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Zeolite-Directed Cascade Reactions: Cycliacyarylation versus Decarboxyarylation of α,β-Unsaturated Carboxylic Acids

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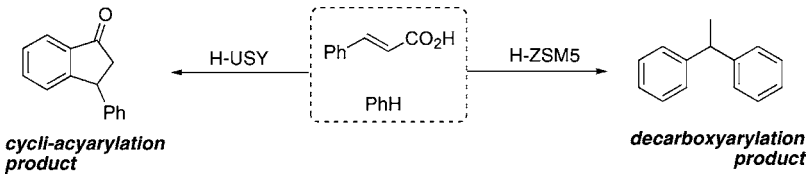
ABSTRACT



The interaction of α,β-unsaturated carboxylic acids with benzene derivatives was investigated in H-zeolites and led to two distinct but competing processes, cycliacyarylation and decarboxyarylation. Interestingly, H-USY selectively induced the cycliacyarylation cascade reaction, whereas H-ZSM5 selectively promoted the decarboxyarylation cascade.

Since the pioneering work of George A. Olah in the early 1960s, liquid superacids have been extensively studied so that they are now accepted as attractive reaction media for organic synthesis.[1] In such media, the so-called "superelectrophilic activation", consisting of the interaction between electron-donating groups and strongly electron-acceptor superacids, is a powerful phenomenon that allows organic reactions that are difficult or even impossible under classical acidic conditions.[2]

Nevertheless, the non-recyclable character of liquid superacids represents their only drawback. Solid acids and especially H-zeolites have been recently regarded as promising green alternatives to liquid media for diverse superacidic-mediated transformations.[3] In this context, we examined if H-zeolites could be green alternatives to triflic acid for the cycliacyarylation of benzene derivatives **1** with α,β-unsaturated carboxylic acids **2** (Scheme 1).

Whereas Friedel−Crafts-type cycliacyarylation was initially investigated using aluminum chloride[4] and heteropolyacids,[5] resulting in low to moderate product yields, it is only very recently that triflic acid was found to be an efficient Brønsted superacid for this transformation (Scheme 1).[6] From a synthetic point of view, this transformation clearly con-

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(1) (a) Olah, G. A.; Prakash, G. K. S.; Sommer, J. *Superacids;* Wiley: New York, 1985. (b) Olah, G. A.; Sommer, J. *Superacid Catalysis;* Baltzer: Bussum, The Netherlands, 1998.

(2) For reviews, see: (a) Olah, G. A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 767−788. (b) Nenajdenko, V. G.; Shevchenko, N. E.; Balenkova, E. S.; Alabugin, I. V. *Chem. Rev.* **2003**, *103*, 229−282. (c) Olah, G. A.; Klumpp, D. A. *Acc. Chem. Res.* **2004**, *37*, 211−220.

(3) For recent examples, see: (a) Koltunov, K. Y.; Walspurger, S.; Sommer, J. *Chem. Commun.* **2004**, 1754−1755. (b) Koltunov, K. Y.; Walspurger, S.; Sommer, J. *Tetrahedron Lett.* **2005**, *46*, 8391−8394.

(4) (a) Koelsch, C. F.; Hochmann, H.; Le Claire, C. D. *J. Am. Chem. Soc.* **1943**, *65*, 59−60. (b) Hart, R. T.; Tebbe, R. F. *J. Am. Chem. Soc.* **1950**, *72*, 3286−3287. (c) Ansell, M. F.; Whitfield, G. F. *Tetrahedron Lett.* **1968**, *9*, 3075−3077.

(5) (a) Allen, J. M.; Johnston, K. M.; Jones, J. F.; Shooter, R. G. *Tetrahedron* **1977**, *33*, 2083−2087. (b) De Castro, C.; Primo, J.; Corma, A. *J. Mol. Catal. A: Chem.* **1998**, *134*, 215−222.

(6) (a) Prakash, G. K. S.; Yan, P.; Török, B.; Olah, G. A. *Catal. Lett.* **2003**, *87*, 109−112. (b) Rendy, R.; Zhang, Y.; McElrea, A.; Gomez, A.; Klumpp, D. A. *J. Org. Chem.* **2004**, *69*, 2340−2347.

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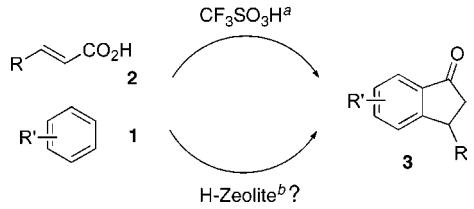
Scheme 1

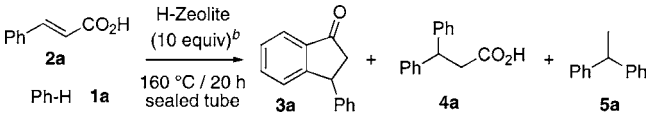


[a] Reported triflic-acid-induced cycliacyarylation. [b] Investigated H-zeolite-catalyzed variant.

stitutes an attractive synthetic tool because it allows the one-pot construction, from simple and inexpensive starting materials,[7] of the indanone skeleton that is encountered in numerous bioactive natural products.[8]

In order to study the feasibility of cycliacyarylation in zeolite frameworks, benzene **1a** and cinnamic acid **2a** were submitted to five H-zeolites possessing different topology/pore size/acidity combinations (Table 1).[9] Except in the case

Table 1. H-Zeolite Screening for the Cycliacyarylation of Benzene **1a** with Cinnamic Acid **2a**[a]



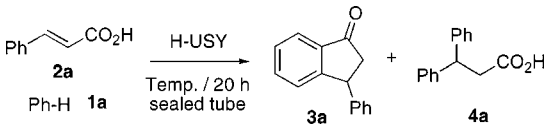
			product distribution (%)[d]		
entry	H-zeolite	conversion[c]	**3a**	**4a**	**5a**
1	H-USY	100%	69	8	*e*
2	H-Y	30%	<5[f]	<5[f]	14
3	H-MOR	95%[g]	19	16	25
4	H-ZSM5	100%	*e*	<5[f]	79
5	H-β	100%	32	26	30

[a] Reagents and reaction conditions: **1a** (solvent), **2a** (1 equiv), H-zeolite (10 equiv), sealed tube, 160 °C, 20 h. [b] Based on the theoretical number of acidic sites.[10] [c] Determined by ^{1}H NMR analysis of the crude mixture. [d] Isolated yields of pure product after complete conversion unless otherwise stated. [e] Not detected even by ^{1}H NMR analysis of the crude mixture. [f] Detected by ^{1}H NMR analysis of the crude mixture. [g] Traces of starting **2a** were detected by ^{1}H NMR analysis of the crude mixture.

of H-Y (entry 2), the use of H-USY, H-MOR, H-ZSM5, and H-β led to the complete conversion of cinnamic acid **2a** to two to three products (entries 1, 3−5). Depending on the nature of the H-zeolite, we observed different product distributions and selectivities. No product selectivity was observed with H-MOR and H-β (entries 3 and 5). The expected 3-phenylindanone **3a** was isolated with yields comparable to the benzene adduct **4a**. Surprisingly, a product **5a** resulting from an unexpected addition−decarboxyarylation was also formed with similar yields. In sharp contrast, H-USY selectively led to the cycliacyarylation product **3a**, while H-ZSM5 promoted almost exclusively the decarboxyarylation leading to **5a** in good yields (entries 1 and 4, respectively).

We then focused on the H-USY-induced cycliacyarylation process, and in order to find the optimal reaction conditions, the right balance between temperature and the number of acidic sites was investigated (Table 2). Temperature clearly

Table 2. H-USY-Induced Cycliacyarylation of Benzene **1a** with Cinnamic Acid **2a**: Reaction Conditions Optimization Studies[a]



	T	H-USY		product distribution[d]	
entry	(°C)	(equiv)[b]	conversion[c]	**3a**	**4a**
1	160	10	100%	69	8
2	130	10	100%	67	6
3	110	10	70%	36	27
4	130	1	0[g]	*e*	*e*
5	130	2	10%	*e*	<5[f]
6	130	5	65%	38	20
7	130	15	100%	72	<5[f]

[a] Reagents and reaction conditions: **1a** (solvent), **2a** (1.0 equiv), H-USY (*n* equiv), sealed tube, 20 h. [b] Based on the theoretical number of acidic sites. [c] Determined by ^{1}H NMR analysis of the crude mixture. [d] Isolated yields of pure product after complete conversion unless otherwise stated. [e] Not detected even by ^{1}H NMR analysis of the crude. [f] Detected by ^{1}H NMR analysis of the crude mixture. [g] Recovery of the starting material.

constitutes a key parameter, and 130 °C proved to be the minimum temperature required to achieve reaction completion (entries 1 and 2 vs 3). The use of stoichiometric or double the amount of acidic sites did not promote any reaction (entries 4 and 5). A 10 molar excess of acidic sites appeared as the minimum required to complete the reaction (entry 2 vs 7 vs 5 and 6). Interestingly, the selectivity increased with the amount of acidic sites, going from a low ratio in favor of the cyclized product **3a** at low acidic site concentration to the almost exclusive formation of **3a** at high concentration (entry 6 vs 2 and 7). It is worth noting that a comparable acidity effect on the reaction selectivity has also been observed in triflic acid.[6b]

With these reaction conditions in hand (15 equiv of H-USY at 130 °C), we explored the scope of this reaction

(7) It is worth noting that cycliacyarylation in zeolites has only been mentioned twice until now: (*i*) with unsuccessful results in ref 5b; (*ii*) with one successful example in ref 3b.

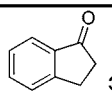
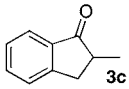
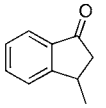
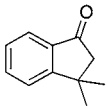
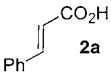
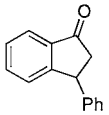
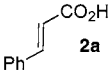
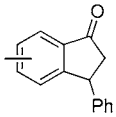
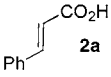
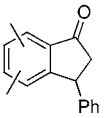
(8) For recent examples of bioactive indanone derivatives, see: (a) Charris, J. E.; Dominguez, J. N.; Gamboa, N.; Rodrigues, J. R.; Angel, J. E. *Eur. J. Med. Chem.* **2005**, *40*, 875−881. (b) Giner, J.-L.; Kehbein, K. A.; Cook, J. A.; Smith, M. C.; Vlahos, C. J.; Badwey, J. A. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2518−2521. (c) Dai, J.; Krohn, K.; Flörke, U.; Draeger, S.; Schulz, B.; Kiss-Szikszai, A.; Antus, S.; Kurtan, T.; van Ree, T. *Eur. J. Org. Chem.* **2006**, *35*, 3498−3506. (d) Charris, J. E.; Lobo, G. M.; Camacho, J. R.; Ferrer, R. E.; Barazarte, A. R.; Dominguez, J. N.; Gamboa, N.; Rodrigues, J. R.; Angel, J. E. *Lett. Drug Des. Discovery* **2007**, *4*, 49−54.

(9) Characteristics of H-zeolites are given in Supporting Information.

(10) For a recent method of determination of Brønsted acidic sites in zeolites, see: Louis, B.; Walspurger, S.; Sommer, J. *Catal. Lett.* **2004**, *93*, 81−84.

by submitting various α,β-unsaturated carboxylic acids **2b**−**d** to benzene (Table 3). Acrylic acid **2b** gave a complex

Table 3. Scope of the H-USY-Induced Cycliacyarylation of Aromatics **1** with Unsaturated Carboxylic Acids **2**[a]

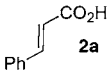
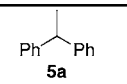
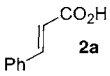
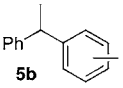
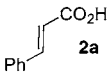
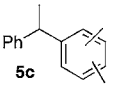
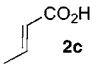
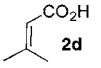
entry	aromatic **1**	unsaturated carboxylic acid **2**	product **3**	yield (%)[b]
1	PhH **1a**	 **2b**	 **3b**	12[c]
2	PhH **1a**	 **2c**	 **3c**	-[d]
3	PhH **1a**	 **2d**	 **3d**	62
4	PhH **1a**	 **2e**	 **3e**	69
5	PhH **1a**	 **2a**	 **3a**	72
6	$PhCH_3$ **1b**	 **2a**	 **3f**	73[e]
7	m-$PhMe_2$ **1c**	 **2a**	 **3g**	69[e]

[a] Reagents and reaction conditions: **1** (solvent), **2** (1.0 equiv), H-USY (15 equiv), sealed tube, 130 °C, 20 h. [b] Isolated yield of pure product. [c] A complex mixture of products was formed. [d] Not detected by ^{1}H NMR analysis of the crude mixture. [e] Isolated as a mixture of regioisomers.

mixture of products from which the expected indanone **3b** could be isolated in only small amounts, **2b** seeming to decompose under reaction conditions (entry 1). The methacrylic acid **2c** did not react under the same conditions (entry 2). In sharp contrast, the more stable 3-methyl acrylic acid derivatives **2d**,**e** reacted with **1a** leading to the corresponding 3-mono- or dimethyl indanones **3d**,**e** in good yields, whatever the substitution (entries 3 and 4). As already shown (Table 2), the phenyl analogue **2a** proved to be the most reactive substrate, yielding the expected 3-phenylindanone **3a** in good yield (entry 5). Therefore, cinnamic acid **2a** was used to look at the role of the aryl reagent. Submitted to toluene and *meta*-xylene **1b**,**c**, **2a** gave the corresponding indanone derivatives **3f**,**g** as expected (entries 6 and 7). They were obtained as a mixture of isomers with good yields, similar to the one obtained with benzene (entries 6 and 7 vs 5), but without selectivity.

We next considered the H-ZSM5-induced decarboxyalkylation, looking for optimal reaction conditions (Table 4, entries 1−6). In this case also, temperature was critical, and 130 °C proved again to be the right temperature (entry 2 vs

Table 4. H-ZSM5-Induced Decarboxyarylation of Carboxylic Acids **2** with Aromatics **1**: Optimization Studies and Scope[a]

entry	Temp (°C)	H-ZSM5 (equiv)[b]	ArH **1**	unsaturated carboxylic acid **2**	product **5**	yield (%)[c]
1	160	10	PhH **1a**	 **2a**	 **5a**	79
2	130	10	PhH **1a**	**2a**	**5a**	78
3	110	10	PhH **1a**	**2a**	**5a**	23[d]
4	130	5	PhH **1a**	**2a**	**5a**	79
5	130	3	PhH **1a**	**2a**	**5a**	78
6	130	1	PhH **1a**	**2a**	**5a**	-[e]
7	130	3	$PhCH_3$ **1b**	 **2a**	 **5b**	64[f]
8	130	3	m-$PhMe_2$ **1c**	 **2a**	 **5c**	61[f]
9	130	3	PhH **1a**	 **2c**	 **5d**	-[e]
10	130	3	PhH **1a**	 **2d**	 **5e**	-[e]

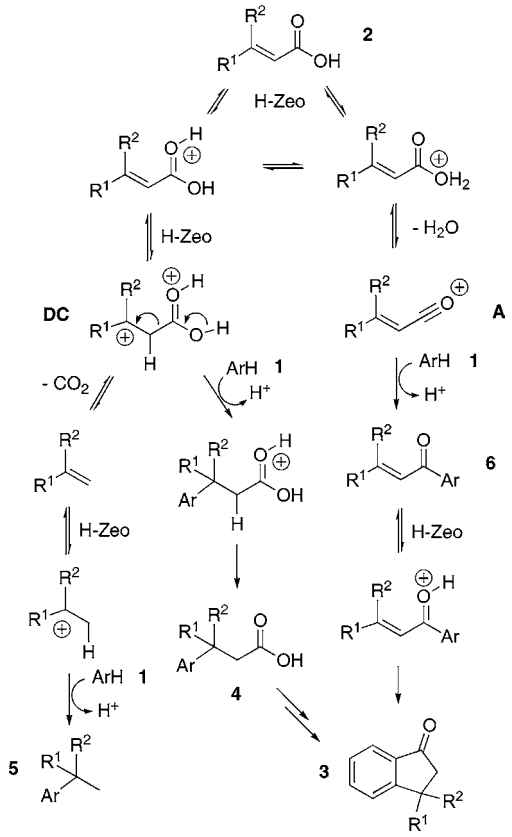
[a] Reagents and reaction conditions: **1** (solvent), **2** (1.0 equiv), H-ZSM5 (*n* equiv), sealed tube, 20 h. [b] Based on the theoretical number of acidic sites. [c] Isolated yields of pure product. [d] Incomplete conversion. [e] Not detected by ^{1}H NMR analysis of the crude mixture. [f] Isolated as a mixture of regioisomers.

1 vs 3). Interestingly enough, the H-ZSM5-mediated decarboxyalkylation required less acidic sites than the H-USY-mediated cyclization, 3 equiv of acidic sites being sufficient to complete the reaction (entries 4−6). The scope of the decarboxyalkylation reaction was then investigated. Toluene **1b** and *meta*-xylene **1c** were thus submitted to cinnamic acid **2a** in the presence of H-ZSM5, and the expected products **5b**,**c** were obtained in good yields (entries 7 and 8) but without selectivity. However, aliphatic α,β-unsaturated acids **2c** and **2d** did not react under the reaction conditions.

The formation of compounds **3**, **5**, and in some cases **4** from **2** in the presence of aryl derivatives **1** clearly involves different and complex cascades of events, probably initiated by protonation within the zeolites (Scheme 2). O-Protonation could indeed lead to an acylium intermediate **A** after water loss. The latter could then react in a Friedel−Crafts reaction with the aryl reagent, leading to an arylenone **6**, which can now cyclize after another protonation to the observed indanone **3**.

The decarboxyarylation could only be explained by the intermediate formation of a doubly protonated form of **2** (e.g. **DC**). Indeed, such dication **DC** could fragment, leading to an alkene, while liberating carbon dioxide. After protonation, this alkene can now react with the aryl derivative **1**, leading to **5**. It is worth noting that only the phenyl-substituted starting material **2a** yielded the decarboxyarylated products **5**, revealing the key role of the ease of protonation (Table 4, entries 1−8 vs 9 and 10).

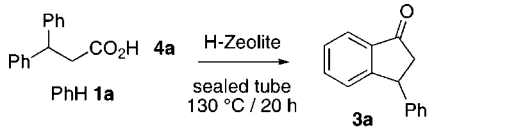
Scheme 2



The dication **DC** could also be trapped by the aryl reagent **1**, leading to β-arylated product **4** observed sometimes (Table 2). This adduct could then also be O-protonated and thus converted to another acylium intermediate which should ultimately lead to indanone **3** via an intramolecular Friedel–Crafts acylation process. The observed variations of the **3a**:**4a** ratio (Table 2) indeed suggest such a pathway.

To clarify this point, compound **4a** was replaced in the presence of benzene in the same conditions (Scheme 3). As proposed, **4a** indeed gave the expected indanone **3a** in H-USY with a yield similar to the one obtained from **2a** (Table 2, entry 7). Interestingly, **4a** remained untouched in H-ZSM5 as expected from the results gained from the zeolite screening (Table 1).

Scheme 3



This striking difference of behavior between H-USY and H-ZSM5, however, remains unclear for the moment.

In summary, we have demonstrated here that the nature of H-zeolites can direct the reaction of α,β-unsaturated carboxylic acids with benzene derivatives. H-USY induces a cycliacyarylation cascade, while H-ZSM5 promotes an unknown decarboxyarylation process. Moreover, since H-USY and H-ZSM5 zeolites are cheap, easily removable (by simple filtration), and recyclable (up to three times without loss of activity), these catalytic systems not only represent green alternatives to the liquid superacidic medium but also should find practical use in the construction of indanone and 1,1-diarylethane derivatives.

Further applications of zeolites in organic synthesis are actively pursued in our laboratories and will be reported in due time.

Acknowledgment. The authors thank the CNRS and the French Ministry of Research as well as the Loker Hydrocarbon Institute, University of Southern California, Los Angeles, for financial support.

Supporting Information Available: Characteristics of H-zeolites used and typical experimental procedures are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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