Table I. Reduction of Trifluoroacetic Acid with Various Catalysts

catalyst[a]	$k_0 \times 10^5$, mol/s·g catalyst
0.1 g of 5% Rh/C	7.6
0.1 g of 5% Rh/Al_2O_3[b]	0.7
0.05 g of Rh black	3.1
0.05 g of Ir black[c]	7.6
0.05 g of $Rh_2O_3 \cdot 5H_2O$	9.5

[a] 1.9 g of CF_3COOH, 11.2 atm of H_2, 113 °C. [b] About 10-min induction period. [c] About 22-min induction period.

[110–200 °C (40–400 atm)] over a supported ruthenium catalyst.[4]

We have now demonstrated that neat trifluoroacetic acid can be reduced in the liquid phase under very mild conditions [50–150 °C (4–12 atm)] to 2,2,2-trifluoroethanol in the presence of a rhodium or iridium catalyst. In about 2–3 h 90% yields can be obtained.

Initial rates of reduction were determined from the slopes of the concentration–time plots. These were derived from the observed pressure drops. No deviation from linearity appeared until about 30% conversion. This indicates that the initial rates are independent of the bulk concentration of trifluoroacetic acid (zero order).

The reaction rate increases with catalyst concentration and reaches a maximum at about 5 wt %. This suggests that at catalyst concentrations higher than ~5% the reaction rate is controlled by the diffusion of hydrogen to the catalyst surface.

The hydrogen pressure dependence was investigated at 73 °C for 2.5 wt % catalyst concentration. For these conditions the initial rate between 6 and 12 atm can approximately be expressed as: $r_0 = 3.8 \times 10^{-7} P^{0.81}$ mol s^{-1}.

An Arrhenius plot between 59 and 82 °C (2.5 wt % catalyst concentration, 11.5 atm of H_2) gives an apparent activation energy of about 8.2 kcal/mol. At higher temperatures there is no further increase of the initial rate constant, perhaps due to decreasing hydrogen solubility in the reaction solution. Various other rhodium and iridium catalysts were also found to be effective for the reduction of trifluoroacetic acid (Table I). The rate of hydrogenation of perfluoropropionic and perfluorobutyric acids at comparable reaction conditions is about 20 times lower.

These results represent the first example of an easy preparation of 2,2,2-trifluoroethanol from trifluoroacetic acid. Furthermore, our data strongly suggest that perfluorocarboxylic acids should be used only with caution as solvents for liquid-phase hydrogenations over platinum metal catalysts since they are directly reducible.

Experimental Section

Chemicals. Highest purity trifluoroacetic acid (PCR Research Chemicals, Inc. redistilled and iron free) and commercially available catalysts (Strem Chemicals, Inc., Alfa) were used in all hydrogenation reactions. All organic chemicals were analyzed for purity by gas chromatography (Porapak QS column) prior to use.

Hydrogenation Procedure. The hydrogenation reactions were carried out in thick-wall glass reactors attached to the metal line and to the pressure gauge (0–20 atm). The volume of the whole system, including the reactor, was 0.206 L. The acid and an appropriate amount of catalyst were charged into the reactor. After degassing, the reaction mixture was pressurized with hydrogen in a constant temperature oil bath. The contents of the reactor were stirred with a magnetic stirrer. The course of the reaction was followed by the pressure decrease. The products were analyzed by GC (Porapak QS column), using pentafluorobenzene as an internal standard.

Registry No. Trifluoroacetic acid, 76-05-1; 2,2,2-trifluoroethanol, 75-89-8.

Reactions of Trinitrotoluenes with Sodium Borohydride in a Phase Transfer Catalytic System

Yoshiyuki Okamoto* and S. T. Attarwala[†]

Department of Chemistry, Polytechnic Institute of New York, Brooklyn, New York 11201

Received March 23, 1979

Aromatic mononitro compounds are not attacked by sodium borohydride under mild conditions, and under rigorous conditions the reactions afford azo and azoxy compounds.[1,2] With *m*-dinitrobenzene and 1,3,5-trinitrobenzene, the aromatic ring is reduced.[3,4] However, the reaction of *o*-dinitrobenzene with sodium borohydride yields nitrobenzene and benzofurazan in low yield.[5]

It is known that the nitro group on the meta position of 2,3,4- and 2,4,5-trinitrotoluene is readily replaced by nucleophiles.[6] During the production of 2,4,6-trinitrotoluene about 5% of the crude product comprises unsymmetrical isomers, principally the 2,3,4- and 2,4,5-trinitrotoluenes, which are commonly removed by treating the crude trinitro product with aqueous sodium sulfite. The unsymmetrical trinitro isomers are converted into the water-soluble sodium 2,4-dinitrotoluene-3- and -5-sulfonates.[7]

Investigations for the conversion of both 2,3,4- and 2,4,5-trinitrotoluenes to 2,4-dinitrotoluene are of obvious interest because the dinitrotoluene can be nitrated further to yield symmetrical 2,4,6-trinitrotoluene. Thus, the reactions of these trinitrotoluenes with sodium borohydride were investigated.

Results and Discussion

The reaction of 2,4,5-trinitrotoluene with sodium borohydride was carried out in diglyme under a nitrogen atmosphere at room temperature (23–24 °C). Samples were taken at 15-min time intervals and treated with dilute aqueous HCl solution. Products were extracted with CH_2Cl_2 and analyzed using a high-pressure liquid chromatograph (LC). The results show that the reaction gives 2,4-dinitrobenzene at a slow rate.

Recently phase-transfer catalysis has been recognized as a general and versatile technique applicable to many organic syntheses. The technique appeared as a method for overcoming problems of mutual solubility as well as offering the potential for activation of anions.[8] Thus an investigation on the reaction of trinitrotoluene with sodium borohydride in the presence of a phase-transfer catalyst was initiated. The two-phase systems consisted of trinitrotoluene in methylene chloride[9] and an aqueous solution of sodium borohydride with a small amount of ethylhexadecyldimethylammonium bromide (EHDMABr). The two-phase system was vigorously stirred or shaken in a separatory funnel at room temperature. The products

---

(4) German Patent 1 944 381, September 2, 1969.

[†] Abstracted in part from M.S. Thesis of S. T. Attarwala, Polytechnic Institute of New York, 1979.

Table I. Reactions of Trinitrotoluenes with $NaBH_4$[a]

	reaction time, min							
	15		30		60		180	
EHDMABr concn, mol	% 2,4,5-TNT	% 2,4-DNT	% 2,4,5-TNT	% 2,4-DNT	% 2,4,5-TNT	% 2,4-DNT	% 2,4,5-TNT	% 2,4-DNT
0[b]	85.0	15.0	73.9	26.1	66.0	34.0	51.5	48.5
0.000013[c]	93.2	6.8	92.7	7.3	91.6	8.4		
0.000026[c]	83.0	17.0	78.3	21.6	71.8	28.2		
0.000053[c]	20.3	79.7	13.9	86.1	12.4	87.5		
	15		30		60			
	% 2,3,4-TNT	% 2,4-DNT	% 2,3,4-TNT	% 2,4-DNT	% 2,3,4-TNT	% 2,4-DNT		
0.000026[c]	65.6	34.4	57.0	43.0	52.5	47.5		
0.000053[c]	46.4	53.6	19.6	80.4	8.2	91.8		

[a] Initial concentration: $NaBH_4$ = 0.0060 mol, TNT = 0.0020 mol. [b] In diglyme homogeneous solution. [c] Using a phase-transfer catalysis in CH_2Cl_2–H_2O system.

were analyzed by LC and the results are shown in Table I.

Under similar conditions, the reaction of 2,4,6-trinitrotoluene with $NaBH_4$ yields ring reduction products instead of the displacement of a nitro group. The competition reactions of *sym*- and *unsym*-trinitrotoluenes with $NaBH_4$ showed that the rate of the disappearance of *sym*-trinitrotoluene is faster than that of *unsym*-trinitrotoluene. These results suggested that, for the reaction with *sym*-trinitrotoluene, the hydride reacts initially on the electron-deficient carbon at the 3-position and forms the Meisenheimer adduct,[10] which subsequently leads to the ring reduction.[11] In the case of *unsym*-trinitrotoluene, nitro groups are twisted out of the benzene ring plane and the hydride reacts at the most electron-deficient position of 3 or 5 of 2,3,4- and 2,4,5-trinitrotoluenes. The labile nitro group is displaced with the hydride and yields 2,4-dinitrotoluene.

Experimental Section

Melting points were taken in a Thomas-Hoover melting point apparatus and uncorrected infrared spectra were determined in Nujol mulls with a Perkin-Elmer 457 R spectrophotometer. NMR spectra were obtained with a Varian A-60 spectrometer using tetramethylsilane as internal reference. A Water Associates ALC-GPC-201 liquid chromatograph was used for all subsequent analyses. The typical chromatographic analytical procedures are as follows. The reaction samples were treated with 6 N HCl and extracted with methylene chloride. The methylene chloride solution was washed with distilled water and filtered through 0.45-μm millipore filter (Millipore Corp., Bedford, Mass.). A CN-μ-bondapak column was employed with a mixture of cyclohexane and methylene chloride (9:1) as a mobile phase at the flow rate 1.9 mL/min with a resulting pressure of 1000 psi, UV detector (254 mm wavelength monitor) set at 0.1 absorbance units full scale (AUFS) sensitivity.

Materials. Trinitrotoluenes. 2,4,6-Trinitrotoluene was obtained from Eastman Organic Chemicals and recrystallized from ethanol solution, mp 82 °C. 2,3,4- and 2,4,5-trinitrotoluenes were synthesized by the methods described in the literature, mp 112 °C (lit.[12] mp 111 °C), mp 105 °C (lit.[12] mp 104.5 °C), respectively. Phase-transfer catalyst ethylhexadecyldimethylammonium bromide (EHDMABr) was obtained from Eastman Kodak Co. The surfactant was washed with anhydrous ether and then recrystallized twice from hot methanol.[13] Sodium borohydride was obtained from Alfa Division, Ventron. Cyclohexane and methylene chloride used as the mobile-phase compositions were a special LC–UV grade obtained from Burdick and Jackson (Muskegon, Mich.) and no further purification was necessary.

Reactions of Trinitrotoluenes with $NaBH_4$ in Diglyme. 2,4,5-Trinitrotoluene (0.46 g, 0.002 mol) was dissolved in 30 mL of dry diglyme. To this solution, 30 mL of a diglyme solution of $NaBH_4$ (0.24 g, 0.006 mol) was added slowly with stirring under N_2 atmosphere at room temperature (23–24 °C). The color of the solution was immediately turned to deep blue. After each 15-min time interval 0.8 mL of reaction mixture was removed. The solution was treated with 6 N HCl and then extracted with methylene chloride. The methylene chloride solution was washed with water and the solution was made up to 25 mL. The solution was analyzed by LC.

Reactions of Trinitrotoluenes with $NaBH_4$ in the Presence of a Cationic Surfactant (EHDMABr). 2,4,5-Trinitrotoluene (0.46 g, 0.002 mol) was dissolved into 30 mL of methylene chloride. To this solution, 30 mL of an aqueous solution of $NaBH_4$ (0.24 g, 0.006 mol) and a known amount of EHDMABr was added. The heterogeneous solution was shaken vigorously in a separatory funnel at room temperature. The methylene chloride solution (0.9 mL) was sampled at given time intervals and treated with 6 N HCl. The methylene chloride solution was washed with water and made up to 25 mL. The solution was analyzed by LC.

Competition Reactions of Trinitrotoluenes with $NaBH_4$. Equimolar amounts of 2,4,5- and 2,4,6-trinitrotoluenes (2 g each, 0.0088 mol) were dissolved into 200 mL of methylene chloride. To this solution, 200 mL of an aqueous solution of $NaBH_4$ (1 g, 0.025 mol) and the surfactant (0.0004 mol) was added slowly and the solution was stirred vigorously. The sample (2 mL) was taken at given time intervals and analyzed. The results found that the molar ratio of 2,4,5- and 2,4,6-trinitrotoluenes was 1:1 at the initial, 1:0.5 at 10 min, 1:0.35 at 15 min, and 1:0.25 at 30 min, respectively. The three repeated experimental results agreed with these findings.

Isolation of Reaction Products. 2,4,5-Trinitrotoluene (3.5 g, 0.015 mol) was dissolved into 100 mL of methylene chloride.

---

(1) E. Schenker, *Angew. Chem.*, **73**, 81(1961).

(2) R. D. Hutchins, D. W. Lawson, L. Rua, C. Milewski, and B. Marganoff, *J. Org. Chem.*, **36**, 803 (1971).

(3) (a) T. Severin and R. Schmitz, *Chem. Ber.*, **95**, 1417 (1962); (b) T. Severin and M. Adam, *Chem. Ber.*, **96**, 403 (1963).

(4) L. A. Kaplan, *J. Am. Chem. Soc.*, **86**, 740 (1964).

(5) K. J. Bird, I. D. Rae, and A. M. White, *Aust. J. Chem.*, **26**, 1683 (1973).

(6) D. L. Brady, S. W. Hewetson, and L. Klein, *J. Chem. Soc.*, 2400 (1924).

(7) E. E. Gilbert, *Propellants Explosives*, **2**, 118 (1977).

(8) W. P. Weber and G. W. Gokel, "Phase Transfer Catalysis in Organic Synthesis", Springer-Verlag, Berlin, 1977.

(9) The advantages of using methylene chloride as a reaction medium for tetraalkylammonium borohydride have been reported by D. J. Raber and W. C. Guida, *J. Org. Chem.*, **41**, 690 (1976).

(10) L. A. Kaplan and A. R. Siedle, *J. Org. Chem.*, **36**, 937 (1971).

(11) V. A. Sokolova, M. D. Beldyrev, B. F. Gidaspov, and T. N. Timofeeva, *Zh. Org. Khim.* (*U.S.S.R.*), **8** (6), 1243 (1972).

(12) W. H. Dennis, D. H. Rosenblatt, W. G. Blucher, and C. L. Coon, *J. Chem. Eng. Data*, **20** 2 (1975).

(13) J. H. Fendler and E. J. Fendler, "Catalysis in Micellar and Macromolecular Systems", Academic Press, New York, 1975, Chapter 3, pp 1–55.

To this solution, 100 mL of an aqueous solution of $NaBH_4$ (1.9 g, 0.050 mol) and EHDMABr (0.0006 mol) was added and stirred vigorously for 1 h under a N_2 atmosphere. The organic layer was separated and treated with 20 mL of 6 N HCl, and then washed thoroughly with distilled water. The solution was dried over anhydrous $MgSO_4$, the solvent was then evaporated, and a pale yellow solid (2.36 g) was obtained. The solid was recrystallized from absolute ethanol and it was found that the product corresponded to the 2,4-dinitrotoluene (no melting point depression, IR, identified, 1.66 g, yield 60%).

Acknowledgment. We thank Dr. E. E. Gilbert for his helpful suggestions.

Registry No. 2,4,6-Trinitrotoluene, 118-96-7; 2,3,4-trinitrotoluene, 602-29-9; 2,4,5-trinitrotoluene, 610-25-3; sodium borohydride, 16940-66-2; 2,4-dinitrotoluene, 121-14-2.

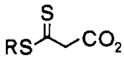
Facile Synthesis of β-Thioxo Esters from β-Enamino Esters

Frank DiNinno* and Ernest V. Linek

Merck Sharp & Dohme Research Laboratories, Rahway, New Jersey 07065

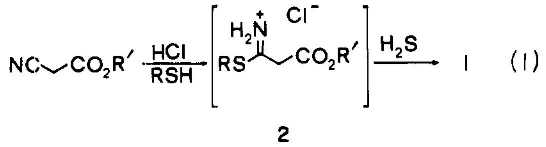
Received April 17, 1979

An integral part of our synthetic approach to 2-thioalkyl-substituted penems[1] required the use of β-thioxo esters, and in particular 1,1-dithiomalonates **1**. The



1

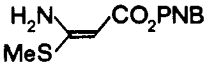
synthesis of such compounds and related substances has been accomplished by utilization of the classical modified Pinner reaction (eq 1), as exemplified by Scheithauer and



(1)

2

Mayer.[2] In addition, this method has been utilized as an approach to the synthesis of dithio esters in general.[3] However, we have found that application of this procedure, for our purposes, in which Pinner intermediate **2**, derived from *p*-nitrobenzyl cyanoacetate and methyl mercaptan ($R = CH_3$, $R' = CH_2C_6H_4\text{-}p\text{-}NO_2 \equiv PNB$), when exposed to hydrogen sulfide for 10 min under the usual conditions[2] (dry pyridine, room temperature) gave after 2 h only a 7% yield of the desired dithioate **1** and a 60% yield of the neutralization product of **2**, β-enamino ester **3**.[4] As a result



3

of this finding, we have developed a simple, efficient modification of this method which: (a) provides useful yields of these thiocarbonyl compounds in relatively short reaction times; (b) circumvents the prolonged administration of the highly toxic hydrogen sulfide gas; and (c) offers an alternative method for the synthesis of other β-thioxo esters.

In general, it was found that β-enamino esters **4** (R^1 = alkyl, aryl, thioalkyl) were readily transformed into the corresponding thiocarbonyl compounds **5** (eq 2) when

4 5 (2)

treated with trifluoroacetic acid (TFA) in dry DMF at ambient temperature or below followed by the introduction of gaseous hydrogen sulfide for relatively short times (1–30 min). Typically, the β-thioalkyl-substituted enamines **4** (R^1 = SR) required both longer reaction times and greater amounts of H_2S for good conversions to dithiomalonates, as compared to the extremely rapid reactions of the corresponding β-alkyl- and aryl-substituted enamines, as illustrated by the examples in Table I.

Although it is apparent that these simple modifications constitute a circuitous thiolytic Pinner reaction for the synthesis of 1,1-dithiomalonates, several criticalities are noteworthy which reflect the potential advantages of the procedure. For example, with entry 3 in the table, it was demonstrated, after an extensive developmental effort, that the corresponding Pinner adduct **2** (eq 1) could be *directly* converted to the dithio ester **5** in high yield (80%). However, when this set of optimum conditions was applied to the analogous transformation for entry 4, none of the corresponding dithioate was detected. In contrast then, the results depicted in the table for these entries clearly demonstrate the reliability and efficiency of the method. Aside from the fact that the majority of the β-enamino ester precursors of dithiomalonates were conveniently synthesized by neutralization of intermediate **2** with dry pyridine, it should be noted that in certain cases this common intermediate may not be available, thus rendering the direct production of **1** impossible. Entry 2 illustrates such a case since exposure of (9-anthryl)methyl cyanoacetate and methyl mercaptan to gaseous HCl in dry benzene or dioxane instantaneously produced 9-(chloromethyl)anthracene and cyanoacetic acid quantitatively. Since the requisite β-enamino ester for this entry can be made by an alternative means, this procedure then offers a successful solution to the synthesis of dithiomalonates possessing functionalities that may be incompatible with the Pinner process.

Finally entries 5–7 demonstrate the generality of the method for the *facile* synthesis of β-thioxo esters, in which the primary advantages over existing, popular methods[5] are as previously stated. It should be noted that although eq 2 depicts these entries **5** in a thioketo form, they in fact exist exclusively as the *cis*-enethiol tautomer.[6] In this

---

(1) DiNinno, F.; Linek, E. V.; Christensen, B. G. *J. Am. Chem. Soc.*, **1979**, *101*, 2210.

(2) Scheithauer, S.; Mayer, R. *Chem. Ber.* **1967**, *100*, 1413.

(3) See for example: Hoffmann, R.; Hartke, K. *Justus Liebigs Ann. Chem.* **1977**, 1743. Poupart, J.; Bruylants, A.; Crooy, P. *Synthesis.* **1972**, 622, and references cited therein.

(4) It should be noted that certain β-enamino esters have been converted to β-thioxo esters under these conditions: Bleisch, S.; Mayer, R. *Z. Chem.* **1964**, *4*, 146.

(5) See for example: (a) Duus, F. *J. Org. Chem.* **1977**, *42*, 3123. (b) Duus, F. *Tetrahedron.* **1974**, *30*, 3753. (c) Duus, F. *Ibid.* **1972**, *28*, 5923, and references cited therein.

(6) For an excellent discussion of this subject, see Duus, F. *Tetrahedron.* **1968**, *24*, 5323, and ref 5b and 5c.

(7) This β-enamino ester, mp 91–92 °C ($Me_2CHOH\text{-}CH_2Cl_2$), was prepared by a series of transformations in which (9-anthryl)methyl cyanoacetate (mp 144–145 °C, $Me_2CHOH\text{–}CH_2Cl_2$), prepared in 76% yield as described by Kornblum and Scott[8] from cyanoacetic acid and (9-anthryl)methyl chloride, was converted to the corresponding thioamide (64%, H_2S, Et_3N, EtOH, $CHCl_3$), mp 168 °C ($Me_2CO\text{–}Me_2CHOH$), and methylated (MeI, K_2CO_3, $Me_2CO\text{–}MeCN$ (2:1); 100%).