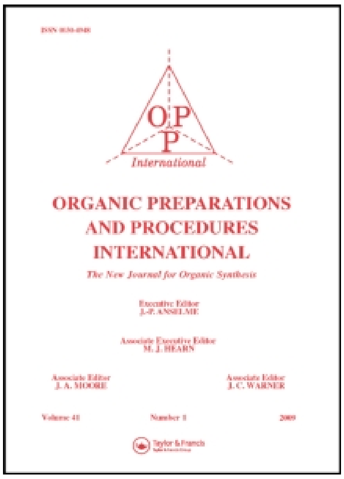
This article was downloaded by:
On: *27 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Organic Preparations and Procedures International

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

THE PREPARATION OF 5-CHLORO-2-INDOLINONE BY DIRECT CHLORINATION OF 2-INDOLINONE

Paul Pranc[a]
[a] Lilly Research Laboratories, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, Indiana

To cite this Article Pranc, Paul(1990) 'THE PREPARATION OF 5-CHLORO-2-INDOLINONE BY DIRECT CHLORINATION OF 2-INDOLINONE', Organic Preparations and Procedures International, 22: 1, 104 — 105

To link to this Article: DOI: 10.1080/00304949009356676

URL: http://dx.doi.org/10.1080/00304949009356676

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

REFERENCES

1. C. S. LeHoullier and G. W. Gribble, J. Org. Chem., 48, 2364 (1983).

2. H. Hart, A. Bashir-Hashemi, J. Lou and M. A. Meador, Tetrahedron, 42, 1641 (1986).

3. C. T. Lin and T. C. Chou, Synthesis, 8, 628, (1988).

4. S. L. Crump, J. Netka and B. Rickborn, J. Org. Chem., 50, 2746 (1985).

5. The reagents employed were: a) $NaBH_4/CF_3COOH/THF$ [Gribble et al. Synthesis, 1, 143 (1982)]. b) $LTBAH/Et_3B$. c) $TiCl_4/LAH/Et_3N/THF$ [Xing et al. J. Org. Chem., 47, 70, (1982)]. d) Lithium naphthalenide [Polovsky et al. ibid., 39, 3010, (1974)]. e) Zn/AcOH [Bhatt and Reddy, Tetrahedron Lett., 21, 3627 (1980)]. Procedures (a) and (b) gave no 6 while the other ones gave only poor yields.

6. R. J. Moss and B. Rickborn, J. Org. Chem., 47, 5391 (1982).

****

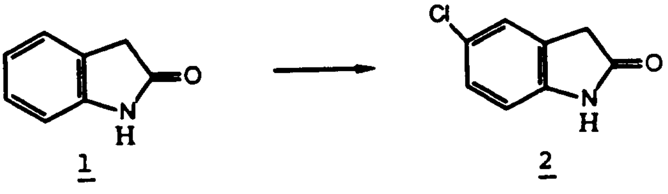
THE PREPARATION OF 5-CHLORO-2-INDOLINONE BY DIRECT CHLORINATION OF 2-INDOLINONE

Submitted by (4/28/89)

Paul Pranc

Lilly Research Laboratories
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, Indiana 46285

5-Chloro-2-indolinone (2) is an important chemical intermediate used in the synthesis of compounds reported to be useful in the treatment of anxiety[1] and as anti-inflammatory agents.[2] A recent patent[3] reviews the literature methods for preparing 2 and reports a two-step synthesis of 2, starting with 5-chloroindole. All of these methods require several steps. The bromination of 2-indolinone (1) yields 5-bromo-2-indolinone[4], but apparently no one has reported the chlorination of 1. This paper describes the preparation of 2 from 1 by direct chlorination.



EXPERIMENTAL SECTION

The NMR spectra were obtained on a G. E. QE-300 spectrometer. The mass spectrum (MS) was taken using a CEC 21-110 spectrometer. Melting points were determined on a Mel-Temp apparatus and are uncorrected. The reactions were monitored by TLC on silica gel plates (Kieselgel 60), visualized by UV or iodine.

5-Chloro-2-indolinone (2).- Oxindole (1) (100.0 g, 0.75 mol) was dissolved in 2 L of water at 90°. Chlorine (52.9 g, 0.75 mol), by weight difference, was then bubbled into the hot solution over a period of 40 min. A brown precipitate formed during the chlorine addition. Stirring was continued for another 0.5 hr. After cooling to room temperature, the crude brown colored solid was collected and crystallized from 1 L of ethanol to yield 49.4 g (39%) of clear small crystals of 2, mp. 194-196°, lit.[5,6] mp. 195-196°; TLC: Rf 0.43, EtOAc. MS: m/e 167 (M^+). ^1H NMR (DMSO-d_6): δ 10.5 (s, 1H, -NH-, exch. with D_2O), 7.2 (m, 2H, aromatic), 6.8 (d, 1H, aromatic), 3.5 (s, 2H, -CH_2-). The NMR is identical with that reported for authentic material.[7]

Anal. Calcd. for C_8H_6ClNO: C, 57.33; H, 3.61; N, 8.36; Cl, 21.15
Found: C, 57.48; H, 3.57; N, 8.18; Cl, 21.24

REFERENCES

1. B. B. Molloy, U. S. Patent 3,882,236 (1975); Chem. Abstr., 83, 79075y (1975).
2. S. B. Kadin, U. S. Patent 4,556,672 (1985); Chem. Abstr., 105, 24187d (1986).
3. A. Marfat, U. S. Patent 4,761,485 (1988); Chem. Abstr., 110, 38887x (1989).
4. W. C. Sumpter, M. Miller and L. N. Hendrick, J. Am. Chem. Soc., 67, 1656 (1945).
5. W. B. Wright, Jr. and K. H. Collins, ibid., 78, 221 (1956).
6. T. V. RajanBabu, B. L. Chenard and M. A. Petti, J. Org. Chem., 51, 1704 (1986).
7. J. M. Muchowski, Can. J. Chem., 48, 422 (1970).

****