Microwave-induced, solvent-free transformations of benzoheteracyclanones by HTIB (Koser's reagent)

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Dedicated to Professor Sándor Antus on the occasion of his 60th birthday

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Abstract

The microwave-activated reactions of [hydroxy(tosyloxy)iodo]benzene (HTIB) with various chromanones, thiochromanones and dihydroquinolones under solvent-free conditions have been studied. In addition to the common dehydrogenation reaction, 2,3-migration also has been observed in the case of flavanone and 2,2-disubstituted chromanones. 3-Tosyloxychromanones were isolated from the reaction of chromanone and 2-methylchromanone for the first time. Substrates with nucleophilic heteroatoms such as thiochromanones and 2-phenyl-2,3-dihydro-4-quinolone reacted by electrophilic attack of the heteroatom.

Keywords: Chromanones, 2,3-dihydro-4-quinolones, hypervalent iodine reagent, microwave irradiation, thiochromanones, tosyloxylation

Introduction

[Hydroxy(tosyloxy)iodo]benzene[1] (HTIB, Koser's reagent) and related hypervalent iodine derivatives have become widely used reagents for synthetic organic chemistry during the last decades, and excellent overviews of their chemistry have been forthcoming in several papers.[2] The most frequently exploited reactions of HTIB and the other [(arylsulfonyloxy)(hydroxy)iodo]benzene analogues are the α-sulfonyloxylation of ketones (or their enol derivatives), sulfonyloxylation of double bonds, phenyliodination and oxidation, and all of these approaches have been utilized in the synthesis of various heterocyclic systems[2]. A survey of the literature reveals continuous efforts to develop these reagents and the conditions for their use. Some recent examples are preparation of isoflavones from 2'-hydroxychalcones by

means of a polymer-supported reagent,[3] α-tosyloxylation in ionic liquids,[4] α-hydroxylation of ketones by HTIB in DMSO-water mixtures,[5] oxidative α-tosyloxylation of alcohols into α-tosyloxy aldehydes and ketones[6] or the use of [hydroxy(2,4-dinitrobenzenesulfonyloxy)iodo]benzene (HDNIB).[7]

Microwave (MW) irradiation is an efficient and environmentally-benign method to activate various organic transformations to afford products in higher yields in shorter reaction periods. In this class of MW-assisted reactions, solvent-free syntheses are of particular interest and importance in view of their simplicity, tunability and ease of work-up.[8] MW activation was utilized advantageously in the α-tosyloxylation of acetophenones by HTIB in the presence of K10 clay and the generated tosylates were successfully transformed into thiazoles and imidazo[2,1-*b*]thiazoles.[9]

In continuation of our studies in the field of cyclic α-(arylsulfonyloxy)ketones and oxygen-containing heterocycles, we decided to investigate the reaction of various chromanone derivatives and their sulfur or nitrogen-containing analogues with HTIB under MW irradiation and solvent-free conditions, and the most characteristic results are presented here.

Results and Discussion

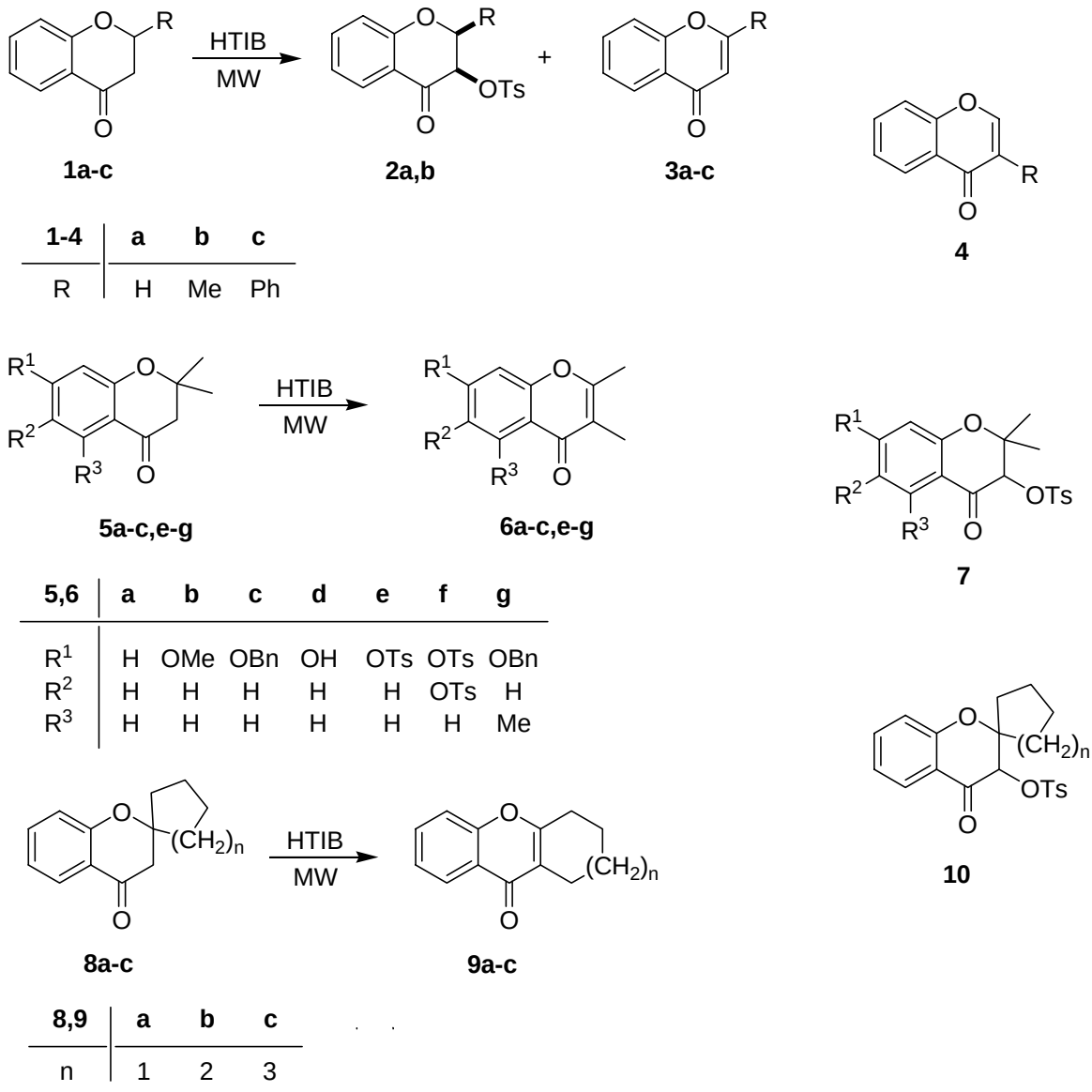
First, we searched for the most efficient MW-inactive support for use of the highly sensitive 2,2-dimethyl-7-methoxychromanone (**5b**) as a test molecule. MW irradiation and subsequent work-up afforded the expected 2,3-dimethyl-7-methoxychromone (**6b**) in addition to some unidentified, highly polar products which could be removed easily by filtration through a short pad of silica or by short-column chromatography (Scheme 1, Table 1). The structure of the product was in accordance with literature data, Prakash and his coworkers[10] have observed the same 2,3-methyl migration and dehydrogenation in refluxing acetonitrile using ultrasound activation.

Table 1. Effect of the support on the MW-induced reaction of 2,2-dimethyl-7-methoxy-chromanone (**5b**) with HTIB[a]

Entry	Support	MW Irradiation (min)	Conversion[b] (%)	Yield[c] (%)
1	None	4x1	80	41
2	Montmorillonite K-10	20x1	29	46
3	Al_2O_3 (neutral)	20x1 + 15x2	57	53
4	$CaCO_3$	20x1 + 5x2	80	59
5	Na_2SO_4	12x1	88	61

[a] According to the General Procedure (Experimental Part) by treating 1.00 mmol of **5b** with 1.20 mmol of HTIB, elution with hexane-ethyl acetate (1:1, v/v). [b] Calculated on the basis of the recovered starting material. [c] Refers to pure isolated products, the values are normalized to 100% conversion.

The results summarized in Table 1 reveal a decisive role for the support. Surprisingly, poor conversion and low yield was found using Montmorillonite K10 and neutral alumina. Inorganic salts such as $CaCO_3$ or Na_2SO_4 gave much better conversions. Good conversions also have been achieved without any support, but the yield was lower due to secondary reactions causing the decomposition of the product. Taking the length of the irradiation period, conversions and yields into consideration, we chose Na_2SO_4 as the carrier for further experiments.



1-4	a	b	c
R	H	Me	Ph

5,6	a	b	c	d	e	f	g
R^1	H	OMe	OBn	OH	OTs	OTs	OBn
R^2	H	H	H	H	H	OTs	H
R^3	H	H	H	H	H	H	Me

8,9	a	b	c
n	1	2	3

Scheme 1

The reactions of chromanone (**1a**) and 2-methylchromanone (**1b)** afforded a mixture of the 3-tosyloxychromanones **2a,b** and the corresponding chromones **3a,b** under the optimized conditions (Table 2, Scheme 1). It was noteworthy that, in the case of **1b** the oxidative

sulfonyloxylation took place with complete diastereoselectivity; only the *cis* diastereomer could be detected and isolated. The relative configuration of the obtained *cis*-2-methyl-3-tosyloxychromanone (**2b**) has been determined on the basis of the small value for the $^3J_{2H,3H}$ coupling constant (3.7 Hz). Earlier, Liebscher and coworkers have reported values of $^3J_{2H,3H}$ = 12.4 Hz for *trans*-3-hydroxy-2-propylchromanone and $^3J_{2H,3H}$ = 6.0 Hz for *cis*-3-hydroxy-2-methylchromanone. The stereochemistry of the *cis*-3-hydroxy-2-methyl-2,3-dihydro-4*H*-naphto[2,3-*b*]pyran-4-one also has been proven by X-ray crystallography.[11] In spite of the low yields of tosylates **2a,b**, the method has some synthetic value since 3-arylsulfonyloxychromanones were practically unknown. The only exception, 3-[(4-nitrobenzenesulfonyl)oxy]chromanone, was obtained from 4-acetoxy-2*H*-1-chromene with *bis*(4-nitrobenzenesulfonyl) peroxide.[12] Further, no tosylates **2a,b** have been isolated previously from the reaction of substrates **1a,b** and HTIB in hot acetonitrile with or without sonication,[10] proving again the beneficial effect of MW irradiation.

On the contrary, when flavanone (**1c**) was treated with HTIB no tosylate **2c** was obtained and the reaction yielded a mixture of flavone (**3c**) and isoflavone (**4c**) (Table 2, Scheme 1). This result is in accordance with the literature data. According to Prakash *et al.*, 3-tosyloxyflavanone was never observed using classical heating and the product ratio depended strongly on the conditions. In boiling acetonitrile or propionitrile, isoflavone (**4c**) was the major product accompanied with a small amount of flavone (**3c**) and methyl 2-phenyl-2,3-dihydrobenzofuran-3-carboxylate.[13] The change of the solvent to methanol resulted in a dramatic shift as flavone (**3c**) became the major product, accompanied by some *cis*-3-methoxyflavanone and methyl 2-phenyl-2,3-dihydrobenzofuran-3-carboxylate.[14] The oxidative rearrangement of flavanone (**1c**) also has been performed using other reagents such as iodobenzene diacetate/*p*-toluenesulfonic acid in acetonitrile, iodosobenzene/methanesulfonic acid in methylene chloride or acetonitrile[2] or various thallium(III) reagents.[15]

Table 2. Reaction of chromanones **1a-c** with HTIB under MW irradiation using Na_2SO_4 support

Entry	Starting material	HTIB (equiv.)	MW irradiation (min)	Eluent[a]	Conversion[b] (%)	Yield[c] (%) **2**	**3**	**4**
1	**1a**	1.2	6x1	A	70	6.1	45	0
2		2.4	8x1	B	63	12	62	0
3	**1b**	1.2	3x1	B	85	32	28	0
4		2.4	3x1	B	100	25	19	0
5	**1c**	1.2	4x1	A	100	0	25	20
6		2.4	2x1	B	95	0	13	47

[a] A: dichloromethane, B: dichloromethane, components of low R_f were eluted by ethyl acetate and re-chromatographed using hexane-ethyl acetate (1:1, v/v).
[b] Calculated on the basis of the recovered starting material. [c] Refers to pure isolated products, the values are normalized to 100% conversion.

The treatment of various substituted 2,2-dimethylchromanones **5a-c,e-g** with HTIB under our MW conditions afforded the corresponding 2,3-dimethylchromones **6a-c,e-g** (Table 3, Scheme 1). The use of higher amounts of HTIB resulted in an increase in the conversion in all cases, but the yields were significantly lower due to the decomposition of the primary products formed. This tendency is quite conspicuous in the case of 7-benzyloxy-2,2,5-trimethylchromanone (**5g**) where the aromatic ring is highly activated and, therefore, sensitive to the competitive attack of the electrophilic reagent (Table 3, Entries 9,10). For the same reason, the reaction of 2,2-dimethyl-7-hydroxychromanone (**5d**) failed to give any desired rearranged product **6d**. The latter was prepared by the acid-catalyzed debenzylation of the protected derivative **6c**.

Table 3. Reaction of 2,2-disubstituted chromanones **5a-c,e-g, 8a-c** with HTIB under MW irradiation using Na_2SO_4 support

Entry	Starting material	HTIB (equiv.)	MW irradiation (min)	Eluent[a]	Conversion[b] (%)	Product	Yield[c] (%)
1	**5a**	1.2	8x1	A	64	**6a**	85
2		2.4	6x1	C	100		78
3	**5b**	1.2	6x1	C	65	**6b**	60
4		2.4	6x1	C	89		37
5	**5c**	1.2	5x1	D	80	**6c**	80
6	**5e**	1.2	6x1	C	81	**6e**	85
7	**5f**	1.2	6x1	A	52	**6f**	84
8		2.4	6x1	C	93		71
9	**5g**	1.2	8x1	D	64	**6g**	28
10		2.4	6x1	D	92		3.7
11	**8a**	1.2	6x1	D	82	**9a**	82
12		2.4	6x1	D	100		73
13	**8b**	1.2	3x1	A	75	**9b**	97
14		2.4	2x1	A	100		76
15	**8c**	1.2	4x1	D	63	**9c**	80
16		2.4	2x1	D	100		57

[a] A: dichloromethane, C: dichloromethane-acetone (10:1, v/v), D: 1,2-dichloroethane.
[b] Calculated on the basis of the recovered starting material. [c] Refers to pure isolated products, the values are normalized to 100% conversion.

The 2,3-alkyl migration and dehydrogenation also was observed in the reaction of the 2-spirochromanones **8a-c** to give the corresponding tricyclic products **9a-c** in good-to-excellent yields. The same reaction had been observed previously from the treatment of the spirochromanones with HTIB in hot acetonitrile, with or without ultrasound activation,[10] or with thallium(III) trinitrate in hot acetonitrile.[16] Based on the results, we can conclude that the

rearrangement is expected only with 2,2-disubstituted chromanones or 2-substituted chromanones containing a group of high migrating capability (e.g. aryl). HTIB-induced dehydrogenation and migration of spirochromanones offers a useful method for the synthesis of various naturally-occurring and/or biologically active targets and some such molecules containing a tetrahydroxanthone moiety are shown in Figure 1. To the best of our knowledge, the only exploitation of this approach has been presented by Gabutt *et al.*[21] who accomplished the synthesis of the rotenoid core.

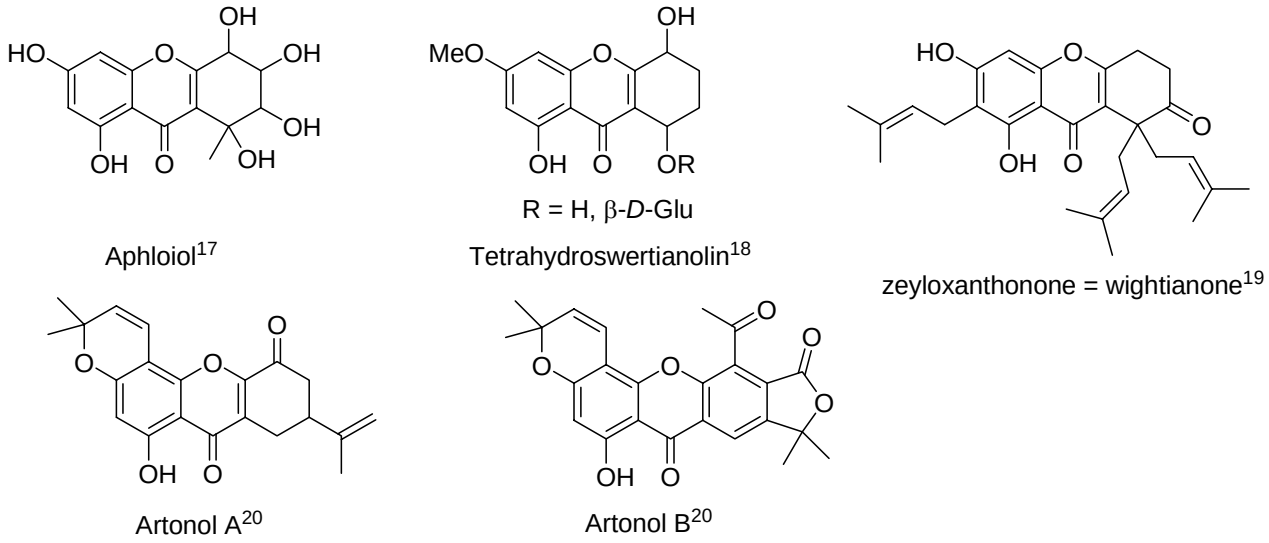


Figure 1

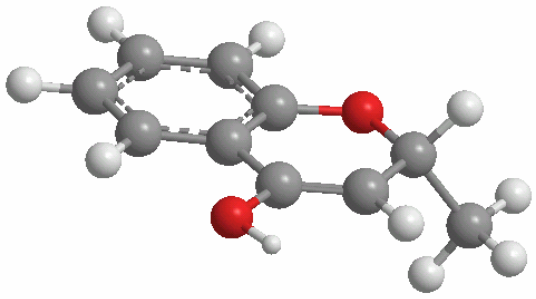
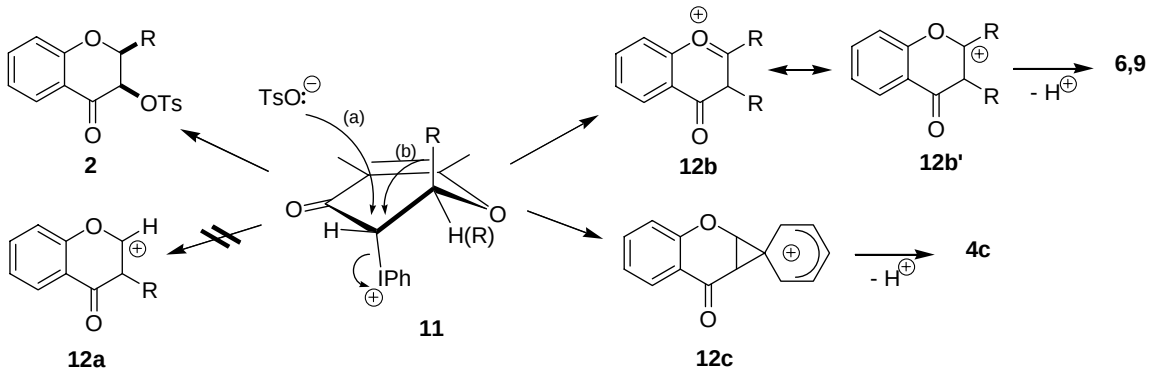


Figure 2

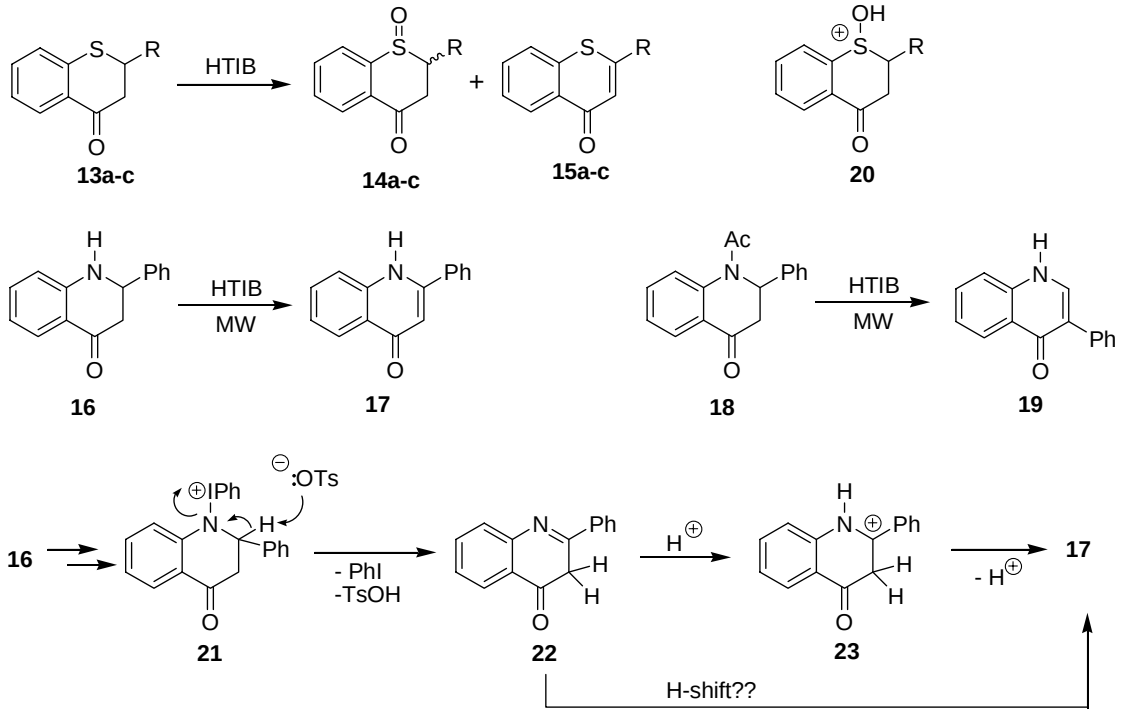
The obtained results can be integrated in a single mechanism. According to the literature,[2] the reacting species in the HTIB-mediated reactions is the 3-phenyliodonio intermediate **11** which has a *trans* relative configuration in the case of 2-substituted chromanones. The preferred formation of this diastereomer can be rationalized in terms of the optimized[22] conformation of the enol of the chromanone (see Figure 2) which allows attack of the HTIB only from the opposite side. S_N2 attack of the tosylate anion results in the stereoselective formation of chromanone **2** (arrow (a), Scheme 2) while the migration of the antiperiplanar alkyl or alkylene group by the loss of iodobenzene (arrow (b), Scheme 2) results in the formation of the resonance-stabilized cation **12b**.



Scheme 2

The lack of an electron-donating 2-alkyl substituent in cation **12a** makes it more unstable and hinders the migration in the case of 2-methylchromanone (**1b**). On the other hand, it seems very likely that the migration in the flavanone (**1c**) takes place *via* the phenonium intermediate **12c**.

We have investigated also some heteroanalogs of chromanones. Treatment of 1-thiochromanone **13a** with HTIB under MW irradiation afforded the corresponding sulfoxide **14a**, accompanied by a small amount of 1-thiochromone **15a**. Surprisingly, the same product **14a** was obtained in nearly the same yield *without any MW activation* simply by intimately mixing the reagents and the support. 2-Substituted-1-thiochromanones **13b,c** gave similar results, affording the sulfoxides **14b,c** with low-to moderate diastereoselectivity (Scheme 3, Table 4).



Scheme 3

Oxidation of sulfides to sulfoxides without apparent overoxidation to sulfones by [methoxy(tosyloxy)iodo]benzene (MTIB), obtained from HTIB and trimethyl orthoformate,[23] or by HTIB or HCIB in methylene chloride,[24] or by in situ generated HTIB in acetonitrile[25] has been reported, but this is the first case where a heterogenous, solid-phase reaction has been observed. Our finding offers a new and easy entry to heterocyclic sulfoxides.

Table 4. Reaction of thiochromanones **13a-c** and dihydroquinolones **16,18** with HTIB under MW irradiation using Na_2SO_4 support

Entry	Starting material	HTIB (equiv.)	MW irradiation (min)	Eluent[a]	Conversion[b] (%)	Yield[c] (%) **14** (*trans*/*cis*)	**15/17**	Others
1	**13a**	1.2	2x1	E	84	39 (-)	11	-
2		2.4	2x1	E	100	12 (-)	9.9	-
3		2.4	none	E	95	37 (-)	traces	-
4	**13b**	2.4	none	F	100	38 (79:21)	9.1	-
5	**13c**	2.4	none	F	56	66 (59:41)	traces	-
6	**16**	2.4	2x1	E	55	-	12	-
7	**18**	2.4	3x1	G	74	-	-	**19**: 15

[a] E: ethyl acetate, F: toluene-ethyl acetate (4:1, v/v), G: ethyl acetate-hexane (8:1, v/v)
[b] Calculated on the basis of the recovered starting material. [c] Refers to pure isolated products, the values are normalized to 100% conversion.

Finally, the reactivity of 2,3-dihydro-4-quinonolones **16, 18** was tested since previously very little had been published on the reaction of dihydroquinolones with hypervalent iodine reagents. 2-Aryl-2,3-dihydro-4-quinolones were reported to afford 4-alkoxy-2-arylquinolines in the presence of HTIB, trialkyl orthoformate and perchloric acid[26] and 2-aryl-4-quinolones upon treatment with iodobenzene diacetate and potassium hydroxide in methanolic solution.[27] Under our conditions, both substrates reacted sluggishly and low conversions were found even by using higher amounts of HTIB. The substitution on the nitrogen plays a decisive role since 2-phenyl-2,3-dihydro-4-quinolone (**16**) gave the dehydrogenated 2-phenyl-4-quinolone (**17**) as the sole product while 1-acetyl-2-phenyl-2,3-dihydro-4-quinolone (**18**) yielded the migrated 3-phenyl-4-quinolone (**19**) (Scheme 3, Table 4). Neither of these reactions has considerable synthetic value but each provides important mechanistic information. Similarly to the sulfur-containing substrates where the sulfoxidation proceeds by an electrophilic attack on the sulfur atom and runs *via* the intermediate **20**, HTIB attacks the nucleophilic nitrogen atom in the dihydroquinolone **16** giving the phenyliodonium intermediate **21** and then finally the quinolone **22**. This latter intermediate transforms into the final product, either by a hydrogen shift or by a protonation-deprotonation sequence (Scheme 3). The acylation of the nitrogen in compound **18** stops its nucleophilic character and directs the transformation to the enol mechanism shown in Scheme 2. This duality proves for the higher reactivity of nucleophilic heteroatoms toward HTIB in comparison with double bonds.

In conclusion, the reaction of 2-unsubstituted and 2-alkylchromanones with HTIB was found to give the corresponding, hitherto unknown 3-tosyloxy derivatives, in addition to dehydrogenation, whereas dehydrogenation and/or 2,3-migration was observed with other chromanones. Attack at the nucleophilic heteroatom was observed in the reactions of 1-thiochromanones or 2-phenyl-2,3-dihydro-4-quinolone, giving the corresponding sulfoxides or the dehydrogenated product, respectively.

Experimental Section

General Procedures. Column chromatography was performed on Kieselgel 60 or Kieselgel 40. – Melting points: Boetius hot-stage, uncorrected values. – IR: Perkin Elmer 16 PC-FT-IR; KBr pellets unless otherwise stated. – NMR: Bruker WP 200 SY, Bruker AM 360 (200 or 360 MHz for ^{1}H; 50 or 90 MHz for ^{13}C). Recorded in $CDCl_3$ solution unless otherwise stated. Chemical shifts are given in δ relative to an internal standard TMS (δ = 0) or to the residual $CHCl_3$ (δ = 7.26 for ^{1}H NMR and δ = 77.0 for ^{13}C NMR). – Elemental analysis: Carlo Erba EA 1106 CHN analyzer. Starting materials **1a** and **13a** were purchased while **1b**,**c**, **5a-g, 8a-c**, **16** and **18** were synthesized according to literature methods.

General procedure for the microwave-induced reactions
Benzoheteracyclanone **1a-c**, **5a-c,e-g, 8a-c**, **16**, or **18** (1 mmol), HTIB (1.2 or 2.4 mmol) and anhydrous sodium sulfate (5 g) were mixed thoroughly and irradiated in a household microwave oven (2.45 GHz, 700 W) with a one-minute break between two exposures (for details see Tables 1-4). The mixture was washed with dichloromethane (4x30 mL), concentrated *in vacuo* and the residue was submitted to short-column chromatography. Conversion and yields are shown in the Tables. Known products **3a-c**, **4c** were identified by TLC comparison, m.p. and ^{1}H NMR spectra.
3-Tosyloxychromanone (2a). For the conditions see Table 2. Mp 125-128 ^{o}C (hexane-EtOAc). IR: 1690 (C=O), 1606, 1478, 1466, 1364 (SO_2), 1314, 1218, 1192, 1174 (SO_2), 1008, 942, 908, 852, 814, 774, 738 cm^{-1}. ^{1}H NMR: 2.48 (s, 3H, 4′-Me), 4.55 (dd, *J* = 10.0, 11.0 Hz, 1H, 2-H_{ax}), 4.66 (dd, *J* = 5.1, 11.0 Hz, 1H, 2-H_{eq}), 5.17 (dd, *J* = 5.1, 10.0 Hz, 1H, 3-H), 7.04 (d, *J* = 8.4 Hz, 1H, 8-H), 7.11 (m, 1H, 6-H), 7.50 (d, *J* = 8.4 Hz, 2H, 3′,5′-H), 7.61 (m, 1H, 7-H), 7.75 (d, *J* = 9.0 Hz, 1H, 5-H), 7.90 (d, *J* = 8.4 Hz, 1H, 2’,6’-H). ^{13}C NMR: 21.6 (4′-Me), 69.8 (C-2), 75.5 (C-3), 118.7 (C-8), 122.9 (C-6), 128.1 (C-5), 129.0 (C-2′,6′), 130.9 (C-3′,5′), 134.2 (C-1′), 137.6 (C-7), 146.5 (C-4′), 162.0 (C-8a), 185.5 (C-4). Anal. Calcd. for $C_{16}H_{14}O_5S$ (318.34): C, 60.37; H, 4.43. Found: C, 60.11; H, 4.59.
***cis*-2-Methyl-3-tosyloxychromanone (2b).** For the conditions see Table 2. Mp 104-105 ^{o}C (hexane-abs. EtOH). IR: 1694 (C=O), 1610, 1466, 1370, 1364 (SO_2), 1312, 1188, 1178 (SO_2), 972, 948, 846, 684 cm^{-1}. ^{1}H NMR: 1.50 (d, *J* = 7.0 Hz, 3H, 2-Me), 2.45 (s, 3H, 4′-Me), 4.75 (m, 1H, 2-H), 5.10 (d, *J* = 3.7 Hz, 1H, 3-H), 6.96 (d, *J* = 8.4 Hz, 1H, 8-H), 7.0 (m, 1H, 6-H), 7.34 (d, *J* = 8.4 Hz, 2H, 3’,5’-H), 7.50 (m, 1H, 7-H,), 7.72 (dd, *J* = 1.8, 8.0 Hz, 1H, 5-H), 7.84 (d, *J* = 8.4

Hz, 2H, 2′,6′-H). ^{13}C NMR: 14.5 (2-Me), 21.6 (4′-Me), 75.3 (C-3), 77.5 (C-2), 118.1 (C-8), 119.0 (C-4a), 121.8 (C-6), 127.3 (C-5), 128.0 (C-3′,5′), 129.7 (C-3′,5′), 133.0 (C-1′), 136.8 (C-7), 145.2 (C-4′), 159.8 (C-8a), 185.1 (C-4). Anal. Calcd. for $C_{17}H_{16}O_5S$ (332.37): C, 61.43; H, 4.85. Found: C, 61.70; H, 4.69.

2,3-Dimethylchromone (6a). For the conditions see Table 3. Mp 93-94 °C (hexane) (Lit.[28] 97-99 °C, lit.[29] 91-93 °C). IR: 1632 (C=O), 1609 (C=C), 1470, 1400, 1173, 772 cm^{-1}. ^{1}H NMR: 2.06 (s, 3H, 2-Me), 2.42 (s, 3H, 3-Me), 7.32-7.39 (m, 2H, 6,8-H), 7.60 (m, 1H, 7-H), 8.20 (dd, *J* = 1.3, 7.9 Hz, 1H, 5-H). ^{13}C NMR: 9.8 (3-Me), 18.3 (2-Me), 116.9 (C-3), 117.6 (C-8), 122.7 (C-4a), 124.5, 125.9 (C-5, C-6), 133.0 (C-7), 156.0 (C-8a), 162.0 (C-2), 178.1 (C-4).

2,3-Dimethyl-7-methoxychromone (6b). For the conditions see Table 3. Mp 122-123 °C (hexane-EtOAc). (Lit.[30] 127 °C). IR: 1640 (C=O), 1618 (C=C), 1604, 1574, 1442, 1040, 1352, 1246 (C-O-C), 1204, 826 cm^{-1}. ^{1}H NMR: 2.03 (s, 3H, 2-Me), 2.37 (s, 3H, 3-Me), 3.87 (s, 3H, 7-OMe), 6.75 (d, *J* = 1.3 Hz, 1H, 8-H), 6.91 (dd, *J* = 1.3, 9.6 Hz, 1H, 6-H), 8.09 (d, *J* = 9.6 Hz, 1H, 5-H). ^{13}C NMR: 9.9 (3-Me), 18.4 (2-Me), 55.6 (7-OMe), 99.6 (C-8), 113.8 (C-6), 116.4 (C-3), 127.1 (C-5), 157.4 (C-8a), 161.2 (C-2), 163.4 (C-7), 177.3 (C-4).

7-Benzyloxy-2,3-dimethylchromone (6c). For the conditions see Table 3. Mp 92.5-93.5 °C (hexane). IR: 1644 (C=O), 1610 (C=C), 1442, 1398, 1344, 1244 (C-O-C), 1182, 1098, 746, 708 cm^{-1}. ^{1}H NMR: 2.02 (s, 3H, 2-Me), 2.36 (s, 3H, 3-Me), 5.12 (s, 2H, CH_2), 6.83 (d, *J* = 1.3 Hz, 1H, 8-H), 6.99 (dd, *J* = 1.3, 8.3 Hz, 1H, 6-H), 7.34-7.45 (m, 5H, Ph), 8.09 (d, *J* = 8.3 Hz, 1H, 5-H). ^{13}C NMR: 9.9 (3-Me), 18.4 (2-Me), 70.4 (CH_2), 100.8 (C-8), 114.3 (C-6), 116.5, 116.8 (C-3, C-4a), 127.3, 127.5, 128.3, 128.7 (C-5, C-2′,6′, C-3′,5′, C-4′), 135.9 (C-1′), 157.4 (C-8a), 161.2 (C-2), 162.5 (C-7), 177.3 (C-4). Anal. Calcd. for $C_{18}H_{16}O_3$ (280.32): C, 77.12; H, 5.75. Found: C, 76.89; H, 5.94.

2,3-Dimethyl-7-tosyloxychromone (6e). For the conditions see Table 3. Mp 109-110 °C (hexane-EtOAc). IR: 1636 (C=O), 1612 (C=C), 1444, 1376 (SO_2), 1192, 1174 (SO_2), 1092, 868, 822, 814, 734 cm^{-1}. ^{1}H NMR: 2.04 (s, 3H, 2-Me), 2.40 (s, 3H, 3-Me), 2.46 (s, 3H, 4'-Me), 6.85 (dd, *J* = 2.1, 8.8 Hz, 1H, 6-H), 7.22 (d, *J* = 2.1 Hz, 1H, 8-H), 7.33 (d, *J* = 8.0 Hz, 2H, 3′,5′-H), 7.73 (d, *J* = 8.0 Hz, 2H, 2′,6′-H), 8.08 (d, *J* = 8.8 Hz, 1H, 5-H). ^{13}C NMR: 9.8 (3-Me), 18.3 (2-Me), 21.6 (4′-Me), 111.7 (C-8), 117.4 (C-3), 119.0 (C-6), 121.4 (C-4a), 127.7 (C-5), 128.6 (C-2′,6′), 130.1 (C-3′,5′), 132.1 (C-1′), 146.1 (C-4′), 152.7 (C-7), 156.2 (C-8a), 162.6 (C-2), 177.3 (C-4). Anal. Calcd. for $C_{18}H_{16}O_5S$ (344.38): C, 62.78; H, 4.68. Found: C, 62.99; H, 4.88.

2,3-Dimethyl-6,7-ditosyloxychromone (6f). For the conditions see Table 3. Mp 166-169 °C (EtOH). IR: 1646 (C=O), 1617 (C=C), 1478, 1448, 1381(SO_2), 1356, 1194, 1179 (SO_2), 1084, 830, 817, 734, 706, 694 cm^{-1}. ^{1}H NMR: 2.02 (s, 3H, 2-Me), 2.38 (s, 3H, 3-Me), 2.45, 2.46 (2xs, 2x3H, 4′,4″-H), 7.29 (m, 4H, 3′,5′,3″,5″-H), 7.47 (s, 1H, 8-H), 7.66 (m, 4H, 2′,6′,2″,6″-H), 7.86 (s, 1H, 5-H). ^{13}C NMR: 9.8 (3-Me), 18.3 (2-Me), 21.6 (4′, 4″-Me), 113.8 (C-8), 117.4 (C-3), 120.8 (C-6), 121.5 (C-4a), 128.7, 128.8 (C-5, C-2′,6′, C-2″,6″), 130.0 (C-3′,5′, C-3″,5″), 131.9, 132.4 (C-1, C-1′), 138.5 (C-6)*, 145.1 (C-7)*, 146.1, 146.4 (C-4′, C-4″), 153.9 (C-8a), 162.8 (C-2), 176.4 (C-4). [*interchangeable] Anal. Calcd. for $C_{25}H_{22}O_8S_2$ (514.56): C, 58.36; H, 4.31. Found: C, 58.12; H, 4.37.

7-Benzyloxy-2,3,5-trimethylchromone (6g). For the conditions see Table 3. Mp 108-112 °C (hexane-EtOAc). IR: 1654 (C=O), 1612 (C=C), 1570, 1454, 1280, 1180, 1156, 756 cm^{-1}. ^1H NMR: 1.98 (s, 3H, 2-Me), 2.32 (s, 3H, 3-Me), 2.82 (s, 3H, 5-Me), 5.10 (s, 2H, CH_2), 6.69 (d, *J* = 1.2 Hz, 1H, 8-H), 6.74 (br s, 1H, 6-H), 7.32-7.45 (m, 5-H, Ph). ^{13}C NMR: 10.0 (3-Me), 18.1 (2-Me), 23.1 (5-Me), 70.1 (CH_2), 98.9 (C-8), 115.4, 117.2 (C-3, C-4a), 116.4 (C-6), 127.5, 128.7 (C-2',6', C-3',5'), 128.2 (C-4'), 136.1 (C-1''), 142.5 (C-5), 158.9 (C-8a), 159.4 (C-2), 161.1 (C-7), 179.3 (C-4). Anal. Calcd. for $C_{19}H_{18}O_3$ (294.35): C, 77.53; H, 6.16. Found: C, 77.72; H, 5.98.

2,3-Dimethyl-7-hydroxychromone (6d). A mixture of 7-benzyloxy-2,3-dimethylchromone (**6c**) [280 mg, 0.999 mmol], 48% hydrogen bromide (3 mL) and acetic acid (6 mL) was refluxed for 15 min, then poured on crushed ice, filtered off and washed with water to give pure **6d**. Mp 268-271 °C (EtOH). IR: 3208 (OH), 1632 (C=O), 1592, 1570, 1406, 1246 (C-O), 1188, 1102, 862 cm^{-1}. ^1H NMR (DMSO-d_6): 1.90 (s, 3H, 2-Me), 2.35 (s, 3H, 3-Me), 6.76 (d, *J* = 1.1 Hz, 1H, 8-H), 6.87 (dd, *J* = 1.1, 8.6 Hz, 1H, 6-H), 7.85 (d, *J* = 8.6 Hz, 1H, 5-H), 10.64 (s, 1H, 7-OH). ^{13}C NMR (DMSO-d_6): 10.6 (3-Me), 19.0 (2-Me), 102.6 (C-8), 115.4 (C-6), 115.8, 116.1 (C-3, C-4a), 127.7 (C-5), 158.0 (C-8a), 162.2, 163.0 (C-2, C-7), 176.8 (C-4). Anal. Calcd. for $C_{11}H_{10}O_3$ (190.19): C, 69.46; H, 5.30. Found: C, 69.67; H, 5.25.

1,2,3,4-Tetrahydroxanthen-9-one (9a). For the conditions see Table 3. Mp 100-100.5 °C (hexane). (Lit.[16] 88-89 °C). IR: 2946 (CH_2), 1640 (C=O), 1622 (C=C), 1570, 1474, 1464, 1424, 1410, 1156, 768 cm^{-1}. ^1H NMR: 1.74, 1.86 (2xm, 2x2H, 2,3-H), 2.56, 2.63 (2xt, *J* = 6.2 Hz and 6.4, 2x2H), 1,4-H), 7.21 (m, 2H, 5,7-H), 7.57 (m, 1H, 6-H), 8.17 (dd, *J* = 1.2, 7.9 Hz). ^{13}C NMR: 21.0, 21.6, 21.9 (C-2,3,4), 28.1 (C-1), 117.6 (C-5), 118.4 (C-9a), 123.1 (C-8a), 124.3, 125.7 (C-7,8), 132.9 (C-6), 155.9 (C-5a), 163.9 (C-10a), 177.6 (C-9).

7,8,9,10-Tetrahydrobenzo[b]cyclohepta[e]pyran-11(6*H*)-one (9b). For the conditions see Table 3. Mp 79-80.5 °C (hexane). (Lit.[16] 82-83 °C). IR: 2924 (CH_2), 1632 (C=O + C=C), 1608, 1574, 1466, 1446, 1402, 1322, 1158, 762 cm^{-1}. ^1H NMR: 1.61 (m, 2H, 8-H), 1.75, 1.84 (2xm, 2x2H, 7,9-H), 2.80, 2.87 (2xm, 2x2H, 6,10-H), 7.32-7.40 (overlapping dd and m, 2H, 2,4-H), 7.61 (m, 1H, 3-H), 8.22 (dd, *J* = 1.5, 7.9Hz, 1H, 1-H). ^{13}C NMR: 22.11, 24.74, 26.22, 31.8, 34.6 (C-6,7,8,9,10), 117.6 (C-4), 122.6, 122.8 (C-10a,11a), 124.3 (C-1), 125.81 (C-2), 132.6 (C-3), 155.5 (C-4a), 168.8 (C-5a), 176.8 (C-11).

6,7,8,9,10,11-Hexahydrobenzo[b]cycloocta[e]pyran-12(6*H*)-one (9c). For the conditions see Table 3. Mp 87-89 °C (hexane). (Lit.[16] 90-91 °C). IR: 2930 (CH_2), 1632 (C=O + C=C), 1612, 1574, 1466, 1456, 1400, 1334, 1224, 1188, 1128, 780, 764 cm^{-1}. ^1H NMR: 1.50 (m, 4H, 8,9-H), 1.72, 1.84 (2xm, 2x2H, 7,10-H), 2.73, 2.81 (2xt, *J* = 6.0 Hz, 2x2H, 6,11-H), 7.33-7.41 (overlapping dd and m, 2H, 2,4-H), 7.61 (m, 1H, 3-H), 8.21 (dd, *J* = 0.9, 8.1 Hz, 1H, 1-H). ^{13}C NMR: 22.6, 26.0, 26.1, 28.8, 29.0, 31.2 (C-6,7,8,9,10,11), 117.6 (C-4), 120.4, 122.8 (C-11a,12a), 124.2 (C-1), 125.6 (C-2), 132.6 (C-3), 155.9 (C-4a), 166.1 (C-5a), 176.8 (C-12).

2-Phenyl-4-quinolone (17). For the conditions see Table 4. Mp 245-250 °C (MeOH). (Lit.[31] 252-254 °C). IR: 3432 (NH), 3064, 2964, 1632 (C=O + C=C), 1580, 1546, 1504, 1472, 1450, 1432, 1256, 1140, 770 cm^{-1}. ^1H NMR (DMSO-d_6): 6.38 (s, 1H, 3-H), 7.40 (m, 1H, 6-H), 7.62 (m, 3H, 3',4',5'-H), 7.71 (m, 1H, 7-H), 7.81 (d, *J* = 8.3 Hz, 1H, 8-H), 7.88 (m, 2H, 2',6'-H), 8.14

(d, *J* = 7.8 Hz, 1H, 5-H), 11.77 (s, 1H, NH). ^{13}C NMR (DMSO-d_6): 107.3 (C-3), 117.8 (C-8), 123.1 (C-6), 124.6 (C-4'), 127.3 (C-2',6'), 128.9 (C-3',5'), 129.6 (C-2), 130.3 (C-5), 131.7 (C-7), 134.2 (C-4a), 140.4 (C-8a), 150.8 (C-1'), 176.8 (C-4).

3-Phenyl-4-quinolone (19). For the conditions see Table 4. Mp 250-253 ^{o}C (MeOH). (Lit.[32] 255-257 ^{o}C, Lit.[33] 268-269 ^{o}C). ^{1}H NMR (DMSO-d_6): 7.33 (m, 1H, 6-H), 7.39-7.45 (m, 3H, 3',4',5'-H), 7.63 (d, *J* = 8.0 Hz, 1H, 8-H), 7.71 (m, 1H, 7-H), 7.77 (dd, *J* = 1.1, 7.3 Hz, 1H, 2',6'-H), 8.20 (d, *J* = 6.2 Hz, 1H, 2-H), 8.23 (d, *J* = 7.9 Hz, 1H, 5-H), 12.11 (d, *J* = 6.2 Hz, 1H, NH). ^{13}C NMR (DMSO-d_6): 118.7 (C-8), 120.5 (C-3), 124.2, 126.1, 127.1 (C-5,6,4'), 126.1 (C-4a), 128.5, 129.0 (C-2',6', C-3',5'), 132.4 (C-7), 136.4 (C-1'), 138.7 (C-2), 139.6 (C-8a), 175.6 (C-4).

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