mmol) with 2 (6.28 g, 0.080 mol) yielded 8.32 g (70%) of 4-chloropentyl acetate: bp 92–95 °C (15 torr) [lit.[12] bp 82 °C (10 torr)]; ^{1}H NMR (neat) δ 4.05 (m, 3 H, CHCl and $AcOCH_2$), 1.97 (s, 3 H, CH_3CO), 1.90–1.65 (m, 4 H, CH_2CH_2), 1.60–1.40 (d, J = 7 Hz, 3 H, $CClCH_3$); IR 1750 cm^{-1} (carbonyl).

Reaction of 2,5-Dimethyltetrahydrofuran with 2. Reaction of 2,5-Me_2THF (30.0 g, 0.299 mol) in the presence of 4 (360 mg, 0.612 mmol) with 2 (4.71 g, 0.060 mol) yielded 8.63 g (81%) of 5-chloro-2-hexyl acetate: bp 90–93 °C (13 torr) [lit.[11] bp 85–87 °C (15 torr)]; ^{1}H NMR (neat) δ 5.10–4.70 (m, 1 H, AcOCH), 4.30–3.70 (m, 1 H, CHCl), 1.95 (s, 3 H, CH_3CO), 1.85–1.65 (m, 4 H, CH_2CH_2), 1.45–1.30 (d, J = 6 Hz, 3 H, $AcOCCH_3$), 1.15–1.05 (d, J = 6 Hz, 3 H, $CClCH_3$); IR 1730 cm^{-1} (carbonyl).

Reaction of Oxetane with 2. Reaction of oxetane (10.7 g, 0.185 mol) in the presence of 3 (530 mg, 1.37 mmol) with 2 (2.90 g, 0.037 mol) yielded 2.35 g (47%) of 3-chloropropyl acetate: bp 65–68 °C (15 torr) [lit.[13] bp 166–175 °C (760 torr)]; ^{1}H NMR (neat) δ 4.35–4.05 (t, J = 6 Hz, 2 H, $AcOCH_2$), 3.85–3.50 (t, J = 6 Hz, 2 H, CH_2Cl), 2.2–1.95 (m, 5 H, CH_3CO and CH_2); IR 1750 cm^{-1} (carbonyl).

Reaction of Tetrahydropyran with 2. Reaction of THP (29.0 g, 0.340 mol) in the presence of 4 (360 mg, 0.612 mmol) with 2 (5.34 g, 0.068 mol) yielded 6.35 g (57%) of 5-chloropentyl acetate: bp 90–92 °C (10 torr) [lit.[14] bp 104 °C (18 torr)]; ^{1}H NMR (neat) δ 4.25–3.90 (t, J = 6 Hz, 2 H, $AcOCH_2$), 3.65–3.40 (t, J = 6 Hz, 2 H, CH_2Cl), 1.97 (s, 3 H, CH_3CO), 1.85–1.40 (m, 6 H, $CH_2CH_2CH_2$); IR 1750 cm^{-1} (carbonyl).

Reaction of *p*-Dioxane with 2. Reaction of *p*-dioxane (48.4 g, 0.550 mol) in the presence of 4 (350 mg, 0.60 mmol) with 2 (8.63 g, 0.106 mol) yielded 3.90 g (22%) of 2-(2-chloroethoxy)ethyl acetate: bp 93–95 °C (4.0 torr); ^{1}H NMR (C_6D_6) δ 4.20–3.97 (t, 4 H, $AcOCH_2$ and CH_2Cl), 3.50–3.25 (t, 4 H, CH_2OCH_2), 1.8 (s, 3 H, CH_3CO); IR 1750 (carbonyl), 1150 cm^{-1} (ether).

Acknowledgment. This work was supported by the Robert A. Welch Foundation (Grant AI-306).

Registry No. 1, 109-99-9; 2, 75-36-5; 3, 16405-35-9; 4, 12073-36-8; $CH_3CO_2CH_2(CH_2)_2CH_2Cl$, 6962-92-1; $C_6H_5CO_2CH_2(CH_2)_2CH_2Cl$, 946-02-1; $CH_3CO_2CH_2(CH_2)_2CH_2Br$, 4753-59-7; $CH_3CH_2(CH_2)_2CHClCH_3$, 36978-15-1; $CH_3CO_2CH(CH_3)(CH_2)_2CHClCH_3$, 84602-36-8; $CH_3CO_2CH_2CH_2CH_2Cl$, 628-09-1; $CH_3CO_2CH_2(CH_2)_3CH_2Cl$, 20395-28-2; $CH_3CO_2CH_2CH_2OCH_2CH_2Cl$, 14258-40-3; C_6H_5COCl, 98-88-4; CH_3COBr, 506-96-7; *trans*-[$Pt(C_2H_4)py Cl_2$], 12078-66-9; [$Rh_2(C_2H_4)_4Cl_2$], 12122-73-5; 2-CH_3THF, 96-47-9; 2,5-$(CH_3)_2$THF, 1003-38-9; oxetane, 503-30-0; tetrahydropyran, 142-68-7; *p*-dioxane, 123-91-1.

(12) King, J. A.; McMillan, F. H. *J. Am. Chem. Soc.* **1946**, *68*, 1774.
(13) McElvain, S. M.; Curry, M. J. *J. Am. Chem. Soc.* **1948**, *70*, 3781.
(14) Synerholm, M. E. *J. Am. Chem. Soc.* **1947**, *69*, 2581.

Novel 1,2-Ester Transposition Reactions

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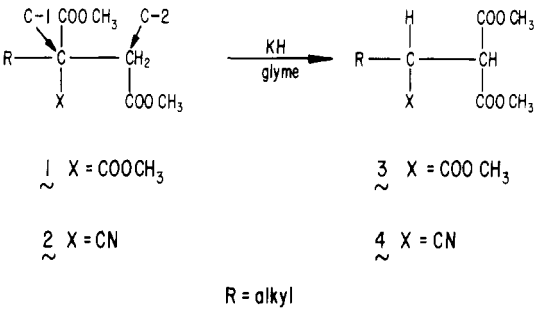
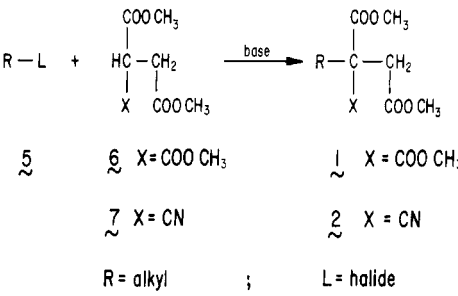
We report a novel 1,2-ester transposition reaction observed during the study of the heavily ester-packed intermediates for synthesis of the experimental anticancer compound Carbethimer (N-137) and its analogues.[1] We have found that in both 1-substituted trimethyl ethane-1,1,2-tricarboxylate **1** and 1-substituted dimethyl cyanoethane-1,2-dicarboxylate **2** systems, treatment with potassium hydride (KH; Scheme I) causes the C-1 ester to migrate cleanly to the adjacent terminal carbon (C-2) to give **3** and **4**, respectively.

(1) J. E. Fields, S. S. Asculai, J. H. Johnson, and R. K. Johnson, *J. Med. Chem.*, **25**, 1060 (1982).

Scheme I



Scheme II



Results and Discussion

The starting materials **1** and **2** for the above rearrangement study were prepared by condensation of the corresponding alkyl halide **5** with trimethyl ethane-1,1,2-tricarboxylate (**6**) or dimethyl 1-cyanoethane-1,2-dicarboxylate (**7**; Scheme II). Treatment of the above alkylation adducts **1** and **2** with KH in 1,2-dimethoxyethane (glyme) leads to this "1,2-ester walk" to the corresponding isomers **3** and **4**. The essentially pure terminal diesters were obtained after acidic workup. We also noticed that this "1,2-ester walk" was extensively inhibited in systems having an additional substituent on C-2. For example, when **8** was subjected to the above condition, the dehydrocyanation and decarbomethoxylation products **9** and **10** were observed[2] (Scheme III).

The structures of the rearranged compounds were established by their ^{1}H NMR and mass spectra. The mass spectroscopic data are very informative. A characteristic pattern of mass fragmentation of the rearranged esters shows the preferential McLafferty rearrangement fragment[3] (e.g., m/e 132 ion), while the spectra of the starting materials indicate the "normal cleavage" ions (e.g., m/e 202 ion; Chart I). Unambiguous structural evidence for this 1,2-ester migration was obtained for the reactions with R = CH_3. The ^{1}H NMR spectra of the rearranged products (i.e., **3** or **4**, R = CH_3) showed three-hydrogen doublets for the methyl absorption, while the ^{1}H NMR spectra of the starting materials (i.e., **1** or **2**, R = CH_3) were three-hydrogen singlets.

To our knowledge this 1,2-ester migration reaction is unprecedented in the literature.[4] A suggested mechanistic

(2) The elimination products were identified by GC/MS analysis. **9**: m/e (relative intensity) 276 (6), 245 (5), 185 (12), 172 (27), 105 (100). High-resolution MS calcd for $C_{16}H_{20}O_4$ (M^+) m/e 276.1362, found m/e 276.1357. **10**: m/e (relative intensity) 218 (27), 159 (88), 129 (55), 117 (100). High-resolution MS calcd for $C_{14}H_{18}O_2$ (M^+) m/e 218.1307, found m/e 218.1299.
(3) F. W. McLafferty, "Interpretation of Mass Spectra", 2nd ed., W. A. Benjamin, New York, 1973, p 58.
(4) An analogous 1,3-ester migration, namely, the "abnormal" Michael addition, was reported by Holder and Lapworth: N. Holder and A. Lapworth, *J. Chem. Soc.*, 2368 (1931). See also: G. A. Swan, *J. Chem. Soc.*, 1939 (1965); E. Bergman and P. Ginsburg, *Org. React.*, **10**, 191–7 (1959).

0022-3263/83/1948-0753$01.50/0

Scheme III

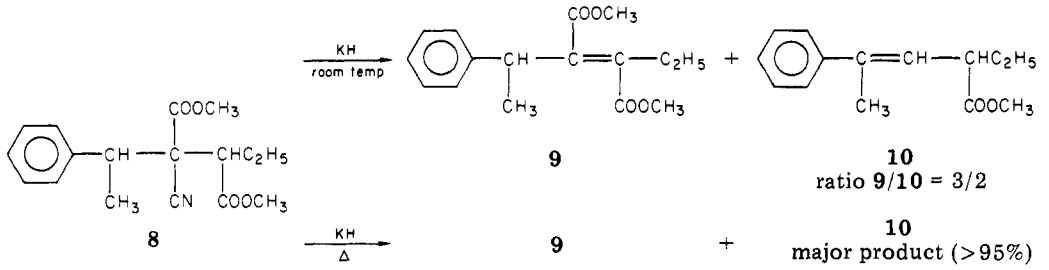


Chart I

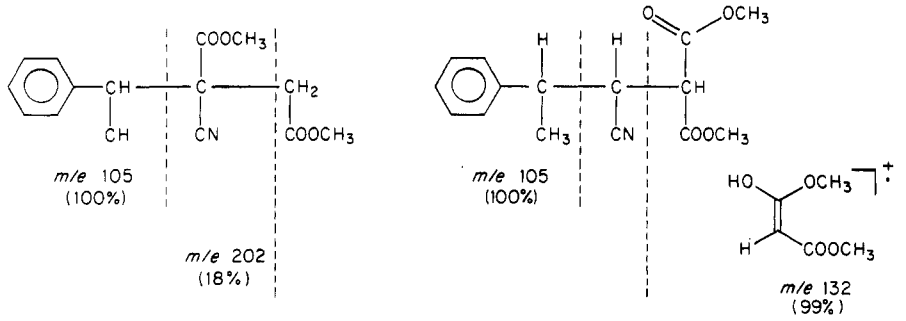
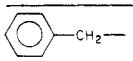
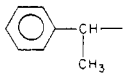


Table I. Physical and Spectral Data for Compounds 1-4

R	compd	yield,[b] %	mp, °C	^{1}H NMR ($CDCl_3$), δ	MS,[c] m/e (rel intensity)
	1[a]	88	oil	7.1 (m, 5 H), 3.6 (s, 6 H), 3.5 (s, 3 H), 3.3 (s, 2 H), 2.7 (s, 2 H)	294 ($M^{+\cdot}$, 14), 221 (14), 203 (18), 91 (58)
	3[a]	80	51-53[d]	7.2 (s, 5 H), 3.6 (s, 6 H), 3.5 (s, 3 H), 2.8-3.6 (m, 4 H)	294 ($M^{+\cdot}$, 12), 203 (10), 163 (88), 132 (52), 131 (56), 91 (55)
CH_3	1[9]	85	oil	3.7 (2 s, 9 H), 3.0 (s, 2 H), 1.6 (s, 3 H)	187 ($M^{+\cdot} - OCH_3$, 46), 159 (39), 145 (14), 127 (79)
	3[a,9]	85	43-46[d]	3.6-3.8 (m, 1 H), 3.6-3.8 (3 s, 9 H), 3.0-3.1 (m, 1 H), 1.2 (d, 3 H)	187 ($M^{+\cdot} - OCH_3$, 20), 159 (62), 132 (85), 127 (100)
	2[a]	80	82.5-83.5[e]	7.3 (s, 5 H), 3.7 (s, 3 H), 3.4 (s, 3 H), 3.1 (m, 3 H), 1.5 (d, 3 H)	275 ($M^{+\cdot}$, 7), 244 (5), 202 (18), 105 (100)
	4[f]	84	oil	7.3 (m, 5 H), 3.7 (2 s, 6 H), 3.0-3.7, (m, 3 H), 1.5 (d, 3 H)	275 ($M^{+\cdot}$, 2), 244 (5), 144 (22), 132 (99), 105 (100)
CH_3	2[10]	81	oil	3.9 (s, 3 H), 3.7 (s, 3 H), 3.0 (d, 2 H), 1.7 (s, 3 H)	154 ($M^{+\cdot} - OCH_3$, 28), 126 (14), 112 (2), 74 (15)
	4[10]	82	oil	3.8 (s, 6 H), 3.4-3.7 (m, 2 H), 1.4 (d, 3 H)	154 ($M^{+\cdot} - OCH_3$, 17), 132 (42), 126 (27), 69 (70)

[a] Acceptable elemental analyses (C, H, N) were obtained. [b] Crude yields. [c] $M^{+\cdot}$ + 1 ions were obtained by CI mode. [d] Recrystallized from ether/petroleum ether. [e] Recrystallized from ethyl acetate/petroleum ether. [f] Mixture of diastereoisomers.

rationale is outlined in Scheme IV. The anion 11 initiated by KH undergoes a Dieckmann-type reaction resulting in a cyclopropyl intermediate 12. The key feature of this suggested mechanism is the proton transfer step 13 → 14. Intermediate 14, possessing the favorable electronic structure of the doubly stabilized anion, is protonated or alkylated by the addition of water or methyl iodide,[5] respectively. On the other hand, the unsuccessful rearrangement reaction observed in 8 may be due to the lack of the favored electronic character as in 14.

Experimental Section

General Procedures. All KH reactions were conducted under nitrogen. Glyme was distilled from calcium hydride and was stored over 4A molecular sieves. Commercial 35% KH in oil (Aldrich) was used. ^{1}H NMR spectra of deuteriochloroform solutions with tetramethylsilane acting as internal standard (δ = 0 ppm) were taken on Varian T-60 or EM-390 spectrometers. Mass spectral data were obtained with either a Finnigan 4000 GC/MS or a Varian CH7A spectrometer. Melting points were determined on a Reichert hot-stage microscope and were uncorrected. Microanalyses were performed by Galbraith Laboratories, Knoxville, TN.

General Procedure for the Preparation of Trimethyl 1-Alkylethane-1,1,2-tricarboxylate (1) and Dimethyl 1-Alkyl-1-cyanoethane-1,2-dicarboxylate (2). A mixture of trimethyl ethane-1,1,2-tricarboxylate (6,[6] or dimethyl 1-cyanoethane-1,2-dicarboxylate, 7[7]), 1.2 equiv of alkyl halide, and 1.5 equiv of pulverized potassium carbonate in dimethyl sulfoxide[8] was stirred at room temperature. The reaction was monitored by VPC (OV-101 column). Ice–water was added after the reaction

(5) The alkylation product 15 displayed the following properties: ^{1}H NMR ($CDCl_3$) δ 7.2 (s, 5 H), 3.65 (s, 6 H), 2.6–3.5 (m, 3 H), 1.6 (s, 3 H); MS, m/e (relative intensity) 244 ($M^{+\cdot} - OCH_3$, 1), 184 (7), 146 (100), 129 (6), 114 (54), 91 (73). Molecular ion of 15 was confirmed by CI technique.

(6) C. A. Bischoff, *Ber. Dtsch. Chem. Ges.* **29**(1), 966 (1896).

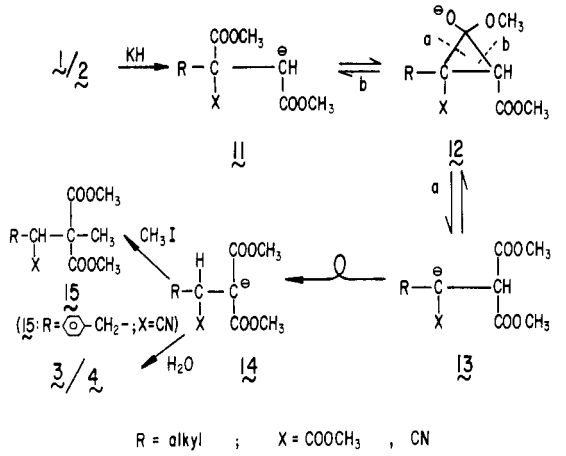
(7) This material was prepared from methyl cyanoacetate and methyl chloroacetate by the potassium carbonate method (see ref 8). It gave satisfactory spectroscopic data with bp 73–74 °C (1 mmHg).

(8) D. A. White, *Synth. Commun.*, 1, 559 (1977).

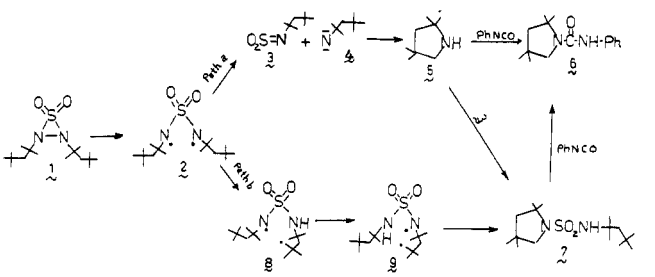
(9) D. A. Tysee and M. M. Baizer, *J. Org. Chem.*, **39**, 2819 (1974).

(10) D. A. White, *J. Chem. Soc., Perkin Trans.* 1, 1926 (1976).

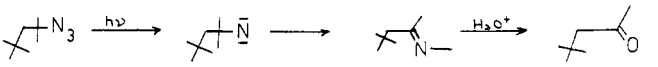
Scheme IV



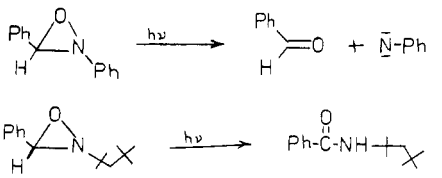
Scheme I



Scheme II



Scheme III



was completed. To this mixture was added cold dilute hydrochloric acid until the reaction mixture was neutralized. This mixture was extracted several times with ether, and the combined organic layers were washed sequentially with cold sodium bicarbonate, water, and brine and then dried over magnesium sulfate. The solvent was removed. The desired products were obtained in about 80–88% yields. The materials were then used in the KH reactions without further purification. The physical and spectral data for these products are shown in Table I.

General Procedure for the KH Reactions. An excess amount of KH (35% in oil, 3 mmol) was washed several times with petroleum ether in a three-necked round-bottomed flask. After removal of petroleum ether, 3 mL of glyme was added. To this slurry was added dropwise a solution of 1.5 mmol of 1 (or 2) in 3 mL of glyme. The reaction mixture was stirred at room temperature for 3 h or under reflux for 0.5 h. The resulting solution was then cooled in an ice bath before cold water or methyl iodide (1.7 mmol in 2 mL of glyme) was cautiously added. Workup as described in the above alkylation reactions gave 80–93% yields of essentially pure rearranged products. Table I lists the properties of the rearranged compounds.

Acknowledgment. We thank Drs. M. J. Holm and F. B. Zienty for their helpful discussions and encouragement. We are also indebted to Dr. K. Wood, Mr. R. C. Scheibel, and Mr. R. Fuhrhop for obtaining mass spectra and for valuable discussions.

Registry No. 1 (R = CH_2Ph), 84454-40-0; 2 (R = $CH(CH_3)Ph$), 84454-41-1; 3 (R = CH_2Ph), 84454-42-2; 4 (R = $CH(CH_3)Ph$) (isomer 1), 84454-43-3; 4 (R = $CH(CH_3)Ph$) (isomer 2), 84454-44-4; 6, 40967-67-7; 7, 6283-71-2; 8, 84454-45-5; 9, 84454-46-6; 10, 84454-47-7; 15, 84454-48-8.

Decomposition of *N*,*N*-Dialkylthiadiaziridine 1,1-Dioxides: A Mechanistic Revision

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Received August 30, 1982

Recently,[1] we reported that the thermal decomposition of di-*tert*-octylthiadiaziridine 1,1-dioxide in benzene or toluene gives rise to a pyrrolidinyl sulfamide (7). At that time we thought that while it was possible to conceive of an intramolecular path for formation of this sulfamide (7), the fact that urea 6 was formed in presence of phenyl isocyanate provided evidence for the existence of free 2,2,4,4-tetramethylpyrrolidine (5). This pyrrolidine was thought to arise from *tert*-octylnitrene (4) by γ-hydrogen insertion since similar cyclizations of arylnitrenes and carbonylnitrenes were known[2] and since this *tert*-octylnitrene rearrangement conveniently explained the product distribution.[1] It was recognized, however, that no alkylnitrene insertions of this type had previously been substantiated.[2]

It now appears that the reaction sequence as illustrated in path a of Scheme I may be incorrect. When sulfamide 7 is heated in the presence of phenyl isocyanate under conditions identical with those for its formation, pyrrolidinylurea 6 is formed in 60% yield. Thus the formation of urea 6 is not singularly evidence of the existence free pyrrolidine 5 because sulfamide 7, once formed, is capable of dissociation, presumably to 3 and 5, and the latter is trapped by phenyl isocyanate.

In addition, attempts to independently generate *tert*-octylnitrene failed to produce any tetramethylpyrrolidine. For example, irradiation of *tert*-octyl azide in ether followed by aqueous acid workup gave methyl neopentyl ketone as the only isolated product. This is consistent with methyl migration (concerted or from nitrene) to give imine which is hydrolyzed to ketone in the workup (Scheme II) and is a well-known reaction.[3,4]

It has been reported that photochemical decomposition of oxaziridines produce nitrenes[3] (Scheme III). For this reason 3-phenyl-2-*tert*-octyloxaziridine was prepared via peracid oxidation of the imine. However, irradiation of this oxaziridine produced *N*-*tert*-octylbenzamide as the only isolated product.

We conclude that thiadiaziridines probably do not generate alkylnitrenes upon thermolysis but more likely rearrange by an intramolecular pathway, perhaps as indicated in path b in Scheme I.

Experimental Section

Reaction of *N*-(1,1,3,3-Tetramethylbutyl)-*N*-(2,2,4,4-tetramethyltetramethylene)sulfamide with Phenyl Iso-

(1) Timberlake, J. W.; Alender, J. A.; Garner, A. W.; Hodges, M. L.; Özmeral, C.; Szilagyi, S.; and Jacobus, J. O. *J. Org. Chem.* **1981**, *46*, 2082.

(2) Lwowski, W. "Nitrenes"; Wiley: New York, 1970; pp 47–97.

(3) Splitter, J. S.; Calvin, M. *Tetrahedron Lett.* **1968**, 1445.

(4) Sasaki, T.; Eguchi, S. Katada, T.; Hiroaki, O. *J. Org. Chem.* **1977**, *42*, 3741.

0022-3263/83/1948-0755$01.50/0