(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
6 November 2008 (06.11.2008)

PCT

(10) International Publication Number
WO 2008/134325 A1

(51) International Patent Classification:
A01N 33/02 (2006.01)

(21) International Application Number:
PCT/US2008/061189

(22) International Filing Date: 22 April 2008 (22.04.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/915,103	30 April 2007 (30.04.2007)	US
61/027,814	11 February 2008 (11.02.2008)	US
61/028,122	12 February 2008 (12.02.2008)	US

(71) Applicant *(for all designated States except US)*: **ADOLOR CORPORATION** [US/US]; 700 Pennsylvania Drive, Exton, PA 19341 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **LE BOURDONNEC, Bertrand** [FR/US]; 317 Ivy Lane, East Fallowfield, PA 19320 (US). **DOLLE, Roland** [US/US]; 536 Elliott Drive, King Of Prussia, PA 19405 (US).

(74) Agents: **PEASE, Ann M. Caviani** et al.; Dechert LLP, P.O. Box 390460, Mountain View, CA 94039 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(54) **Title:** COMPOSITIONS OF (-)-E-10-OH-NT AND METHODS FOR THEIR SYNTHESIS AND USE

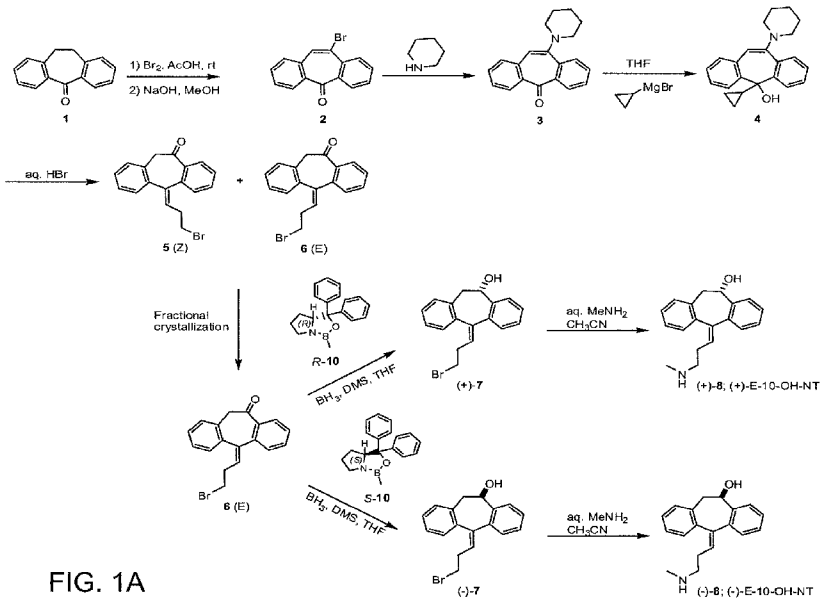


FIG. 1A

(57) **Abstract:** This present disclosure provides compositions comprising E-10-0H-NT metabolites of AT and NT, methods for their synthesis and methods for their use In one embodiment, the compound (-)-E-5-(y-bromopropylidene)-10,11-dihydro-IO-hydroxy-5H-dibenzo[a,d]- cycloheptene. Is prepared by reducing E-5-(y-bromopropylidene)-10,11dihydro-IO-oxo-5H-dibenzo[a,d] ?cycloheptene in the presence of a crural-specific oxazaborolidine catalyst In another embodiment, method for inhibiting uptake of norepinephrine comprising contacting a norepinephrine transporter with a composition comprising E-IO-OH-NT that is enriched in the (-) enantiomer Is described

WO 2008/134325 A1