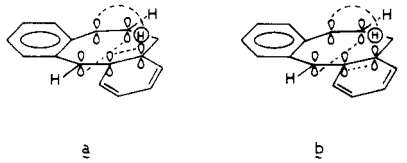


a b

Figure 2.

hydronaphthalene (8) into the dibenzocyclooctatriene 7. In the latter case the end product (7) might arise from 10 via a 1,3- as well as a 1,5-H shift, but irradiation of suitably deuterated 8 revealed that the final step only proceeds by a 1,5-H shift.

A more general reluctance of compounds like 6 and 10 to undergo 1,3-H shifts might explain that photolysis of 1 does not yield the cyclooctatriene derivative 7 because its formation from 6 is only possible via a 1,3-H shift.

Accepting that the product 5 arises from 6, the experimental conditions (254-nm light, no D incorporation) imply that the conversion of 6 → 5 is a thermal, concerted process. Two methods, viz., $\pi^2a + \pi^2a + \sigma^2s$ (Figure 2a) and $\pi^2a + \pi^2s + \sigma^2a$ (Figure 2b), both thermally allowed, are possible to fulfil the steric requirements necessary for the formation of the cis-fused structure of the product 5.

Repeating the analysis of the NMR spectrum of the reaction mixture, obtained by irradiation of 1 in hexane with a broad-spectrum lamp, revealed that 5 is probably also formed under these conditions but in very small amounts (less than 1%).

Apart from the extension of knowledge about the photochemical behavior of phenyl-substituted dihydronaphthalenes, this study may be of some practical value. Two preparations of 5 have been described in the literature. One of them,[4] starting from anthracene, requires a six-step procedure and about 136 working hours to give 5 in 64%; the other[5] starts from cinnamic acid and leads in four steps (ca. 66 h) to an overall yield of 20%. With the photochemical conversion 1 → 5, the latter compound can be obtained in four steps from α-naphthol in 65% yield within 40 h. Especially for the preparation of small samples, it is an attractive, fast, efficient, and simple method.

Experimental Section

The ^1H NMR spectrum was recorded on a Bruker WH90 spectrometer in $CDCl_3$. The mass spectrum was obtained with a VG-7070 mass spectrometer. The UV spectrum was recorded with a Perkin-Elmer 555 instrument.

The preparation of 1 was performed according to the literature.[6] Irradiations were carried out under anaerobic conditions using 10^{-3} M solutions in methanol or hexane. Monochromatic irradiations (254 nm) were done in a Rayonet photochemical reactor fitted with 254-nm lamps or using Philips bactericidal fluorescent tubes. Products were isolated by evaporation of the solvent and crystallization of the residue from methanol. Compound 5 crystallized as colorless needles and melted at 95 °C (lit. mp 95.0–95.5 °C,[5] 95 °C[4]): UV (CH_3OH) λ_{max} (log ϵ) 272 nm (3.40), 265 (3.43), λ_{min} 269 nm (3.06); mass spectrum, m/e 206 (M^+, 100%), 191 (14), 178 (14), 128 (14), 115 (17), 91 (80); NMR (simulated δ from Me_4Si) δ 2.76 (H(4), H(6), $J_{4,5} = J_{5,6} = 3.5$ Hz, $J_{4,4'} = J_{6,6'} = -15.2$ Hz), 3.24 (H(4'), H(6') $J_{4',5} = J_{5,6'} = 7.0$ Hz), 3.40 (H(5) $J_{1,5} = 7.2$ Hz), 4.64 (H(1)), 7.0–7.3 (arom).

Registry No. 1, 16606-46-5; 5, 14090-18-7.

(4) Cristol, S. J.; Jarris, B. B. *J. Am. Chem. Soc.* **1967**, *89*, 401.
(5) Baker, W.; McOrnic, J. F. W.; Parfitt, S. D.; Watlims, D. A. M. *J. Chem. Soc.* **1957**, 4026.
(6) Houben-Weyl, "Methoden der Organische Chemie"; Georg Thieme Verlag: Stuttgart, 1976; Vol. VII 2b, p. 1710.

Asymmetric Reductions by $NaBH_4$ of Ketone–β-Cyclodextrin Complexes

Roberto Fornasier, Fabiano Reniero, Paolo Scrimin,* and Umberto Tonellato*

Centro "Meccanismi di Reazioni Organiche" del C.N.R., Istituto di Chimica Organica, Università di Padova, 35131 Padova, Italy

Received October 16, 1984

The asymmetric reduction of prochiral ketones has been successfully achieved by using chirally modified metal hydrides.[1] Significant asymmetric inductions have also been obtained by the use of achiral reagents in a chiral environment: a 32% optical yield (o.y.) (phenyl *tert*-butyl ketone) was observed in the sodium borohydride reduction in the presence of optically active catalysts under phase-transfer conditions,[2] and up to 78% o.y. (propiophenone) was achieved in the sodium borohydride reduction of ketones bound to the chiral domains of bovine serum albumin.[3]

Cyclodextrins may also provide a chiral binding site[4] capable of including guest ketones and induce "template-directed" chiral reductions. One limited study[3a] reported on a very limited success: carbinols in 0–10% o.y. were obtained from three trifluoromethyl aryl ketones in the presence of a ten-fold molar excess of β-cyclodextrin (β-CD) over the substrate in alkaline aqueous solution. A growing number of reports of successful use of cyclodextrins to achieve kinetic resolutions of racemic substrates[5] or optical induction in reactions involving prochiral centers[6] led us to investigate in more detail the use of these host molecules in the sodium borohydride asymmetric reduction of prochiral ketones. Preliminary experiments carried out in a variety of conditions (in aqueous, DMF, Me_4SO solutions) using different ratios of reactants and cyclodextrins resulted in low optical inductions, about 8% and 7% o.y. at best with 1-naphthyl methyl ketone and 4-phenyl-3-buten-2-one.

We found and here report that significant improvements on these inductions can be obtained by reducing preformed 1:1 β-CD–ketone complexes suspended in a sodium borohydride aqueous alkaline (0.2 M sodium carbonate) solution. After disappearance of the ketone, the reactions were extracted with ether and the resulting alcohols analyzed to ascertain their purity and optical activity and evaluate the o.y.'s.[7] In a few cases where the specific rotation of

(1) (a) Morrison, J. D.; Mosher, H. S. "Asymmetric Organic Reactions"; Prentice Hall: Englewood Cliffs, NJ, 1971. (b) Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1978**, *10*, 175. (c) ApSimon, J. W.; Seguin, R. P. *Tetrahedron.* **1979**, *35*, 2797. (d) Valentine, D., Jr.; Scott, J. W. *Synthesis* **1978**, 329. (e) Mosher, H. S.; Morrison, J. D. *Science (Washington, D.C., 1883-)* **1983**, *221*, 1013 and references therein.
(2) (a) Balcells, J.; Colonna, S.; Fornasier, R. *Synthesis* **1976**, 266. (b) Colonna, S.; Fornasier, R.; Pfeiffer, U. *J. Chem. Soc., Perkin Trans. 1* **1978**, 8. (c) Colonna, S.; Fornasier, R. *Ibid.* **1978**, 371.
(3) (a) Baba, N.; Matsumara, Y.; Sugimoto, T. *Tetrahedron* Lett. **1968**, 4281. (b) Sugimoto, T.; Kokubo, T.; Matsumara, Y.; Miyazaki, J.; Tanimoto, S.; Okano, M. *Bioorg. Chem.* **1981**, *10*, 104.
(4) For recent reviews, see: Szejtli, J. "Cyclodextrins and their Inclusion Complexes"; Akademiai Kiado: Budapest, 1982. Fendler, J. F. "Membrane Mimetic Chemistry"; Wiley: New York, 1982.
(5) (a) Trainor, G. L.; Breslow, R. *J. Am. Chem. Soc.* **1981**, *103*, 154. (b) Breslow, R.; Trainor, G.; Ueno, A. *Ibid.* **1983**, *105*, 2739. (c) van Hooidonk, C.; Gross, C. *Recl. Trav. Chim. Pay-Bas* **1970**, *89*, 845. (d) Fornasier, R.; Scrimin, P.; Tonellato, U. *Tetrahedron Lett.* **1983**, 5541.
(6) (a) Tanaka, Y.; Sakuraba, H.; Nakanishi, H. *J. Chem. Soc., Chem. Commun.* **1983**, 947. (b) Banfi, S.; Colonna, S. *Synth. Commun.* **1983**, *13*, 1049. (c) Czarnik, A. W. *J. Org. Chem.* **1984**, *49*, 924.

0022-3263/85/1950-3209$01.50/0

Table I. Asymmetric Reduction by $NaBH_4$ of Ketone–β-Cyclodextrin Complexes

entry	ketone	alcohol					
		$[\alpha]_D$, deg	solvent (c)	optical yield, %	ref[a]	ee, %	abs config
1	$PhC(O)CH_3$	−1.57	CH_2Cl_2 (4.1)	3.5	7a		S
2	$PhC(O)CH_2CH_3$	+1.20	EtOH (3.3)	3.7	7b		R
3	$PhC(O)CH_2CH_2CH_3$	+0.94	C_6H_6 (3.9)	2.8	7c		R
4	$PhCH_2C(O)CH_3$	+5.00	$CHCl_3$ (4.0)	14.8	7d		S
5	$PhCh_2CH_2C(O)CH_3$	+3.08	C_6H_6 (4.7)	15.9	7e		S
6	(E)-$PHCH{=}CHC(O)CH_3$	−6.75	EtOH (4.75)	36.4	7f	32	S
7	(E)-$PhCH{=}CHC(O)CH_3$[b]	+1.51	EtOH (2.15)	8.2			R
8	m-$CH_3C_6H_4C(O)CH_3$					16	
9	1-$(C_{10}H_7)C(O)CH_3$	+19.12	EtOH (5.45)	26.0	7b		R
10	2-$(C_{10}H_7)C(O)CH_3$	−8.7	EtOH (3.8)	20.1	7g		S
11	1-$(C_{10}H_7)CH{=}CHC(O)CH_3$					4	
12	$FcC(O)CH_3$[c]	+3.32	C_6H_6 (2.5)	10.4	7h		S
13	$FcCH{=}CHC(O)CH_3$[c]					23	
14	n-$C_6H_{13}C(O)CH_3$	+1.60[d]	Et_2O (0.81)	9.0	7i		S

[a] For the maximum value for $[\alpha]_D$ (same solvent and similar c) of the prevailing enantiomer and for its absolute configuration. [b] The 1:1 complex with heptakis(2,6-di-O-methyl)-β-cyclodextrin. [c] Fc = ferrocenyl. [d] $[\alpha]_{546}$.

the alcohol was unknown or uncertain[8] the enantiomeric excess (ee) was determined by the use of the Mosher chiral derivatizing reagent[9] or of a chiral shift reagent. In each case the reduction to alcohol was quantitative[10] and the product isolated in 80–97% yield.

The results summarized in Table I have been obtained under identical standard conditions (see Experimental Section) and were reproducible within 10%.

Assuming that the reaction with sodium borohydride occurs in solution mainly on the complexed ketones,[11] the findings are as follows: (1) the optical induction is larger for substrates where the carbonyl group is removed by one or two carbon atoms from the moiety that is assumed[12] to be included into the cyclodextrins cavity than for ketones where the carbonyl is directly attached to it (phenones, entries 1–3) or too far removed (entry 11); (2) the above structural features, as well as the "meta effect"[13] (entries 1 and 8), and the (opposite and) decreased effect[13,14] (entries 6 and 7) observed on going from β-CD to heptakis-(2,6-di-O-methyl)-β-cyclodextrin (where both the 2- and 6-hydroxyl functions are converted to methoxyl groups) were found quite relevant in the CD's hydroxyl-promoted cleavage of esters[5,13] and clearly indicate that the hydroxyl functions of the cycloamylose are somewhat involved in the asymmetric reduction; (3) hydrogen bonding may play a role. The IR spectra of the solid complexes show a shift of the ketone stretching toward lower frequencies relative to the uncomplexed substrate from 0 to 15 cm^{-1} (from entry 1 to 13: 0, 0, 0, 2, 7, 14, 15, 13, 2, 0, 0, not determined, 12), suggesting[15] the possible formation of hydrogen bonds between the carbonyl and the CD's hydroxyls. Interestingly, the largest shifts are observed for the "best" substrates (except the case of naphthyl derivatives) although there is no simple correlation. Clearly this cannot be taken as definite evidence that hydrogen bonding is a factor in the asymmetric reduction depending on how much these solid state host–guest interactions are maintained in solution.

Thus, a combination of several factors is apparently needed for substantial enantioface selectivity: hydrophobic binding, carbonyl exposure to the CD's rim, where the secondary hydroxyls are located, and decrease of the degrees of freedom of the guest substrate, possibly also through hydrogen bonding. Although the present method, otherwise quite simple from a practical viewpoint, does not offer an alternative way to obtain chiral carbinols of high o.y., optimization of substrates and conditions may lead to substantial improvements.

Experimental Section

Materials. Heptakis(2,6-di-O-methyl)-β-cyclodextrin was synthesized from β-CD and dimethyl sulfate by following a described procedure.[16] 4-(1-Naphthyl)-3-buten-2-one and 4-ferrocenyl-3-buten-2-one were synthesized from 1-naphthylaldehyde and ferrocenylcarboxaldehyde, respectively, according to the literature.[17] The β-cyclodextrin–ketone complexes were prepared by a cocrystallization method. In the standard procedure an equimolar amount of ketone (solid ketones were dissolved in the minimum volume of ethyl ether) was added to a saturated aqueous solution of β-CD. The solution was vigorously stirred for ca. 1 day; the white crystalline precipitate formed was filtered off, washed with ethyl ether, and then dried under vacuum. The stoichiometry of the complexes was in all cases 1:1[18] as determined by ^1H NMR (Me_2SO-d_6, 200 MHz). IR spectra (KBr) were recorded with a Perkin-Elmer 580 B spectrophotometer.

Chiral Reduction. The general procedure for the reduction of the β-cyclodextrin–ketone complexes was as follows: 0.4 mmol of the complex was suspended in 3 mL of 0.2 M aqueous sodium

(7) (a) Nagai, U.; Sishido, T. *Tetrahedron* **1965**, *21*, 1701. (b) Pickard, R. H.; Kenyon, J. *J. Chem. Soc.* **1914**, 1115. (c) Levene, P. A.; Merker, R. E. *J. Biol. Chem.* **1932**, *97*, 379. (d) Schmidt, M.; Lustutz, R.; Crass, V.; Seebach, D. *Chem. Ber.* **1980**, *113*, 1691. (e) Kenyon, J.; Partridge, S. M.; Phillips, H. *J. Chem. Soc.* **1937**, 207. (f) Kenyon, J.; Partridge, S. M.; Phillips, H. *Ibid.* **1936**, 85. (g) Collyer, T. A.; Kenyon, J. *Ibid.* **1940**, 676. (h) Ratajczak, A.; Misterkiewicz, B. *J. Organomet. Chem.* **1975**, *91*, 73. (i) Kenyon, J.; Phillips, H.; Pittman, V. P. *J. Chem. Soc.* **1935**, 1081.

(8) See, e.g.: (a) Sato, T.; Gotoh, Y.; Wakabayashi, Y.; Fujisawa, T. *Tetrahedron Lett.* **1983**, 4123. (b) Soai, K.; Oyamada, H.; Yamanoi, T. *J. Chem. Soc., Chem. Commun.* **1984**, 413.

(9) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(10) In the case of α–β-unsaturated ketones here investigated, only allylic alcohols were formed.

(11) Under the standard reaction conditions the β-cyclodextrin–2-naphthyl methyl ketone complex reacted much faster than the ketone alone.

(12) The phenyl ring (entries 1–8): ref 13 and 5. The unsubstituted aromatic ring of the naphthyl moiety (entries 9–10), see: Fujita, K.; Ejima, S.; Imoto, T. *Tetrahedron Lett.* **1984**, *25*, 3587. The ferrocenyl moiety (entries 12–13), see ref 5 and: Harada, A.; Takahashi, S. J. *J. Chem. Soc., Chem. Commun.* **1984**, 645. The paraffinic chain (entry 14): ref 5d.

(13) van Etten, R. L.; Sebastian, J. F.; Clowes, G. A.; Bender, M. L. *J. Am. Chem. Soc.* **1967**, *89*, 3242, 3253.

(14) In early reports the unsubstituted β-CD's hydroxyls have been assumed to be those at C-2. Later this assignment has been shown to be incorrect, see: Casu, B.; Reggiani, M.; Gallo, G. G.; Vigevani, A. *Tetrahedron* **1968**, *24*, 803.

(15) Colthup, N. B.; Doly, H. L.; Wiberly, S. E. "Introduction to Infrared and Raman Spectroscopy", 2nd ed.; Academic Press: New York, **1975**; pp 284–286.

(16) Szejtli, J.; Liptak, A.; Jodal, I.; Fügedi, P.; Nanasi, P.; Neszmelyi, A. *Starch/Staerke* **1980**, *32*, 165.

(17) (a) Wilds, A. L.; Beck, L. W.; Close, W. J.; Jerassi, C. D.; Johnson, J. A.; Johnson, T. L.; Shunk, C. H. *J. Am. Chem. Soc.* **1947**, *69*, 1985. (b) Kono, H.; Shiga, M.; Motoyama, I.; Hata, K. *Bull Chem. Soc. Jpn.* **1969**, *42*, 3273.

(18) The same substrates failed to give 1:1 complexes with α-CD.

carbonate solution. Sodium borohydride (0.8 mmol) was then added and the slurry vigorously stirred at room temperature until disappearance of the starting material (TLC). Water (10 mL) was then added and the mixture thoroughly extracted with ethyl ether. The ethereal layer was then washed with water (3 × 10 mL) and dried over Na_2SO_4. After evaporation of the solvent, the purity of the resulting alcohols was determined by ^1H NMR or VPC analysis. Rotations were taken at 25 °C, and enantiomeric excesses were determined from the integral ratios of selected ^1H NMR (200 MHz) signals of diastereomeric α-methoxy-α-(trifluoromethyl)phenylacetic acid esters[9] (entries 6, 8, and 11 of Table I) or of the alcohol in the presence of tris[3-((trifluoromethyl)-hydroxymethylene-*d*)camphorato]europium(III) (entry 13).

Acknowledgment. We thank E. Castiglione for his skilled technical assistance and the Ministry of Public Education, Italy, for financial support.

Registry No. $PhCOCH_3$-(β-CD) 1:1 complex, 97150-81-7; $PhCOCH_2CH_3$-(β-CD) 1:1 complex, 97150-82-8; $PhCOCH_2CH_2CH_3$-(β-CD) 1:1 complex, 97150-83-9; $PhCH_2COCH_3$-(β-CD) 1:1 complex, 97150-84-0; $PhCH_2CH_2COCH_3$-(β-CD) 1:1 complex, 97150-85-1; (*E*)-$PhCH{=}CHCOCH_3$-(β-CD) 1:1 complex, 97150-86-2; (*E*)-$PhCH{=}CHCOCH_3$-[heptakis(2,6-di-*O*-methyl)-β-cyclodextrin] 1:1 complex, 97150-87-3; *m*-$CH_3C_6H_4COCH_3$-(β-CD) 1:1 complex, 97150-88-4; 1-$(C_{10}H_7)COCH_3$-(β-CD) 1:1 complex, 97150-89-5; 2-$(C_{10}H_7)COCH_3$-(β-CD) 1:1 complex, 97150-90-8; 1-$(C_{10}H_7)$-$CH{=}CHCOCH_3$-(β-CD) 1:1 complex, 97150-91-9; $FcCOCH_3$-(β-CD) 1:1 complex, 92512-21-5; $FcCH{=}CHCOCH_3$-(β-CD) 1:1 complex, 97150-92-0; *n*-$C_6H_{13}COCH_3$-(β-CD) 1:1 complex, 97150-93-1; (*S*)-$PhCH(OH)CH_3$, 1445-91-6; (*R*)-$PhCH(OH)$-CH_2CH_3, 1565-74-8; (*R*)-$PhCH(OH)CH_2CH_2CH_3$, 22144-60-1; (*S*)-$PhCH_2CH(OH)CH_3$, 1517-68-6; (*S*)-$PhCH_2CH_2CH(OH)CH_3$, 22148-86-3; (*S*)-(*E*)-$PhCH{=}CHCH(OH)CH_3$, 81176-43-4; (*R*)-(*E*)-$PhCH{=}CHCH(OH)CH_3$, 62413-47-2; (*R*)-1-$(C_{10}H_7)CH$-$(OH)CH_3$, 42177-25-3; (*S*)-2-$(C_{10}H_7)CH(OH)CH_3$, 27544-18-9; (*S*)-$FcH(OH)CH_3$, 33136-66-2; (*S*)-*n*-$C_6H_{13}CH(OH)CH_3$, 6169-06-8; $NaBH_4$, 16940-66-2.

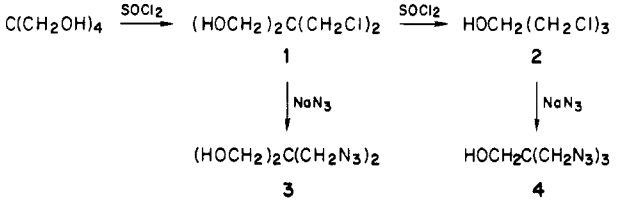
Synthesis of Novel Energetic Compounds. 7. Azido Derivatives of Pentaerythritol

Edgar R. Wilson and Milton B. Frankel*

Rocketdyne, A Division of Rockwell International, Canoga Park, California 91304

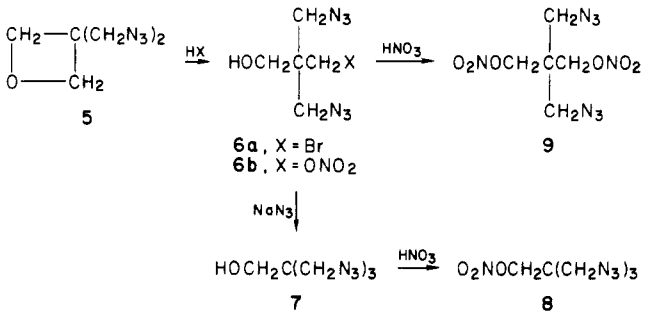
Received January 25, 1985

The synthesis of novel energetic azido compounds has been reported in previous papers of this series.[1] In the current work, it was of interest to prepare diazido and triazido derivatives of pentaerythritol. The initial approach for the synthesis of these compounds was based on the conversion of pentaerythritol to the dichloro (1) and trichloro (2) derivatives,[2] followed by subsequent reaction with sodium azide to give pentaerythritol diazide (3) and pentaerythritol triazide (4). However, this method for the



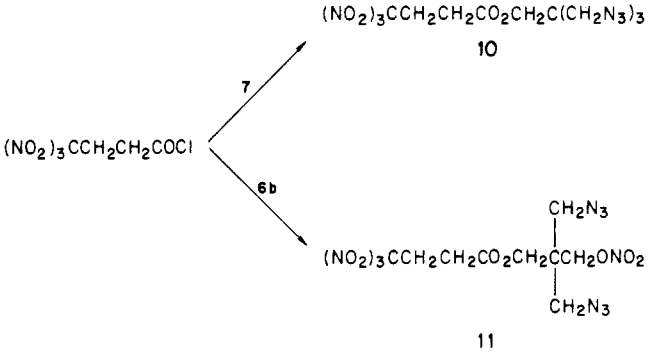
preparation of 1 and 2 gave mixtures of mono-, di-, tri-, and tetrasubstituted products, which were difficult to separate and purify. Consequently, the synthesis of the corresponding azido compounds 3 and 4 by this process did not appear promising, and a better method of synthesis was sought.

In previous work in this laboratory, a facile synthesis of bis(3,3-azidomethyl)oxetane (5) was reported.[3] It has now been found that diazido derivatives of pentaerythritol can be prepared cleanly and in high yield by the treatment of 5 with inorganic acids. In this manner, pentaerythritol diazide monobromide (**6a**) and pentaerythritol diazide mononitrate (**6b**) were prepared. Treatment of **6a** with

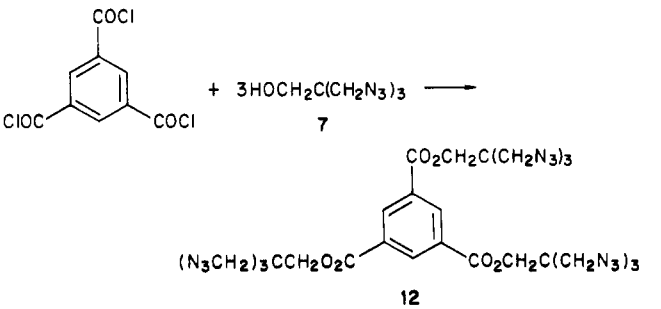


sodium azide gave pentaerythritol triazide (7), which was subsequently nitrated to pentaerythritol triazide mononitrate (8). Nitration of **6b** yielded pentaerythritol diazide dinitrate (9).

The general utility of the alcohols 7 and **6b** as precursors for the preparation of energetic esters was demonstrated. Both alcohols reacted readily with 4,4,4-trinitrobutyryl chloride to form the polyazido/polynitro-substituted esters tris(2,2,2-azidomethyl)ethyl and 3-(nitrooxy)-2,2-bis(azidomethyl)propyl 4,4,4-trinitrobutyrates (**10** and **11**, respectively) in high yields.



Further demonstration of the reactivity of 7 was obtained from its reaction with 1,3,5-benzenetricarboxylic acid chloride to give 1,3,5-tris(2,2,2-azidomethyl)ethyl benzenetricarboxylate (**12**).



Experimental Section

General Procedures. Caution! Most of the products and starting materials described are explosives of moderate to con-

(1) Previous paper in this series; Witucki, E. F.; Wilson, E. R.; Flanagan, J. E.; Frankel, M. B. *J. Chem. Eng. Data* **1983**, *28*, 285.
(2) Mooradian, A.; Cloke, J. B. *J. Am. Chem. Soc.* **1945**, *67*, 942.
(3) Frankel, M. B.; Wilson, E. R. *J. Chem. Eng. Data* **1981**, *26*, 219.

0022-3263/85/1950-3211$01.50/0