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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

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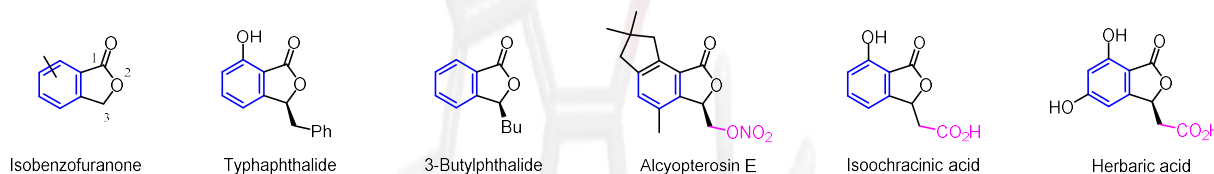
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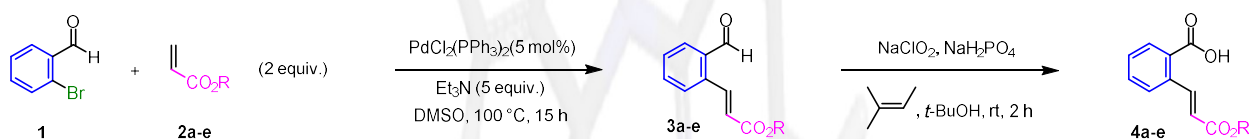
GELAT Fabien, COFFINET Michaël, LEBRUN Stéphane, AGBOSSOU-NIEDERCORN Francine, MICHON Christophe, DENIAU Eric

Univ. Lille, CNRS, Centale Lille, ENSCL, Univ. Artois, UMR 8181-UCCS-Unité de Catalyse et Chimie du Solide, F-59000 Lille, France

Examples of synthetic pharmacologically active isobenzofuranones



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



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

Organocatalyzed regio and diastereoselective halolactonization of **4**



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

Total synthesis of (-)-herbaric acid

