Reaction of 3-Formylchromone-*N*-benzoylhydrazone with Ketenes. Synthesis and Structural Studies of Chromone 1,3,4-Oxadiazolines

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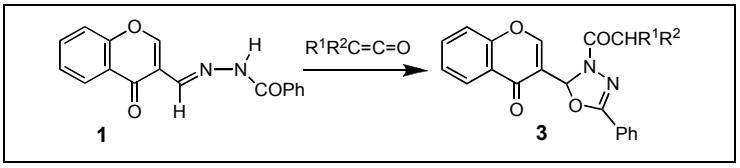
Received July 12, 2006
Revised October 3, 2006



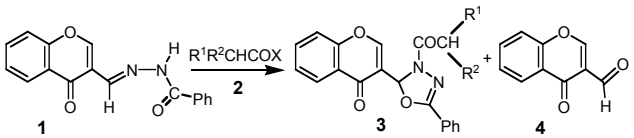
The reaction of 3-formylchromone-*N*-benzoylhydrazone with ketenes, prepared *in situ* from the corresponding acid chlorides **2a**-**d** and the mixed anhydride **2e** was studied. In all cases 2-(4'-oxo-4'*H*-3'-chromyl)-5-phenyl-2,3-dihydro-1,3,4-oxadiazoles (**3**) were isolated in yields varying from 40 to 80%. A full structure assignment of all products has been made on the basis of 1D and 2-D (COSY H-H, COSY C-H, COLOC C-H) NMR spectra. A plausible reaction mechanism is also proposed based on theoretical approaches and experimental results.

J. Heterocyclic Chem., **44**, 425 (2007).

INTRODUCTION

Flavones and chromones are unique molecules because of the availability of their structural framework in a variety of natural products and biologically active molecules [1]. Although 3-formylchromone has emerged as the most valuable synthon for the incorporation of the chromone moiety leading to the synthesis of a variety of heterocycles [2], its synthetic utility is limited due to facile opening of the chromone ring [2–4], hence strategies are being developed to circumvent it [5]. Concerning 3-formylchromone hydrazones, a perusal of the literature revealed that although their antimicrobial activity and bleaching effect [6] as well as their mutagenicity and antimutagenicity were studied [7], their chemistry has not yet been reported. With this in mind, we chose to study the reaction of 3-formylchromone-*N*-benzoylhydrazone with ketenes, since ketenes exhibit a very rich cycloaddition chemistry due to their structural and electronic peculiarities [8], and also because from the few studied reactions between ketenes and 3-formylchromone or 3-formylchromone Schiff bases [4+2] cycloaddition products were mainly isolated [2a]. Another very important feature of chromone chemistry, which lead us to this study, was the fact that chromones substituted by a heterocyclic ring at the 3 position [9a] are known to exhibit a wide range of biological activity such as antialergic, antimicrobial, antifungal, anticholesteric, hypolipidemic and antiblaster action as well stimulate the central nervous system [9b]. On the other hand, the isolated products contain also the 1,3,4-oxadiazoline ring, which is shown to have important biological activities [10], and in addition, constitutes a versatile precursor of reactive intermediates [11].

Scheme 1



		Reaction Conditions		Product	Yield %
2a	R^1 = H, R^2 = Cl, X = Cl	$Et_3N/C_6H_5CH_3$	reflux, 4h	**3a**	38
2b	R^1 = R^2 = Cl, X = Cl	"	"	**3b**	40
2c	R^1 = R^2 = CH_3, X = Cl	"	"	**3c**	60
2d	R^1 = R^2 = Ph, X = Cl	"	"	**3d**	80
2e	R^1 = H, R^2 = OPh, X = OTs	Et_3N/CH_2Cl_2	rt, 24h	**3e**	50

RESULTS AND DISCUSSION

The 3-formylchromone-*N*-benzoylhydrazone (**1**) prepared [6] by condensation of 3-formylchromone with benzohydrazide reacted with ketenes, derived *in situ* by dehydrohalogenation of the corresponding acid chlorides **2** in the presence of triethylamine, and afforded the hitherto unknown 2-chromyl-1,3,4-oxadiazolines **3** (Scheme 1). In the case of chloro- and dichloroketene the 2-chromyl-1,3,4-oxadiazolines **3a** and **3b** were isolated in moderate yield (~40%), whereas in the case of dimethyl- and diphenylketene compounds **3c** and **3d** were obtained in good yield (60-80%).

Furthermore, the reaction of **1** with the mixed anhydride **2e** was studied. The anhydride, a synthetic equivalent of acid chloride, was prepared from phenoxyacetic acid and *p*-toluenesulphonyl chloride in the presence of triethylamine in dichloromethane at room

Table 1

^{13}C, ^{1}H, C-H Correlation and COLOC NMR Data for Compounds **3a** and **3b**.

	Compound **3a**		Compound **3b**		
Position [a]	C	H [b]	C	H [b]	COLOC [c]
2	88.9	6.98 (s)	88.9	7.00 (1H, d, 0.2)	175.1, 156.2
5	157.3		157.9		
6	124.5		124.4		
7,11	127.3	7.87–7.92 (m)	127.5	7.89–7.94 (2H, m)	132.3, 157.9
8,10	128.7	7.41–7.48 (m) [d]	128.8	7.39–7.42 (2H, m)	
9	132.0	7.48–7.55 (m) [e]	132.3	7.48–7.57 (1H, m) [d]	127.5
12	163.1		159.8		
13	41.6	4.53 (2H, s)	63.8	6.87 (1H, s)	
2′	156.3	8.13 (s)	156.2	8.11 (1H, d, 0.2)	175.1, 156.3, 117.4, 88.9
3′	117.9		117.4		
4′	175.3		175.1		
4a′	124.0		123.7		
5′	125.9	8.18 (ddd, 8.0, 1.7, 0.4)	125.9	8.18 (ddd, 8.0, 1.7, 0.4)	134.3
6′	125.9	7.42 (ddd, 8.0, 7.1, 1.1) [f]	125.9	7.42 (ddd, 8.0, 7.1, 1.1) [e]	
7′	134.3	7.70 (ddd, 8.4, 7.1, 1.7)	134.3	7.70 (ddd, 8.4, 7.1, 1.7)	
8′	118.3	7.44 (m) [g]	118.3	7.42–7.50 (m) [f]	125.9, 123.7
8a′	156.2		156.3		

[a] For carbon numbering see Figure 1. [b] The protons on this column are correlated to carbon atoms on the left column via $^{1}J_{C-H}$. Multiplicities and coupling constants ^{n}J (in Hz) in parentheses. [c] Long range ($^{2}J_{C-H}$ and $^{3}J_{C-H}$) correlations between the protons on the left and the carbons stated on this column. [d,e,f,g] Overlapped multiplets, distinguished by homo- and hetero-COSY.

temperature. Under the mild reaction conditions employed, the corresponding chromyloxadiazoline **3e** was isolated in 50% yield. During the reaction time an amount of 3-formyl-*N*-benzoylhydrazone decomposed giving 3-formyl-chromone **4** and benzohydrazide, which reacted further with ketenes to afford the corresponding *N*-benzohydrazides **5a**–**5d** in yields ranging from 3 to 20%.

Structure Assignments The assigned molecular structures of all new compounds **3a**–**e** are based on rigorous spectroscopic analysis including IR, NMR (^{1}H, ^{13}C, COSY H–H, NOESY H–H, HETCOR C–H and COLOC C–H), MS and elemental analysis data. In Tables 1 and 2 the NMR data [^{13}C, ^{1}H and the C–H correlation via one bond (HETCOR C–H) and two and/or three bonds (COLOC C–H)] are presented.

Regarding the structure of compounds **3** the assignment of **3b** is described. From the molecular ion at m/z 402/404/406 (9:6:1) the conclusion could be drawn that **3b** was produced from the reaction of one molecule of **1** with one molecule of dichloroketene, a fact that was also confirmed from the ^{13}C NMR spectrum, where 17 different signals were observed (Table 1). In addition, the presence of the characteristic chromone carbonyl carbon absorption at 175.1 ppm (175.8 in the chromone hydrazone **1**) and of the protonated C(2') carbon absorption at 156.2 ppm, associated with the one proton singlet at δ 8.11, indicated that the chromone moiety remained unaffected. Moreover, the lack of the C=N carbon absorption of the starting material **1** at 140.8 ppm suggested a reaction of the dichloroketene with the hydrazone C=N bond. From the C–H correlated spectrum in the saturated region, the presence of a methine carbon at 63.8 ppm (bearing most probably the dichloroketene chlorine atoms) and the presence of a second methine carbon at 88.9 ppm were established. In addition, this methine proton singlet (δ 7.00) gave COLOC correlations (Figure 1) with the chromone carbonyl carbon at 175.1 ppm and with the C(2') carbon at 156.2 ppm indicating thus that this methine carbon corresponded to the C=N carbon of the starting hydrazone **1**. The downfield shift of this methine carbon (88.9 ppm) was due to the neighboring C=C group, of a nitrogen atom and of a second heteroatom. The lack of a benzoyl carbonyl in combination with the COLOC correlation of the *o*-aromatic protons with the carbon at 156.2 ppm (the former benzoyl carbon of **1** being transformed to a C=N

carbon) supported the hypothesis that the second heteroatom was the former benzoyl oxygen [12].

Reaction Mechanism The reaction is most probably initiated by a nucleophilic attack of the imino hydrazone nitrogen to the carbonyl carbon of the ketene leading to a zwitterionic intermediate **6**. A proton transfer in the zwitterion from the neighboring NH group inactivates the ketene anion and the charge moves to the benzoyl oxygen with subsequent cyclization of the resulting dipolar intermediate **7** leading to the formation of oxadiazolines **3**. An analogous mechanism was previously proposed by us for the reaction of ketenes with *N*-aroyldihydrocyclopenta-pyrazolidinol [13]. However, from the reaction of *N,N*-dialkylhydrazones with ketenes 2-azetidinone derivatives were isolated *via* a Staudinger [2+2] cycloaddition reaction, most probably because of the lack of the N-H moiety [14]. To the contrary, in the present work, the presence of N-H group is responsible for the diversification of the reaction mechanism, as depicted in Scheme 2, leading always to Δ^2-1,3,4-oxadiazoline derivatives **3**.

Following the above approach, the transition structures for the two-step reaction of compound **1** with ketene **2b**, calculated by AM1 method, are depicted in Figure 2.

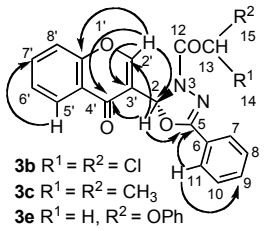
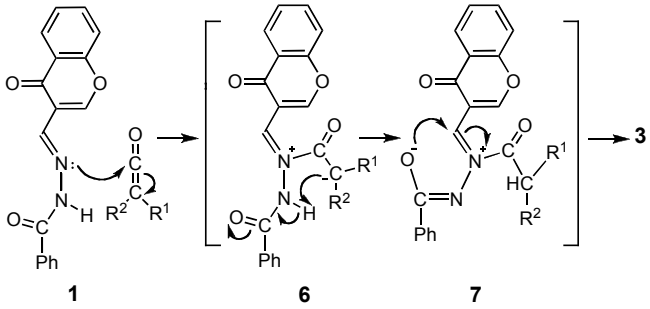


Figure 1. Numbering of skeleton and diagnostic COLOC correlations in compounds **3b**, **3c** and **3e**.

Scheme 2



After the initial proximity of the two reactants in **TS1** and the formation of N(3)-C(12) bond, the C(13) anion approaches and abstracts the H(17) (**TS2**). Next, the benzoyl oxygen gradually approaches the carbon C(2) (**TS3**) and finally gives the product **3b**. In Table 3 the variation in bond lengths or atomic distances from the reactants (compounds **1** and **2b**) to the product, calculated by AM1, can be observed. The H(17) moves to C(13), the bond N(4)-C(5) decreases and the carbonyl bond C(5)-O(1) increases from reactants through **TS1**–**TS2**–**TS3** to the product. Moreover, the net charge values (q_{net}) indicate a change in electron density during the reaction process. The electrons from C(2) = N(3) move to the ketene moiety and after the abstraction of the H-C(7) the charge moves to N(4)-C(5)-O(1) until the final cyclization.

For each located TS after complete optimization only one negative eigenvalue was calculated corresponding to one imaginary frequency assigned to the bonds (shown by the arrows) affected by the moving atom, as depicted in Figure 2. The computed activation energies ($\Delta H^{\#}$) are

Table 2

^{1}H, ^{13}C, C-H Correlation and COLOC NMR Data for Compounds **3c**–**e**.

Position [a]	Compound **3c** C	Compound **3c** H [b]	Compound **3c** COLOC [c]	Compound **3d** C	Compound **3d** H [b]	Compound **3e** C	Compound **3e** H [b]	Compound **3e** COLOC [c]
2	88.3	7.02 (s)	175.4, 156.2, 155.8	88.2	7.09 (s)	89.0	6.98 (s)	175.3, 157.2, 156.4, 118.0
5	156.2			156.2		157.2		
6	124.7			124.5		124.5		
7,11	127.1	7.86–7.93 (m)	156.2	127.2	7.82–7.90 (m)	127.3	7.89–7.95 (m)	157.2, 131.9
8,10	128.6	7.38–7.44 (m) [d]		128.5	7.35–7.45 (m) [d]	128.7	7.38–7.59 (m) [d]	
9	131.5	7.48–7.55 (m)	130.9	131.6	7.25–7.45 (m)	131.9	7.41–7.58 (m) [d]	
12	174.6			169.0		165.2		
13	31.9	3.39, (sept, 7.0)		54.2	6.00, (s)	65.5	5.42, (d, 16.0)	
14	18.2	1.20 (d, 7.0)		138.7 [f], 139.2 [f]		158.2[f]		
				129.0 [g], 129.1 [g]	7.20–7.50 (m)	114.8[g]	6.89–7.05 (m)	121.5
15	18.9	1.23 (d, 7.0)		128.5 [h], 128.5 [h]	7.20–7.50 (m)	129.5[h]	7.22–7.30 (m)	158.2
				127.1 [i], 127.1 [i]	7.20–7.50 (m)	121.5[i]	6.89–7.03 (m)	114.8

Table 2 (continued)

Position [a]	Compound **3c** C	Compound **3c** H [b]	Compound **3c** COLOC [c]	Compound **3d** C	Compound **3d** H [b]	Compound **3e** C	Compound **3e** H [b]	Compound **3e** COLOC [c]
2′	155.8	8.03 (s)	175.4, 156.3, 118.8, 88.3	155.8	7.90 (s)	156.4	8.11 (s)	175.3, 156.3 118.0, 89.0
3′	118.8			118.5		118.0		
4′	175.4			175.3		175.3		
4a′	124.6			124.5		124.2		
5′	125.9	8.19 (dd, 8.0, 1.4)		125.9	8.18 (dd, 8.0, 1.6)	125.9	8.19 (dd, 8.0, 1.6)	134.2
6′	125.7	7.39–7.45 (m) [e]		125.7	7.35–7.45 (m) [e]	125.8	7.41 (ddd, 8.0, 7.0, 1.3) [e]	
7′	134.1	7.67 (ddd, 8.6, 7.0, 1.6)		134.1	7.64 (ddd, 8.5, 7.1, 1.7)	134.2	7.68 (ddd, 8.6, 7.0, 1.6)	125.9
8′	118.2	7.41–7.48 (m) [e]		118.2	7.35–7.45 (m) [e]	118.2	7.46 (dd, 8.0, 1.6) [e]	124.2, 125.8
8a′	156.3			156.2		156.3		

[a] For carbon numbering see Figure 1. [b] The protons on this column are correlated to carbon atoms on the left column via $^{1}J_{C-H}$. Multiplicities and coupling constants ^{n}J (in Hz) in parentheses. [c] Long range ($^{2}J_{C-H}$ and $^{3}J_{C-H}$) correlations between the protons on the left and the carbons stated on this column. [d,e] Overlapped multiplets, distinguished by homo- and hetero-COSY. [f] For C-*ipso* of Ph at C-13. [g] For C-*ortho* of Ph at C-13. [h] For C-*meta* of Ph at C-13. [i] For C-*para* of Ph at C-13.

higher than the experimental ones or those which would have been calculated by DFT computations and are only reliable for relative comparisons of similar reactions [14d,15].

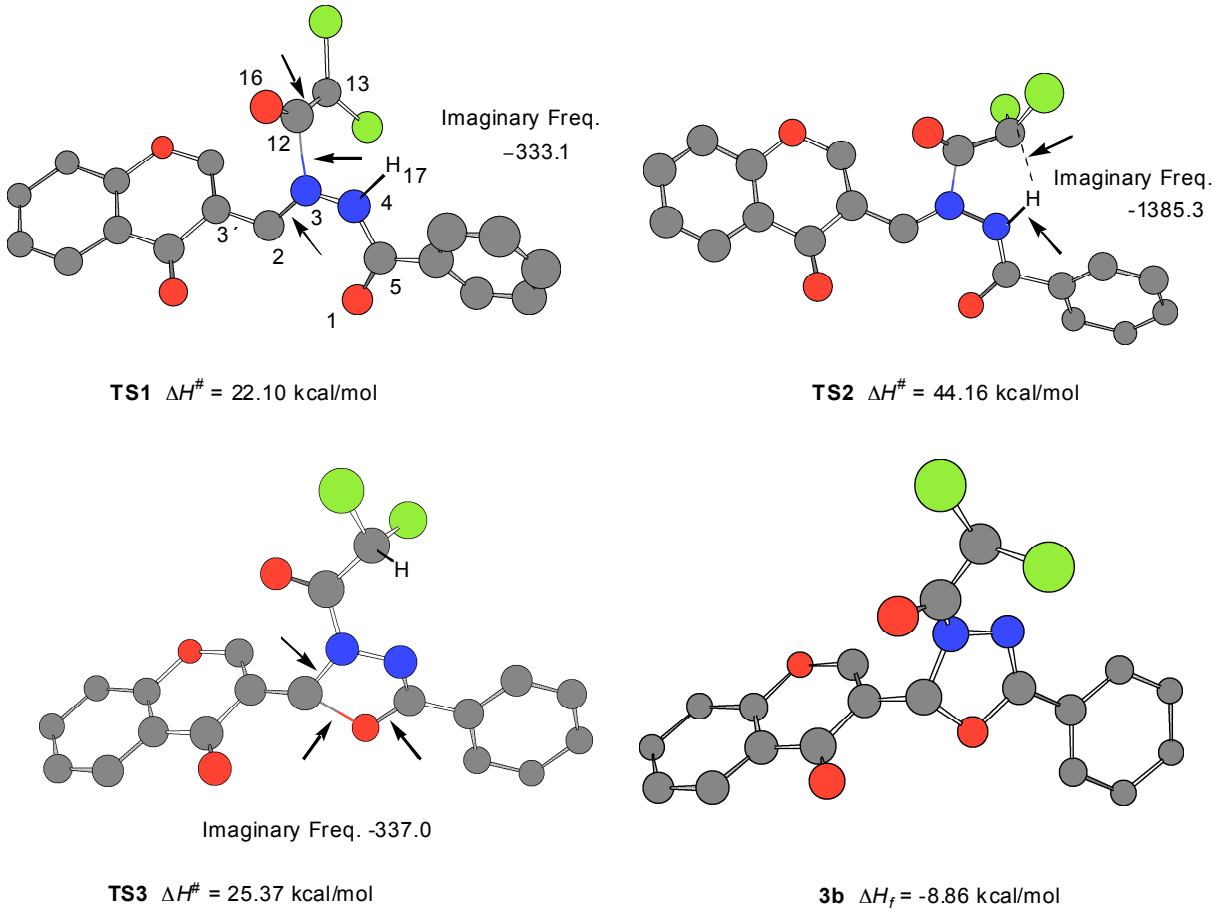


Figure 2. Transition structures calculated by AM1 for the reaction of hydrazone **1** with ketene **2b**. The small arrows show the bonds contributed to the imaginary frequency.

CONCLUSIONS

In conclusion, we have studied the first reaction of 3-formylchromone-*N*-benzoylhydrazone with ketenes leading to the hitherto unknown interesting chromyloxadiazolines **3**. Attention should also be drawn to the fact that in all reactions the chromone moiety remained unchanged. All new compounds are promising targets to study their biological action, because they combine two known independently bioactive rings. For all new compounds full assignment of proton and carbon NMR chemical shifts was achieved. Further investigations of cycloaddition reactions of 3-formylchromone hydrazones are being studied.

EXPERIMENTAL

Melting points were measured on a Kofler hot-stage and are uncorrected. Column chromatography was carried out using Merck silica gel. Petroleum ether refers to the fraction boiling between 60 and 80 °C. NMR spectra were recorded on a Bruker AM 300 spectrometer at 300 MHz for ^{1}H and 75 MHz for ^{13}C, respectively, using $CDCl_3$ as solvent. The chemical shifts are expressed in δ values (ppm) relative to TMS as internal standard for ^{1}H and relative to TMS (0.00 ppm) or to $CDCl_3$ (77.05 ppm) for ^{13}C NMR spectra. Coupling constants ^nJ are reported in Hz. IR spectra were recorded on a Perkin–Elmer 297 spectrometer or on a Perkin–Elmer 1600 series FTIR spectrometer and are reported in wave numbers (cm^{-1}). Low-resolution electron impact mass spectra (EIMS) were obtained on a VG TS-250 instrument and elemental analyses were performed with a Perkin–Elmer 2400-II CHN analyzer. The minimum energy conformation of each compound was computed with the AM1 method [16a] as implemented in the MOPAC package [16b] and referred to vacuum. All geometry optimizations were carried out without symmetry constraints and stationary points were refined by minimization of the gradient norm of the energy to at least 0.05 kcal/mol, using the LET and PRECISE keywords.

Table 3

Comparison of: a) Bond Lengths or Atomic Distances (in Å) and b) Net Atomic Charges (q_{net}) in Reactants (Compounds **1** and **2b**), in various TS during the Reaction of **1** with **2b** and in Product **3b**.

a)

Bonds [a]	Reactants	**TS1**	**TS2**	**TS3**	**3b**
1–2	2.874	2.840	2.828	2.112	1.466
1–5	1.244	1.242	1.250	1.297	1.409
2–3´	1.464	1.458	1.452	1.445	1.498
2–3	1.309	1.312	1.323	1.385	1.504
3–4	1.327	1.341	1.354	1.372	1.370
4–5	1.404	1.410	1.395	1.371	1.327
4–17	1.003	1.006	1.260	2.533	2.661
13–17		2.899	1.506	1.121	1.120
3–12		1.811	1.535	1.440	1.421
12–13	1.323 [b]	1.355	1.491	1.527	1.526
12–16	1.186 [b]	1.215	1.221	1.236	1.236

b)

Atoms	Reactants	**TS1**	**TS2**	**TS3**	**3b**
		q_{net} (Electrons × 10^4, Mulliken)			
1	–3591	–3519	–4108	–4539	–2603
2	–1142	577	703	2017	1355
3	–1064	–1565	–1348	–2226	–3397
4	–4153	–3853	–4064	–3384	–1299
5	3908	3850	3611	2511	1339
17	3297	3290	4402	2624	2444
H-C(2)	2694	2917	2984	2815	2467
12	3126 [b]	3842	3986	3521	3704
13	–2833 [b]	–3632	–3959	–1328	–1366
16	–1513 [b]	–3135	–2740	–2963	–3001
ΔH_f[c]	–3.08 [d]	19.02	41.08	22.56	–8.86

[a] The numbering refers to **TS1** in Figure 2. [b] For ketene **2b**. [c] Enthalpies of formation, in kcal/mol. [d] ΔH_f (**1**) = 11.03; ΔH_f (**2b**) = –14.11.

General Procedure for the Reaction of 3-Formylchromone-*N*-benzoylhydrazone (1) with ketenes. A solution of the appropriately substituted acetyl chloride **2** (3.0 mmoles) in dry toluene (5 mL) was added dropwise under reflux over a period of 20 minutes to a stirred solution of **1** (0.438 g, 1.5 mmoles) in triethylamine (0.45 g, 4.5 mmoles) and dry toluene (40 mL). The reaction mixture was stirred under reflux for 4 hours and then it was washed with a 10% sodium bicarbonate aqueous solution (50 mL). The organic layer was separated, dried and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (7:1) as eluent, slowly increasing the polarity up to 4:1 to give in order of elution: 3-Formylchromone, the chromyloxadiazoline **3** and the benzohydrazide **5**.

Reaction of 3-Formylchromone-*N*-benzoylhydrazone (1) with Chloroacetyl chloride (2a). The following compounds were isolated in order of elution:

3-Formylchromone (0.047 g).

3-(2-Chloroacetyl)-2,3-dihydro-5-phenyl-2-(4-oxo-4*H*-chromen-3-yl)-1,3,4-oxadiazole (3a). White solid in 38% yield, mp 195–197 ° (ethanol); ir (nujol) ν_{max}: 1660, 1635, 1620, 1560 cm^{-1}; ^{1}H and ^{13}C nmr are presented in Table 1; EIMS: m/z (%) 368/370 (25, M^+), 319 (15), 292 (55), 262 (35), 248 (20), 235 (17), 216 (94), 205 (22), 188 (27), 173 (94), 159 (20), 146 (45), 131 (20), 121 (50), 108 (95). *Anal.* Calcd for $C_{19}H_{13}ClN_2O_4$ (368.77): C, 61.88; H, 3.55; N, 7.60. Found: C, 62.09; H, 3.40, N, 7.52.

***N*'-(2-Chloroacetyl)benzohydrazide (5a).** White solid in a yield of 20%, mp 163–165 ° (lit [17a] 165 °).

Reaction of 3-Formylchromone-*N*-benzoylhydrazone (1) with Dihloroacetyl chloride (2b). The following compounds were isolated in order of elution:

3-Formylchromone (0.044 g).

3-(2,2-Dichloroacetyl)-2,3-dihydro-5-phenyl-2-(4-oxo-4*H*-chromen-3-yl)-1,3,4-oxadiazole (3b). White paper like solid in a yield of 40%, mp 231–233 ° (ethanol); ir (nujol) ν_{max}: 1660, 1635, 1620, 1560 cm^{-1}; ^{1}H, ^{13}C and COLOC nmr data are presented in Table 1; EIMS: m/z (%) 402/404/406 (8, M^+), 367/369 (24), 291 (100), 262 (5), 246 (96), 216 (30), 203 (90), 173 (98), 188 (13), 173 (98), 146 (53), 121 (75), 105 (95). *Anal.* Calcd for $C_{19}H_{12}Cl_2N_2O_4$ (403.22): C, 56.60; H, 3.00; N, 6.95. Found: C, 56.51; H, 3.10, N, 7.04.

***N*'-(2,2-Dichloroacetyl)benzohydrazide (5b).** White solid in 20% yield, mp 190–192 ° (lit [17b] 180 °); ^{1}H nmr: δ 6.40 (s, 1 H, 11-H), 7.41–7.46 (m, 2H, (2,6)-H), 7.51–7.56 (m, 1H, 4-H), 7.92–7.94 (m, 2H, (3,5)-H), 10.52 (s, 1 H, 8-H), 10.83 (s, 1 H, 9-H); ^{13}C nmr: δ 64.9 (C-11), 127.7 (C-2,6), 128.3 (C-3,5), 131.9 (C-1), 132.0 (C-4), 162.7 (C-10), 165.6 (C-7); EIMS: m/z (%) 246/248 (25, M^+), 213 (10), 163 (45), 121 (65).

Reaction of 3-Formylchromone-*N*-benzoylhydrazone (1) with Isobutyryl chloride (2c). The following compounds were isolated in order of elution:

3-Formylchromone (0.047 g).

2,3-Dihydro-3-isobutyryl)-2-(4-oxo-4*H*-chromen-3-yl)-5-phenyl-1,3,4-oxadiazole (3c). White paper like solid in a yield of 60%, mp 183–184 ° (ethanol); ir (nujol) ν_{max}: 1660, 1635, 1620, 1560 cm^{-1}; ^{1}H, ^{13}C and COLOC nmr data are presented in Table 2; EIMS: m/z (%) 362 (15, M^+), 292 (35), 291 (100), 188 (10), 173 (33), 147 (20), 133 (18), 121 (35), 105 (84), 77 (55), 71 (47). *Anal*. Calcd for $C_{21}H_{18}N_2O_4$ (362.38): C, 69.60; H, 5.01; N, 7.73. Found: C, 69.73; H, 4.94; N, 7.62.

***N*'-Isobutyrylbenzohydrazide (5c).** White solid in a yield of 16%, mp 185–188 ° (lit [18] 189 °). ^{1}H nmr: δ 1.19 (d, J = 7.3 Hz, 6 H, 2×CH_3), 2.62 (sept, 7.3 Hz, 1 H, 11-H), 7.36–7.41 (m, 2H, (3,5)-H), 7.48–7.52 (m, 1H, 4-H), 7.81–7.84 (m, 2H, (2,6)-H), 9.58 (1 H, s, 8-H), 9.95 (1 H, s, 9-H). EIMS: m/z (%) 206 (100, M^+), 163 (15), 136 (95), 106 (100), 105 (95).

Reaction of 3-Formylchromone-*N*-benzoylhydrazone (1) with Diphenylacetyl chloride (2d). The following compounds were isolated in order of elution:

3-Formylchromone (0.005 g).

2,3-Dihydro-3-(2,2-diphenylacetyl)-2-(4-oxo-4*H*-1-chromen-3-yl)-5-phenyl-1,3,4-oxadiazole (3d). White paper like solid in 80% yield, mp 178–179 ° (ethanol); ir (nujol) ν_{max}: 1635, 1620 cm^{-1}; ^{1}H and ^{13}C nmr data are presented in Table 2; EIMS: m/z (%) 486 (10, M^+), 396 (20), 381 (22), 293 (70), 291 (50), 264 (10), 235 (15), 195 (55), 194 (90), 172 (63), 171 (41), 168 (79), 164 (72), 163 (85), 152 (81), 139 (72), 121 (100), 120 (88), 115 (78), 106 (89), 105 (77).*Anal*. Calcd for $C_{31}H_{22}N_2O_4$ (486.52): C, 76.53; H, 4.56; N, 5.76. Found: C, 76.68; H, 4.52; N, 5.61.

***N*'-(2,2-Diphenylacetyl)benzohydrazide (5d).** White solid in 3% yield, mp 200-201 ° (lit [17c] 202–203 °).

Reaction of 3-formylchromone-*N*-benzoylhydrazone 1 with the anhydride 2e in the presence of triethylamine. A solution of 0.46 g (3.0 mmoles) of phenoxyacetic acid, 0.57 g (3.0 mmoles) of toluene-*p*-sulphonyl chloride, and of 0.61 g (6.0 mmoles) of triethylamine in dry dichloromethane (15 mL) was stirred at room temperature for 10 minutes. To this solution 0.292 g (1.0 mmole) of 3-formylchromone hydrazone **1** was added in dry dichloromethane (2 mL) and the final solution was stirred at room temperature for 24 hours. The reaction mixture was then washed with 10% aqueous sodium bicarbonate solution (10 mL), with water (20 mL) and dried. The solvent was evaporated under reduced pressure and the residue was subjected to column chromatography on silica gel with petroleum ether/ethyl acetate (7:1) as eluent with slowly increasing polarity to give the following compounds in order of elution:

3-Formylchromone. 0.050 g.

2,3-Dihydro-2-(4-oxo-4*H*-chromen-3-yl)-3-(2-phenoxyacetyl)-5-phenyl-1,3,4-oxadiazole (3e). This compound was obtained as yellow solid in a yield of 49%, mp 188–190 ° (ethanol); ir (nujol) ν_{max}: 1685, 1625 cm^{-1}; ^{1}H, ^{13}C and COLOC nmr data are presented in Table 2; EIMS m/z (%) 426 (30, M^+), 333 (6), 321 (40), 319 (55), 305 (20), 291 (45), 290 (53), 280 (10), 262 (35), 248 (12), 230 (25), 216 (95), 205 (28), 188 (25), 173 (90), 172 (95), 146 (70), 131 (90), 121 (80), 120 (72), 108 (89), 107 (90), 106 (97), 105 (92), 103 (100). *Anal*. Calcd for $C_{25}H_{18}N_2O_5$ (426.42): C, 70.42; H, 4.25; N, 6.57. Found: C, 70.60; H, 4.42; N, 6.70.

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