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# Total synthesis of (-)-herbaric acid. Organocatalyzed asymmetric halolactonization of acrylate-type carboxylic acids

Fabien Gelat, Michaël Coffinet, Stephane Lebrun, Francine Agbossou-Niedercorn, Christophe Michon, Eric Deniau

## ► To cite this version:

Fabien Gelat, Michaël Coffinet, Stephane Lebrun, Francine Agbossou-Niedercorn, Christophe Michon, et al.. Total synthesis of (-)-herbaric acid. Organocatalyzed asymmetric halolactonization of acrylate-type carboxylic acids. 9ème Symposium Francophone de Synthèse Totale (SFST), May 2019, Nantes, France. hal-03509948

**HAL Id: hal-03509948**

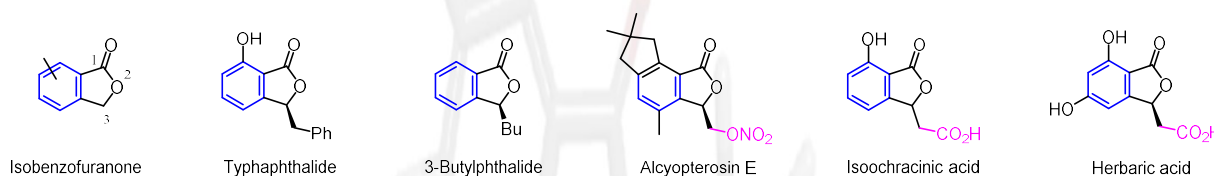
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Submitted on 1 Dec 2023

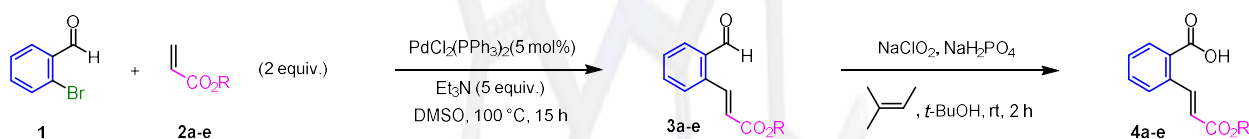
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## Examples of synthetic pharmacologically active isobenzofuranones



## Synthesis of acrylate-type carboxylic acids **4**



Entry	R	Yield (%)	Yield (%)
1	(+)-Menthyl	<b>3a</b> (66)	<b>4a</b> (97)
2	(-)-Menthyl	<b>3b</b> (68)	<b>4b</b> (96)
3	(-)-Borneyl	<b>3c</b> (59)	<b>4c</b> (89)
4	(+)-Isopinocampheyl	<b>3d</b> (64)	<b>4d</b> (91)
5	(+)-Fenchyl	<b>3e</b> (60)	<b>4e</b> (91)

## Organocatalyzed regio and diastereoselective halolactonization of **4**



Entry	4a	R	Catalyst	Additive	Yield (%)	D.e. (%)
1	<b>4a</b>	(+)-Menthyl	-	-	<b>5a</b> (83)	28
2	<b>4a</b>	(+)-Menthyl	QDTC 4-OMe	-	<b>5a</b> (85)	18
3	<b>4a</b>	(+)-Menthyl	QTC 2,4-OMe	-	<b>5a</b> (88)	58
4	<b>4a</b>	(+)-Menthyl	QDTC 4-OMe	PhCO <sub>2</sub> H	<b>5a</b> (85)	10
5	<b>4a</b>	(+)-Menthyl	QTC 2,4-OMe	PhCO <sub>2</sub> H	<b>5a</b> (83)	76
6	<b>4b</b>	(-)-Menthyl	QDTC 4-OMe	PhCO <sub>2</sub> H	<b>5b</b> (82)	74
7	<b>4b</b>	(-)-Menthyl	QDTC 4-OMe	PhCO <sub>2</sub> H	<b>5b</b> (85)	79
8	<b>4b</b>	(-)-Menthyl	QDTC 4-OMe	PhCO <sub>2</sub> H	<b>5b</b> (88) (X=I)	54
9	<b>4b</b>	(-)-Menthyl	QTC 2,4-OMe	PhCO <sub>2</sub> H	<b>5b</b> (88)	32
10	<b>4c</b>	(-)-Borneyl	QDTC 4-OMe	PhCO <sub>2</sub> H	<b>5c</b> (91)	45
11	<b>4c</b>	(-)-Borneyl	QTC 2,4-OMe	PhCO <sub>2</sub> H	<b>5c</b> (88)	15
12	<b>4d</b>	(+)-Isopinocampheyl	QDTC 4-OMe	PhCO <sub>2</sub> H	<b>5d</b> (93)	51
13	<b>4d</b>	(+)-Isopinocampheyl	QTC 2,4-OMe	PhCO <sub>2</sub> H	<b>5d</b> (90)	32
14	<b>4e</b>	(+)-Fenchyl	QDTC 4-OMe	PhCO <sub>2</sub> H	<b>5e</b> (93)	56
15	<b>4e</b>	(+)-Fenchyl	QTC 2,4-OMe	PhCO <sub>2</sub> H	<b>5e</b> (90)	37

## Total synthesis of (-)-herbaric acid

