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# *N*,*N*′-Dichlorobis(2,4,6-trichlorophenyl)urea (CC-2): an Efficient Reagent for the Synthesis of Chemical Weapons Convention-Related Dialkyl-*N*,*N*-dialkylphosphoramidates from Dialkylphosphites

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The present paper describes the one-pot synthesis of dialkyl *N*,*N*-dialkylphosphoramidates (DADAP) from dialkylphosphites and dialkylamines using *N*,*N*′-dichlorobis(2,4,6-trichlorophenyl)urea (CC-2) as chlorinating reagent. DADAP belong to the schedule 2.B.6 category of the Chemical Weapons Convention (CWC), as they are the important markers of the chemical warfare agent tabun and its analogues. The study was undertaken to develop the spectral database of DADAP for verification of CWC. The reported synthetic strategy can be adopted to rapidly synthesize several analogues of DADAP during official proficiency tests.

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## Introduction

Efficient syntheses of reference chemicals required for the verification analysis of chemical warfare agents (CWA) is of paramount importance.[1–6] This field of synthesis and analysis has attracted the attention of several groups owing to the strict verification regime of the Chemical Weapons Convention (CWC).[7,8] The CWC entered into force on 29 April 1997 and prohibits the development, production, stockpiling, and usage of chemical weapons.[9] By April 2007, 184 countries had ratified the convention. The Organisation for Prohibition of Chemical Weapons (OPCW), an international organization, administers the CWC through its stringent verification program. Verification involves collection of samples from production, storage, and suspected sites by inspectors appointed by the OPCW.[9] Generally, inspectors carry out the analysis of collected samples on site; in case of any ambiguity, the samples are sent to at least two off-site laboratories, designated by the OPCW, for unambiguous identification of CWC-related chemicals.[10] Thus, a laboratory willing to undertake the challenging task of off-site analysis of CWC-related chemicals must first achieve the status of 'designated laboratory'.[9,10] A laboratory can become and stay designated only by proving its analytical capabilities in Official Proficiency Tests (PT) conducted by the OPCW.[11–13] The performance of participating laboratories in PT mainly depends on the availability of spectral data of CWC-related chemicals, sample preparation, analytical skills of chemists, judgment, and reporting. It is important to note that a 15-calendar-days timeline is a crucial part in the analysis of PT samples and reporting the results. As the schedules of compounds are based on commercial and past use of chemicals as CWA, the total number of scheduled compounds is several hundred thousand. Hence, their synthesis (in pure form by reported methods) and recording of spectral data is a daunting task. This problem can be obviated by the development of efficient synthetic procedures that can provide pure compounds in the shortest possible period. Rapid synthesis of these compounds in pure form is essential to confirm the structures of analytes identified from their spectroscopic (e.g. gas chromatography–mass spectrometry coupled technique, $^{31}$P NMR spectroscopy, and gas chromatography infrared spectroscopy) analysis. The match of spectra with synthesized compounds is one of the unique ways to report the results of analysis. Furthermore, the spectra and chromatographic data gathered by the synthesis of pure compounds are also helpful in off-site analysis of real samples.

Alkyl *N*,*N*-dialkylphosphoramidocyanidates (ADAPC) are analogues of the highly toxic nerve agent tabun (ethyl *N*,*N*-dimethylphosphoramidocyanidate) that are placed in schedule 1.A.2 of CWC.[9] Based on commercially available $C_1$–$C_{10}$ alcohols, the estimated number of compounds belonging to schedule 1.A.2 is 48 000. Dialkyl *N*,*N*-dialkylphosphoramidates (DADAP) are often produced when tabun or its derivatives are produced in any laboratory or plant.[5] Hence, DADAP are considered as important chemical markers of tabun and its analogues. Consequently, DADAP are included in the schedule 2.B.6 category of CWC and hence are extremely important from a verification view point of the CWC.[14]

Our continued efforts in the field of synthetic and analytical advancement of scheduled chemicals[1–5] have prompted us to further advance the synthesis of DADAP. A plethora of effective chemical approaches have been devised for the preparation of phosphoramidates.[1,2,15–24] Among these, two approaches are worthy of mention here. The first approach

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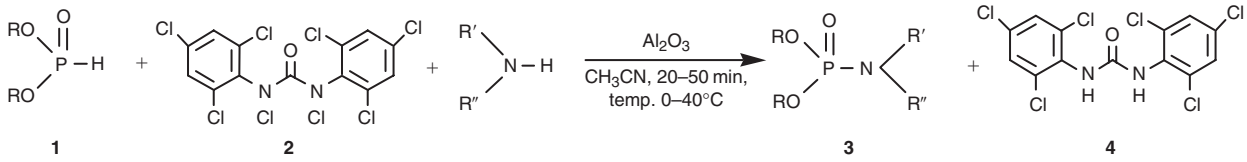


1 2 3 4

**Scheme 1.**

involves the condensation of dialkyl chlorophosphates with dialkylamines in the presence of a base.[20–24] This method requires the synthesis of dialkyl chlorophosphates that are moisture-sensitive and unstable. The second approach involves condensation of *N*,*N*-dialkylphosphoramidic dichloride with alcohols in the presence of $Al_2O_3$ as a solid support.[2] This method is straightforward, yet has a major drawback in the preparation of *N*,*N*-dialkylphosphoramidic dichlorides. The synthesis of these moisture-sensitive intermediates is time-consuming, and requires a strong base and tedious workup. Yet another method involves solution-phase condensation of *N*,*N*-dialkylphosphoramidic dichloride with alcohols in the presence of base,[1] yet it also has the same disadvantages as mentioned above. Thus, state-of-the-art synthesis of DADAP requires a strategy that would permit an expedious, mild, and efficient synthesis of the title compounds. It would be an extra advantage if the synthesis of these compounds could be carried out in one pot without elaborate workup.

We envisaged that if dialkyl chlorophosphate could be produced in situ from dialkylphosphites by an active chlorine-releasing reagent, followed by condensation with dialkylamines, it would generate the required DADAP. For this, we resorted to *N*,*N*′-dichlorobis(2,4,6-trichlorophenyl)urea (CC-2) as an active chlorine-generating reagent,[25–27] and herein report the optimization of reaction parameters.

## Results and Discussion

A typical reaction scheme adopted to generate the DADAP is illustrated in Scheme 1. The dialkyl phosphates **1** were treated with CC-2 **2** to generate the dialkyl chlorophosphates, which were used to phosphorylate different dialkylamines in the same reaction mixture in the presence of activated alumina. In a typical reaction, when dialkyl phosphite was mixed with a suspension of CC-2 in acetonitrile, the corresponding dialkyl chlorophosphate was generated, which was further treated in the same vessel with dialkylamine in the presence of alumina to produce the desired phosphoramidate **3**. Reactions with varying mole ratios of reactants were carried out, and maximum yields were obtained when dialkyl phosphites, CC-2, alumina, and dialkylamines were mixed at molar ratios of 1:0.5:1.5:1.0, respectively. Details of the reaction protocol are described in the Accessory Publication.

To investigate the effect of dialkyl groups on the phosphorylation of dialkylamines, various dialkyl phosphites were treated with diethylamine in the presence of CC-2. Phosphorylation of diisopropyl phosphite with diethylamine was found to be slower (as it took 40 min to complete), in contrast to most of the reactions, which were completed within 20 min. This observation is in accordance with the higher steric demand of the transition state formed in the reaction. Second, this slow reaction can also be explained by the positive inductive effect of the diisopropyl group, which reduces the electrophilic susceptibility of the P=O bond responsible for the nucleophilic attack by dialkylamines. Because of this, reactions of dialkylamines with dimethyl phosphite were faster, and were slowest with diisopropyl phosphate (entry 34, Table 1). Furthermore, while studying the effect of various amines with in situ-generated dialkyl chlorophosphates, we found that the reactions of dimethylamine were faster than that of ethylmethylamine. It was also noticed that the reactivity of the amines decreased with an increase in the chain length. However, diisopropylamine took a somewhat longer time (35–60 min) in each case (Table 1). The results of the present study indicated that the order of reactivity of amines is mainly governed by their steric demand.

The important advantages of this reaction are: (i) its occurrence at room temperature; (ii) short reaction time; and (iii) the by-product bis(2,4,6-trichlorophenyl)urea **4** does not react with amines and is insoluble in any solvent, facilitating its easy isolation and recycling. Recycling of **4** was made possible by removing the alumina from the precipitate by dissolving in alkali solution and obtaining **4** by filtration, which was further converted to CC-2 as per our earlier reported procedure.[26] From the filtrate, the desired products could be obtained in pure form by distillation after distilling off the solvent. This method is advantageous in comparison with the one developed by Atherton and Todd,[20] as it takes place at room temperature and in a single step,[4] whereas the classical method requires additional base (two moles of amines) and a longer reaction time. The method is an advancement over the one developed by Saunders[20b] using *N*-chlorosuccinimide that bears one active chlorine atom per molecule; CC-2 contains two active chlorines, and hence half mole of this latter reagent is sufficient to complete the reaction. The second advantage of using CC-2 is that its dechlorinated product **4** is practically insoluble in the organic solvent, hence facilitating its complete removal by filtration. In contrast, succinimide is soluble in organic solvents and requires extra efforts to remove it from the reaction mixture. To examine the reproducibility of this one-pot concept at higher mole ratio, one mole of diethyl phosphite was treated with 0.5 mol of CC-2 in acetonitrile at room temperature. The reaction mixture was stirred for 15 min; $^{31}$P NMR spectroscopy revealed complete conversion of the diethyl phosphite into the corresponding diethyl chlorophosphate within 15 min. The heterogeneous reaction mixture was cooled to 0°C, and alumina (1.5 mol) was added. Subsequently ethylmethylamine (1 mol) was added slowly. After addition of amine, the reaction mixture was warmed to room temperature and shaken on a vortex shaker. The $^{31}$P NMR spectrum was recorded by drawing a few milligrams of sample from the reaction mixture after 10 min and extracting it with ether. The results of NMR indicated that the signal of diethyl chlorophosphate at $\delta$ 4.14 completely vanished and a new signal appeared at $\delta$ 13.58, which clearly demonstrated the rapid conversion of diethyl chlorophosphate into the corresponding *O*,*O*-diethyl *N*-ethyl-*N*-methyl phosphoramidate. Filtration of the heterogeneous reaction mixture and concentration of the solvent provided the pure product in 92% isolated yield.

**Table 1. One-pot synthesis of dialkyl *N,N′*-dialkyl phosphoramidates from dialkyl phosphites and *N,N′*-dichlorobis(2,4,6-trichlorophenyl)urea (CC-2)[A]**

| Entry | R | R′ | R″ | Time [min] | Temp. [°C] | Yield[B] [%] |
|---|---|---|---|---|---|---|
| 1 | $CH_3$ | $CH_3$ | $CH_3$ | 15 | 25 | 88 |
| 2 | $CH_3$ | $C_2H_5$ | $C_2H_5$ | 20 | 35 | 86 |
| 3 | $CH_3$ | *n*-$C_3H_7$ | *n*-$C_3H_7$ | 30 | 30 | 86 |
| 4 | $CH_3$ | *i*-$C_3H_7$ | *i*-$C_3H_7$ | 35 | 35 | 85 |
| 5 | $CH_3$ | $CH_3$ | $C_2H_5$ | 25 | 30 | 81 |
| 6 | $CH_3$ | *n*-$C_3H_7$ | $C_2H_5$ | 30 | 30 | 80 |
| 7 | $CH_3$ | *i*-$C_3H_7$ | $C_2H_5$ | 25 | 35 | 85 |
| 8 | $CH_3$ | *n*-$C_3H_7$ | $CH_3$ | 25 | 30 | 82 |
| 9 | $CH_3$ | *i*-$C_3H_7$ | *n*-$C_3H_7$ | 30 | 35 | 85 |
| 10 | $CH_3$ | *i*-$C_3H_7$ | $CH_3$ | 30 | 30 | 80 |
| 11 | $C_2H_5$ | $CH_3$ | $CH_3$ | 20 | 25 | 86 |
| 12 | $C_2H_5$ | $C_2H_5$ | $C_2H_5$ | 30 | 30 | 81 |
| 13 | $C_2H_5$ | *n*-$C_3H_7$ | *n*-$C_3H_7$ | 30 | 30 | 85 |
| 14 | $C_2H_5$ | *i*-$C_3H_7$ | *i*-$C_3H_7$ | 35 | 40 | 84 |
| 15 | $C_2H_5$ | $CH_3$ | $C_2H_5$ | 25 | 25 | 92 |
| 16 | $C_2H_5$ | *n*-$C_3H_7$ | $C_2H_5$ | 25 | 30 | 83 |
| 17 | $C_2H_5$ | *i*-$C_3H_7$ | $C_2H_5$ | 30 | 35 | 82 |
| 18 | $C_2H_5$ | *n*-$C_3H_7$ | $CH_3$ | 25 | 25 | 83 |
| 19 | $C_2H_5$ | *i*-$C_3H_7$ | *n*-$C_3H_7$ | 30 | 35 | 82 |
| 20 | $C_2H_5$ | *i*-$C_3H_7$ | $CH_3$ | 30 | 30 | 84 |
| 21 | *n*-$C_3H_7$ | $CH_3$ | $CH_3$ | 30 | 30 | 88 |
| 22 | *n*-$C_3H_7$ | $C_2H_5$ | $C_2H_5$ | 30 | 30 | 86 |
| 23 | *n*-$C_3H_7$ | *n*-$C_3H_7$ | *n*-$C_3H_7$ | 30 | 30 | 84 |
| 24 | *n*-$C_3H_7$ | *i*-$C_3H_7$ | *i*-$C_3H_7$ | 45 | 45 | 80 |
| 25 | *n*-$C_3H_7$ | $CH_3$ | $C_2H_5$ | 30 | 30 | 82 |
| 26 | *n*-$C_3H_7$ | *n*-$C_3H_7$ | $C_2H_5$ | 30 | 35 | 88 |
| 27 | *n*-$C_3H_7$ | *i*-$C_3H_7$ | $C_2H_5$ | 35 | 30 | 81 |
| 28 | *n*-$C_3H_7$ | *n*-$C_3H_7$ | $CH_3$ | 30 | 35 | 84 |
| 29 | *n*-$C_3H_7$ | *i*-$C_3H_7$ | *n*-$C_3H_7$ | 35 | 35 | 82 |
| 30 | *n*-$C_3H_7$ | *i*-$C_3H_7$ | $CH_3$ | 30 | 35 | 88 |
| 31 | *i*-$C_3H_7$ | $CH_3$ | $CH_3$ | 35 | 30 | 82 |
| 32 | *i*-$C_3H_7$ | $C_2H_5$ | $C_2H_5$ | 40 | 40 | 83 |
| 33 | *i*-$C_3H_7$ | *n*-$C_3H_7$ | *n*-$C_3H_7$ | 45 | 50 | 80 |
| 34 | *i*-$C_3H_7$ | *i*-$C_3H_7$ | *i*-$C_3H_7$ | 60 | 50 | 85 |
| 35 | *i*-$C_3H_7$ | $CH_3$ | $C_2H_5$ | 30 | 35 | 81 |
| 36 | *i*-$C_3H_7$ | *n*-$C_3H_7$ | $C_2H_5$ | 40 | 35 | 83 |
| 37 | *i*-$C_3H_7$ | *i*-$C_3H_7$ | $C_2H_5$ | 35 | 35 | 83 |
| 38 | *i*-$C_3H_7$ | *n*-$C_3H_7$ | $CH_3$ | 40 | 35 | 84 |
| 39 | *i*-$C_3H_7$ | *i*-$C_3H_7$ | *n*-$C_3H_7$ | 35 | 40 | 85 |
| 40 | *i*-$C_3H_7$ | *i*-$C_3H_7$ | $CH_3$ | 35 | 40 | 86 |

[A]Reactions were monitored by $^{31}P$ NMR in $CDCl_3$ using 162 MHz NMR.
[B]Reactions were carried out at ambient temperature and the products had satisfactory infrared, NMR, and gas chromatography–mass spectrometry coupled technique (GCMS) data. GCMS data were compared with literature values.[28]

It must be noted that a limitation of this new method is the non-commercial availability of CC-2. Nevertheless, it can be easily prepared and stored in the laboratory using the straightforward method described in ref. [25].

## Experimental

### *General Experimental Procedure*

In a typical experimental procedure, dialkylphosphite (0.2 mol) was added in a suspended solution of *N,N′*-dichlorobis(2,4,6-trichlorophenyl)urea (48.8 g, 0.1 mol) in 150 mL acetonitrile, and the reaction mixture was stirred for 10–30 min. The progress of the reaction was monitored by $^{31}P$ NMR spectroscopy by drawing a few milligrams of reaction mixture to determine the consumption of dialkyl phosphite. A white amorphous precipitate of symmetrical bis(2,4,6-trichlorophenyl)urea **4** formed. When precipitation of **4** ceased, the reaction mixture was cooled to 0°C and neutral alumina (30.60 g, 0.3 mol) was added. The dialkylamine (0.2 mol) was added slowly while shaking the heterogeneous reaction mixture on a vortex shaker. The progress of the reaction was further monitored by $^{31}P$ NMR spectroscopy to determine the consumption of dialkyl chlorophosphate by drawing a few milligrams of reaction mixture and extracting with ether. After completion of the reaction, the white amorphous precipitate of symmetrical bis(2,4,6-trichlorophenyl)urea **4** and alumina was removed by filtration and washed with acetonitrile (3 × 10 mL). The solvent was removed from the filtrate and the product was distilled under vacuum to get pure DADAP. General

experimental details and data for each compound synthesized can be found in the Accessory Publication.

## Conclusions

In conclusion, we have developed a simple, rapid, economical, and efficient one-pot procedure for the preparation of DADAP. The method is very useful to build up the spectral database of CWC-related phosphoramidates. The method could also be extended to prepare other phosphoramidates having biological activity. It will make a useful and an important addition to existing methodologies. In addition to this, the recycling and reusing of the reagent and the convenient workup producing high yields makes it an attractive methodology. Further application of CC-2 in the synthesis of various organic compounds is in progress and will be reported in due course.

## Accessory Publication

General experimental details and data for each compound synthesized are available from the authors or from the *Australian Journal of Chemistry* until November 2011.

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## References

[1] M. Palit, D. Pardasani, A. K. Gupta, P. Shakya, D. K. Dubey, *Anal. Bioanal. Chem.* **2005**, *381*, 477. doi:10.1007/S00216-004-2873-X

[2] P. Shakya, D. K. Dubey, D. Pardasani, M. Palit, A. K. Gupta, *Catal. Commun.* **2005**, *6*, 669. doi:10.1016/J.CATCOM.2005.05.015

[3] A. K. Gupta, P. D. Shakya, D. Pardasani, M. Palit, D. K. Dubey, *Rapid Commun. Mass Spectrom.* **2005**, *19*, 975. doi:10.1002/RCM.1876

[4] J. Acharya, P. D. Shakya, D. Pardasani, M. Palit, D. K. Dubey, *J. Chem. Res.* **2005**, *3*, 194.

[5] A. K. Gupta, M. Palit, D. Pardasani, P. D. Shakya, R. K. Srivastava, D. K. Dubey, *Eur. J. Mass Spectrom.* **2005**, *11*, 309. doi:10.1255/EJMS.741

[6] M. D. Crenshaw, D. B. Cummings, *Phosphorus Sulfur* **2004**, *179*, 1009. doi:10.1080/10426500490459632

[7] (a) O. Kostiainen, *Gas Chromatography in Screening of Chemicals Related to the Chemical Weapons Convention*, in *Chemical Weapons Chemical Analysis: Sample Collection, Preparation, and Analytical Methods* (Ed. Markku Mesilaakso) **2005**, pp. 185–248 (John Wiley & Sons: Chichester, UK).
(b) E. W. J. Hooijschuur, C. E. Kientz, U. A. Brinkman, *J. Chromatogr. A* **2002**, *982*, 177. doi:10.1016/S0021-9673(02)01426-7
(c) R. M. Black, B. Muir, *J. Chromatogr. A* **2003**, *1000*, 253. doi:10.1016/S0021-9673(03)00183-3

[8] (a) E. W. J. Hooijschuur, C. E. Kientz, U. A. Th. Brinkman, *J. Chromatogr. A* **2002**, *982*, 177. doi:10.1016/S0021-9673(02)01426-7
(b) Ch. E. Kientz, *J. Chromatogr. A* **1998**, *814*, 1. doi:10.1016/S0021-9673(98)00338-0

[9] (a) Convention on the Prohibition of the Production, Stockpiling and use of Chemical Weapons and their Destruction, Technical Secretariat of the Organisation for Prohibition of Chemical Weapons **1997**, The Hague; http://www.opcw.nl, accessed 29 April 2007.
(b) W. Krutzsch, R. Trapp, *A Commentary of CWC* **1994** (Martinus Nijhoff: Dordrecht).

[10] (a) *Work Instructions for the Preparation of Test Samples for OPCW Proficiency Tests, QDOC/LAB/WI/PT2* 17 September **2004** (Technical Secretariat OPCW: The Hague).
(b) *Work Instructions for the Evaluation of Results of OPCW Proficiency Tests, QDOC/LAB/WI/PT3* 17 September **2004**.
(c) M. Rautio, *Recommended Operating Procedures for Sampling and Analysis in the Verification of Chemical Disarmament* **1994** (Ministry for Foreign Affairs of Finland: Helsinki).
(d) *Standard Operating Procedure for the Organization of OPCW Proficiency Tests, QDOC/LAB/SOP/PT1* 17 September **2004**.

[11] (a) E. R. J. Wils, *Gas Chromatography/Mass Spectrometry in Analysis of Chemicals Related to the Chemicals Weapons Convention* in *Encyclopedia of Analytical Chemistry* **2000**, p. 979 (Ed. R. A. Meyers) (John Wiley: Chichester, UK).
(b) R. M. Black, J. M. Harrison, in *The Chemistry of Organophosphorus Compounds* (Ed. F. R. Hartley) **1996** (Wiley–Interscience: Chichester, UK).

[12] (a) P. A. D'Agostino, L. R. Provost, *J. Chromatogr. A* **1992**, *598*, 89. doi:10.1016/0021-9673(92)85118-D
(b) D. K. Rohrbaugh, E. W. Sarver, *J. Chromatogr. A* **1998**, *809*, 141. doi:10.1016/S0021-9673(98)00184-8

[13] (a) E. R. J. Wils, *Fresenius'. J. Anal. Chem.* **1990**, *338*, 22. doi:10.1007/BF00322778
(b) H. D. Durst, J. R. Mays, J. L. Ruth, B. R. Williams, R. V. Duevel, *Anal. Lett.* **1998**, *31*, 1429.
(c) E. W. J. Hooijschuur, A. G. Hulst, Ad. L. De Jong, L. P. de Reuver, S. H. Van Krimpen, B. L. M. Van Baar, E. R. J. Wils, C. E. Kientz, U. A. Th. Brinkman, *Trends Anal.Chem.* **2002**, *21*, 116. doi:10.1016/S0165-9936(01)00140-6

[14] (a) M. Mesilaakso, M. Rautio, in *Encyclopedia of Analytical Chemistry* **2000**, p. 899 (John Wiley: Chichester, UK).
(b) M. Mesilaakso, *Chemical Weapons Convention Chemicals Analysis* **2005** (John Wiley & Sons: Chichester, UK).

[15] J. I. G. Cadogan, R. K. Mackie, J. A. Maynard, *J. Chem. Soc. C* **1967**, 1356.

[16] H. E. Baumgarten, R. A. Setterquist, *J. Am. Chem. Soc.* **1959**, *81*, 2132. doi:10.1021/JA01518A028

[17] I. Kers, J. Stawinski, *Tetrahedron Lett.* **1998**, *39*, 1219. doi:10.1016/S0040-4039(97)10734-1

[18] L. A. Adams, R. J. Cox, J. S. Gibson, M. B. Mayo-Martin, M. Walter, W. Whittingham, *Chem. Commun.* **2002**, 2004. doi:10.1039/B206199F

[19] J. K. Chen, R. G. Schultz, D. H. Lloyd, S. M. Grayaznov, *Nucleic Acids Res.* **1995**, *23*, 2661. doi:10.1093/NAR/23.14.2661

[20] (a) F. R. Atherton, H. T. Openshaw, A. R. Todd, *J. Chem. Soc.* **1945**, 660. doi:10.1039/JR9450000660
(b) M. Goldwhite, B. C. Saunders, *J. Chem. Soc.* **1955**, 3564.

[21] P. K. Chakravarty, W. J. Greenlee, W. H. Parsons, A. A. Partchett, P. Combs, A. Roth, R. D. Busch, T. N. Mellin, *J. Med. Chem.* **1989**, *32*, 1886. doi:10.1021/JM00128A033

[22] J. M. Desmarchelier, T. R. Fukuto, *J. Org. Chem.* **1972**, *37*, 4218. doi:10.1021/JO00798A066

[23] D. E. C. Corbridge, B. V. Amsterdam, *Phosphorus: an Outline of its Chemistry, Biochemistry and Technology, 4th edn* **1990**, Ch. 5, p. 403 (Elsevier: Amsterdam).

[24] G. M. Kosolapoff, L. Maier, in *Organic Phosphorus Compounds* **1973**, Vol. 6 (John Wiley & Sons: New York, NY).

[25] D. K. Dubey, R. C. Malhotra, R. V. Vaidyanathswamy, R. Vijayaraghavan, *J. Org. Chem.* **1993**, *64*, 8301.

[26] R. Vijayaraghavan, P. Kumar, D. K. Dubey, R. Singh, *Biomed. Environ. Sci.* **2002**, *15*, 25.

[27] (a) P. D. Shakya, D. K. Dubey, D. Pardasani, M. Palit, A. K. Gupta, *J. Chem. Res.* **2005**, 821.
(b) B. C. Bag, K. Sekhar, D. K. Dubey, M. Sai, R. S. Dangi, M. P. Kaushik, C. Bhattacharya, *Org. Process Res. Dev.* **2006**, *10*, 505. doi:10.1021/OP060002P

[28] *Central OPCW Analytical Database, ver. 6*, Released September **2004** (Technical Secretariat of OPCW: The Hague).