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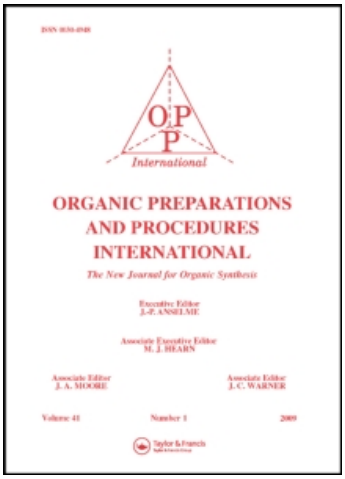

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

SUBSTITUTED 3,4-DIHYDROXYCINNOLINES

Manuel Lora-Tamayo[a]; Berta Marco[a]; Carmen Sender[a]
[a] Centro Nacional de Quimica Organica, C.S.I.C., Madrid-6, SPAIN

To cite this Article Lora-Tamayo, Manuel , Marco, Berta and Sender, Carmen(1978) 'SUBSTITUTED 3,4-DIHYDROXYCINNOLINES', Organic Preparations and Procedures International, 10: 6, 298 — 300
To link to this Article: DOI: 10.1080/00304947809355056
URL: http://dx.doi.org/10.1080/00304947809355056

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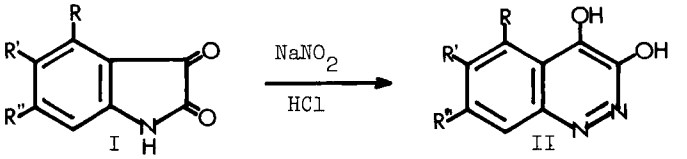
SUBSTITUTED 3,4-DIHYDROXYCINNOLINES

Submitted by Manuel Lora-Tamayo*, Berta Marco and Carmen Sender (7/5/78)

Centro Nacional de Quimica Organica, C.S.I.C.
Juan de la Cierva, 3
Madrid-6, SPAIN

Four new 3,4-dihydroxycinnolines (IIa-d) have been prepared in 70-90% yields by a generalization of the method previously described [M. Lora-Tamayo, B. Marco and P. Navarro, Org. Prep. Proced. Int., 8, 45 (1976)]. The starting isatins (Ia-d) were obtained by cyclization of the correspond-



a) R = R'' = CH_3, R' = H b) R = R'' = H, R' = CH_3

c) R = R'' = H, R' = OCH_3 d) R = R'' = H, R' = Cl

ing isonitroso acetanilides with polyphosphoric acid.

EXPERIMENTAL

General Procedure.- To a stirred solution of I (1 g) in 50 ml of N sodium hydroxide cooled below 0°, was added a solution of the equivalent amount of sodium nitrite in 5 ml of water. Then, 100 ml of conc. hydrochloric acid previously cooled to -5° were added, and the mixture was stirred for 5 min. at the same temperature. The resulting diazonium salt solution was added dropwise to a solution of stannous chloride dihydrate (in a ratio of 2:1 with respect to the starting isatin) in 100 ml of conc. hydrochloric acid. The suspension formed was stirred for one hour at 0° and filtered at room temperature, affording the 3,4-dihydroxycinnoline (II) which was recrystallized from acetic acid. Small additional amounts of the compound were obtained by extracting the acid filtrate with ethyl acetate.

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3,4-Dihydroxy-5,7-dimethylcinnoline [IIa, 0.86 g. (80%)] obtained as a yellow solid identified mp. 213-214°, from 1 g (0.0056 mole) of 4,6-dimethylisatin.

Anal. Calcd. for $C_{10}H_{10}N_2O_2$: C, 63.14; H, 5.29; N, 14.73.

Found: C, 62.89; H, 5.44; N, 14.51.

IR: (KBr, cm^{-1}): 3400-2300, 1695, 1635, 1625, 1575, 1525, 1460, 1375, 1360, 1255, 1220, 1180, 1150, 1075, 1055, 1045, 840, 825, 790, 760.

NMR (DMSO-d_6, δ): 2.3-2.9 (m, 6H, $2CH_3$), 6.5-7.4 (m, 3H, 2H, aromat. and 1OH), 10.1-12.5 (broad m, 1H, OH). MS: m/e (%): 190 (52, M^+), 172 (98), 162 (36), 144 (50), 131 (6), 117 (100), 116 (20), 91 (12), 90 (13).

3,4-Dihydroxy-6-methylcinnoline [IIb, 0.94 g. (85%)] obtained as a white-yellow solid, mp. 292-293° from 1 g (0.062 mole) of 5-methylisatin.

Anal. Calcd. for $C_9H_8N_2O_2$: C, 61.35; H, 4.75; N, 15.90.

Found: C, 61.24; H, 4.49; N, 15.66.

IR: (KBr, cm^{-1}): 3400-2300, 1685, 1678, 1490, 1380, 1245, 1170, 795, 770.

NMR (DMSO-d_6, δ): 2.5 (s, 3H, CH_3), 7.2-7.8 (m, 2H, aromat.), 8.0 (m, 1H, aromat.), 12.5-12.8 (broad m, 2H, HO). MS: m/e (%): 176 (100, M^+), 158 (12), 131 (33), 130 (44), 107 (18), 105 (1), 77 (15), 76 (5).

3,4-Dihydroxy-6-methoxycinnoline [IIc, 0.76 g. (71%)]obtained as a white solid identified, mp. 281-282° from 1 g (0.0056 mole) of 5-methoxyisatin.

Anal. Calcd. for $C_9H_8N_2O_3$: C, 56.24; H, 4.19; N, 14.57.

Found: C, 56.27; H, 4.14; N, 14.46.

IR (KBr, cm^{-1}): 3400-2300, 1690, 1665, 1625, 1585, 1480, 1365, 1285, 1240, 1215, 1170, 1160, 1120, 1050, 1020, 945, 825, 800, 780, 745.

NMR (DMSO-d_6, δ): 3.9 (s, 3H, OCH_3), 7.0-7.9 (3H, aromat.), 12.1-14.1 (broad, m, 2H, HO). MS: m/e (%): 192 (100, M^+), 177 (36), 133 (17), 118 (9), 105 (10), 104 (2), 78 (6), 76 (2).

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6-Chloro-3,4-dihydroxycinnoline [IId, 1.04 g. (96%)] obtained as a yellow solid, mp. 180-181°, from 1 g (0.0055 mole) of 5-chloroisatin.

Anal. Calcd. for $C_8H_5N_2O_2Cl$: C, 48.87; H, 2.54; N, 14.25; Cl, 18.02.
Found: C, 48.52; H, 2.64; N, 13.98; Cl. 17.84.

IR (KBr, cm^{-1}): 3400-2300, 1675, 1575, 1495, 1480, 1465, 1420, 1370, 1270, 1250, 1235, 1165, 1035, 925, 860, 800, 775. NMR (DMSO-d_6, δ): 7.38-7.95 (m, 3H, 2H aromat. and 1 OH), 8.1-8.2 (m, 1H, aromat.), 12.6-14.6 (broad m, 1H, OH). MS: m/e (%): 196 (100, M^+), 197 (10), 198 (36), 179 (18), 152 (17), 124 (15), 122 (15), 111 (1), 76 (2).

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X-RAY CRYSTAL STRUCTURE ANALYSES OF ISOMERIC CYCLOADDUCTS OF 3-PICOLINE-N-OXIDE WITH p-CHLOROPHENYL ISOCYANATE

Submitted by (6/14/78)

Takuzo Hisano,* Toshikazu Matsuoka, Masataka Ichikawa, and Keiji Muraoka

Faculty of Pharmaceutical Sciences
Kumamoto University
5-1 Oe-hon-machi
Kumamoto 862
JAPAN

Tetsuya Komori, Kazunobu Harano and Yoshiteru Ida

Faculty of Pharmaceutical Sciences
Kyushu University
Maidashi, Higashi-ku
Fukuoka 812
JAPAN

Arild T. Christensen

Syntex Analytical Instruments, Inc.
10040 Bubb Road
Cupertino, CA 95014
USA

The X-ray crystal analysis of the two products (I and II) isolated from the reaction of 3-picoline N-oxide with p-chlorophenyl isocyanate con-