Supplementary Material

Radical scavenging activity and pharmacokinetic properties of coumarin-hydroxybenzohydrazide hybrids

Marko R. Antonijević[1,2] ,Edina H. Avdović[1], Dušica M. Simijonović[1], Žiko Milanović[1], Ana Amić[3], Zoran S. Marković[1*]

[1]*University of Kragujevac, Institute for Information Technologies, Department of Science, Jovana Cvijića bb, 34000 Kragujevac, Serbia*
[2]*University of Kragujevac, Faculty of Science, Department of Chemistry, Radoja Domanovića 12, 34000 Kragujevac, Serbia*
[3]*Department of Chemistry, Josip Juraj Strossmayer University of Osijek, Ulica cara Hadrijana 8A, 31000 Osijek, Croatia; aamic@kemija.unios.hr*
**Correspondence: e-mail address: zmarkovic@uni.kg.ac.rs ; phone number: +38134/610-01-95*

Table S1: Thermodynamic parameters for radical scavenging activity of investigated compounds with alkoxy radicals (kJ mol^{-1}).

With **alkoxy** radicals		**HAT**	**SET-PT**		**SPLET**		**HAT**	**SET-PT**		**SPLET**	
		Δ_rG_{HAT}	Δ_rG_{SET}	Δ_rG_{PT}	Δ_rG_{SPL}	Δ_rG_{ET}	Δ_rG_{HAT}	Δ_rG_{SET}	Δ_rG_{PT}	Δ_rG_{SPL}	Δ_rG_{ET}
		Water					**Benzene**				
•OCH$_3$											
3a	C7"-NH	**-81**	225	-307	**-166**	85	**-86**	417	-504	**-229**	143
	C2"-OH	**-44**		-270	**-92**	48	**-32**		-450	**-133**	101
3b	C7"-NH	**-80**	214	-294	**-146**	66	**-86**	403	-489	**-204**	118
	C4"-OH	**-53**		-267	**-118**	64	**-51**		-454	**-171**	120
3c	C7"-NH	**-81**	219	-278	**-143**	64	**-86**	402	-488	**-203**	117
	C4"-OH	**-61**		-280	**-101**	39	**-57**		-459	**-157**	100
3d	C7"-NH	**-79**	180	-259	**-168**	89	**-83**	424	-506	**-233**	150
	C2"-OH	**-75**		-256	**-110**	35	**-60**		-484	**-157**	97
	C3"-OH	**-73**		-253	**-103**	30	**-58**		-482	**-146**	88
3e	C7"-NH	**-76**	200	-277	**-145**	68	**-84**	418	-502	**-206**	122
	C3"-OH	**-85**		-285	**-119**	35	**-86**		-504	**-179**	93
	C4"-OH	**-83**		-283	**-129**	46	**-84**		-503	**-192**	107
•OCH$_2$CH$_3$											
3a	C7"-NH	**-79**	228	-307	**-166**	87	**-83**	415	-498	**-224**	140
	C2"-OH	**-41**		-269	**-92**	50	**-29**		-444	**-127**	98
3b	C7"-NH	**-77**	217	-294	**-145**	68	**-83**	400	-483	**-198**	115
	C4"-OH	**-51**		-267	**-118**	67	**-48**		-448	**-166**	117
3c	C7"-NH	**-78**	221	-278	**-142**	67	**-83**	400	-483	**-197**	114
	C4"-OH	**-59**		-280	**-100**	42	**-54**		-453	**-151**	97
3d	C7"-NH	**-76**	183	-259	**-168**	92	**-80**	421	-501	**-227**	148
	C2"-OH	**-73**		-256	**-110**	38	**-57**		-478	**-152**	94
	C3"-OH	**-70**		-253	**-102**	32	**-55**		-476	**-141**	86
3e	C7"-NH	**-74**	203	-277	**-145**	71	**-81**	416	-497	**-200**	119
	C3"-OH	**-82**		-285	**-119**	37	**-83**		-499	**-173**	90
	C4"-OH	**-80**		-283	**-128**	48	**-81**		-497	**-186**	105
•OCH(CH$_3$)$_2$											
3a	C7"-NH	**-85**	222	-307	**-166**	81	**-90**	405	-495	**-221**	130
	C2"-OH	**-48**		-270	**-92**	44	**-36**		-441	**-124**	88
3b	C7"-NH	**-83**	211	-294	**-146**	62	**-90**	390	-480	**-195**	105
	C4"-OH	**-57**		-268	**-118**	61	**-55**		-445	**-163**	108
3c	C7"-NH	**-85**	215	-278	**-143**	61	**-90**	390	-480	**-194**	104
	C4"-OH	**-65**		-280	**-101**	36	**16**		-450	**-148**	88
3d	C7"-NH	**-82**	177	-259	**-168**	86	**-87**	411	-498	**-225**	138
	C2"-OH	**-79**		-256	**-111**	32	**-64**		-475	**-149**	85
	C3"-OH	**-76**		-253	**-103**	26	**-62**		-473	**-138**	76
3e	C7"-NH	**-80**	197	-277	**-145**	65	**-88**	406	-494	**-197**	109
	C3"-OH	**-88**		-285	**-119**	31	**-90**		-496	**-171**	81
	C4"-OH	**-87**		-284	**-129**	42	**-88**		-494	**-183**	95
•OC(CH$_3$)$_3$											
3a	C7"-NH	**-90**	221	-311	**-170**	81	**-95**	401	-496	**-221**	126
	C2"-OH	**-52**		-274	**-96**	44	**-41**		-442	**-125**	85
3b	C7"-NH	**-88**	210	-298	**-150**	62	**-94**	386	-481	**-196**	102
	C4"-OH	**-61**		-272	**-122**	61	**-60**		-446	**-163**	104
3c	C7"-NH	**-89**	215	-282	**-147**	60	**-95**	386	-481	**-195**	101
	C4"-OH	**-69**		-284	**-105**	35	**-65**		-451	**-149**	84
3d	C7"-NH	**-87**	177	-263	**-172**	86	**-91**	407	-499	**-225**	134
	C2"-OH	**-83**		-260	**-115**	31	**-69**		-476	**-150**	81
	C3"-OH	**-81**		-257	**-107**	26	**-67**		-474	**-138**	72
3e	C7"-NH	**-84**	197	-281	**-149**	65	**-93**	402	-494	**-198**	105
	C3"-OH	**-93**		-289	**-123**	31	**-94**		-496	**-171**	77
	C4"-OH	**-91**		-288	**-133**	42	**-93**		-495	**-184**	91

Table S2: Thermodynamic parameters for radical scavenging activity of investigated compounds with peroxy radicals (kJ mol^{-1}).

With **peroxy** radicals		**HAT**	**SET-PT**		**SPLET**		**HAT**	**SET-PT**		**SPLET**	
		$\Delta_r G_{HAT}$	$\Delta_r G_{SET}$	$\Delta_r G_{PT}$	$\Delta_r G_{SPL}$	$\Delta_r G_{ET}$	$\Delta_r G_{HAT}$	$\Delta_r G_{SET}$	$\Delta_r G_{PT}$	$\Delta_r G_{SPL}$	$\Delta_r G_{ET}$
		Water					**Benzene**				
•OOCH$_3$											
3a	C7“-NH	**-1**	261	-262	**-122**	120	**-7**	439	-461	**-186**	179
	C2“-OH	**36**		-225	**-47**	83	**48**		-406	**-90**	137
3b	C7“-NH	**1**	250	-249	**-101**	101	**-6**	439	-445	**-161**	154
	C4“-OH	**27**		-223	**-73**	100	**29**		-411	**-128**	156
3c	C7“-NH	**-1**	255	-234	**-98**	98	**-6**	451	-445	**-160**	153
	C4“-OH	**19**		-236	**-56**	75	**16**		-416	**-114**	137
3d	C7“-NH	**2**	216	-214	**-124**	125	**-3**	460	-463	**-190**	187
	C2“-OH	**5**		-211	**-66**	71	**19**		-441	**-114**	133
	C3“-OH	**8**		-209	**-58**	65	**22**		-438	**-103**	125
3e	C7“-NH	**4**	236	-232	**-100**	104	**-4**	455	-459	**-162**	158
	C3“-OH	**-4**		-240	**-75**	70	**-6**		-461	**-136**	130
	C4“-OH	**-3**		-239	**-84**	81	**-5**		-459	**-149**	144
•OOCH$_2$CH$_3$											
3a	C7“-NH	**-2**	266	-267	**-127**	125	**-6**	456	-462	**-187**	181
	C2“-OH	**36**		-230	**-52**	88	**48**		-408	**-91**	139
3b	C7“-NH	**0**	254	-254	**-106**	106	**-5**	441	-447	**-162**	156
	C4“-OH	**27**		-228	**-78**	105	**29**		-412	**-129**	159
3c	C7“-NH	**-1**	259	-239	**-103**	104	**-6**	441	-446	**-161**	155
	C4“-OH	**18**		-241	**-61**	79	**24**		-417	**-115**	139
3d	C7“-NH	**1**	221	-220	**-129**	130	**-2**	462	-460	**-191**	189
	C2“-OH	**5**		-216	**-71**	75	**20**		-462	**-115**	136
	C3“-OH	**7**		-214	**-63**	70	**22**		-461	**-104**	127
3e	C7“-NH	**4**	241	-237	**-105**	109	**-4**	457	-464	**-164**	160
	C3“-OH	**-5**		-245	**-80**	75	**-5**		-442	**-137**	132
	C4“-OH	**-3**		-244	**-89**	86	**-4**		-440	**-150**	146
•OOCH=CH$_2$											
3a	C7“-NH	**-16**	216	-232	**-92**	75	**-20**	399	-419	**-144**	124
	C2“-OH	**21**		-195	**-17**	38	**34**		-365	**-48**	82
3b	C7“-NH	**-15**	204	-219	**-71**	56	**-20**	384	-404	**-119**	101
	C4“-OH	**12**		-193	**-43**	55	**15**		-369	**-86**	99
3c	C7“-NH	**-16**	209	-233	**-68**	54	**-20**	383	-403	**-118**	98
	C4“-OH	**4**		-206	**-26**	30	**9**		-374	**-72**	81
3d	C7“-NH	**-14**	171	-185	**-94**	80	**-17**	405	-421	**-148**	131
	C2“-OH	**-10**		-181	**-36**	26	**6**		-399	**-72**	78
	C3“-OH	**-8**		-179	**-28**	20	**8**		-397	**-61**	69
3e	C7“-NH	**-11**	191	-202	**-70**	59	**-18**	399	-417	**-121**	103
	C3“-OH	**-20**		-210	**-45**	25	**-20**		-419	**-94**	74
	C4“-OH	**-18**		-209	**-54**	36	**-18**		-418	**-107**	89

Table S3: Thermodynamic parameters for radical scavenging activity of investigated compounds with chlorinated methyl-peroxy radicals (kJ mol^{-1}).

With **chlorinated Me-peroxy** radicals		**HAT**	**SET-PT**		**SPLET**		**HAT**	**SET-PT**		**SPLET**	
		$\Delta_r G_{HAT}$	$\Delta_r G_{SET}$	$\Delta_r G_{PT}$	$\Delta_r G_{SPL}$	$\Delta_r G_{ET}$	$\Delta_r G_{HAT}$	$\Delta_r G_{SET}$	$\Delta_r G_{PT}$	$\Delta_r G_{SPL}$	$\Delta_r G_{ET}$
		Water					**Benzene**				
$ClCH_2OO$•											
3a	C7“-NH	**-26**	198	-224	**-83**	58	**-31**	374	-405	**-131**	99
	C2“-OH	**12**		-187	**-9**	21	**23**		-351	**-34**	58
3b	C7“-NH	**-24**	187	-211	**-63**	38	**-31**	359	-390	**-105**	75
	C4“-OH	**2**		-184	**-35**	37	**4**		-355	**-73**	77
3c	C7“-NH	**-25**	192	-195	**-60**	35	**-31**	359	-390	**-104**	74
	C4“-OH	**-6**		-197	**-18**	12	**-1**		-360	**-58**	57
3d	C7“-NH	**-23**	153	-176	**-85**	62	**-28**	380	-408	**-135**	107
	C2“-OH	**-20**		-173	**-27**	8	**-5**		-385	**-59**	54
	C3“-OH	**-17**		-170	**-20**	3	**-3**		-383	**-48**	45
3e	C7“-NH	**-21**	173	-194	**-62**	41	**-29**	375	-404	**-107**	78
	C3“-OH	**-29**		-202	**-36**	8	**-31**		-406	**-81**	50
	C4“-OH	**-27**		-200	**-45**	18	**-29**		-404	**-93**	64
Cl_2CHOO•											
3a	C7“-NH	**-35**	169	-204	**-63**	28	**-39**	343	-381	**-106**	68
	C2“-OH	**2**		-166	**11**	-9	**16**		-327	**-10**	26
3b	C7“-NH	**-33**	157	-191	**-42**	9	**-38**	328	-366	**-81**	43
	C4“-OH	**-7**		-164	**-15**	8	**-3**		-331	**-48**	45
3c	C7“-NH	**-34**	162	-175	**-39**	5	**-38**	327	-366	**-80**	42
	C4“-OH	**-15**		-177	**3**	-17	**-9**		-336	**-34**	25
3d	C7“-NH	**-32**	124	-156	**-65**	33	**-35**	349	-384	**-110**	75
	C2“-OH	**-29**		-153	**-7**	-21	**-12**		-361	**-35**	22
	C3“-OH	**-26**		-150	**-1**	-27	**-10**		-359	**-24**	13
3e	C7“-NH	**-30**	144	-174	**-42**	12	**-36**	343	-380	**-83**	47
	C3“-OH	**-38**		-182	**-16**	-22	**-38**		-382	**-56**	18
	C4“-OH	**-36**		-180	**-25**	-11	**-36**		-380	**-69**	33
Cl_3COO•											
3a	C7“-NH	**-38**	147	-185	**-44**	7	**-41**	315	-356	**-81**	40
	C2“-OH	**-1**		-148	**30**	-31	**47**		-301	**15**	-2
3b	C7“-NH	**-36**	136	-172	**-23**	-13	**-40**	300	-340	**-55**	15
	C4“-OH	**-10**		-145	**4**	-14	**-5**		-305	**-23**	18
3c	C7“-NH	**-37**	141	-178	**-21**	-16	**-40**	300	-340	**-55**	14
	C4“-OH	**-18**		-158	**21**	-39	**-11**		-311	**-9**	-2
3d	C7“-NH	**-35**	102	-137	**-46**	11	**-37**	300	-358	**-85**	48
	C2“-OH	**-32**		-134	**12**	-43	**-15**		-336	**-9**	-5
	C3“-OH	**-29**		-131	**19**	-49	**-12**		-333	**2**	-14
3e	C7“-NH	**-33**	122	-155	**-23**	-10	**-40**	316	-354	**-57**	19
	C3“-OH	**-41**		-163	**3**	-44	**-39**		-356	**-31**	-9
	C4“-OH	**-39**		-161	**-6**	-33	**-38**		-354	**-43**	5

Table S4: Thermodynamic parameters for RAF mechanistic pathway of inactivation of $CH_3O^{\bullet}$ by investigated compounds (kJ mol^{-1}).

	Compound	Position	Water	Benzene
$CH_3O^{\bullet}$	**3a**	C5”	25.4	23.0
		C6”	-1.5	0.4
		C7	17.9	15.5
	3b	C5”	19.3	16.9
		C6”	18.9	11.7
		C7	17.7	12.0
	3c	C5”	28.5	24.7
		C6”	6.0	0.6
		C7	20.6	17.5
	3d	C5”	27.1	25.3
		C6”	-9.3	-13.8
		C7	20.5	16.1
	3e	C5”	26.7	23.8
		C6”	6.9	2.9
		C7	17.9	14.0

Table S5: Thermodynamic parameters for RAF mechanistic pathway of inactivation of $CH_3CH_2O^{\bullet}$ by investigated compounds (kJ mol^{-1}).

	Compound	Position	Water	Benzene
$CH_3CH_2O^{\bullet}$	**3a**	C5”	30.1	28.4
		C6”	11.2	5.3
		C7	21.1	19.9
	3b	C5”	23.4	21.6
		C6”	23.0	16.7
		C7	22.2	17.3
	3c	C5”	36.2	30.0
		C6”	15.0	4.7
		C7	24.9	24.9
	3d	C5”	35.7	29.8
		C6”	-5.0	-10.4
		C7	22.6	21.5
	3e	C5”	33.8	29.4
		C6”	13.8	1.3
		C7	27.2	21.3

Table S6: Thermodynamic parameters for RAF mechanistic pathway of inactivation of $(CH_3)_2CHO^{\bullet}$ by investigated compounds (kJ mol^{-1}).

	Compound	Position	Water	Benzene
$(CH_3)_2CHO^{\bullet}$	**3a**	C5”	33.0	29.4
		C6”	6.7	2.4
		C7	23.8	16.8
	3b	C5”	19.5	18.1
		C6”	23.1	16.0
		C7	17.3	13.2
	3c	C5”	35.3	28.9
		C6”	12.4	6.8
		C7	23.0	16.6
	3d	C5”	37.6	33.1
		C6”	-6.8	-10.8
		C7	25.4	19.1
	3e	C5”	27.4	27.3
		C6”	12.1	0.8
		C7	21.8	18.2

Table S7: Thermodynamic parameters for RAF mechanistic pathway of inactivation of $(CH_3)_3CO^{\bullet}$ by investigated compounds (kJ mol^{-1}).

	Compound	Position	Water	Benzene
$(CH_3)_3CO^{\bullet}$	**3a**	C5”	30.8	26.1
		C6”	17.6	13.3
		C7	35.7	39.8
	3b	C5”	38.0	32.6
		C6”	33.0	26.1
		C7	32.8	30.7
	3c	C5”	47.8	36.4
		C6”	23.4	16.4
		C7	43.9	39.3
	3d	C5”	49.5	44.9
		C6”	2.4	-0.1
		C7	35.5	38.0
	3e	C5”	44.7	42.6
		C6”	16.9	18.1
		C7	41.4	37.2

Table S8: Thermodynamic parameters for RAF mechanistic pathway of inactivation of $CH_3COO^{\bullet}$ by investigated compounds (kJ mol^{-1}).

	Compound	Position	Water	Benzene
$CH_3OO^{\bullet}$	**3a**	C5”	95.7	87.4
		C6”	73.4	67.5
		C7	89.0	85.7
	3b	C5”	85.0	85.6
		C6”	91.2	83.3
		C7	86.2	84.3
	3c	C5”	99.9	93.5
		C6”	59.2	68.1
		C7	89.7	90.7
	3d	C5”	98.0	94.2
		C6”	59.2	53.6
		C7	89.7	89.8
	3e	C5”	104.5	97.0
		C6”	80.8	75.0
		C7	95.2	91.2

Table S9: Thermodynamic parameters for RAF mechanistic pathway of inactivation of $CH_3CH_2OO^{\bullet}$ by investigated compounds (kJ mol^{-1}).

	Compound	Position	Water	Benzene
$CH_3CH_2OO^{\bullet}$	**3a**	C5”	91.0	85.9
		C6”	72.6	62.6
		C7	91.8	90.1
	3b	C5”	92.6	88.8
		C6”	90.3	82.1
		C7	91.7	88.1
	3c	C5”	85.4	80.3
		C6”	79.5	71.5
		C7	96.2	92.6
	3d	C5”	94.0	92.1
		C6”	62.6	51.6
		C7	92.0	92.1
	3e	C5”	88.6	86.8
		C6”	79.8	70.9
		C7	94.5	92.9

Table S10: Thermodynamic parameters for RAF mechanistic pathway of inactivation of CH_2=CHOO• by investigated compounds (kJ mol^{-1}).

	Compound	Position	Water	Benzene
CH_2=CHOO•	**3a**	C5”	83.4	82.8
		C6”	63.7	59.2
		C7	73.9	72.6
	3b	C5”	82.8	81.7
		C6”	78.6	72.5
		C7	74.6	73.2
	3c	C5”	87.8	84.8
		C6”	68.6	61.9
		C7	74.7	82.0
	3d	C5”	86.0	85.0
		C6”	48.7	44.3
		C7	74.3	75.1
	3e	C5”	86.6	79.7
		C6”	72.2	63.1
		C7	78.1	77.5

Table S11: Thermodynamic parameters for RAF mechanistic pathway of inactivation of $ClCH_2OO$• by investigated compounds (kJ mol^{-1}).

	Compound	Position	Water	Benzene
$ClCH_2OO$•	**3a**	C5”	86.9	81.0
		C6”	66.4	67.1
		C7	56.7	60.7
	3b	C5”	86.4	76.6
		C6”	82.8	82.4
		C7	61.5	56.0
	3c	C5”	95.5	92.5
		C6”	70.2	60.1
		C7	67.7	72.6
	3d	C5”	92.7	81.8
		C6”	57.0	47.8
		C7	61.1	67.8
	3e	C5”	88.8	85.4
		C6”	78.0	64.0
		C7	74.1	63.4

Table S12: Thermodynamic parameters for RAF mechanistic pathway of inactivation of $Cl_2CHOO^{\bullet}$ by investigated compounds (kJ mol^{-1}).

	Compound	Position	Water	Benzene
$Cl_2CHOO^{\bullet}$	**3a**	C5”	64.8	55.5
		C6”	45.9	42.0
		C7	64.3	61.1
	3b	C5”	54.0	60.7
		C6”	65.5	60.6
		C7	63.4	62.7
	3c	C5”	62.8	63.5
		C6”	48.7	43.4
		C7	69.3	60.2
	3d	C5”	63.7	69.8
		C6”	30.2	24.2
		C7	65.6	57.2
	3e	C5”	68.1	67.2
		C6”	55.7	51.3
		C7	71.0	65.2

Table S13: Thermodynamic parameters for RAF mechanistic pathway of inactivation of $Cl_3COO^{\bullet}$ by investigated compounds (kJ mol^{-1}).

	Compound	Position	Water	Benzene
$Cl_3COO^{\bullet}$	**3a**	C5”	51.6	60.7
		C6”	35.6	33.7
		C7	49.0	49.8
	3b	C5”	56.1	57.9
		C6”	51.3	56.1
		C7	55.1	55.4
	3c	C5”	63.4	53.9
		C6”	43.8	40.6
		C7	54.9	59.5
	3d	C5”	54.9	58.6
		C6”	22.7	19.4
		C7	48.9	61.8
	3e	C5”	53.9	56.4
		C6”	40.4	43.5
		C7	55.0	54.8

Table S14: Thermodynamic parameters describing the second step (RAF) of the radical scavenging reaction following the HAT-RAF mechanism in triplet spin state (kJ mol^{-1}).

Compounds		Water			Benzene		
Triplet		$(CH_3)_3CO^{\bullet}$	$CH_2{=}CHOO^{\bullet}$	$Cl_3COO^{\bullet}$	$(CH_3)_3CO^{\bullet}$	$CH_2{=}CHOO^{\bullet}$	$Cl_3COO^{\bullet}$
3a	C5”	35	85	63	32	84	63
	C6”	33	69	45	27	67	44
	C7”	39	85	64	28	87	66
3b	C5”	32	86	58	28	85	59
	C6”	46	89	61	45	88	60
	C7”	41	86	68	38	85	67
3c	C5”	28	71	39	48	90	62
	C6”	15	56	28	33	77	48
	C7”	22	70	49	43	85	64
3d	C5”	33	83	58	34	84	61
	C6”	19	56	30	18	54	30
	C7”	43	87	60	40	85	56
3e	C5”	33	88	56	41	88	56
	C6”	32	73	55	31	73	46
	C7”	38	86	68	47	82	68

Table S15: Thermodynamic parameters describing the second step (RAF) of the radical scavenging reaction following the HAT-RAF mechanism in singlet spin state (kJ mol^{-1}).

Compounds		Water			Benzene		
Singlet		$(CH_3)_3CO^{\bullet}$	$CH_2{=}CHOO^{\bullet}$	$Cl_3COO^{\bullet}$	$(CH_3)_3CO^{\bullet}$	$CH_2{=}CHOO^{\bullet}$	$Cl_3COO^{\bullet}$
3a	C5”	-114	-54	-47	-110	-50	-70
	C6”	33	86	67	44	96	78
	C7”	28	104	92	55	69	42
3b	C5”	-19	56	41	20	97	80
	C6”	40	100	78	62	114	89
	C7”	42	72	57	11	85	42
3c	C5”	-33	40	31	22	90	68
	C6”	-40	15	-5	10	63	48
	C7”	23	52	24	20	68	42
3d	C5”	-121	-59	-74	-117	-56	-70
	C6”	-44	8	-12	-43	5	-14
	C7”	25	103	88	54	71	45
3e	C5”	-18	62	55	23	100	86
	C6”	-15	42	20	30	67	50
	C7”	40	70	41	23	65	36

Table S16: Gibbs Free Energies of the optimized structures of biradical species (in Hartree)

Biradical specie		Singlet		Triplet	
		Water	Benzene	Water	Benzene
3a	C2”-O˙ and C7”-N˙	-1178.33	-1178.32	-1178.35	-1178.34
3b	C4”-O˙ and C7”-N˙	-1178.34	-1178.33	-1178.35	-1178.35
3c	C4”-O˙ and C7”-N˙	-1292.84	-1292.83	-1292.85	-1292.84
3d	C2”-O˙ and C7”-N˙	-1253.56	-1253.55	-1253.59	-1253.58
	C3”-O˙ and C7”-N˙	-1253.61	-1253.60	-1253.59	-1253.58
	C2”-O˙ and C3”-O˙	-1253.61	-1253.60	-1253.55	-1253.55
3e	C3”-O˙ and C7”-N˙	-1253.57	-1253.56	-1253.59	-1253.58
	C4”-O˙ and C7”-N˙	-1253.58	-1253.57	-1253.59	-1253.58
	C3”-O˙ and C4”-O˙	-1253.61	-1253.60	-1253.55	-1253.55

Table S17: Drug-likeness rules and bioavailability score

SwissADME

Compounds	Lipinski	Ghose	Veber	Egan	Muegge	Violations	Bio-availability score
3a	Yes	Yes	Yes	Yes	Yes	0	0.55
3b	Yes	Yes	Yes	Yes	Yes	0	0.55
3c	Yes	Yes	Yes	Yes	Yes	0	0.55
3d	Yes	Yes	Yes	Yes	Yes	0	0.55
3e	Yes	Yes	Yes	Yes	Yes	0	0.55

ADMET Lab2.0

Compounds	Lipinski	Pfizer	GSK	Golden triangle	Natural product-likenees	QED	Synthetic accesbility (SA)Score*
3a	Yes	Yes	Yes	Yes	Yes	Too complex	2.339
3b	Yes	Yes	Yes	Yes	Yes	Too complex	2.304
3c	Yes	Yes	Yes	Yes	Yes	Too complex	2.379
3d	Yes	Yes	Yes	Yes	Yes	Attractive	2.495
3e	Yes	Yes	Yes	Yes	Yes	Attractive	2.445

*****Compounds with the SA score <6 are considered easy to synthetise

Table S18: Predicted pharmacokinetic parameters of investigated compounds by ADMET Lab 2.0 server.

Compound	**HIA (GI)**	**BBB**	**Log*Kp* (cm/s)**	**P−gp substrate**	**CYP1A2 inhibitor**	**CYP2C19 inhibitor**	**CYP2C9 inhibitor**	**CYP2D6 inhibitor**	**CYP3A4 inhibitor**
3a	>30%	No	−5.17	No	Yes	No	Yes	No	No
3b	>30%	No	−5.06	No	Yes	No	Yes	No	No
3c	>30%	No	−5.20	No	Yes	No	Yes	No	Yes
3d	>30%	No	−5.65	No	Yes	No	Yes	No	Yes
3e	>30%	No	−5.57	No	Yes	No	No	No	Yes

Table S19: HOMO orbital energies of investigated biradical species in triplet and singlet spin states.

Compound		HOMO	
		Spin state	
	Positions	Singlet	Triplet
3a	C2”-O• and C7”-N•	-0.28378	-0.26117
3b	C4”-O• and C7”-N•	-0.28115	-0.26775
3c	C4”-O• and C7”-N•	-0.26872	-0.26413
3d	C2”-O• and C7”-N•	-0.2778	-0.25316
	C3”-O• and C7”-N•	-0.27959	-0.28172
	C2”-O• and C3”-O•	-0.23737	-0.3041
3e	C3”-O• and C7”-N•	-0.27645	-0.26053
	C4”-O• and C7”-N•	-0.27335	-0.26439
	C3”-O• and C4”-O•	-0.23623	-0.30339

Table S20: HAT-RC mechanism of radical scavenging activity for compounds **3a-3e** (kJ mol^{-1}).

Compound	Water			Benzene		
	$(CH_3)_3CO^•$	$CH_2=CHOO^•$	$Cl_3COO^•$	$(CH_3)_3CO^•$	$CH_2=CHOO^•$	$Cl_3COO^•$
3a	-81	-30	-53	-83	-33	-54
3b	-86	-39	-63	-88	-35	-61
3c	-83	-29	-58	-87	-34	-61
3d	-79	-27	-53	-81	-28	-54
3e	-84	-33	-64	-86	-35	-67

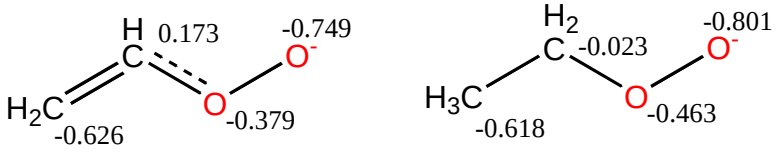


Figure S1: NBO charge distribution of $CH_2=CHOO^-$ (left) and $CH_3CH_2OO^-$ (right)

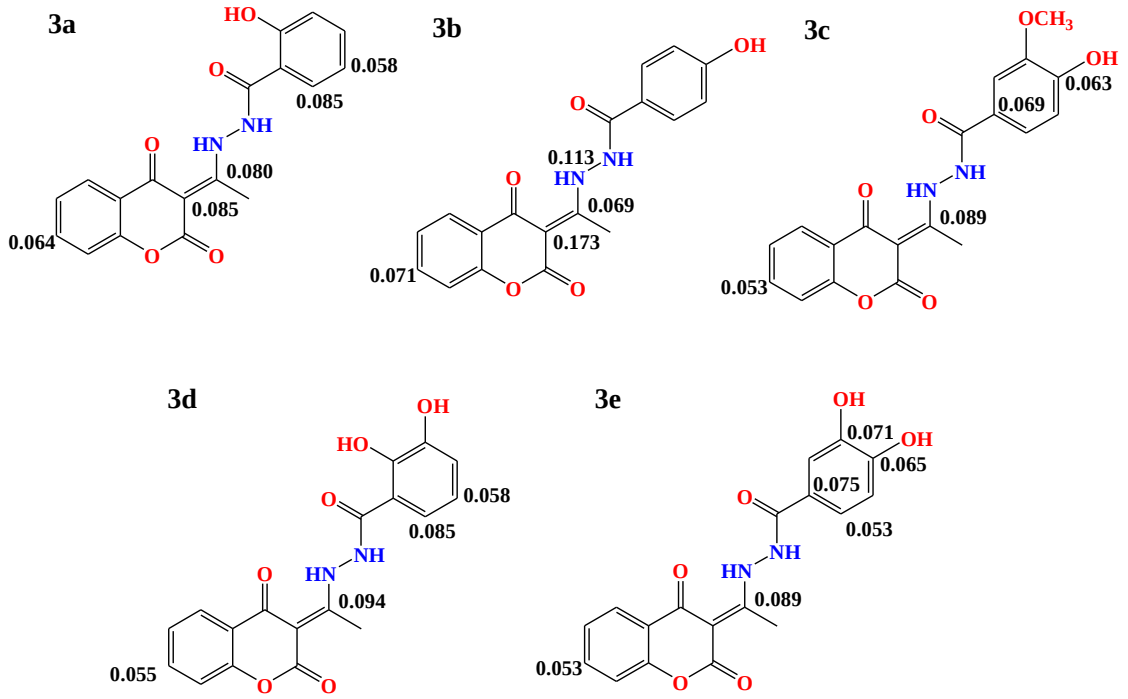
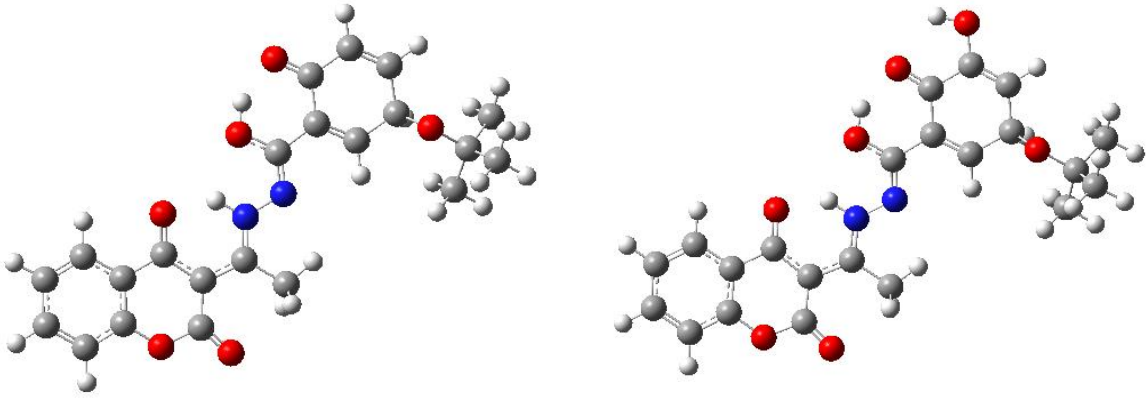


Figure S2: Fukui index values for investigated compounds with values higher than 0.05 presented



3aC5″-OC(CH3)3 **3d**C5″-OC(CH3)3

Figure S3: Optimised structures of the compounds stabilised by hydrogen transfer from C2″-OH to C7″=O

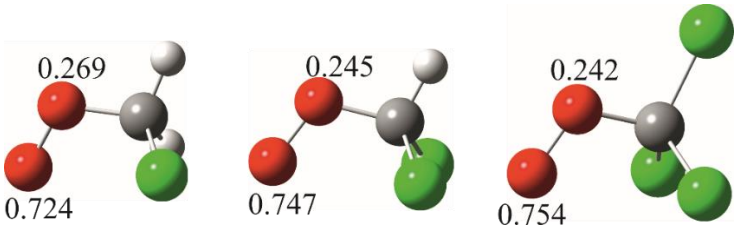


Figure S4. NBO spin distribution on the oxygen atoms of chlorinated methyl radicals

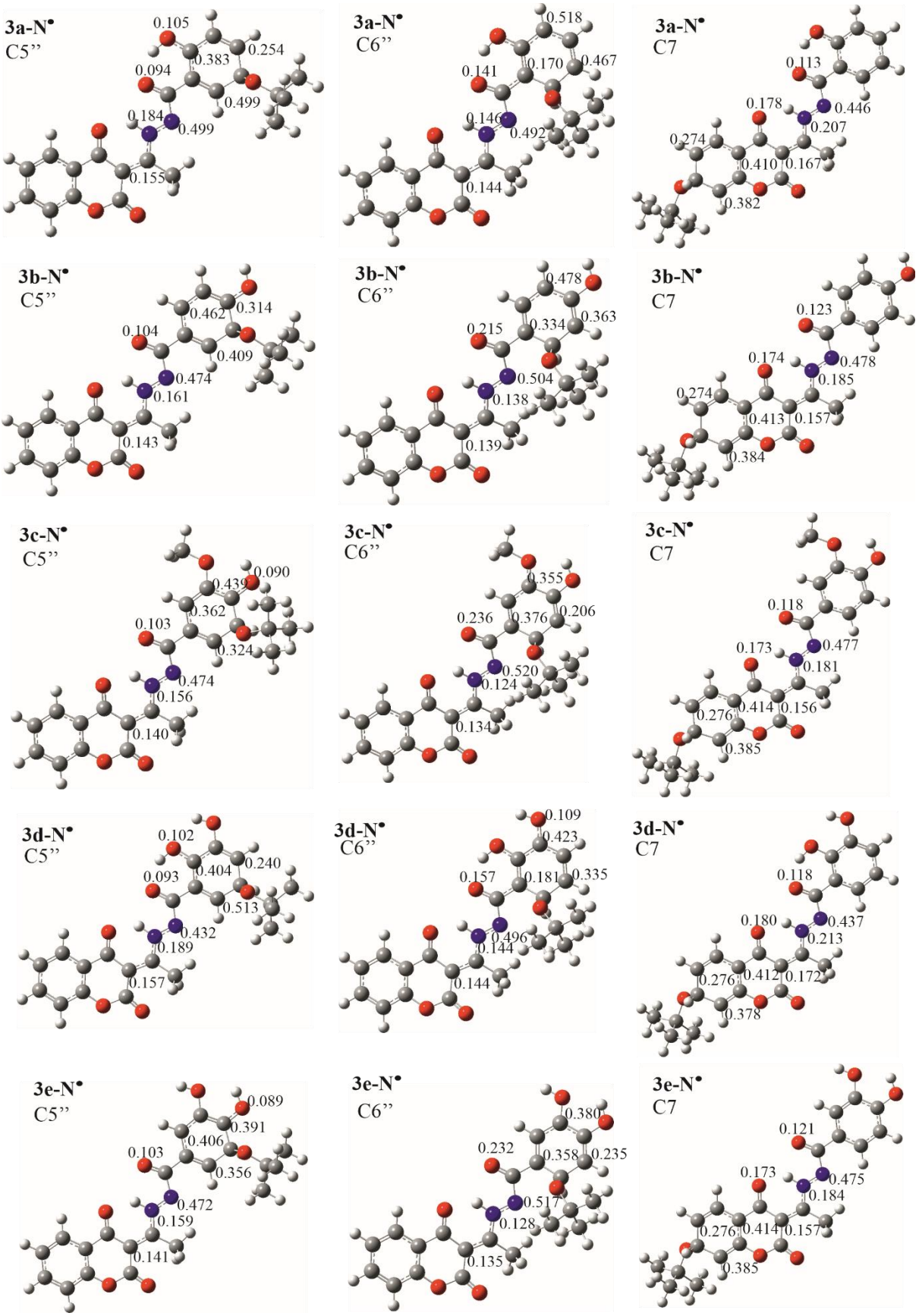


Figure S5. NBO spin distribution for adducts obtained in HAT-RAF mechanism with $(CH_3)_3CO^{\bullet}$