acetic acid amide (7), and *N*-[(acetylthio)methyl]thioglycolic acid amide (8).

The NMR data were as follows: (1) δ 2.37 (s), 2.40 (s), 3.60 (s), 4.65 (d, J = 6.4 Hz); (2) δ 2.19 (t, J = 6.3 Hz), 2.58 (t, J = 8.7 Hz), 3.30 (d, J = 6.3 Hz), 4.40 (dd, J_{SH} = 8.7 Hz, J_{NH} = 6.2 Hz); (7) δ 2.40 (s), 2.54 (t, J = 8.7 Hz), 3.60 (s), 4.36 (dd, J_{SH} = 8.7 Hz, J_{NH} = 6.2 Hz); (8) δ 2.16 (t, J = 6.3 Hz), 2.40 (s), 3.33 (d, J = 6.3 Hz), 4.69 (d, J = 6.4 Hz).

Integration over appropriate peaks indicated that the reaction mixture contained 1, 2, 7, and 8 in the ratio 20:37.5:37.5:5.

2,9-Bis(*p*-methoxyphenyl)-1,3,8,10-tetrathiacyclotetradecane-5,12-diene (11). Crude **10** (0.40 g, 0.0030 mol) obtained by hydrolysis of **9** in 1.2 N methanolic hydrogen chloride[8] was mixed with 0.42 g (0.003 mol) of anisaldehyde in 150 mL of methylene chloride. One drop of boron trifluoride etherate was added, and the mixture was kept overnight at room temperature. The precipitate was filtered, washed with ethanol, and recrystallized from large amounts of pyridine. The product (0.6 g, 75% yield) melted at 244 °C; mass spectrum (11 eV), m/e (rel intensity) 476 (<1), 358 (9), 270 (15); an NMR spectrum could not be obtained due to the insolubility of the sample.

Anal. Calcd for $C_{24}H_{28}O_2S_4$: C, 60.5; H, 5.92; S, 26.9. Found: C, 60.4; H, 5.80; S, 26.4.

Acknowledgment. This work was supported by the Swedish Natural Science Research Council and the Royal Physiographic Society in Lund.

Registry No. 1, 71831-11-3; 2, 71831-12-4; 3, 71831-13-5; 4, 71831-14-6; 7, 71831-15-7; 8, 71831-16-8; 9, 71831-17-9; 10, 55443-61-3; 11, 71831-18-0; *N*-(chloromethyl)chloroacetamide, 3659-52-7.

Supplementary Material Available: The crystallographic data for 4 [fractional coordinates (Table I), bond distances (Table II), and bond angles (Table III)] (2 pages). Ordering information is given on any current masthead page.

Aldehyde Syntheses. Study of the Preparation of 9,10-Anthracenedicarboxaldehyde

Yang-i Lin,* S. A. Lang, Jr., Christina M. Seifert,[1] R. G. Child, G. O. Morton, and P. F. Fabio

American Cyanamid Company, Medical Research Division, Pearl River, New York 10965

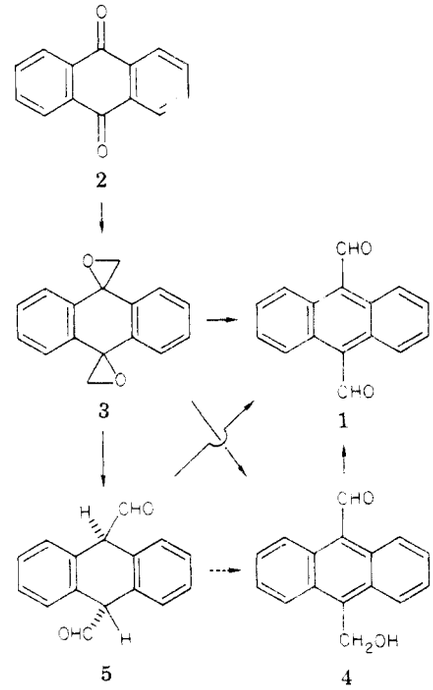
Received May 8, 1979

9,10-Anthracenedicarboxaldehyde (1) is the key intermediate for the synthesis of compounds with biological activity.[2] None of the three reported methods for the synthesis of 1 is convenient or economical. One method[3] involves a low-yield multistep synthesis starting from anthraquinone (2). The other two methods employ respectively dichloromethylation of anthracene[4] and lithiation of 9,10-dibromoanthracene[3] in their synthetic sequences. Since anthraquinone (2) and its substituted derivatives are readily available, a new practical synthesis of 1 from 2 has been sought.

Results and Discussion

We have developed new high-yield three-step syntheses of 1 starting from 2. *trans*-Dispiro[oxirane-2,9′(10′*H*)-anthracene-10′,2″-oxirane] (3)[5] was prepared in 94% yield by the reaction of anthraquinone with dimethylsulfonium methylide which was generated in situ by reacting trimethylsulfonium iodide with sodium hydride in dimethyl sulfoxide. The epoxide functions of 3 may open in two different modes depending on reaction conditions. Under mild and selective conditions, the epoxide moieties of 3 open in a stepwise fashion leading to the formation of 10-hydroxymethyl-9-anthraldehyde (4); for example, the rearrangement of 3 with lithium bromide in acetonitrile at 60 °C gave 4 in quantitative yield. Secondarily, the addition of dilute boron trifluoride etherate solution into a solution of 3 in ether at −45 °C also gave 4 but in 52% yield. Under more drastic conditions, however, both epoxide functions of 3 open simultaneously leading to *trans*-9,10-dihydro-9,10-anthracenedicarboxaldehyde (5); for example, the addition of an etheral solution of 3 to a dilute boron trifluoride etherate solution at 0 °C gave 5 in 95% yield. Furthermore, the treatment of 3 with boron trifluoride etherate at room temperature led to the formation of 1 in low yield (Scheme I).

Scheme I



The structure of 5 was determined by single-crystal X-ray methods.[6] The stereochemistry of the two aldehyde functions is trans. The center of the molecule coincides with a crystallographic inversion center, and the central ring is an extremely distorted chair form with torsion angles of approximately 4°. In agreement with our expectation, both NMR and IR spectra of 5 were similar but different from those of its cis isomer,[7] which was synthesized by oxidation of *cis*-9,10-dihydro-9,10-ethanoanthracene-11,12-diol with potassium periodate.

The oxidation of 4 by dimethyl sulfoxide in the presence of a sulfur trioxide–pyridine complex and triethylamine[8] at room temperature gave 1 in 95% yield.

Attempts to rearrange 5 to 4 with triethylamine in ether or with lithium bromide in acetonitrile led to the formation

(1) A 1978 summer intern from Smith College.
(2) K. C. Murdock, F. E. Durr, and R. B. Angier, in preparation.
(3) G. Rio and B. Sillion, *C. R. Hebd. Seances Acad. Sci.*, **244**, 623 (1957).
(4) B. H. Klanderman, *J. Org. Chem.*, **31**, 2618 (1966).
(5) T. J. McCarthy, W. F. Connor, and S. M. Rosenfeld, *Synth. Commun.*, **8** (6), 379 (1978).
(6) F. M. Lovell, N. A. Peterkinson, Y. Lin, R. G. Child, and S. A. Lang, Jr., in preparation.
(7) R. G. Child, S. A. Lang, Jr., V. J. Lee, and Y. Lin, in preparation. NMR ($CDCl_3$) δ 4.92 (d, J = 2.2 Hz, 2), 7.40 (s, 8), 9.40 (d, J = 2.2 Hz, 2); IR (KBr) 2800, 1720, 1480, 1450, 1380, 1300, 1240, 1120, 1010, 772, 755, 682 cm^{-1}.
(8) J. R. Parikh and W. von E. Doering, *J. Am. Chem. Soc.*, **89**, 5505 (1967).

0022-3263/79/1944-4701$01.00/0

Table I. Rate of Rearrangement of 3 to 4 in Acetonitrile Containing 0.289 M LiBr

temp, C	time, h	% 3	10^5k, s^{-1} [a]	% 4	10^5k, s^{-1} [b]
22 ± 1	7	83		18	
22 ± 1	13	59	1.03 ± 0.05[c]	37	1.04 ± 0.04[c]
22 ± 1	19	47		50	
22 ± 1	26	40		64	
60 ± 0.5	0.5	54	34.2	41	29.2

[a] The rate of the disappearance of 3. [b] The rate of the formation of 4. [c] Calculated by least-squares fit of ln (mol fraction of 3 or 4) vs. time; we thank Dr. J. B. Collins for analysis of the rate data.

of **1** respectively in 46 or 75% yield, and no appreciable amount of **4** was formed.

The use of acetonitrile as the reaction medium for the rearrangement of **3** to **4** is an improvement over reported conditions which employed benzene and HMPA.[9] The rearrangement of **3** to **4** with lithium bromide in acetonitrile was kinetically investigated. The results of kinetic data are summarized in Table I. Good pseudo-first-order behavior was observed within 5% standard deviation of the rate constant. The rate of the disappearance of **3** was equal to the rate of the formation of **4** within the experimental error. The NMR product analysis indicated that not even a trace of **5**, **6**, or **7** was formed or accumulated during the reaction. The kinetic study thus implied that **3** under the catalytic effect of lithium bromide rearranged to the reactive intermediate, presumably **6**, which then

6

7

rapidly rearranged to **4**; in other words, k_2 was much greater than k_1.

$$3 + \text{LiBr} \xrightarrow{k_1} 6 \xrightarrow{k_2} 4 \qquad (1)$$

Experimental Section

All melting points were taken on a Mel-Temp apparatus. NMR spectra were obtained on a Varian Model HA-100 spectrometer; chemical shifts (δ) are in ppm relative to internal tetramethylsilane. Mass spectra were recorded on A.E.I. MS 902. IR spectra were obtained on Perkin-Elmer Model 21.

***trans*-Dispiro[oxirane-2,9′[10′*H*]-anthracene-10′,2″-oxirane] (3).**[5] To a stirred mixture of 9.72 g (0.202 mol) of sodium hydride (50% oil dispersion) and 18.7 g (0.090 mol) of **2** in 560 mL of dry dimethyl sulfoxide at room temperature in the dark and under argon was added dropwise a solution of 41.26 g (0.202 mol) of trimethylsulfonium iodide in 340 mL of dry dimethyl sulfoxide over a period of 30 min. The reaction mixture was stirred for an additional hour and filtered through a sintered glass funnel. The filtrate was poured into 1500 mL of ice water and allowed to stand for 20 min. The crystals were collected and washed with water to give 20.2 g (94%) of **3** as colorless crystals: mp 119–121 °C (lit.[5] mp 121.5–122 °C); NMR ($CDCl_3$) δ 3.20 (s, CH_2, 4), 7.34 (s, aromatic, 8).

***trans*-9,10-Dihydro-9,10-anthracenedicarboxaldehyde (5).** A mixture of 0.10 mL of boron trifluoride etherate in 40 mL of anhydrous ether and 2.0 g of potassium carbonate was stirred at 0 °C for 10 min. A solution of 0.500 g of **3** in 20 mL of anhydrous ether was added. The resulting mixture was stirred at 0 °C for an additional 2 min and filtered. The ether filtrate was washed twice with a mixture of 10 mL of saturated sodium bicarbonate solution and 10 mL of ice water, dried over anhydrous sodium sulfate, and filtered. After removal of the ether, 0.495 g (95%) of yellow crystals, mp 126–133 °C, was obtained. Recrystallization from ether/hexane gave 0.384 g of **5** as yellow crystals: mp 132–135 °C; NMR ($CDCl_3$) δ 4.90 (d, J = 3.2 Hz, methine, 2), 7.38 (m, aromatic, 8), 9.30 (d, J = 3.2 Hz, CHO, 2); IR (potassium bromide) 2840, 2730, 1720, 1490, 1450, 1120, 1030, 1010, 750, 505, 450 cm^{-1}.

Anal. Calcd for $C_{16}H_{12}O_2$: C, 81.3; H, 5.12. Found: C, 81.1; H, 5.28.

10-(Hydroxymethyl)-9-anthraldehyde (4). Method A. To a solution of 4.00 g (0.0462 mol) of lithium bromide in 150 mL of dry acetonitrile was added 2.36 g (0.0100 mol) of **3**. The reaction mixture was stirred at 60 °C in the dark for 16 h and then cooled to −40 °C in a dry ice–acetone bath. The resulting crystals were collected by filtration and washed with water, giving 2.2 g (93%) of **4** as yellow crystals: mp 182–184 °C; NMR (Me_2SO-d_6) δ 5.42 (s, methylene, 2), 7.4–8.0 (m, aromatic, 4), 8.3–8.7 (m, aromatic, 2), 8.7–9.2 (m, aromatic, 2), 11.38 (s, CHO, 1); IR (potassium bromide) 3440, 1680 cm^{-1}; M^+ at m/e 236.

Anal. Calcd for $C_{16}H_{12}O_2$: C, 81.3; H, 5.12. Found: C, 81.1; H, 5.38.

Method B. To a solution of 0.500 g of **3** in 50 mL of anhydrous ether at −45 °C was added dropwise a solution of 0.060 mL of boron trifluoride etherate in 2.0 mL of anhydrous ether. The reaction mixture was stirred at −45 °C for 10 min, allowed to warm up to −30 °C in 5 min, and poured into a mixture of 20 mL of cold saturated sodium bicarbonate solution and 30 mL of ether. The ether solution was washed with an additional 20 mL of saturated sodium bicarbonate solution, dried over anhydrous sodium sulfate, and filtered. After removal of the ether, the yellow solid residue was recrystallized from acetonitrile to give 0.25 g (52%) of **4** as yellow crystals, mp 182–184 °C.

9,10-Anthracenedicarboxaldehyde (1) from 4. To a solution of 1.20 g (0.0050 mol) of **4** in a mixture of 14 mL of dry dimethyl sulfoxide at room temperature was added a solution of 4.80 g (0.030 mol) of sulfur trioxide–pyridine complex in 25 mL of dry dimethyl sulfoxide. The reaction mixture was stirred at room temperature for 50 min and then poured into 200 mL of water. The crystals were collected and washed with water to give 1.15 g (95%) of **1** as orange crystals, mp 244–245 °C (lit.[3] mp 241–244 °C).

9,10-Anthracenedicarboxaldehyde (1) from 5. Method A. Oxygen was bubbled through a solution of 0.40 g of lithium bromide in 20 mL of acetonitrile for 10 min. To the acetonitrile solution was added 0.240 g of **5**. The reaction mixture was stirred and kept under oxygen at 60 °C for 22 h. After removal of the acetonitrile, the orange residue was washed with water to give 0.22 g of **1**, mp 225–230 °C. Recrystallization from a mixture of Me_2SO and chloroform gave 0.178 g (75%) of orange crystals, mp 241–243 °C.

Method B. To a solution of 0.24 g of **5** in 15 mL of acetonitrile was added a solution of 0.30 mL of triethylamine in 5 mL of acetonitrile. The reaction mixture was stirred at room temperature for 4 h and then cooled in an ice bath. The orange precipitate was collected by filtration to give 0.136 g of **1**, mp 224–228 °C. Recrystallization from a mixture of Me_2SO and chloroform gave 0.110 g (46%) of orange crystals, mp 243–245 °C.

Kinetic Studies of the Rearrangement of 3 to 4. To a solution of 400 mg of lithium bromide in 16.0 mL of dry acetonitrile (0.289 M) was added 280 mg of **3**. The reaction mixture was stirred in the dark at room temperature (22 ± 1 °C) or at 60 ± 0.5 °C. At intervals, 4.0-mL aliquots were withdrawn and added to 50 mL of ether. The ether solutions were washed with 3 × 15 mL portions of water and dried over sodium sulfate. After removal of the ether, the residues were dissolved in a mixture of deuterated dimethyl sulfoxide (3 parts), deuterated chloroform (1 part) and a few drops of deuterated methanol. The NMR spectra indicated that the products consisted of **3** and **4** and that not a trace of **5**, **6**, and **7** was present. The rate of the rearrangement of **3** to **4** was based on the integrations of the signals at δ 3.26 (of **3**) and 5.52 (of **4**), using the integration of aromatic protons (δ 7.0–9.1) as an internal standard. The results of kinetic studies are summarized in Table I.

Acknowledgment. We wish to thank Mr. L. Brancone and staff for microanalyses and Dr. W. Gore and staff for

(9) B. Rickborn and R. M. Gerkin, *J. Am. Chem. Soc.*, **93**, 1693 (1971).

the spectral data. We are grateful to Dr. J. D. Albright for helpful discussion on Me_2SO oxidation.

Registry No. 1, 7044-91-9; 2, 84-65-1; 3, 71774-87-3; 4, 71774-88-4; 5, 71774-89-5.

Lithium–Methylamine Studies. 3. Reduction of Carboxamides

Angela O. Bedenbaugh,* Albert L. Payton, and John H. Bedenbaugh

Department of Chemistry, University of Southern Mississippi, Hattiesburg, Mississippi 39401

Received December 8, 1978

Benkeser et al.[1] have reduced a number of aliphatic carboxamides to alcohols or aldehydes electrolytically with lithium chloride in methylamine. In those cases in which aldehyde was the primary product, ethanol, an effective proton donor in this system, had been added to the solution. In the electrolytic procedure of Benkeser, *N*-methylalkanamides and *N,N*-dimethylalkanamides produced aldehydes in about 50% yield, while unsubstituted carboxamides were reduced in 25% or lower yield.

Since lithium–amine reduction may differ from electrolytic reduction, we herein report reduction of carboxamides by lithium–methylamine and compare the results with those of amide reduction by the electrolytic–methylamine method of Benkeser.

Results and Discussion

Carboxamides of varying molecular weight and nitrogen substituents were investigated. Reduction of about 0.1 mol of pentanamide, octanamide, *N*-methylpentanamide, *N*-methylhexanamide, and *N*-methyloctanamide with either 2 or 3 equiv of lithium produced only trace amounts of aldehyde. The results of reductions of some other amides with lithium in methylamine are shown in Table I. The unexpectedly small amount of aldehyde formed in the case of *N,N*-dicyclohexylpentanamide is attributed to condensation of the reduction product during the isolation procedure. The percentage of reduced product observed when the amide is added to lithium in solution is less than when lithium is added to the amide in solution. For example, *N,N*-dimethyloctanamide added to a lithium solution produces 27.3% octanal in contrast to the 51.7% octanal produced when lithium is added to dissolved *N,N*-dimethyloctanamide. When lithium is added to dissolved amide, amide reaction (with lithium already in solution) as well as lithium dissolution are occurring during most of the reaction period. The resultant concentration of dissolved, unreacted lithium at any time is considerably lower than 0.23 M (when all added lithium is dissolved but unreacted); hence, the relative concentrations of various reducing species[2] are dependent on the order of addition of reactants.

After treatment of *N,N*-dimethyldecanamide and *N,N*-diethyldecanamide with lithium–methylamine (nonacidic isolation procedure) the product obtained was subjected to a second lithium–methylamine reduction. The yields from these consecutive reductions were 75.3% *N*-methyldecylamine and 20.0% *N*-methyldecanamide from *N,N*-dimethyldecanamide and 76.4% *N*-methyldecylamine with 14.4% *N*-methyldecanamide from *N,N*-diethyldecanamide. Any *N*-methylalkanamide observed must arise from transamidation between starting amide and methylamide ion. Since *N*-methylalkanamides were shown to be relatively resistant to reduction, the percentage of *N*-methylalkanamide formed (15–20%) should be a rough approximation of the extent of the side reaction which forms the *N*-methylalkanamide. This is supported by the 15 and 30% *N*-methylalkanamide isolated in two separate instances as indicated in Table I.

When the product isolation procedure involves basic conditions, imine is obtained; but if the aqueous solution becomes acidic during the extraction process, aldehyde is obtained. No *N*-methylalkylamine is observed among the reaction products, thus indicating that imine was not present during the reduction since it has been shown that imine is readily reduced to amine by lithium in methylamine.[3] The absence of significant quantities of alcohol (formed rapidly from aldehyde in this system[1,3]) in the reaction products leads to the conclusion that little aldehyde is present in the reaction. Since neither aldehyde nor imine appear to be present in the reduction, we have concluded that a carbinolamine anion is a stable intermediate.

When 4 equiv of absolute ethanol was added to *N*-methyloctanamide in methylamine prior to addition of 8 equiv of lithium, a mixture containing 1-octanol and octanal in about a 3:1 ratio was observed. *N,N*-Dimethyloctanamide, when subjected to the same reaction conditions, yielded a slightly higher percentage of alcohol; however, 14.3% *N*-methyloctylamine was obtained from the reduction with no aldehyde being observed. This is

Table I. Reduction of Amides with Lithium in Methylamine

amide	reduction medium[a]	amt Li, equiv	yield of aldehyde, %[b]
$CH_3(CH_2)_3CONHCH_3$	0.423 (6)	2	4.39
$CH_3(CH_2)_6CONHCH_3$	0.113 (10)[c]	6	13.2[f]
$CH_3(CH_2)_3CON(CH_3)_2$	0.139 (8)	2	45.0
$CH_3(CH_2)_4CON(CH_3)_2$[h]	0.0907 (8)[c]	2	48.4
$CH_3(CH_2)_6CON(CH_3)_2$[h]	0.116 (10)[c]	2	51.7
$CH_3(CH_2)_8CON(CH_3)_2$[h]	0.0998 (6)	2	57.9[g]
$CH_2(CH_2)_8CON(CH_2CH_3)_2$[h]	0.0826 (6)	2	54.3[g]
$CH_3(CH_2)_3CON(C_6H_{11})_2$[h]	0.0848 (0.23)	2	trace[d,e]

[a] In all of these reactions 500 mL of methylamine was used, the first value is moles of amide and the reaction time, in hours, is in parentheses. [b] The products reported were identified by IR and NMR spectra. [c] The solution was blue, indicating imcomplete reaction of all added lithium when the reaction was quenched. [d] The product gave a positive (2,4-dinitrophenyl)hydrazine test. [e] See the Experimental Section for details of this reduction. [f] Isolated as *N*-octylidenemethylamine. [g] *N*-Methyldecanamide was also isolated (29.2% from *N,N*-dimethyldecanamide and 13.7% from *N,N*-diethyldecanamide). [h] Certain physical constants (d, n_D, MR_D) of this compound are reported in *J. Chem. Eng. Data*, 21, 247 (1976).

(1) R. A. Benkeser, H. Watanabe, S. J. Mels, and M. A. Sabol, *J. Org. Chem.*, **35**, 1210 (1970).
(2) R. L. Dye, *Acc. Chem. Res.*, **1**, 306 (1968).
(3) A. O. Bedenbaugh, J. H. Bedenbaugh, W. A. Bergin, and J. D. Adkins, *J. Am. Chem. Soc.*, **92**, 5774 (1970).

0022-3263/79/1944-4703$01.00/0