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MICROPOROUS SOLIDS FOR THE SELECTIVE BROMINATION OF A DITERPENE RESIN ACID

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Abstract. The liquid-phase bromination of methyl dehydroabietate with bromine or NBS in the presence of microporous solids has been investigated. The reactions were fast and easily performed and the highest yield and regioselectivity were obtained with the system bromine/montmorillonite K10.

Considerable advances are being achieved in the area of electrophilic aromatic substitution, where microporous solids, as catalysts, are playing a significant role either influencing product selectivity or in the development of cleaner technologies.[1,2]

Recent reports[3,4] on the high yield and selective monobromination of aromatic substrates with zeolites promped us to use similar catalysts for the bromination of dehydroabietic acid **1**, an available intermediate for the chemical conversion of pine rosin to compounds with biological activity[5] or with industrial interest.[6]

In the literature,[7] two procedures for the bromination of dehydroabietic acid **1** have been described. Direct bromination of **1**, with a solution of bromine in carbon tetrachloride, led to a mixture of bromine derivatives in low yield. In another procedure, involving sulphonation of **1**, followed by substitution and esterification, methyl 12-bromo-dehydroabietate **2** was obtained with a global yield *ca.* 70%. The minute yield in the first case and the time consuming procedure, including the use of concentrated sulfuric acid, in the second, led us to apply the method of Smith[4] for the direct bromination of methyl dehydroabietate **1a** (Scheme).

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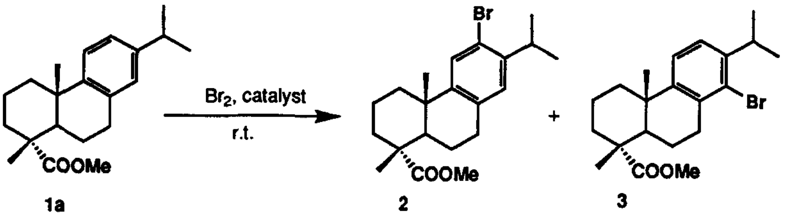

Scheme

Zeolites and conditions similar to those used by Smith[4] were initially applied to **1a**. The results obtained (Table 1) with two Y zeolite [Si/Al=5.2 and 12] in the acid form (HY) showed low conversions (40 and 46 %) with the formation of methyl 12-bromodehydroabietate **2** and methyl 14-bromodehydroabietate **3**, as well as, a mixture of other brominated compounds (GC/MS) which were not isolated. An increase in regioselectivity (7 to 31 %) observed when the zeolite [Si/Al=5.2] was in the sodium form, agrees in terms of selectivity with the results obtained by Sasson[3] and Smith[4] for the bromination of toluene using a NaY zeolite. Since our results for the bromination of methyl dehydroabietate **1a** in those conditions, are low when compared with those early reported[3,4] for smaller aromatic compounds, such as toluene and derivatives, we decide to use clays whose structural interlamellar spaces [> 12.4 Å][8] are larger than Y zeolite pores [7.4 Å].[9]

Indeed, the use of montmorillonite K10 or sepiolite G, in similar amount and conditions, led to higher conversions (93 or 87%) than with Y zeolites, the selectivity on **2** being higher (72%)

Table 1 - Bromination of methyl dehydroabietate **1a** with different zeolite and clay catalysts.[a)]

Catalyst [Si/Al]	Conversion (%)	Product[b)](%) **2**	**3**	Other	Selectivity to **2** (%)
NaY [5.2]	39	12	7	20	31
HY [5.2]	40	3	8	29	7
HY [12]	46	19	12	15	41
Mont. K10	93	67	12	14	72
Sepiolite G	87	38	26	23	44

a) Bromination of **1a** (0.21 mmol) with bromine (1.4 eq) over the catalyst (0.2 g) in CH_2Cl_2 (2 mL) at r. t. for 30 min. b) Determined by quantitative GC.

with K10, allowing its isolation and complete characterization. The isomer **3** was characterized by proton NMR and GC/MS in a mixture of **2** and **3**.

The higher activity of the clays as compared to zeolites for this reaction is probably due to lesser diffusional constraint of the hydrophenantrenic structure of **1a** in the clays, allowing the access of the large molecules to the active centers of the catalyst.

To improve reaction yield and selectivity, different conditions in terms of temperature, source and amount of bromine or K10 were used.

As it can be seen on Table 2, the results obtained for bromination of **1a** over K10 (0.66 g/mmol) with different amounts of bromine show an increase of both conversion and selectivity to **2** with bromine till a maximum of 1.7 eq. It was also noticed an increase in regioselectivity when bromine was added dropwise with reaction temperature maintained under 5°C.

Table 2 - Bromination of **1a** over K10 (0.66 g/mmol) with different temperatures and amounts of bromine.

Br_2 (eq.)	Conv.(%)		Product (%)a) **2**		**3**		Other		Selectivity to **2** (%)	
Temp.	r.t.	0-5 °C	r.t.	0-5 °C	r.t.	0-5 °C	r.t.	0-5 °C	r.t.	0-5 °C
1.2	82	-	56	-	8	-	18	-	68	-
1.4	89	85	71	70	10	9	11	6	80	82
1.5	-	89	-	73	-	10	-	5	-	82
1.7	89	96	55	84	8	9	26	2	62	88
1.8	-	90	-	75	-	9	-	6	-	84

a) Determined by quantitative GC.

The effect of K10 was studied in a further set of reactions at 0-5°C with a constant amount of bromine (1.7 eq.). From the results on Table 3 it can be seen that the highest conversion (96 %) and selectivity (88 %) on methyl 12-bromo-dehydroabietate **2** were obtained for 0.66 mg/mmol of K10.

The bromination of dehydroabietic acid **1** performed under those reaction conditions showed similar conversion but lower selectivity, as can be seen by the results (obtained after methylation) presented in the last entry of Table 3.

Similar procedure was also carried out using *N*-bromosuccinimide (NBS), a more simple to handle and widely used brominating reagent, as source of bromine.[10]

Table 3 - Bromination of **1a** with bromine (1.7 eq.) and different amounts of K10, at 0-5°C, after 30 min.

K10 (g/mmol)	Conv. (%)	Product (%)a) 2	 3	 Other	Selec. to **2** (%)
-	55	22	6	27	40
0.48	79	66	8	6	84
0.66	96	84	9	2	88
0.72	95	84	9	3	88
0.97	83	62	7	14	75
0.66	93	51	20	22	55

a) Determined by quantitative GC.

Table 4 - Bromination of **1a** over K10 with different solvents and amount of *N*-Bromosuccinimide (NBS), after 24 hours at room temperature.

NBS (eq.)	K10 (g/mmol)	Solvent	Conv. (%)	Productsa) (%) 2	 3	 Other	Select. **2** (%)
1.1	-	CH_2Cl_2	0	-	-	-	-
1.1	0.48	CH_2Cl_2	65	41	17	7	63
1.1/0.48b)		CH_2Cl_2	63	49	8	6	78
1.1	0.97	CH_2Cl_2	82	55	13	14	67
1.1/0.97b)		CH_2Cl_2	71	51	10	10	72
1.1	1.45	CH_2Cl_2	78	51	9	18	65
2.0	0.97	CH_2Cl_2	85	49	14	22	58
1.1	-	CH_3CN	85	72	11	2	85
2.0	-	CH_3CN	79	67	10	2	85
1.1	0.97	CH_3CN	87	74	13	-	85
1.1	1.45	CH_3CN	83	71	13	-	86
2.0	0.97	CH_3CN	84	62	12	-	74

a) Determined by quantitative GC. b) Preparation of supported NBS/K10: To a solution of NBS (80 mg) in CH_2Cl_2 (5 mL) in the dark, was added K10 (200 or 400 mg) under stirred. After 10 min. the solvent was evaporated till dryness and the residue of NBS/K10 immediatly used in the reactions.[2]

Two diferent amounts of NBS (1.1 and 2.0 eq.) were employed for reactions carried out in the dark, either in dichloromethane or in acetonitrile and varying the amount of K10.
The results obtained after 24 hours (Table 4) show that in dichloromethane the reaction did not take place without catalyst in spite of the increase of conversion with the increase of NBS or K10. Small improvement on selectivity of **2** was obtained when NBS was supported on K10 by a procedure early described[2] for other electrophylic aromatic substituted reactions (Table 4, entries 3 and 5). Best conversion and selectivity were achieved in acetonitrile which did not suffer significative changes with or without catalyst. This different behaviour with the solvents suggests a solvent dependent mechanism. In spite of the high regioselectivity obtained in acetonitrile with NBS, the conversions are lower and the reactions times longer than those with the bromine/K10 system.

All these results demonstrate that an acidic clay (K10) can be used as catalyst in the bromination of dehydroabietic acid **1** or its methyl ester **1a** with bromine, with considerable practical and regioselective advantages over the procedures previously reported. The reactions are fast, high-yielding, the work-up simple and have the added advantage given by the possibility of regeneration and reuse of the solid catalyst.
Testing the application of the method to other aromatic diterpenes and large aromatic molecules is currently under way in order to expand its range of application.

Bromination of Methyl Dehydroabietate. Typical procedure:

Bromination with bromine. To a solution of methyl dehydroabietate **1a** (0.52 g, 1.656 mmol) in dry dichloromethane (5 mL), gently stirred in a 50 ml round-bottomed flask, is added the solid catalyst in the indicated amount, followed by a solution of bromine in dichloromethane (5 mL) through a dropping funnel over 20 min, maintaining the temperature under 5°C. After 30 min. of reaction, the catalyst was filtered and the solid washed at least three times with 5 mL portions of warm solvent. The combined filtrates were washed with saturated aqueous sodium bisulphite solution (2x20 mL)and then dried over anhydrous sodium sulphate. After evaporation of the solvent, the residue was dried and recrystalized from diethyl ether and methanol to give white crystals of methyl 12-bromodehydroabietate **2** (0.46 g, 71 %), m.p. 139-140 °C (lit.[7] 140.5 - 141 °C); IR ($CHCl_3$) 1718 (C=O), 1085 (C-Br) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (3H, *s*, 10-Me), 1.19 (3H,*d* (7), 16-Me or 17-Me, 1.21 (3H,*d* (7), 17-Me or 16-Me, 1.26 (3H,*s*, 4-Me), 1.43 (2H, *m*, 1-H_a and 6-H_a), 1.74 (5H, *m*, 6-H_e, 2-H_2 and 3-H_2), 2.18 [1H, *dd* (12, 1.8), 5-H], 2.24 (1H, *brd*, (12) 1-H_e), 2.83 [1H, *dt* (4.5), 7-H_a], 2.82 (1H, *dt* (4.5), 7-H_e), 3.28 [1H, *sept* (7), 15-H, 3.66 (3H, *s*, 18-OMe), 6.91 (1H, *s*, 11-H), 7.36 (1H, *s*, 14-H); ^{13}C NMR ($CDCl_3$) δ: 37.8 (C-1), 18.4 (C-2), 36.6 (C-3), 47.5 (C-4), 44.5 (C-5), 21.5 (C-6), 29.5 (C-7), 121.4 (C-8), 148.9 (C-9), 37.0 (C-10), 128.5 (C-11), 144.0 (C-12), 134.4 (C-13), 127.1 (C-14), 32.3 (C-15), 22.8 (C-16 or C-17), 23.0 (C-17 or C-16), 178.9 (C-18), 16.5 (C-19), 25.0 (C-20), 52.0 (C-21); m/z 392 [$M^{+\cdot}$] (82), 317 (100), 275 (55).

Data for methyl 14-bromodehydroabietate **3**: ^{1}H NMR ($CDCl_3$) δ 1.19 (3H, *s*, 10-Me), 1.22 (3H,*d* (7), 16-Me or 17-Me, 1.24 (3H,*d* (7), 17-Me or 16-Me, 1.27 (3H,*s*, 4-Me), 2.18 (1H, *m*, 5-H], 2.29 (1H, *brd* (12) 1-H_e), 2.79 (1H, *m*, 7-H_a), 2.97 (1H, *m*, 7-H_e), 3.44 [1H, *sept* (7), 15-H], 3.67 (3H, *s*, 18-OMe), 7.09 (1H, *d* (8), 11-H or 12-H), 7.21 (1H, *d* (8), 12-H or 11-H); m/z 392 [$M^{+\cdot}$] (80), 315 (100), 277 (50).

Bromination with NBS. To a solution of methyl dehydroabietate **1a** (130 mg, 0.41 mmol) in dry solvent (5 mL), gently stirred in a 25 ml round-bottomed flask at room temperature and protected from light, the clay is added followed by NBS (or the supported NBS/K10) in a indicated amount. After 24 h the reaction mixture was worked up as above.

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