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REACTION OF CHALCONES WITH N-BROMOSUCCINIMIDE. SYNTHESIS OF AURONES

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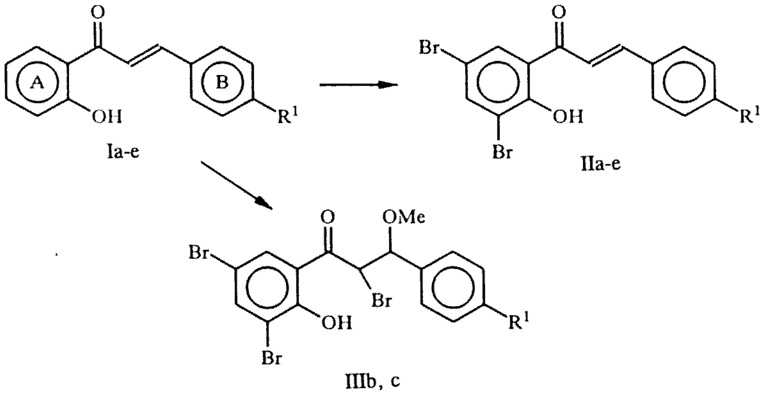
The reaction of 2'-OR-4-R^1 chalcone with N-bromosuccinimide is reported. It was found that the structure of the product depends on the nature of the substituents R and R^1. The prepared α-bromo-β-methoxydihydrochalcones were converted to the corresponding aurones.

Well known reactions in the chemistry of flavonoids include the conversion of α-halo-β-alkoxydihydrochalcones to aurones (the Wheeler reaction [1]), the conversion of α-halo-β-hydroxydihydrochalcones with the epoxides, and of 3-hydroxyflavanones to 3-hydroxyflavones (the Rasoda–Limaye reaction [2, 3]). It would appear that the starting materials for these reactions might be obtained from the readily available chalcone dibromides [4]. However the β-placed bromine in the dibromides is only replaced by such nucleophiles as water and alcohols when the B ring of the dibromide contains a para orientated electron donor substituent [5]. Bien et al. found [6] that chalcone bromohydrins can be prepared by reaction with N-bromoacetamide in aqueous tetrahydrofuran with the presence of catalytic amounts of perchloric acid. Donnelly et al. [7] have improved this method and bromomethoxylated different chalcones using N-bromo-succinimide (NBS) in methanol.

By a detailed study of the reactions of 2'-NHR- chalcones (R = H, Ac, Ts) with NBS in methanol we have found that there can occur either bromination in the ring (R = H or Ts) or bromomethoxylation (R = Ac) depending on the nature of the substituent.

In this work we report the reaction of 2'-OR-4-R^1-chalcones with NBS together with an investigation into the effect of the nature of R and R^1 on the final product.

Reaction of 2'-OR-4-R^1-chalcones (Ia-e) with NBS in methanol was monitored using TLC and by PMR spectroscopy following disappearance of the starting chalcone. It was found that full conversion of chalcones Ia, c-e needs 2.5 moles of NBS. The main products of the reactions are the dibromochalcones IIa, c-e. The side products in the reaction mixture are dihydrochalcone III, IVc and dibromide Vc-e.



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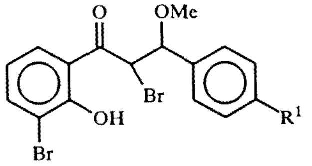
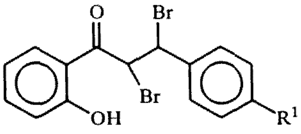


IVb,c

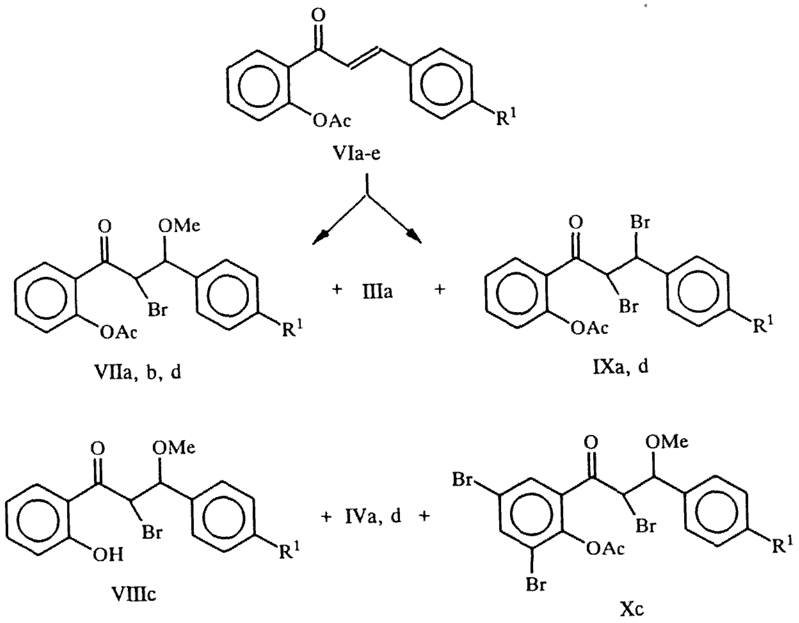


Vb-e

a R^1 = H, b R^1 = OMe, c R^1 = Me, d R^1 = Br, e R^1 = NO$_2$

In the case of chalcone Ib, addition of less than 1.25 moles of NBS gives the dibromochalcone IIb whereas addition of 2.5 moles gives the dihydrochalcone IIIb as the main product. There are also significant amounts of IVb and Vb in the reaction mixture.

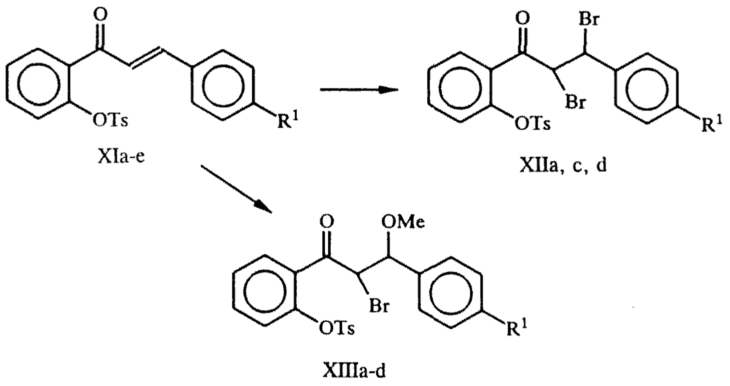
Reactions of 2′-acetoxy-4-R^1-chalcones (VIa-e) with NBS also gives various products. Addition of 1.25 mole of NBS to VIa gives the dihydrochalcone VIIa in good yield. With 2.5 moles of NBS there are formed the desacyl compound IVa and, after removal of IVa, the dihydrochalcone IXa in the mother liquor. Further NBS (3.5 mole) gives a mixture of VIIa and IIIa. Under similar conditions the main product from chalcone VIb and 2.5 moles of NBS is the dihydrochalcone VIIb.



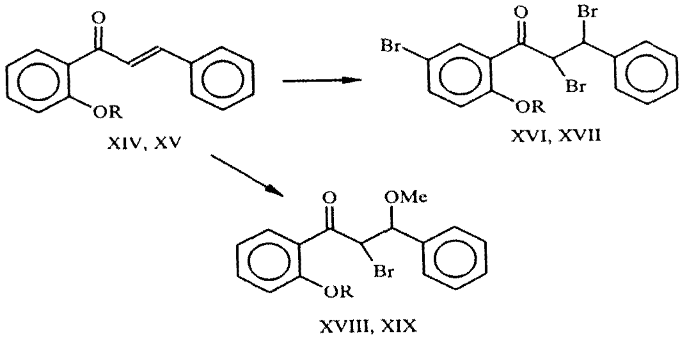
Chalcone VIc gives VIIIc and, after its removal, mainly Xc in the mother liquor. Under analogous conditions, chalcone VId gives dihydrochalcone IVd along with VIId and IXd. Chalcone VIe forms a complex mixture of products which could not be analyzed using NMR spectroscopy. These results disagree with the reports of Donnelly and coworkers [7, 9] who report that 2′-acetoxy-4′(5′)R-chalcones (R = H, OMe, Me, NO$_2$, Cl) and NBS give only the corresponding 2′-acetoxy-4′(5′)-α-bromo-β-methoxyhydrochalcones.

2′-Tosylchalcone (XIb) is converted to dihydrochalcone XIIIb when the molar ratio of NBS is less than 1.25. Addition of 2.5 or 3.5 moles of NBS XIa gives the dibromide XIIa in 23 and 57% yields respectively.

The mother liquors also contain XIIIa (70 and 20% respectively). Chalcones XIc, d gives mainly products XIIc, d and XIIIc, d in smaller amounts. Compound XIe is unreactive, even with a large excess of NBS. Conversion to XIId and XIIId was not observed and only starting material was recovered from the reaction mixture.



The main product of reaction of chalcone XIV with 2.5 moles of NBS is XVI together with a small amount of XVIII. Under similar conditions, chalcone XV gives an equimolar mixture of dihydrochalcones XVII and XIX.



XIV, XVI, XVIII R = Me; XV, XVII, XIX R = CH_2Ph

The structures of the brominated products obtained in the above reactions were confirmed using elemental analysis and IR and PMR spectroscopy (see Tables 1 and 2).

The results obtained show that the structure of the main product obtained when treating 2′-OR-4-R^1 chalcones with NBS is determined by the nature of the substituents R and R^1.

The α-bromo-β-methoxydihydrochalcones (III, IV, VII, and X) react in moderate yields with methanolic base to give the corresponding aurones (XX-XXII).

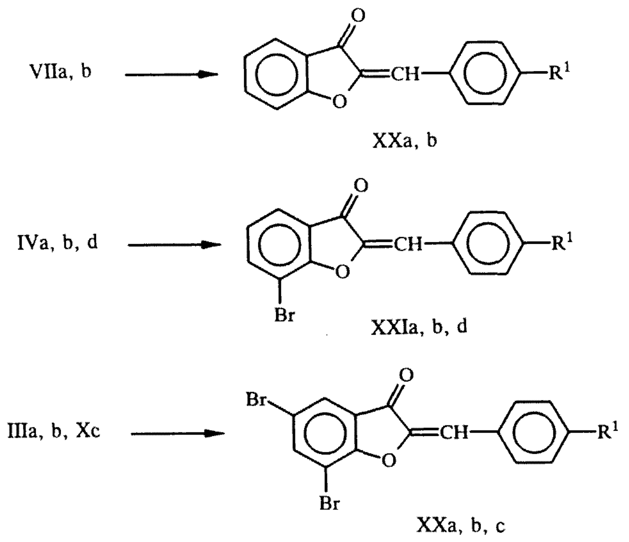


TABLE 1. Physical Parameters for the Products from Reaction of 2'-OR-Chalcones with NBS

Starting material	Molar ratio of NBS	Product	Empirical formula	mp, °C (lit. mp)	Yield, % (solvent)
Ia	2,5	IIa	$C_{15}H_{10}Br_2O_2$	149...151 (150...151 [1])	59 (EtOH—EtOAc)
Ib	1,25	IIb	$C_{16}H_{12}Br_2O_3$	164...166	15 (MeOH)
Ib	2,5	IIIb	$C_{17}H_{15}Br_3O_4$	142...143	40 (MeOH)
		IVb[*2]	$C_{17}H_{16}Br_2O_4$	—	40
		Vb[*2]	$C_{16}H_{14}Br_2O_3$	—	10
Ic	2,5	IIc	$C_{16}H_{12}Br_2O_2$	144...156	52 (MeOH)
		IIIc[*2]	$C_{17}H_{15}Br_3O_3$	—	20
		IVc[*2]	$C_{17}H_{16}Br_2O_3$	—	10
		Vc[*2]	$C_{16}H_{14}Br_2O_2$	—	10
Id	2,5	IId	$C_{15}H_9Br_3O_2$	203...205	85 (EtOH—EtOAc)
		Vd[*2]	$C_{15}H_{11}Br_3O_2$	—	10
VIa	1,25	VIIa	$C_{18}H_{17}BrO_4$	84...86 (84...86 [1])	78 (hexane)
VIa	2,5	IVa	$C_{16}H_{14}Br_2O_3$	185...187 (57...62 [1])	63 (hexane)
		IXa[*2]	$C_{17}H_{14}Br_2O_3$	—	20
VIa	3,5 (54 h)	IIIa	$C_{16}H_{13}Br_3O_3$	138...140	37 (hexane)
		VIIa	$C_{18}H_{17}BrO_4$	84...86 (85...86 [1])	25 (hexane)
VIb	2,5	VIIb[*2]	$C_{19}H_{19}BrO_5$	Syrup	90
VIc	2,5	VIIIc	$C_{17}H_{17}BrO_3$	98...99	20 (hexane)
		Xc[*2]	$C_{19}H_{17}Br_3O_4$	—	60
VId	2,5	IVd	$C_{16}H_{13}Br_3O_3$	140...141	52 (hexane)
		VIId[*2]	$C_{18}H_{16}Br_2O_4$	—	20
		IXd[*2]	$C_{17}H_{13}Br_3O_3$	—	10
VIe	2,5	Complex mixture		—	—
XIa	2,5	XIIa	$C_{22}H_{18}Br_2O_4S$	139...141 (139...141 [9])	23 (MeOH)
		XIIIa[*2]	$C_{23}H_{21}BrO_5S$	Syrup	50
XIa	3,5	XIIa	$C_{22}H_{18}Br_2O_4S$	139...141	57 (MeOH)
		XIIIa[*2]	$C_{23}H_{21}BrO_5S$	—	20
XIb	1,25	XIIIb[*2]	$C_{24}H_{23}BrO_6S$	Syrup	100
XIc	2,5	XIIc[*2]	$C_{23}H_{20}Br_2O_4S$	Syrup	90
		XIIIc[*2]	$C_{24}H_{23}BrO_5S$	Syrup	10
XId	2,5	XIId[*2]	$C_{23}H_{17}Br_3O_4S$	Syrup	90
		XIIId[*2]	$C_{23}H_{20}Br_2O_5S$	Syrup	10
XIe	2,5	XIe	$C_{22}H_{17}O_6S$	148...150 (MeOH)	60
		XIIe[*2]	$C_{23}H_{17}Br_3O_4S$	Syrup	20
		XIIIe[*2]	$C_{23}H_{20}Br_2O_5S$	Syrup	10
XIV	2,5	XVI	$C_{17}H_{16}Br_2O_3$	109...110 (MeOH)	60
		XVIII[*2]	$C_{17}H_{17}BrO_3$	—	20
XV	2,5	XVII[*2]	$C_{23}H_{20}Br_2O_3$	Syrup	50
		XIX[*2]	$C_{23}H_{21}BrO_3$	Syrup	50[*]

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[*] Yield of product after crystallization.

[*2] Yield according to PMR data.

TABLE 2. PMR Spectra Data for Chalcones and Dihydrochalcones

Compound	Chemical shift, δ, ppm									
	phenol ring protons					olefin and dihydroolefin protons		benzene ring protons		
	2'-R	3'-H	4'-H	5'-H	6'-H	α-H	β-H	2,6-H	3,5-H	4-R
1	2	3	4	5	6	7	8	9	10	11
IIa	OH; 13,5	—	—		8,05...7,4					
IIb	OH; 13,65	—	7,85	—	8,00	H; 7,50	H; 7,95	7,63	6,95	OCH_3; 3,95
IIc	OH; 13,65	—	7,85	—	8,00	H; 7,50	H; 7,95	7,65	7,25	CH_3; 2,45
IId	OH; 13,45	—	7,85	—	8,00	H; 7,50	H; 7,95	7,65	7,55	—
IIe	OH; 13,20	—	8,4...7,6	—	8,60	8,4...7,6		8,4...7,55		—
IIIa	OH; 12,60	—	7,85	—	7,95	H; 5,05	H; 4,85; OCH_3; 3,15	7,45	7,45	H; 7,45
IIIb	OH; 12,60	—	7,85	—	7,95	H; 5,05	H; 4,75; OCH_3; 3,15	7,40	7,00	OCH_3; 3,85
IIIc	OH; 12,55	—	7,85	—	7,95	H; 5,05	H; 4,80; OCH_3; 3,15	7,00...7,60		CH_3; 2,35
IVa	OH; 12,05	—	7,00...7,50		7,85	H; 5,20	H; 4,85; OCH_3; 3,15	7,00...7,50		
IVb	OH; 12,00	—	7,00...7,50		7,80	H; 5,15	H; 4,85; OCH_3; 3,20	7,00...7,50		OCH_3; 3,90
IVc	OH; 12,05	—	7,00...7,50		7,90	H; 5,15	H; 4,75; OCH_3; 3,15	7,00...7,50		CH_3; 2,35
IVd	OH; 11,95	—	7,00...7,60		7,85	H; 5,15	H; 4,85; OCH_3; 3,20	7,00...7,50		—
Va	OH; 12,0		7,00...7,55			H; 5,70	H; 5,55	7,00...7,55		
Vb	OH; 12,0		7,00...7,55			H; 5,70	H; 5,50	7,00...7,55		CH_3; 2,30
Vc	OH; 12,05		7,00...7,55			H; 5,60	H; 5,30	7,00...7,55		—
Vd	OH; 12,0		7,20...7,00			H; 5,65	H; 5,40	7,00...7,50		—
VIIa	Ac; 2,35	7,15	7,60	7,40	7,90	H; 5,05	H; 4,75; OCH_3; 3,20	7,40	7,40	7,40
VIIb	Ac; 2,40	7,20	7,60	7,30	7,90	H; 5,05	H; 4,70; OCH_3; 3,15	7,30	6,95	OCH_3; 3,85
VIIc	Ac; 2,35		7,00...7,60		7,85	H; 5,05	H; 4,75; OCH_3; 3,20	7,00...7,60		CH_3; 2,35
VIIIb	OH; 12,00	7,00	7,55	7,00	7,85	H; 5,25	H; 4,85; OCH_3; 3,20	7,40	7,25	CH_3; 2,40
IXa	Ac; 2,35		7,00...7,95			H; 5,90	H; 5,65	7,00...7,95		

TABLE 2 (continued)

1	2	3	4	5	6	7	8	9	10	11
IX d	Ac; 2,35		7,00...7,95			H; 5,95	H; 5,65	7,00...7,95		
X c	Ac; 2,35	—	7,80	—	7,95	H; 5,00	H; 4,75; OCH_3; 3,15	7,20	7,30	CH_3; 2,45
XI e	CH_3; 2,40		7,20...8,25			7,20...8,25		7,2...8,25		
XII a	CH_3; 2,45		7,35...7,90			H; 5,95	H; 5,50	7,35...7,90		
XII c	CH_3; 2,45		7,30...7,90			H; 5,70	H; 5,45	7,30...7,90		
XII d	CH_3; 2,40		7,10...7,90			H; 5,95	H; 5,50	7,10...7,90		—
XII e	CH_3; 2,45		7,10...8,00			H; 6,05	H; 5,60	7,00...8,00		—
XIII a	CH_3; 2,35		7,85...7,25			H; 5,15	H; 4,65; OCH_3; 3,15	7,85...7,25		
XIII b	CH_3; 2,40		7,85...6,95			H; 5,15	H; 4,65; OCH_3; 3,15	6,95...7,85		OCH_3; 3,90
XIII c	CH_3; 2,35		7,85...7,25			H; 5,15	H; 4,60; OCH_3; 3,20	7,30...7,85		CH_3; 2,45
XIII d	CH_3; 2,35		7,85...7,25			H; 5,15	H; 4,70; OCH_3; 3,15	7,30...7,85		—
XIII e	CH_3; 2,40		7,85...7,25			H; 5,15	H; 4,90; OCH_3; 3,20	7,30...7,85		—
XVI	OCH_3; 3,95	6,90	7,60	7,45	7.95	H; 5,45	H; 4,80; OCH_3; 3,20	7,4...7,5		
XVII	CH_2; 5,25	7...7,5	7,90	7...7,5	8,00	H; 5,50	H; 4,80; OCH3; 3,15	7,4...7,5		
XVIII	OCH_3; 3,80		7,0...7,8			H; 5,60	H; 4,75; OCH_3; 3,30	7,0...7,8		
XIX	CH_2; 5,65		7,7...7,9				OCH_3; 3,15	7,7...7,9		

TABLE 3. Physical Parameters for Aurones and α-Bromochalcones

Starting material	Product	Empirical formula	mp, °C (lit. mp)	Yield, % (solvent)
III a	XXII a	$C_{15}H_8Br_2O_2$	164...165	70 (EtOH)
III b	XXII b	$C_{16}H_{10}Br_2O_2$	194...196	30 (EtOH)
IV a	XXI a	$C_{15}H_9BrO_2$	179...181	43 (EtOH)
IV b	XXI b	$C_{16}H_{11}BrO_3$	151...152	30 (EtOH)
IV d	XXI d	$C_{15}H_8Br_2O_2$	141...142	58 (MeOH)
VII a	XX a	$C_{15}H_{10}O_2$	110...111 (108 [1])	88 (EtOH)
VII b	XX b	$C_{16}H_{12}O_3$	134...136 (135...136 [1])	70 (MeOH)
XI c	XXII c	$C_{16}H_{10}Br_2O_2$	155...157	70 (EtOH)
XIII a	XXIII a	$C_{22}H_{17}BrO_4S$	138...139 (138...140 [8])	45 (EtOH)
XIII b	XXIII b	$C_{23}H_{19}BrO_5S$	139...141	66 (MeOH)
XIII c	XXIII c	$C_{23}H_{19}BrO_4S$	85...86	45 (EtOH)
XIII d	XXIII d	$C_{22}H_{16}Br_2O_4S$	172...174	70 (EtOH)

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*Yield of product after crystallization.

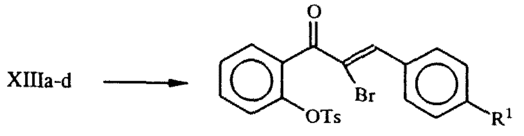
TABLE 4. Spectroscopic Parameters for Aurones XX-XXII and α-Bromochalcones XXIII

Compound	IR		^1H NMR, δ, ppm, $CDCl_3$
	$\nu_{C=C}$	$\nu_{C=O}$	
XX a	1656	1712	7,95 (2H, dd, $J = 8$ and 1,5 Hz. 2',6'-H), 7,85 (1H, dd, $J = 7$ and 1 Hz, 4-H), 7,65 (1H, m, 6-H), 7,50...7,25 (5H, m, 5,7,3',4',5'-H), 6,90 (1H, s, $H\beta$)
XX b	1650	1700	7,90 (d, $J = 10$ Hz, 2',6'-H), 7,80 (1H, dd, $J = 7{,}0$ and 1,5 Hz, 4-H), 7,60 (1H, m, 6-H), 7,40...7,00 (4H, m, 5,7,3',5'-H), 6,90 (1H, s, $H\beta$), 3,90 (3H, s, OCH_3)
XXI a	1642	1704	7,90 (2H, dd, $J = 8$ and 1,5 Hz, 2',6'-H), 7,75 (1H, dd, $J = 7$ and 1,5 Hz, 4-H), 7,50...7,25 (6H, m, 5,6,7,3',4',5'-H), 6,90 (1H, s, $H\beta$)
XXI b	1646	1700	7,90 (2H, d, $J = 8$ Hz, 2',6'-H), 7,85 (1H, dd, $J = 7{,}0$ and 1,5 Hz, 4-H), 7,60...7,00 (4H, m, 5,6,3',5'-H), 6,90 (1H, s, $H\beta$), 3,90 (3H, s, OCH_3)
XXI d	1648	1704	7,85 (2H, d, $J = 8$ Hz, 2',6'-H), 7,65 (1H, dd, $J = 7{,}0$ and 1,5 Hz, 4-H), 7,60...7,30 (4H, m, 5,6,3',5'-H), 6,85 (1H, s, $H\beta$)
XXII a	1646	1710	7,95 (1H, d, $J = 1$ Hz, 4-H), 7,90 (1H, d, $J = 1$ Hz, 6-H), 7,85 (2H, dd, $J = 12$ and 1 Hz, 2',6'-H), 7,60...7,40 (3H, m, 5,3',4'-H), 6,90 (1H, s, $H\beta$)
XXII b	1642	1702	8,00 (2H, d, $J = 8$ Hz, 2',6'-H), 7,95 (1H, d, $J = 1{,}5$ Hz, 4-H), 7,85 (1H, d, $J = 1{,}5$ Hz, 6-H), 7,00 (2H, d, $J = 8$ Hz, 3',5'-H), 6,95 (1H, s, H_b), 3,90 (3H, s, OCH_3)
XXII c	1646	1708	7,90 (2H, d, $J = 8$ Hz, 2',6'-H), 7,95 (1H, d, $J = 1{,}5$ Hz, 4-H), 7,85 (1H, $J = 15$ Hz, 6-H), 7,30 (2H, d, $J = 8$ Hz, 3',5'-H), 6,95 (1H, s, $H\beta$), 2,40 (3H, s, OCH_3)
XXIII a	1600	1666	7,85...7,20 (13H, m, ArH), 7,50 (1H, s, $H\beta$), 2,30 (3H, s, CH_3)
XXIII b	1590	1656	7,90...6,95 (12H, m, ArH), 7,45 (1H, s, $H\beta$), 3,90 (3H, s, OCH_3), 2,25 (3H, s, CH_3)
XXIII c	1592	1660	7,75...7,15 (12H, m, ArH), 7,45 (1H, s, $H\beta$), 2,40 (3H, s, CH_3), 2,25 (3H, s, CH_3)
XXIII d	1598	1664	7,75...7,25 (12H, m, ArH), 7,50 (1H, s, $H\beta$), 2,35 (3H, s, CH_3)

TABLE 5. Mass Spectra of XXI and XXII

Compound	MS (*m/z*, %)
XXI a	302 (98, M+2), 300 (100, M^+), 272 (6, M-CO), 220 (33, M-HBr), 198 (35, $M-C_6H_5—C{\equiv}CH$), 170 (35, $M-C_9H_6O$), 102 (37, $C_6H_5C{\equiv}CH$)
XXI b	332 (10, M+2), 330 (10, M^+), 299 (4, $M-OCH_3$), 252 (100, M+2-HBr), 132 (58, $CH_3OC_6H_4C{\equiv}CH$)
XXI c	380 (80, M+2), 378 (40, M^+), 300 (100, M+2-HBr), 299 (60, M-Br), 220 (17, 299-Br), 180 (14, $BrC_6H_4C{\equiv}CH$)
XXII a	380 (100, M+2), 378 (50, M^+), 350 (7, M-CO), 299 (20, M-Br), 276 (20, $M-C_6H_5C{\equiv}CH$), 248 (14, $M-C_9H_6O$), 102 (28, $C_6H_5C{\equiv}CH$)
XXII b	410 (78, M+2), 408 (38, M^+), 380 (17, M-CO), 328 (4, M-HBr), 276 (5, $C_7H_2Br_2O_2$), 197 (6, $C_7H_3O_2Br$), 132 (100, $CH_3OC_6H_4C{\equiv}CH$)
XXII c	394 (80, M+2), 392 (40, M), 364 (5, M-CO), 312 (10, M-HBr), 276 (10, $C_7H_2Br_2O_2$), 197 (6, $C_7H_3O_2Br$), 115 (50, $CH_3C_6H_4C{\equiv}CH$)

In similar conditions the 2′-tosyl derivatives (XIIIa-d) give the α-bromochalcones XXIIIa-d.



XXIIIa-d

The structures of compounds XX and XXIII were confirmed by elemental analysis and by IR, PMR, and mass spectral analysis.

EXPERIMENTAL

Melting points were determined on a Kofler apparatus. IR Spectra were measured on a Perkin-Elmer 283 spectrometer for KBr tablets. PMR Spectra were obtained on a WP 200 SY instrument (200 MHz) using $CDCl_3$ solvent and TMS internal standard. Mass spectra were measured on a VG-7035 instrument with electron impact excitation of 70 eV. TLC was carried out on kieselguhr 60 F_{254} plates (DC-Alurolle, Merck) using toluene–ethyl acetate (4:1) as eluent.

Reaction of 2′-OR-4-R¹-Chalcones with N-Bromosuccinimide. General Method. NBS (2.5 mole) was added to a solution of chalcones I, VI, XIa-e, XIV, or XV (2 mmoles) in methanol (40 ml) and stirred at room temperature. When starting material was identified in the product after 24 h, a further 2.5 moles of NBS was added. After standing for 24 h, the precipitate was filtered and recrystallized from the solvent given in Table 1. When a precipitate was not produced the filtrate was diluted with water and extracted with methylene chloride. The organic layer was dried with calcined $MgSO_4$, the solvent removed *in vacuo*, and the residue crystallized and analyzed using PMR spectroscopy.

Physical and spectral data for the products are given in Tables 1 and 2 respectivrely.

General Method for Preparing Aurones (XXa, b, XXIa, b, d and XXIIIa-c) and 2′-OTs-α-Bromo-4-R-chalcones (XXIIIa-d). A solution of α-bromo-β-methoxydihydrochalcone (IIIa, b, IVa, b, d, VIIa, b, Xc, or XIIIa-d, 1 mmole) in methanol (10 ml) was treated with an 8% aqueous solution of sodium hydroxide (1 ml) for 24 h. The reaction mixture was diluted with water and the precipitate filtered and crystallized from the solvent given in Table 3. The physical and spectral data for the products is given in Tables 3 and 4 and 5 respectively.

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REFERENCES

1. J. A. Donnelly, M. J. Fox, and T. C. Sharma, Tetrahedron, **35**, 875 (1979).
2. S. D Limaye, Rasayanam, **2**, 1 (1950).
3. F. M. Dean, Naturally Occurring Oxygen Ring Compounds, Butterworths, London (1963), p. 348.

4. Gy. Litkei, R. Bognar, and J. Ando, Acta Chim. Acad. Sci. Hung., **76**, 95 (1973).
5. F. Fisher and W. Arlt, Chem. Ber., **97**, 1910 (1964).
6. S. Bien, M. Beer, and E. Flohr, Israel J. Chem., **5**, 51 (1967).
7. J. Donnelly and J. L. Higginbotham, Monatsh. Chem., **122**, 83 (1991).
8. Gy. Litkei, T. Mester, T. Patonay, and R. Bognar, Acta Chim. Acad. Sci. Hung., **101**, 53 (1979).
9. J. A. Donnelly and C. L. Higginbotham, Tetrahedron, **46**, 7219 (1990).