mL). The mixture was stirred for 30 min. The resulting solution of lithium diisopropylamide was cooled to −30 °C and a solution of acetophenone dimethylhydrazone (0.91 g, 5.6 mmol) in anhydrous THF (5 mL) was added with stirring. The resulting light yellow solution was stirred at ~20 °C for 30 min and cooled to −30 °C. A solution of 2-trifluoromethylchromone (1.0 g, 4.7 mmol) in anhydrous THF (5 mL) was added. The reaction mixture was stirred at ~20 °C for 12 h and hydrolyzed with water (50 mL). The product was extracted with ether (20 mL). The organic layer was separated, dried, and concentrated. The resulting light yellow oil was triturated with pentane to initiate crystallization. The solid product was filtered off and recrystallized from hexane to give compound **8** (0.40 g, 22%) as light yellow crystals, m.p. 129—130 °C. Found (%): C, 63.95; H, 5.13; N, 7.44. $C_{20}H_{19}F_3N_2O_3$. Calculated (%): C, 63.82; H, 5.09; N, 7.44. IR, ν/cm$^{-1}$: 3300 (OH), 1695 (C=C), 1605 (arom.). $^1$H NMR ($CDCl_3$), δ: 2.72 (s, 6 H, 2 Me); 3.19 (d, 1 H, C<u>H</u>H, $J$ = 13.9 Hz); 3.50 (d, 1 H, CH<u>H</u>, $J$ = 13.9 Hz); 5.69 (s, 1 H, H(3)); 7.10 (dd, 1 H, H(8), $J_o$ = 8.2 Hz, $J_m$ = 1.1 Hz); 7.16 (ddd, 1 H, H(6), $J_o$ = 7.8 and 7.5 Hz, $J_m$ = 1.1 Hz); 7.25—7.31 (m, 3 H, H(7), H(3′), H(5′)); 7.36 (m, 1 H, H(4′)); 7.47—7.50 (m, 2 H, H(2′), H(6′)); 7.66 (dd, 1 H, H(5), $J_o$ = 7.8 Hz, $J_m$ = 1.6 Hz); 9.3 (br.s, 1 H, OH).

**Ethyl 3′-phenyl-2-trifluoromethylspiro[4*H*-chromene-4,5′,4′,5′-dihydro-1*H*-pyrazole]-1′-carboxylate (9)** was obtained from 2-trifluoromethylchromone and acetophenone *N*-ethoxycarbonylhydrazone as described above for compound **8** by hydrolysis of the reaction mixture with dilute HCl (1 : 3). The yield of compound **9** was 26%, light yellow crystals, m.p. 201—202 °C (toluene—hexane). Found (%): C, 62.55; H, 4.14; N, 6.93. $C_{21}H_{17}F_3N_2O_3$. Calculated (%): C, 62.69; H, 4.26; N, 6.96. IR (KBr), ν/cm$^{-1}$: 1721 (C=O), 1602, 1585 (arom.). $^1$H NMR ($CDCl_3$), δ: 0.7—1.4 (br.s, 3 H, Me); 3.61 (d, 1 H, C<u>H</u>H, $J$ = 17.8 Hz); 3.81 (d, 1 H, CH<u>H</u>, $J$ = 17.8 Hz); 3.9—4.4 (br.s, 2 H, $OCH_2$); 5.75 (s, 1 H, H(3)); 7.10—7.16 (m, 2 H, H(6), H(8)); 7.30—7.34 (m, 2 H, H(5), H(7)); 7.41—7.45 (m, 3 H, H(3′), H(4′), H(5′)); 7.77—7.79 (m, 2 H, H(2′), H(6′)).

**2-Phenacyl-2-trifluoromethylchroman-4-one (10)** was obtained from 2-trifluoromethylchromone and acetophenone anil as described for compound **8** by hydrolysis of the reaction mixture with dilute HCl (1 : 3). The yield of compound **10** was 69%, m.p. 81—82 °C (hexane—$CCl_4$). Compound **10** has been described earlier.[10]

This work was financially supported by the Civilian Research and Development Foundation of the United States (CRDF) and the Ministry of Education and Science of the Russian Federation (Grant Nos EK-005-X1 and Y1-005-04).

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*Received June 24, 2005;*
*in revised form February 1, 2006*