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Nitric acid in dichloromethane solution. Facile preparation from potassium nitrate and sulfuric acid

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Abstract—Pure dry HNO₃ can be liberated from KNO₃ with 96% H_2SO_4 directly into CH_2Cl_2 to yield solutions of variable concentration for use in a number of organic reactions. The present method efficiently replaces the employment of 100% HNO₃ in some synthetic applications, avoiding the problems associated in storage and handling the acid. © 2001 Elsevier Science Ltd. All rights reserved.

Commercial 100% HNO₃ in CH_2Cl_2 solution has recently proved to be a very useful reagent in organic synthesis, either in regio-controlled electrophilic aromatic nitration¹ or in the deprotection of *t*-butyl esters of carboxylic acid² and amino acid derivatives.³ Despite some reports assessing potential explosion hazards in handling HNO₃- CH_2Cl_2 mixtures,⁴ we have never experienced any problem in using such solutions. Nevertheless, purchasing, storage and handling of 100% HNO₃ may represent difficulties, due to the strong oxidising



Entry	Substrate (1) ^b	React. Time (h)	Conversion (%) ^c	Product (2) ^b	Isomer Ratio (o-/m-/p-, rel.%)
1	PhCH ₂ COOMe (1a)	24	>99 (97)	2a	75/8/17
2 ^d	PhCH ₂ COOMe (1a)	1	>99 (93)	2a	49/14/37
3	PhCH ₂ CHO (1b)	2 ^e	97 (95)	2b	84/3/13
4	PhCH ₂ COMe (1c)	2 ^e	97 (92)	2c	85/5/10
5	PhCH ₂ COPh (1d)	24	>99 (93)	2d	86/4/10

Table 1. Nitration of aromatic substrates by KNO₃-H₂SO₄ in CH₂Cl₂ (Scheme 1)^a

^a Unless otherwise specified, finely powdered KNO₃ (50.0 mmol) was treated with the appropriate amount of 96% H₂SO₄ (47.5 mmol) and the mixture stirred for 15 min at room temperature; CH₂Cl₂ (25.0 mL) was added to the homogeneous slurry so obtained and the mixture cooled at 0°C with vigorous stirring. A solution of the substrate 1 (5.0 mmol) in CH₂Cl₂ (8.0 mL) was added dropwise and the stirring continued at room temperature for the required time. The reaction mixture was then poured into 10% aqueous Na₂SO₄ (30 mL) and the separated organic phase washed with 10% aqueous Na₂SO₄ (2×20 mL), dryed over anhydrous Na₂SO₄, concentrated to dryness and the products obtained conveniently purified.^{1b}

^b All substrates and products are commercially available (Aldrich, Milano, Italy) or have been reported elsewhere.^{1b}

^d The reaction was carried out as reported above using: 25.0 mmol KNO_3 -23.8 mmol 96% H_2SO_4 in 1.5 mL CH_2Cl_2 and 0.5 mL CH_2Cl_2 to dissolve the substrate.

^e After 24 h extensive oxidation took place.

^c Reported conversions were determined by ¹H NMR on intact reaction mixtures, after dilution with CDCl₃: only mononitration was observed. Isolated yields are in parentheses.

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nature of the acid. Moreover, its inherent instability,⁵ producing nitrogen oxides and H_2O on storage, modifies its properties favouring, inter alia, unwanted oxidations and causes dilution ending up in loss of titre as well as miscibility with CH_2Cl_2 . For such reasons, a method circumventing these drawbacks would be highly desirable.

Consequently, we decided to consider the possibility of producing a solution of pure HNO₃ in CH_2Cl_2 , suitable for any subsequent synthetic purpose, by freeing the acid with concentrated H₂SO₄ in situ from some readily available and cheap nitrate. Nitric acid inorganic salts are in general very stable chemicals and among them KNO₃ is common, cheap, nature friendly and safe to handle.6 We found that the use of finely powdered KNO_3 and an equimolecular amount of H_2SO_4 , to be stirred with the solid (slightly exothermic reaction) for 1 h at rt with protection from light and eventual extraction of the slurry with three portions of dry solvent, gave pure CH₂Cl₂ solutions of HNO₃ with a molarity of ca. 1.2. The efficiency of the process was above 80%, as could be established alkalimetrically after thorough extraction of the organic phase with H_2O .

As the result of a few preliminary experiments, a typical preparation involved mixing finely powdered KNO_3 (100 mmol, 10.1 g) with concentrated H_2SO_4 (96%, 98.8 mmol, 5.5 mL) with efficient stirring, for 1 h at rt in the dark with protection from external moisture. Lumps that form during this process should be carefully broken

down. The colourless homogeneous slurry so obtained was then stirred three times (10 min) with portions of CH_2Cl_2 (1×30 mL and 2×20 mL) and the resulting extracts combined and filtered through a sintered glass septum and used as such in desired applications. For analytical purposes, the whole organic solution was extracted with H₂O (3×30 mL) and the combined aqueous phase submitted to the necessary assays (alkalimetric titration, BaCl₂ and KMnO₄ tests, ion chromatography), after subtraction of suitable blanks. The CH₂Cl₂ solution (ca. 70 mL) was found to average 1.19 M HNO₃ (83% recovered yield of the acid) and was free of H₂SO₄, as well as HCl originating by decomposition of the solvent (<30 mg/L SO_4^{2-} , <0.3 mg/L Cl^{-}). In addition, ion chromatography and a negative KMnO₄ test ruled out the presence of nitrogen products of lower oxidation state. When needed, the solution of HNO₃ so obtained can be concentrated by removal of part of the solvent by distillation at atmospheric pressure.

We have tested the solutions so obtained against two reactions employing HNO₃ in CH₂Cl₂ (Tables 1 and 2): more conveniently, the substrate could be present already in the extraction solvent. In order to optimise the KNO₃–H₂SO₄ ratio necessary for the completion of the nitration reaction, a set of experiments was performed where the reactants (Table 1, entry 1) were treated with increasing amounts of H₂SO₄. After 24 h at rt, the following conversions were observed: KNO₃/H₂SO₄ 1.00:0.75 (mol/mol), 70%; 1.00:0.85, 91%; 1.00:0.95, >99%.

G-COO <i>t</i> Bu	KNO ₃ -H ₂ SO₄ CH ₂ Cl ₂	G-COOH	+	<i>t</i> BuONO ₂
3	a, G = Me_3C b, G = $PhCH_2$ c, G = Ph d, G = L-ZHN(Me)CH	4		5

Scheme 2.

Table 2. Nitrolysis of t-butyl esters of carboxylic acids by $KNO_3-H_2SO_4$ in CH_2Cl_2 (Scheme 2)^a

Entry	Substrate (3) ^b	G	Conversion (%) ^c	Product (4) ^b	Yield (%)
1	3a	Me ₃ C	>99	4a	86
2	3b	PhCH ₂	>99	4b	92
3	3c	Ph	>99	4c	93
4 ^d	3d	L-ZHN(Me)CH	98	4d	88

^a Unless otherwise specified, finely powdered KNO₃ (40.0 mmol) was treated with the appropriate amount of 96% H₂SO₄ (38.0 mmol) and the mixture stirred for 15 min at room temperature; CH₂Cl₂ (10.0 mL) was added to the homogeneous slurry obtained and the mixture cooled at 0°C with vigorous stirring. A solution of the substrate **3** (20.0 mmol) in CH₂Cl₂ (10.0 mL) was added dropwise and the stirring continued at 0°C for 2 h. After this time, the reaction mixture was poured into 10% aqueous Na₂CO₃ (120 mL) and Et₂O (50.0 mL) was added. The separated organic phase was discarded and the aqueous phase made acidic with 37% HCl (ca. 3.5 mL), and extracted with Et₂O (3×30 mL). The combined ethereal phase was washed with 10% aqueous Na₂SO₄ (1×30 mL), dryed over anhydrous Na₂SO₄, concentrated to dryness and the product **4** obtained conveniently purified.^{2,3}

^b All substrates and products are commercially available (Aldrich, Milano, Italy) or have been reported elsewhere.^{2,3}

^c Reported conversions were determined by ¹H NMR on intact reaction mixtures after dilution with CDCl₃.

^d The reaction was carried out as reported above using: 70.0 mmol KNO₃-66.0 mmol 96% H₂SO₄ in 10.0 mL CH₂Cl₂ and 10.0 mL CH₂Cl₂ to dissolve the substrate.

Nitration^{1,2} (Scheme 1) and nitrolytic³ (Scheme 2) reactions were best performed by mixing CH_2Cl_2 solutions of the appropriate substrate with a suitable amount of the preformed KNO_3 -H₂SO₄ slurry, as reported in Tables 1 and 2. The results obtained were, in all cases, coincidental with those afforded by reactions in which commercial fuming (*d*=1.51) HNO₃ was employed in CH_2Cl_2 .^{1–3}

In conclusion, in view of the peculiar behaviour of HNO_3 in the aprotic solvent CH_2Cl_2 , readily available solutions prepared and described here are expected to offer further advantages and opportunities with respect to known reactions of the neat acid, as well as reactions of the acid at different concentrations in H_2O or H_2SO_4 . Moreover, the reaction producing HNO_3 , being only slightly exothermic ($\Delta H^\circ = -21.1$ kJ mol⁻¹),⁷ proves suitable for any scale-up purpose.

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