

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>

A NEW AND CONVENIENT PREPARATION OF 3-BROMO-4-CHLORONITROBENZENE

Kantilal Kosandal^a; A. K. S. Bhujanga Rao^a; C. Gundu Rao^a; B. B. Singh^a

^a R&D Centre, Reckitt & Colman of India Limited, Hosur, Tamil Nadu, INDIA

To cite this Article Kosandal, Kantilal, Rao, A. K. S. Bhujanga, Rao, C. Gundu and Singh, B. B. (1991) 'A NEW AND CONVENIENT PREPARATION OF 3-BROMO-4-CHLORONITROBENZENE', *Organic Preparations and Procedures International*, 23: 3, 395 – 396

To link to this Article: DOI: 10.1080/00304949109458221

URL: <http://dx.doi.org/10.1080/00304949109458221>

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.

A NEW AND CONVENIENT PREPARATION OF 3-BROMO-4-CHLORONITROBENZENE

Submitted by Kantilal Kosandal, A. K. S. Bhujanga Rao,
(12/12/90) C. Gundu Rao and B. B. Singh*

*R&D Centre, Reckitt & Colman of India Limited
Plot 176, SIPCOT Industrial Complex
Hosur-635 126, Tamil Nadu, INDIA*

In the course of our studies on the synthesis of the potent antibacterials "fluoroquinolones",¹ 3-bromo-4-chloronitrobenzene was needed on a large scale. A low yield multi-step synthesis involving exhaustive purification has been described.² Although several mild methods are available for bringing about electrophilic bromination of activated aromatic compounds, very few have been reported for deactivated rings. We now describe a simple one-step preparation of 3-bromo-4-chloronitrobenzene by the bromination of easily available *p*-chloronitrobenzene.

The first method attempted involving the use of liquid bromine, mercuric oxide and sulfuric acid, gave only a 20% conversion after 8 hrs of reflux.³ The second procedure⁴ was modified by changing the mode of addition of potassium bromate and by raising the temperature to 80°. The progress of the reaction was monitored by gas chromatography [OV-1(10%) 6 ft, 110-10-220°]. The results are summarized in the Table. This reaction has been optimized on one mole scale and could easily be carried out on a large scale.

TABLE. Bromination of *p*-Chloronitrobenzene

Method	Temp. (°C)	Time (hrs)	Conversion ^a	Yield ^b
Br ₂ , HgO	70	3	15%	
H ₂ SO ₄ , CCl ₄		6	18%	
		8	21%	
KBrO ₃ , H ₂ SO ₄	30	5	0%	
	80	5	94%	85%

a) Based on GC analysis. b) Isolated pure product.

EXPERIMENTAL SECTION

3-Bromo-4-chloronitrobenzene.- To a 3 L three-neck flask, fitted with a mechanical stirrer, a reflux condenser and a thermometer, were added water (800 ml), conc. sulfuric acid (800 ml) and *p*-chloronitrobenzene (157 g). The well stirred mixture was heated to 80° and potassium bromate (187 g) was added in portions over a period of 3 hrs. Stirring was continued for a further period of 2 hrs

and the reaction mixture was poured onto crushed ice (500 g). The precipitated solid was collected, washed with water and sucked dry. Recrystallization from toluene afforded 200 g (85%) of pure 3-bromo-4-chloronitrobenzene, mp. 62°, lit.² 61°.

REFERENCES

1. M. P. Wentland and J. B. Cornett, "Annual Reports in Medicinal Chemistry", 20, 145 (1985); H. Koga, A. Itoh, S. Murayama, S. Suzue and T. Irikura, *J. Med. Chem.*, 23, 1358 (1980).
2. S. S. Berg, *J. Chem. Soc.*, 1991 (1949).
3. S. A. Khan, M. A. Munawar and M. Siddiq, *J. Org. Chem.*, 53, 1799 (1988).
4. J. J. Harrison, J. P. Pellegrini and C. M. Selwitz, *ibid.*, 46, 2169 (1981).

A CONVENIENT SYNTHESIS OF (2S)-2-AMINO-3-PHENYLPROPANOL

Submitted by Ramalinga Dharanipragada, Arled Alarcon and Victor J. Hruby*
(12/19/90)

Department of Chemistry
University of Arizona, Tucson, AZ 85721

(2S)-2-Amino-3-phenylpropanol (**2**) is the precursor to a chiral auxiliary introduced by Evans and co-workers.¹ It is synthesized from L-phenylalanine (**1**) by reduction with borane-dimethyl sulfide.² This reaction is exothermic and as Gaze and Evans² note "the potential vigor of this exotherm cannot be overemphasized". In addition, dimethyl sulfide (stench) is produced as a side-product. Since we recently had occasion to synthesize the title compound in our studies related to the asymmetric synthesis of unusual amino acids³ and needed rather large amounts of it, we sought a safer alternative procedure. We have adopted a procedure developed by Giannis and Sanhoff⁴ for the reduction of valine and proline and found that reduction of L-phenylalanine (**1**) with lithium borohydride in the presence of chlorotrimethylsilane⁴ provides the desired compound **2** in 83% yield. The merits of this procedure are its relative ease of execution and safety. In view of the immense utility of chiral auxiliaries of Evans and co-workers in organic synthesis,⁵ we expect our procedure to be very useful.