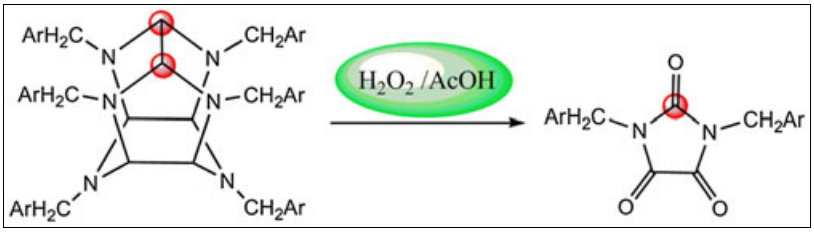
Green Synthesis of 1,3-Dibenzylimidazolidine-2,4,5-triones by Oxidation of Hexabenzylhexaazaisowurtzitanes

Ahmad Khorramabadi-zad,[a]* Mohammad Azadmanesh,[a] and Yadollah Bayat[b]

[a]Faculty of Chemistry, Bu-Ali Sina University, Hamedan 6517838695, Iran
[b]Department of Chemistry, Malek Ashtar University of Technology, P.O. Box 16765-3454, Tehran, Iran
*E-mail: khoram@gmail.com

Additional Supporting Information may be found in the online version of this article.
Received September 12, 2016
DOI 10.1002/jhet.2831
Published online 00 Month 2017 in Wiley Online Library (wileyonlinelibrary.com).



Herein, a novel and convenient procedure is described for the preparation of 1,3-dibenzylimidazolidine-2,4,5-triones. This method is based on a multi-stage oxidation of hexabenzylhexaazaisowurtzitanes by hydrogen peroxide in acetic acid, leading to the title compounds in relatively good yields.

J. Heterocyclic Chem., **00,** 00 (2017).

INTRODUCTION

Five-membered rings containing two heteroatoms are privileged structures with proven utility in medicinal chemistry [1]. One example of such a heterocycle comprises imidazoline and imidazolidine. Imidazolines are biologically active pharmacophores and synthetic intermediates in medicinal chemistry [2–12]. Another member of this family is imidazolidine-2,4,5-trione (commonly known as parabanic acid) and its derivatives; they are used in preparation of alkylidene and imino-substituted hydantoins by their reactions with Wittig reagents [13]. Parabanic acid has a pronounced herbicidal action, controlling the growth of unwanted plants.

Although parabanic acid, the main skeleton of the titled compounds, is produced as a byproduct during synthesis of 1,1-diamino-2,2-dinitroethylene (DADE) as an energetic material [14], few processes have been published for the preparation of substituted parabanic acid and its derivatives, for example, reaction of trimethylsilyl cyanide with aryl isocyanates [15] and the reaction of urea derivatives with oxalyl chloride [13].

It is interesting that in our laboratory, however, 1,3-dibenzylimidazolidine-2,4,5-trione (a derivative of parabanic acid sold at about 40 $ per 1mg), was unexpectedly formed during oxidation of hexabenzyl-hexaazaisowurtzitane (HBIW). The latter compound is itself the very starting material for the synthesis of hexanitrohexaazaisowurtzitane (also called HNIW and CL-20). CL-20 is the most powerful explosive known having higher performance than other conventional explosives for which various synthesis methods have been reported without going into details. Because of the importance of CL-20 in areas such as missile industry, developing new procedures for its preparation may be of economic value. One way to achieve CL-20 is to start with hexaacetylhexaazaisowurtzitane (HAIW). This compound has been prepared from HBIW through a costly, multi step, and time-consuming reaction.

Therefore, direct conversion of HBIW into HAIW, by the reaction of *N*-oxide intermediate with acetyl chloride (through the presumed Polonovski rearrangement) was attempted. For this purpose, HBIW was treated with H_2O_2 in acetic acid. However, instead of the above said intermediate, a white crystalline compound was formed, which was found to be 1,3-dibenzylimidazolidine-2,4,5-trione (Fig. 1, R=H). The successful synthesis of 1,3-dibenzylimidazolidine-2,4,5-trione, prompted us to prepare other derivatives of this compound. For this purpose, three other derivatives of HBIW were synthesized according to the procedure of Nielsen and coworkers [16], and subjected to the above said oxidation reaction (Fig. 1, R= 2-Cl, 4-CH_3, 4-OCH_3).

RESULTS AND DISCUSSION

As was mentioned earlier, our main purpose was to synthesize HAIW from HBIW by Polonovski rearrangement of the *N*-oxide intermediate in the presence of acetyl chloride. However, instead of *N*-oxide intermediate, the oxidation of HBIW led merely to a crystalline compound which was confirmed to be 1,3-dibenzylimidazolidine-2,4,5-trione.

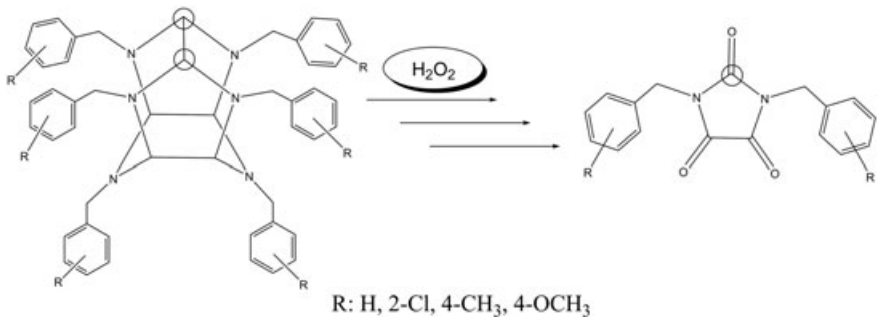


Figure 1. Synthesis of 1,3-dibenzylimidazolidine-2,4,5-triones from HBIWs.

To explain this phenomenon, it is reasonable to first consider the structure of HBIW. Its X-ray analysis shows that C_1–C_7 bond length (Fig. 2, circled atoms) is longer than normal sp^3–sp^3 carbon bond [17], which may be due to the strained molecular skeleton of this compound weakening the C_1–C_7 bond.

In addition, according to a previous report, the C_1–C_7 bond in HBIW is broken in the presence of $CuCl_2$ (as a mild oxidizing agent) in pyridine [18]. It is therefore logical to conclude that the reaction may follow a similar pathway in the presence of H_2O_2 and acetic acid (Fig. 3). Furthermore, based on a reported oxidative cleavage of HBIW in the presence of CAN [19], it is plausible that in the first step of the proposed mechanism a dication species (II) is formed. This dication is then hydroxylated by H_2O to III (step 2) which is itself oxidized to IV. In the following steps, the remaining C—H bonds are successively oxidized to C-OOAc ones (V), the oxidative cleavage of which leads to the desired product (VI).

CONCLUSION

In summary, a new oxidation system (H_2O_2/AcOH) was developed for the synthesis of 1,3-dibenzylimidazolidine-2,4,5-triones from HBIWs with good yields. H_2O_2/AcOH mixture is equivalent to peracetic acid which is a strong and benign oxidizing agent. The advantages of this procedure over previously reported ones (which have made use of an unsafe reagent such as oxalyl chloride [13] or the highly toxic trimethylsilyl chloride [15]) are that it is highly efficient and sustainable using a cheap, easily available, green, and non-toxic environmentally friendly reagent for defragmentation of HBIW and its derivatives. In short, while highly expensive 1,3-dibenzylimidazolidine-2,4,5-trione has been previously prepared from urea and oxalyl chloride, it was shown that this compound and its analogues could be synthesized from corresponding HBIW derivatives.

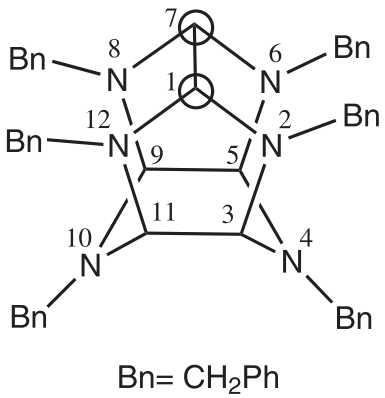


Figure 2. HBIW structure.

EXPERIMENTAL

IR spectra were recorded using KBr. ^{1}H NMR, ^{13}C NMR, and DEPT spectra were run in $CDCl_3$. Mass spectra were recorded on a Shimadzu QP 1100 BX Mass Spectrometer All chemicals and solvents were purchased and used as received. HBIW and its derivatives were synthesized according to the procedure of Nielsen and coworkers [16], primarily washed with ethanol and then recrystallized from ethyl acetate. All spectral data of the products are fully consistent with those of the reported ones.

General procedure for the synthesis of 1,3-dibenzylimidazolidine-2,4,5-triones. In 20 mL of acetic acid, 10 mmol of HBIW was dissolved; the reaction vessel was placed in ice bath into which was poured 40 mL of 35% H_2O_2 by dropping funnel in 5 min. Reaction temperature was raised to 70°C during 5 h after which the solution color was changed from red to orange. The mixture was then cooled to room temperature, 30 mL of water was added, and the yellow precipitate was collected and washed with two portions of 20 mL of 50% ethanol. Recrystallizing the crude solid in acetone/water (5/2) afforded white crystals (see Table 1 for melting points and reaction yields).

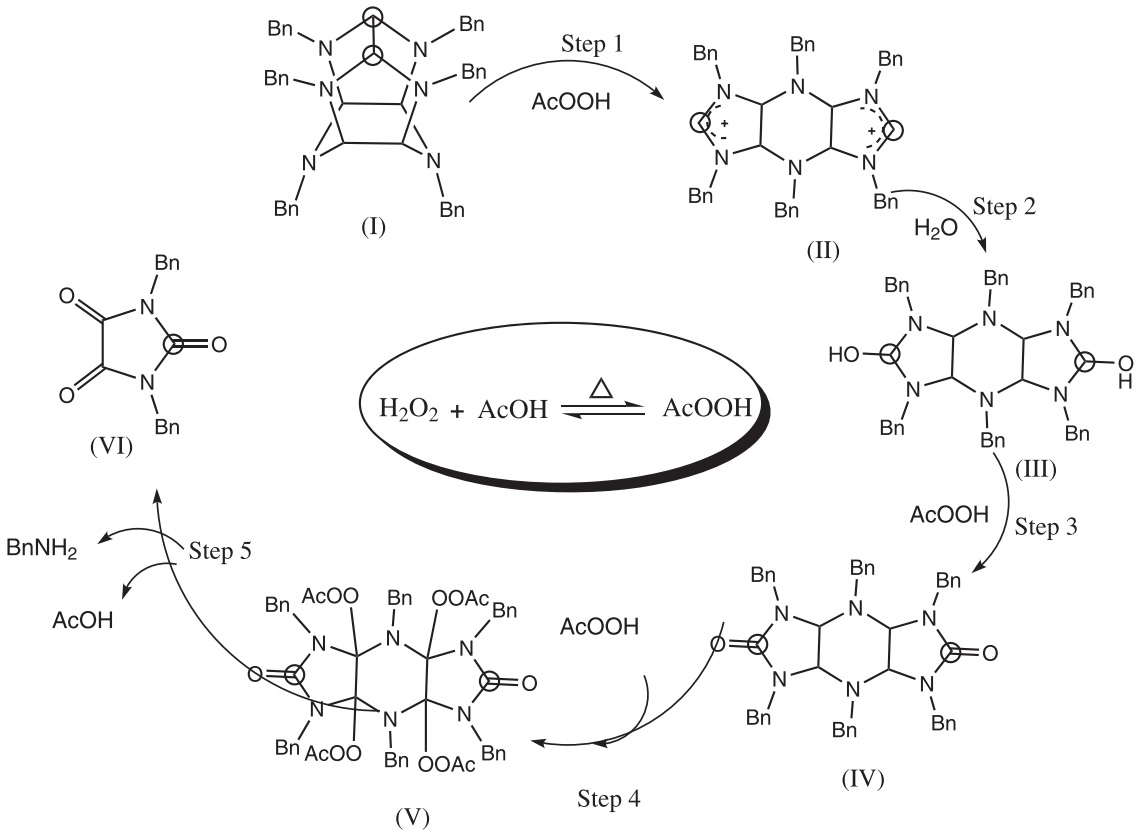


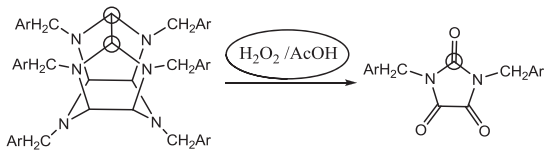
Figure 3. Plausible mechanism for the oxidation of HBIW by H_2O_2/AcOH.

Spectral data of the unsubstituted product (Table 1, entry 1) is fully compatible with the previously reported ones [20]. The other derivatives of 1,3-dibenzylimidazolidine-2,4,5-trione, synthesized by this procedure, were fully characterized by their ^{1}H NMR, ^{13}C NMR, IR, and Mass spectra (see vide infra and supplementary document).

Spectral data of 1,3-dibenzylimidazolidine-2,4,5-trione derivatives. ***1,3-dibenzylimidazolidine-2,4,5-trione (2a).*** ^{1}H-NMR (250 MHz, $CDCl_3$) δ4.76 (s,4H), 7.25–7.38 (m,10H); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ43.0, 128.7, 129.0, 134.4, 153.4, 156.4; DEPT (135, $CDCl_3$): 43.0 (CH_2), 128.6, 129.0; MS (*m/z*): 294 (M^+); IR (KBr, cm^{-1}): 3032, 1728, 1448, 1412, 1146, 731, 696, 613, 562, 454.

Table 1

Synthesis of 1,3-dibenzylimidazolidine-2,4,5-trione derivatives.



1 **2**

Ar = a: C_6H_5; b: 2-ClC_6H_4; c: 4-$CH_3C_6H_4$; d: 4-$OCH_3C_6H_4$

Entry	Ar	Product	Melting point (°C)	Yield (%)
1	C_6H_5	2a	167–169	53
2	2-ClC_6H_4	2b	198–201	45
3	4-$CH_3C_6H_4$	2c	151–153	57
4	4-$OCH_3C_6H_4$	2d	145–147	15

1,3-bis(2-chlorobenzyl)imidazolidine-2,4,5-trione (2b). ^{1}H-NMR (500 MHz, $CDCl_3$) δ4.96 (s, 2H), 7.24–7.33 (m, 3H), 7.39 (d, J = 6.82 Hz, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ41.4, 127.6, 130.3, 130.4, 130.5, 131.9, 133.8, 153.4, 156.4; Anal. Found for $C_{17}H_{12}Cl_2N_2O_3$: C, 56.15; H, 3.27; N, 7.64. Calcd: C, 56.22; H, 3.33; N, 7.71; MS (*m/z*): 363 (M^+); IR (KBr, cm^{-1}): 3065, 3011, 1817, 1778, 1728, 1442, 1417, 1356, 1149, 754, 637, 513.

1,3-bis(4-methylbenzyl)imidazolidine-2,4,5-trione (2c). ^{1}H-NMR (500 MHz, $CDCl_3$) δ2.33 (s, 3H), 4.71 (s, 2H), 7.14 (d, J = 7.82 Hz, 2H), 7.27 (d, J = 7.96 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ21.6, 43.1, 129.3, 130.0, 131.9, 138.9, 153.8, 156.8; Anal. Found for $C_{19}H_{18}N_2O_3$: C, 70.55; H, 5.53; N, 8.73. Calcd: C, 70.79; H, 5.63; N, 8.69; MS (*m/z*): 322 (M^+); IR (KBr, cm^{-1}): 2924, 2856, 1821, 1728, 1518, 1447, 1409, 1353, 1147, 1061, 905, 793, 768, 523.

1,3-bis(4-methoxybenzyl)imidazolidine-2,4,5-trione (2d). ^{1}H-NMR (500 MHz, $CDCl_3$) δ3.78 (s, 3H), 4.65 (s, 2H), 6.85 (d, J = 8.43 Hz, 2H), 7.32 (d, J = 8.40 Hz, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ42.8, 55.7, 114.7, 127.1, 130.9, 153.9, 156.8, 160.2; Anal. Found for $C_{19}H_{18}N_2O_5$: C, 64.32; H, 5.01; N, 7.84. Calcd: C, 64.40; H, 5.12; N, 7.91; MS (*m/z*): 354 (M^+); IR (KBr, cm^{-1}): 2965, 2939, 2835, 1819, 1783, 1725, 1614, 1515, 1454, 1439, 1408, 1355, 1287, 1249, 1180, 1147, 1030, 828, 811, 603, 539.

Acknowledgements. We gratefully acknowledge the support of this work by the Research Council of Bu-Ali Sina University. We specially thank Professor Issa Yavari (Tarbiat Modares University, Tehran, Iran) for his highly fruitful discussions.

REFERENCES AND NOTES

[1] Kurz, T.; Widyan, K. Tetrahedron Lett 2004, 45, 7049.
[2] Hayashi, T.; Kishi, E.; Soloshonok, V. A.; Uozumi, Y. Tetrahedron Lett 1996, 37, 4969.
[3] Jung, M. E.; Huang, A. Org Lett 2000, 2, 2659.
[4] Lin, Y. R.; Zhou, X. T.; Dai, L. X.; Sun, J. J Org Chem 1997, 62, 1799.
[5] Langlois, Y.; Dalko, P. I. Org Chem 1998, 63, 8107.
[6] Doyle, M. E.; Egan, J. M. Pharmacol Rev 2003, 55, 105.
[7] Meidute-Abaraviciene, S.; Mosen, H.; Lundquist, I.; Salehi, A. Acta Physiol 2009, 195, 375.
[8] Touzeau, F.; Arrault, A.; Guillaumet, G.; Scalbert, E.; Pfeiffer, B.; Rettori, M. C.; Renard, P.; Merour, J. Y. J Med Chem 2003, 46, 1962.
[9] Masajtis-Zagajewska, A.; Majer, J.; Nowicki, M. Hypertens Res 2010, 33, 348.
[10] Li, H. Y.; Drummond, S.; DeLucca, I.; Boswell, G. A. Tetrahedron 1996, 52, 11153.
[11] Vinodkumar, R.; Vaidya, S. D.; Siva Kumar, B. V.; Bhise, U. N.; Bhirud, S. B.; Mashelkar, U. C. Eur J Med Chem 2008, 43, 986.
[12] Navarrete-Vázquez, G.; Rojano-Vilchis, M. M.; Yépez-Mulia, L.; Meléndez, V.; Gerena, L.; Hernández-Campos, A.; Castillo, R.; Hernández-Luis, F. Eur J Med Chem 2006, 41, 135.
[13] Üngören, S. H.; Kani, I.; Günay, A. Tetrahedron Lett 2012, 53, 4758.
[14] Latypov, N. V.; Bergman, J.; Langlet, A.; Wellmar, U.; Bemm, U. Tetrahedron 1998, 54, 11525.
[15] Inaba, S.-I.; Ojlma, I. J Organomet Chem 1979, 169, 171.
[16] Nielsen, A. T.; Nissan, R. A.; Vanderah, D. J.; Coon, C. L.; Gilardi, R. D.; George, C. F.; Flippen-Anderson, J. J Org Chem 1990, 55, 1459.
[17] Crampton, M. R.; Hamid, J.; Millar, R.; Ferguson, G. J Chem Soc, Perkin Trans 1993, 2, 923.
[18] Sysolyatin, S. V.; Lobanova, A. A.; Chernikova, Y. T.; Sakovich, G. V. Russ Chem Rev 2005, 74, 757.
[19] Guan, X. P.; Yan, H.; Sun, J. G.; Yu, Y. Z. Molecules 1999, 4, 69.
[20] García-Egido, E.; Paz, J.; Iglesias, B.; Muñoz, L. Org Biomol Chem 2009, 7, 3991.