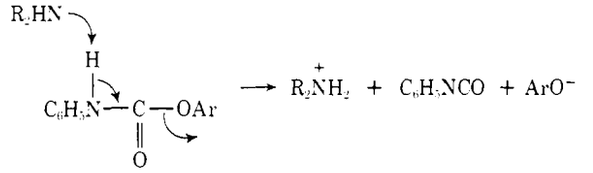
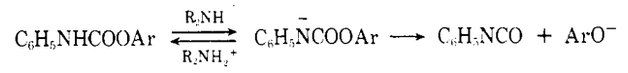
(2) E2 mechanism



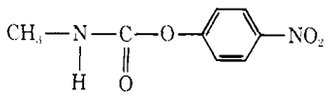
(3) E1cB mechanism



The following results remove the cyclic concerted mechanism as an acceptable possibility. Both diethylamine and triethylamine were found to catalyze the formation of isocyanate from Ia. The triethylamine-catalyzed elimination is first order in amine below 0.1 M amine ($k_2 = 4.5 \times 10^{-2}$ M^{-1} sec^{-1}, toluene, 25.0°).[7] The diethylamine reaction is both first order and second order in amine with the former predominating below 0.1 M amine ($k_2 = 2.2 \times 10^{-2}$ M^{-1} sec^{-1}, toluene, 25.0°). Comparison of the corresponding bimolecular rate constants for the secondary and tertiary amines shows that triethylamine is a twofold better catalyst than diethylamine. Of the three mechanisms above, only the first is inconsistent with this comparison. Triethylamine lacks the necessary N proton to participate in the cyclic pathway. We conclude that the concerted mechanism is incorrect.

Both of the remaining mechanisms entail charge formation. One would predict, therefore, that carbamate aminolysis should be subject to a sizable solvent effect, and this was found to be the case. The reaction of triethylamine with Ia is three orders of magnitude faster in acetonitrile than in toluene.

No evidence was collected which distinguishes the E2 from the E1cB-type mechanism. There does seem, however, to be considerable N–H breakage in the transition state, because Ia reacts over 200 times faster than p-nitrophenyl N-methylcarbamate (II) with triethylamine in toluene.



II

In conclusion, we have found that the aminolysis of Ia prefers an ionic mechanism despite the nonpolar medium and despite the availability of a seemingly feasible concerted pathway. The lack of a concerted proton transfer from a secondary amine to the "ether" oxygen of Ia during the proton abstraction suggests that there is little carbonyl carbon–oxygen bond cleavage in the transition state. If bond cleavage were appreciable, then the cyclic mechanism would be favored because p-nitrophenoxide is undoubtedly a stronger base than an aliphatic amine in a hydrocarbon solvent.[8,9] Our results can also be viewed in terms of the postulate that intramolecular proton transfer is most probable when a cyclic transition state can accommodate a linear arrangement of the donor atom, proton, and acceptor atom.[10] The absence of a cyclic mechanism for aminolysis of Ia might, therefore, stem from the inability of a six-membered ring to attain such a relationship.

Experimental Section

Materials. p-Nitrophenyl N-phenylcarbamate was prepared by refluxing equimolar amounts of p-nitrophenol and phenyl isocyanate in dry toluene for 3 hr. Recrystallization and drying gave pale yellow crystals, mp 148–150° (lit. mp 153–155°,[11] 149–150° [12]).

Anal. Calcd for $C_{13}H_{10}N_2O_4$: C, 60.46; H, 3.90; N, 10.85. Found: C, 60.50; H, 3.91; N, 10.87.

p-Nitrophenyl N-methyl-N-phenylcarbamatewas prepared from p-nitrophenol, N-methyl-N-phenylcarbamoylchloride, and triethylamine in toluene. The product was purified by liquid chromatography and by crystallization to give a 6% yield of product melting at 62–64°.

Anal. Calcd for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.44; N, 10.29. Found: C, 61.83; H, 4.50; N, 10.36.

p-Nitrophenyl N-methylcarbamate was obtained by mixing p-nitrophenol and methyl isocyanate in anhydrous diethyl ether with a trace of triethylamine, mp 162–163° (lit.[2a] mp 157.5–159°).

Kinetics. A stoppered cuvette containing 3.00 ml of a toluene solution of an aliphatic amine (0.01–0.1 M) was equilibrated at 25.0° within the thermostated cell comparment of a Cary 14 spectrophotometer. A small amount (25 μl) of a toluene solution of Ia was then added to the cuvette such that the initial substrate concentration was 8.7×10^{-5} M. The production of p-nitrophenol (measured by the increase in absorbance at 322 nm) was then traced as a function of time.[13] Pseudo-first-order rate constants were secured by processing the absorbance–time data in the usual manner.

Acknowledgment. This work was supported in part by the National Science Foundation.

Registry No.—Ia, 6320-72-5; Ib, 49839-35-2; II, 5819-21-6; diethylamine, 109-89-7; triethylamine, 121-44-8.

References and Notes

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(2) For information on the mechanism of carbamate hydrolyses, see (a) M. L. Bender and R. B. Homer, *J. Org. Chem.*, **30**, 3975 (1965); (b) A. Williams, *J. Chem. Soc., Perkin Trans. 2*, 808 (1972); (c) L. N. Frost and A. F. Hegarty, *J. Chem. Soc., Chem. Commun.*, 82 (1973).
(3) The reaction of Ib is too slow to measure under our reaction conditions; therefore 10^4 is only a *minimum* rate difference.
(4) The rate difference cannot be attributed to steric effects on a BAC2 mechanism because diisopropylamine reacts with Ia nearly as rapidly as does diethylamine.
(5) The same argument has been used in a study of the alkaline hydrolysis of carbamates (ref 2a).
(6) Y. Furuya, *et al.*, *Tetrahedron*, **24**, 2367 (1968), studied the mechanism of aminolysis of p-nitrophenyl N-phenylcarbamate by aniline in dioxane at 80°. Since they did not consider the possibility of an isocyanate intermediate, we feel that their work ought to be reexamined in the light of our results.
(7) At concentrations well above 0.1 M triethylamine, the k_{obsd} *vs.* [amine] plot curves downward. The origin of this effect has not yet been established.
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Selectivity in the Free-Radical Reduction of Lactones with Trichlorosilane[1]

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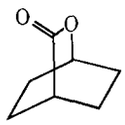
Each of the generally recognized methods for converting lactones to cyclic ethers suffers from distinct structural limitations. For instance, Adams catalyst in an acidic medium will reduce δ-lactones to the corresponding ethers but fails completely with γ- and ϵ-lactones.[2] Pettit's reagents derived from complex metal hydrides and boron trifluoride are very effective when the alcohol portion of the lactone is tertiary, but the yields of ethers decrease

dramatically as substitution at the alcohol portion is decreased.[3] Published results suggest a further limitation to the Pettit procedure when the lactone is part of an otherwise flexible system that can adopt a more favorable conformation by ring opening. For instance, Bruice[4] has reported that no ether is formed on reduction of 2-oxabicyclo[2.2.2]octan-3-one (1) with BF_3–B_2H_6 and we have encountered a similar failure with 6-oxabicyclo[3.2.1]octan-7-one (2). Each of these lactones are esters of secondary



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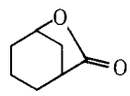
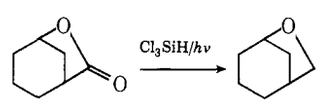


2

alcohols and would normally be expected to afford moderate amounts of ether. Failure to do so presumably indicates that the preferred conformations of ring-opened intermediates derived from 1 and 2 are such as to preclude ready recyclization to the desired ethers.[5] Thus the successful applications of the Lewis acid–metal hydride reagents have generally occurred when the lactone ring was either part of a strain-free or conformationally restricted system. We wish to report here that the radical-induced reduction of lactones by trichlorosilane circumvents many of the problems previously mentioned and further that the reaction can exhibit remarkable selectivity.

There have been several recent reports describing the reduction of simple esters and lactones with trichlorosilane on ultraviolet irradiation.[6] Tsurugi's thorough work has established that the reduction proceeds by a radical chain process, greatly diminishing the opportunity for ring opening *via* ionic intermediates. We anticipated that the application of Tsurugi's method to more complex lactones might well be of value.

In practice this prediction was realized when lactones 2 and 4 were smoothly converted to the cyclic esters by irra-



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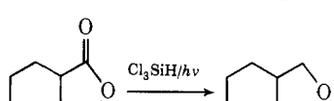
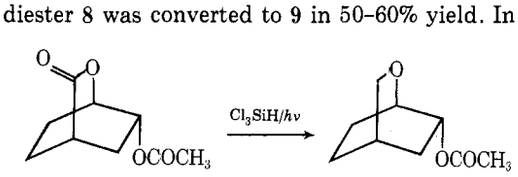


4 5

diation in the presence of excess trichlorosilane. Perhaps of greater interest was the selectivity shown when the lactone contained additional ester groupings. For instance, reaction of lactone acetate 6 with 2 equiv of trichlorosilane afforded ether 7 in 73% yield.[7] In a similar manner lactone diester 8 was converted to 9 in 50–60% yield. In each



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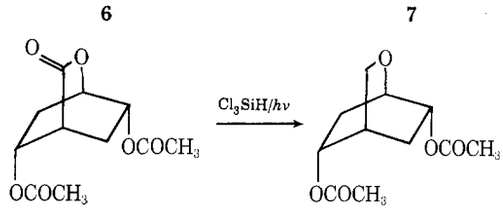

8 9

case the lactone carbonyl was selectively reduced. Current observations suggest that the observed selectivity is steric in origin, although this remains to be rigorously demonstrated.

Although the work reported herein describes the direct one-step conversion of lactones to polycyclic ethers, there is some question as to other fuctionality which may be present. For instance, Tsurugi[6a] has noted the inhibitory effect of added aromatic compounds to the reaction medium and the propensity for reaction between $\cdot SiCl_3$ and other unsaturated centers is known. We are currently examining the scope of this reaction in detail.

Experimental Section

The ir spectra were recorded on Perkin-Elmer 137 and 237 spectrophotometers. Nmr spectra were determined on a Varian A-60 spectrometer or a Jeol MH-100 spectrometer and are reported in δ units downfield from TMS. Gas chromatographic analyses were performed on a Hewlett-Packard Model 700 laboratory gas chromatograph equipped with dual flame ionization detectors. A flow rate (N_2) of 35 ml/min through 6 ft × 0.125 in. columns (5% SE-30 on Chromosorb P) was employed. Microanalyses were performed by Atlantic Microlabs, Inc., Atlanta, Ga., and M-H-W Laboratories, Garden City, Mich. Yields have not been optimized.

6-Oxabicyclo[3.2.1]octane (3). A. A solution of 478 mg (3.80 mmol) of lactone 2 and 29 mg (0.04 ml, 0.2 mmol) of di-*tert*-butyl peroxide in 2.06 g (1.60 ml, 15.2 mmol) of trichlorosilane was degassed (0.01 mm) with three freeze–pump–thaw cycles, sealed in a Pyrex tube, and irradiated for 2.5 hr with a Hanovia 450-W medium-pressure ultraviolet lamp. The resulting clear solution was diluted with 50 ml of CH_2Cl_2 and then the excess trichlorosilane was destroyed by the careful addition (0°, stirring) of 10 ml of water and 2.5 ml of 10% NaOH solution. The aqueous layer was extracted with CH_2Cl_2 (3 × 25 ml) and the combined organic layer was washed with saturated brine (50 ml) and dried ($MgSO_4$). Gas chromatographic analysis of this dilute solution showed a single peak identical with authentic material prepared in B. Careful removal of the solvent and distillation (sublimation) of the residue in the Kugelrohr manner (110°, 33 mm) afforded 126 mg (27.5%)[8] of semisolid residue, spectroscopically identical with the ether prepared in B.[9]

B. An ether solution of 204 mg (2.42 mmol) of lactone 2 was reduced with excess lithium aluminum hydride. The resulting crude diol and 2 mg of *p*-toluenesulfonic acid were distilled (sublimed) as above (110°, 33 mm) to give 160 mg (59.4%) of a waxy solid, which exhibited a single peak on gas chromatographic analysis (100°, 2.3 min), identical with the ether prepared in A: nmr (CCl_4) δ 1.43–2.50 (broad, 9 H), 3.78 (m, 2 H, $-CH_2O-$), 4.25 (broad, 1 H, –CHO).

***trans*-8-Oxabicyclo[4.3.0]nonane (5).**[10] **A.** A solution of 500 mg (3.57 mmol) of lactone 4 (prepared by the method of Bloomfield[11]), 26 mg (0.033 ml, 0.18 mmol) of di-*tert*-butyl peroxide, and 1.94 g (1.44 ml, 14.3 mmol) of trichlorosilane was degassed and sealed in a Pyrex tube as described above. Irradiation as before for 2 hr followed by a similar work-up (CH_2Cl_2, NaOH, NaCl, $MgSO_4$) and concentration at 200 mm led to 410 mg of mobile oil which was distilled in the Kugelrohr manner (85°, 33 mm) to give 373 mg (83%) of colorless liquid identical with that produced in B. Occasionally the presence of minor amounts (10–20%) of cis ether was apparent from the nmr spectrum, which showed complex absorption centered at δ 3.64.

B. A solution of trans diol [derived from reducing 5.0 g (35.7 mmol) of trans lactone 4 with excess lithium aluminum hydride], 20 ml of water, and 1 ml of concentrated H_2SO_4 was steam distilled, additional water being added as necessary to maintain the original volume. When organic material stopped collecting, the distillate was saturated with potassium carbonate and extracted with ether (3 × 10 ml). The combined ether layers were washed with brine (50 ml), dried ($MgSO_4$), and concentrated at 200 mm. Distillation of the residue afforded 3.5 g (78%) of pure ether, bp 73–77° (20 mm) [lit.[10] bp 70° (20 mm)], homogeneous by gas chromatography (150°, 1.3 min): nmr (CCl_4) δ 0.84–1.63 (broad, 8 H), 1.81 (broad, 2 H), 2.09 (m, 2 H), 3.64 (m, 4 H).

6-*endo*-Acetoxy-2-oxabicyclo[2.2.2]octan-3-one (6). A. A solution of 10.3 g (65.0 mmol) of 3α,4β-dihydroxycyclohexane-1α-carboxylic acid (13)[12] in 200 ml of acetic anhydride was slowly heated under nitrogen to 180–185° and maintained at that temperature for 1 hr. Removal of the acetic anhydride *in vacuo* gave 13 g of a light yellow oil, vacuum distillation of which afforded 4.72 g

(40%) of a colorless liquid: bp 111–120° (0.05 mm); ir (CCl_4) 1774 and 1755 cm^{-1} (C=O); nmr (CCl_4) δ 1.90 (broad, 5 H), 2.10 (s, 3 H, $COCH_3$), 2.50 (broad, 2 H), 4.55 (broad, 1 H), 5.00 (m, 1 H).

Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.61; H, 6.41.

B. Oxidation of Ether 7 with Ruthenium Tetroxide.[13] To a solution of 200 mg (1.28 mmol) of ether **7** in 50 ml of carbon tetrachloride was added 2 ml of a carbon tetrachloride solution of ruthenium tetroxide [prepared by stirring 0.1 g (0.49 mmol) of ruthenium trichloride and 0.5 g (2.32 mmol) of sodium periodate in 25 ml of carbon tetrachloride and 10 ml of water for 20 hr] and a solution of 0.5 g (2.32 mmol) of sodium periodate in 25 ml of water. After the mixture was stirred vigorously for 2 days, isopropyl alcohol was added and the mixture was filtered. Concentration of the organic layer afforded 129 mg (55%) of lactone **6**, identical with material prepared in A.

6-*endo*-Acetoxy-2-oxabicyclo[2.2.2]octane (7). A. A solution of 5.59 g (30.0 mmol) of lactone **6**, 8.31 g (61 mmol) of trichlorosilane, and 0.22 g (1.5 mmol) of di-*tert*-butyl peroxide in a Pyrex tube (35 × 1.5 cm) was degassed by four freeze–pump–thaw cycles (0.01 mm). The tube was sealed and then irradiated as before for 4 hr. The contents of the tube were then poured into 200 ml of ether and 10% sodium hydroxide was added carefully until no further reaction occurred. After filtration, the filtrate was washed with saturated sodium bicarbonate (25 ml) and brine (25 ml), dried ($MgSO_4$), and concentrated. Distillation of the resulting oil in the Kugelrohr manner afforded 3.78 g (73%) of a light oil (70–80°, 0.01 mm): ir (CCl_4) 1740 cm^{-1} (C=O); nmr (CCl_4) δ 1.30–2.50 (broad, 7 H), 2.08 (s, 3 H, $COCH_3$), 3.70 (broad, 3 H, H_2COCH), 4.90 (m, 1 H, $HCOCOCH_3$).

Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.66; H, 8.06.

5-*endo*-Carbomethoxy-7-*endo*-acetoxy-2-oxabicyclo[2.2.2]octane (9). A solution of 5.0 g (21.0 mmol, freshly recrystallized) of lactone **8**,[14] 7.01 g (52.0 mmol) of trichlorosilane, 0.241 g (1.65 mmol) of di-*tert*-butyl peroxide, and 30 ml of tetrahydrofuran (doubly distilled from $LiAlH_4$) was placed in a Pyrex tube (35 × 1.5 cm) and degassed by eight freeze–pump–thaw (0.01 mm) cycles. The tube was sealed and irradiated as before for 12 hr at 50° (heat lamp) and at a distance of 11.5 cm from the lamp. Volatile material was removed by vacuum distillation (30°, 20 mm) and the residue was dissolved in a slurry of 100 ml of ethyl ether and 3 g of sodium bicarbonate. Water was added dropwise until gas evolution ceased. After stirring for 0.5 hr the mixture was dried ($CaCl_2$), filtered, and concentrated to give a light residue. Distillation afforded 2.40 g (50%) of product, bp 95–100° (0.04 mm), that was homogeneous by gas chromatography (160°, 5.0 min):[15] ir (CCl_4) 1745 cm^{-1} (C=O); nmr (CCl_4) δ 1.5–2.4 (broad, 6 H), 2.05 (s, 3 H, $COCH_3$), 3.65 (s, 3 H, $COOCH_3$), 3.75 (broad, 3 H, H_2COCH), 4.90 (m, 1 H, $HCOCOCH_3$).

Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.89; H, 7.07. Found: C, 57.64; H, 6.86.

Registry No.—**2**, 4350-83-8; **3**, 279-87-8; **4**, 7702-72-9; **5**, 10479-79-5; **6**, 51608-92-5; **7**, 51608-93-6; **8**, 51608-94-7; **9**, 51608-95-8; **13**, 23477-88-5; *trans*-1,2-cyclohexanedimethanol, 25712-33-8.

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(5) The presence of ionic intermediates which might undergo ring opening is inferred from the highly acidic nature of the medium and the normal mode of hydride attack on carboxyl derivatives. Furthermore, the parallel increase in reduction efficiency with increasing substitution suggests ionic intermediates.
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(7) When the reduction of **6** was carried out with 4 equiv of trichlorosilane, the major product (60% yield) was the ethyl ether formed by further reduction of the acetate of **7**.
(8) Gas chromatographic analysis of the crude reaction mixture showed that ether **3** was the only volatile product present and that it had been formed in 67% yield (*p*-xylene internal standard). The low isolated yield is ascribed to its extreme volatility and resultant loss during work-up.
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(14) Details of the synthesis of triester **8** from *trans*-1,2,3,6-tetrahydrophthalic anhydride (75% yield) will be reported at a later date.
(15) The major contaminant in the reduction of **8** resulted from attack at the acetate carbonyl and ranged randomly from 15 to 35%.

Methoxymethyl Isocyanate from Thermal Rearrangement of 5-Methoxymethyldioxazolone

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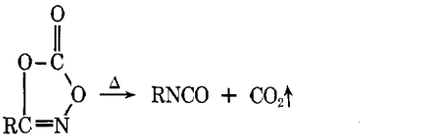
The acid-catalyzed reactions[1] of *N*-methylol and *N*-methoxymethyl derivatives have been utilized industrially. The formation of resins and modifications of cellulose employing urea–formaldehyde and melamine–formaldehyde chemistry are examples. Interst has developed in methoxymethyl isocyanate (MMI) as a modifying agent for incorporating *N*-methoxymethyl sites onto reactive polymers.[2-5] Such modifications have resulted in thermosetting lacquers, coatings, and resins suitable for industrial applications. Our efforts in this area were initially complicated by problems encountered in the synthesis of MMI.

The reported[3] synthesis of MMI involves the reaction of chloromethyl methyl ether with sodium cyanate in a mixed solvent system composed of DMF and a hydrocarbon, and isolation of the MMI by distillation (90°, 760 mm). We found the yields of MMI by this method to be low and variable. The highest yield of MMI we have realized by this procedure is 45%. The MMI was codistilled with toluene from the reaction mixture containing DMF–toluene as solvents. The utilization of this MMI–toluene solution was previously reported.[6] We would like to report a superior synthetic route for the generation of MMI in excellent yields in a hydrocarbon solvent.

The thermal rearrangement of dioxazolones (nitrile carbonates) to aliphatic and aromatic isocyanates has been well documented.[7-12] The nature and scope of the rearrangement have not, however, been thoroughly investigated. We have applied the aforementioned thermal rearrangement of nitrile carbonates to the synthesis of MMI. The precursor dioxazolone (**3**) was prepared as shown in eq 2.



(1)

Ethyl methoxyacetate (**1**) was treated with hydroxylamine in methanol to produce methoxyacetohydroxamic acid (**2**). The hydroxamic acid **2** was then treated with excess phosgene, which resulted in the isolation of methoxymethyldioxazolone (**3**) in excellent yield.

The dioxazolone **3** could be easily handled and was not a lachrymator. Analysis (neat) by differential scanning calo-