Organic Process Research & Development

TECHNICAL NOTE

pubs.acs.org/OPRD

A Safe Two-Step Process for Manufacturing Glycidyl Nitrate from Glycidol Involving Solid−Liquid Phase-Transfer Catalysis

José R. Ochoa-Gómez[†,*] and Juan J. Blanco-Gómez[‡]

[†]Universidad Alfonso X el Sabio, Department of Industrial Technology, Avda de la Universidad 1, 28696 Villanueva de la Cañada, Madrid, Spain, and Tecnalia Research and Innovation, Tecnalia-Energy, Department of Bioenergy, Parque Tecnológico de Álava, Leonardo Da Vinci, 11, 01510 Miñano, Álava, Spain

[‡]Reuser S.L., C/Chile 10, Edificio Madrid 92, Oficina 43, 28290 Las Rozas, Madrid, Spain

ABSTRACT: A new and safer two-step process for manufacturing glycidyl nitrate from glycidol is reported. In the first step glycidyl tosylate is obtained by reacting glycidol with *p*-tosyl chloride in the presence of triethylamine according to any one of the well-known procedures for obtaining tosyl esters described in the literature. In the second step, glycidyl tosylate is reacted with $NaNO_3$ in refluxing acetonitrile under solid−liquid phase-transfer catalysis conditions using tetrabutylammonium nitrate as catalyst. Acetonitrile and the phase-transfer catalyst were recycled 12 times without deactivation, yielding 99% pure glycidyl nitrate in a cumulative isolated yield of 81.5% with a catalyst turnover number of 85.7 mol substrate per mol phase-transfer catalyst. This procedure avoids the use of the dangerous reactants used in the current manufacturing processes of glycidyl nitrate and could be useful as a safe and general method for obtaining nitrate esters.

INTRODUCTION

Glycidyl nitrate (GN) is a valuable chemical used for manufacturing energetic polymers such as hydroxy-terminated poly(glycidyl nitrate) which in turn is used as a component of high-energy binder matrices in propellant compositions.[1] GN has been synthesized from glycidol by a two-step procedure in which glycidyl tosylate (GT) is obtained from glycidol and tosyl chloride (TsCl) in a first step, and GT is converted into GN in a second step by reacting with concentrated (70 wt %) HNO_3 at 10 °C or less under N_2 atmosphere,[2,3] from glycidol in a single step by reaction with N_2O_5 in an inert solvent such as dichloromethane at temperatures between −10 °C and −20 °C,[4] and from glycerol in a two-step synthesis in which dinitroglycerol is first obtained by reacting glycerol with concentrated (90 wt %) HNO_3 in CH_2Cl_2 at temperatures below 15 °C, and subsequently it is reacted with 50 wt % NaOH in CH_2Cl_2 at temperatures below 25 °C to yield GN.[5] All of these synthetic methods have in common the use of hazardous chemicals (N_2O_5 and concentrated HNO_3) and/or the formation of dangerous intermediates and/or byproduct such as dinitroglycerol and nitroglycerin. However, green and safer synthetic pathways of energetic materials for defense and space applications are currently desired.[6]

In this contribution, a safe and easy process for manufacturing GN from glycidol avoiding the above-mentioned drawbacks is described (Scheme 1). The procedure consists of two steps: (a) step 1: synthesis of GT by reacting glycidol with TsCl in the presence of triethylamine (TEA) to scavenge the HCl formed and (b) step 2: synthesis of GN by reacting GT with solid $NaNO_3$ in refluxing acetonitrile (ACN) using tetrabutylammonium nitrate (TBAN) as a solid−liquid phase-transfer catalyst (PTC). This synthetic pathway could be used as a safe and general method for obtaining nitrate esters useful as explosives and pharmaceuticals.

RESULTS AND DISCUSSION

Manufacturing of Glycidyl Tosylate (GT) (Step 1). The preparation of tosyl esters is a well-known reaction which often proceeds in yields higher than 90% in the presence of a base such as triethylamine.[7,8] Consequently, we have not studied this step at this process development stage but instead we have used commercially available GT.

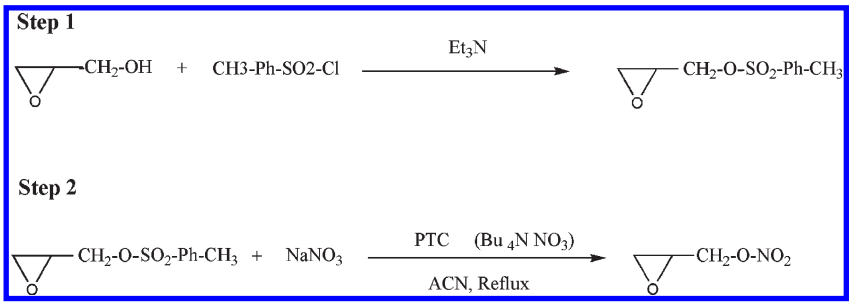
Manufacturing of Glycidyl Nitrate from Glycidyl Tosylate (Step 2). No GN formation was detected in a series of preliminary experiments carried out using solid $NaNO_3$ as nucleophile and molten GT as both solvent and reactant at temperatures between 50 and 100 °C. However, reaction was observed in aprotic organic solvents such as dimethylacetamide (DMA) and dimethylformamide (DMF). For instance, a 95% yield (HPLC, not isolated) was obtained in DMA after 5 h, but temperatures close to 100 °C were needed, and glycidol was formed as a byproduct probably by base-catalyzed hydrolysis of GT due to the presence of water, always present in trace amounts in such hygroscopic solvents. Likewise, glycerol 1-mononitrate was detected in very low amounts together with acetic acid resulting from GN and solvent hydrolysis, respectively. On the other hand, the proximity between the boiling points of GN (179.7 °C) and DMA (165 °C) was a drawback for a straightforward isolation of GN in high purity. ACN is a solvent that could facilitate the isolation of GN because it is easily removed from a reaction mixture by evaporation at mild temperatures, but no reaction was observed in said solvent after 7 h under reflux, very probably due to the insolubility of $NaNO_3$ in ACN which makes NO_3^- not available for reaction with GT.

Special Issue: Safety of Chemical Processes 11

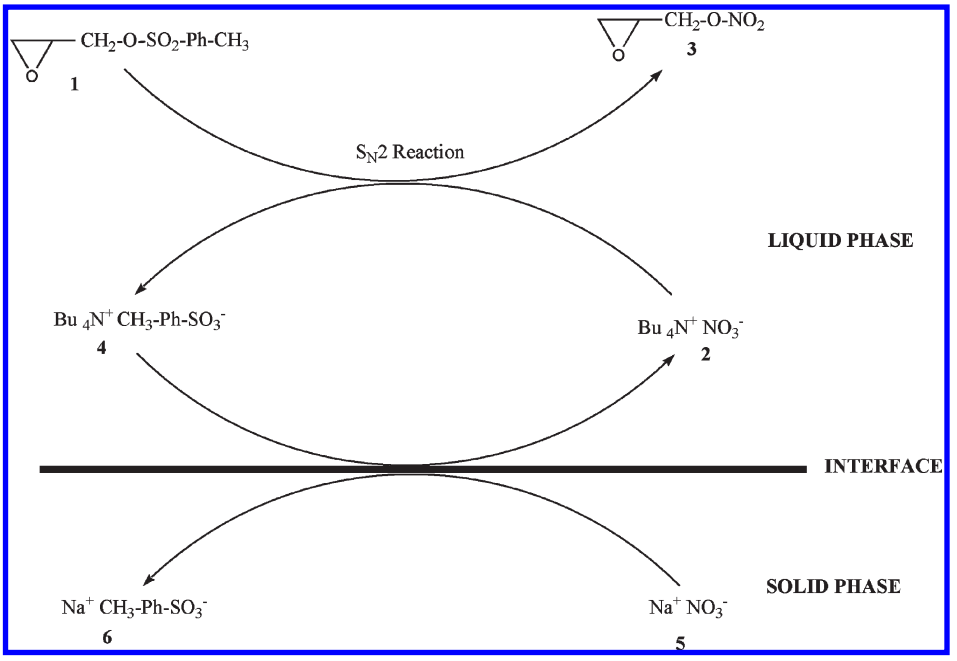
Received: March 17, 2011
Published: April 19, 2011

dx.doi.org/10.1021/op200066e | *Org. Process Res. Dev.* 2011, 15, 1454–1457

Scheme 1. Proposed two-step synthesis of glycidyl nitrate from glycidol (PTC = phase-transfer catalyst)



Scheme 2. Schematic representation of step 2



Phase-transfer catalysis is a well-known methodology for facilitating interphase transfer of species, making reactions between reagents in two immiscible phases possible.[9,10] Consequently, we thought that the reaction could proceed in ACN if NO_3^- could be transferred from the solid phase to the liquid one by means of a PTC soluble in ACN. Quaternary ammonium salts are typical PTC, but we decided to reject quaternary ammonium halides as PTCs because their halide anions could act as nucleophiles yielding the corresponding epihalohydrins. Finally, we decided that the best choice was to use a quaternary ammonium nitrate because nitrate was the desired nucleophile for the intended reaction. Tetrabutylammonium nitrate (TBAN) was ultimately chosen as PTC to be tested in this reaction. According to our hypothesis, the reaction should proceed as depicted in Scheme 2. TBAN **2** would be solubilized in ACN and could react with GT **1** through a S_N2 mechanism to give the desired product **3** and tetrabutylammonium *p*-tolylsulfonate **4**. The latter would react at the solid−liquid interface with $NaNO_3$ **5** in the solid phase, yielding sodium *p*-tolylsulfonate **6**, which would precipitate from the reaction medium, and TBAN **2**, thereby achieving the transference of the nitrate ion from the solid to the liquid phase and allowing the reaction to proceed to completion.

Our hypothesis was confirmed by reacting GT (0.25 mol), $NaNO_3$, and TBAN in a 1:1.5:0.14 molar ratio, respectively, in refluxing ACN (60 g, 82 °C) for 6 h under vigorous stirring. GN yield was 58% by HPLC, and 99% pure GN was isolated in a 34% yield after workup. A much higher isolated yield of 76% was obtained by carrying out the reaction under the same conditions but in a 1:3.2:0.14 GT/$NaNO_3$/TBAN molar ratio, indicating that GT/$NaNO_3$ molar ratio is a key parameter although its influence on conversions and yields has not been deeply studied. The residue obtained after workup consisted of quaternary ammonium salt, unreacted GT (in low amounts as detected by TLC with $CHCl_3$ as eluent, UV detection at 254 nm), and undistilled GN. Then, the possibility of recycling this residue was studied by adding fresh GT (0.25 mol) and $NaNO_3$ in a 1:3.2 molar ratio and recycling the ACN previously recovered by evaporation. No amount of TBAN was added. Reaction was then repeated under the same conditions, and the residue obtained after workup was successively recycled by adding into it fresh GT and $NaNO_3$ at the above-mentioned molar ratio, and using the recovered acetonitrile from the former reaction as solvent.

Results are depicted in Figure 1. As it can be seen, the isolated cumulative yield increases slightly with the number of recycles

dx.doi.org/10.1021/op200066e |*Org. Process Res. Dev.* 2011, 15, 1454–1457

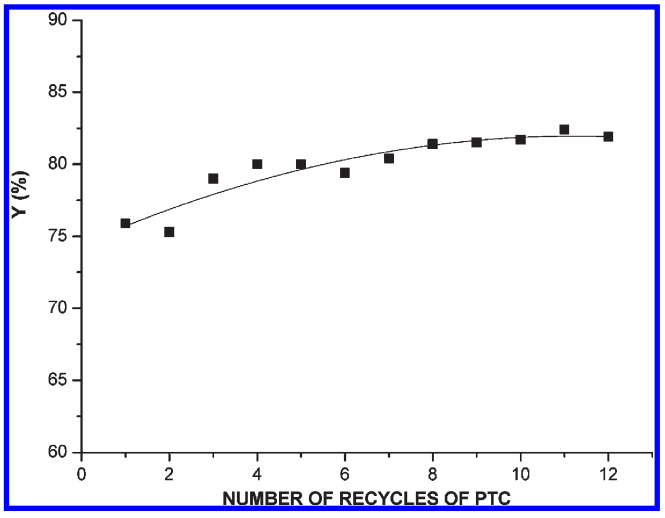


Figure 1. Cumulative isolated glycidyl nitrate yield (Y) versus the number of recycles of phase-transfer catalyst (PTC) and solvent.

from 76% at run 1 to 81.5% at run 8 and then remains constant. Catalyst turnover number (TON) was 85.7 mol substrate/mol PTC (69.8 mol of isolated GN per mol of PTC) and probably may be significantly increased according to the results shown in Figure 1 in which no loss in catalyst activity is observed.

The reaction was also carried out on a 2-L scale with the same results.

Ideas for Process Optimization. In our opinion, any project for process optimization should address at least the following items:

(a) **Reduction of Solvent Inventory.** In a further development of step 1 the same solvent, ACN, used in step 2 should be the first choice.

(b) **Process Intensification.** If items (a) works successfully, a process intensification of the overall process could be easily carried out; after completion of step 1, the reaction mixture is filtered to remove the precipitate of TEA hydrochloride, and the filtrate consisting of a solution of GT in ACN is directly used in step 2 without further purification.

(c) **TEA Recovery in Step 1.** TEA hydrochloride obtained as byproduct can be treated with aqueous NaOH to release TEA which can be easily separated by distillation and recycled to the TsCl synthesis, or alternatively, TEA can be recovered by treating an aqueous solution of TEA hydrochloride by electrohydrolysis with bipolar membranes,[11,12] generating a useful aqueous HCl stream at the same time.

(d) **Recovery of Excess $NaNO_3$ and Sodium *p*-Tolylsulfonate in Step 2.** A solid mixture consisting of unreacted $NaNO_3$ and sodium *p*-tolylsulfonate is obtained as waste in step 2, but taking into account the different characteristics of both salts, their separation by solid−liquid extraction or fractional crystallization must not be a difficult task, bearing in mind that $NaNO_3$ can be recycled to this step even with a relatively large amount of sodium *p*-tolylsulfonate as impurity. After a suitable treatment (for instance, acidification to give the free acid) isolated sodium *p*-tolylsulfonate could be reused for manufacturing the raw material, TsCl, to be used in step 1.

(e) **Safety Data.** Even though step 2 does not seem to be a problematic reaction according to the laboratory observations, the acquisition of reaction safety data by reaction calorimetry and DSC is strongly recommended prior to any further scale-up.

CONCLUSIONS

By taking into account the high yields (often >90%) usually obtained in the synthesis of tosyl esters (step 1), the overall isolated yield of the process herein outlined may be about 75%, a good yield, taking into account that the process has not been optimized. The process is safer than those currently used for manufacturing GN, and the catalyst turnover number was 85.7 mol substrate/mol PTC (69.8 mol of isolated GN per mol of PTC) equivalent to a specific consumption of the phase-transfer catalyst as low as 0.036 kg/kg isolated GN, an amount which can even be further reduced because no catalyst deactivation was observed after 12 recycles. The solvent, ACN, is easily recovered by distillation and recycled. At first, the characteristics of the waste streams generated in step 1 (TEA hydrochloride) and in step 2 (a mixture of $NaNO_3$ and sodium-*p*-toluenesulfonate) should enable, after a relatively easy treatment, a recovery of $NaNO_3$ and the regeneration of TEA and *p*-toluenesulfonyl chloride, all of them to be recycled into the process. Considering that the process has not been optimized, the results obtained are very promising for industrial application.

EXPERIMENTAL SECTION

Materials. All chemicals were chemically pure reagents. TBAN was synthesized by neutralizing a 40 wt % aqueous solution of tetrabutylammonium hydroxide with 20 wt % aqueous nitric acid. After water evaporation at vacuum in a rotatory evaporator, cooling of the concentrated solution, filtering off the precipitated product, and drying at 100 °C overnight, TBAN was obtained as a white solid (mp ranged from 110 to 120 °C, depending on the batch).

Analytical Methods. GN was quantified (wt %) by HPLC using a Perkin-Elmer chromatograph model 3B and a UV detector Perkin-Elmer LC-75 at 195 nm, according to the procedure described by Kaplan et al.[13] ^{1}H NMR spectra were measured with a Varian VXR-200 spectrometer (200 MHz) at 25 °C in $CDCl_3$ using tetramethylsilane as internal reference standard. IR spectra were recorded in a Perkin-Elmer FTIR spectrometer model Spectrum 2000. GN purity was also calculated as the percentage of nitrogen relative to the theoretical one as determined by elemental analysis using a LECO CHN-800 analyzer.

Synthesis of Glycidyl Nitrate (GN). GT (0.25 mol), $NaNO_3$ (0.83 mol), TBAN (0.034 mol), and ACN (60 g) are charged into the reactor described above, and the reaction mixture was refluxed (85 °C) for 6 h under vigorous stirring. Sodium *p*-tolylsulfonate precipitated off with time as a pearly looking solid, causing a significant amount of foam. Consequently, it is advisible to keep the volume of the reaction mixture equal to or below 60% of that of the reactor. Then, the solid obtained consisting of a mixture of unreacted sodium nitrate and sodium *p*-tolylsulfonate was filtered off and washed with ACN. ACN in the combined filtrates was recovered by distillation at 100 mmHg and 50 °C and can be reused in further reactions. The residue was distilled at 1−3 mmHg at a boiler temperature ≤100 °C for avoiding GN degradation. Glycidyl nitrate distillates were obtained as a clear liquid, yielding 22.6 g (0.19 mol, 76% yield) with a purity of 99% as determined by elemental analysis and HPLC.

dx.doi.org/10.1021/op200066e |*Org. Process Res. Dev.* 2011, 15, 1454–1457

Elemental analysis. Calculated: C (30.26%), H (4.23%), N (11.76%), O (53.75%); Found: C (30.09%), H (4.17%), N (11.65%), O (54.09%).

^{1}H NMR: δ ($CDCl_3$) 2.72 (1H, dd); 2.92 (1H, t); 3.29 (1H, m); 4.77 (1H, dd); 4.34 (1H, dd) ppm.

IR: ν max (film): 1632, 1424, 1343, 1280, 1133, 997, 968, 908, 858, 756, 663 cm^{-1}.

AUTHOR INFORMATION

Corresponding Author

*jrochoag@telefonica.net.

ACKNOWLEDGMENT

The contribution of Mr. José M[a] Garrido to the experimental work is gratefully acknowledged.

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