1645, 1605 cm^{-1}; mass spectrum, m/e (relative intensity) 349 (19), 257 (100), 228 (30). Anal. Calcd for $C_{25}H_{19}NO$: C, 85.93; H, 5.48. Found: C, 85.87; H, 5.54.

5′-Bromo-1,1′:3′,1″-terphenyl (21). The general procedure was followed, but with 2,4,6-tribromoiodobenzene (**20**)[17] in place of **1**, and the mixture was heated at reflux for 1.5 h before quenching with aqueous HCl. The usual workup gave, after chromatography (silica gel, hexane eluent), 80% of **21** which was recrystallized from benzene–ethanol: mp 105–106 °C (107.5–109 °C after sublimation); ^{1}H NMR δ 7.46–7.50 (m, 7 H), 7.58–7.64 (m, 4 H), 7.70 (s, 2 H). Anal. Calcd for $C_{18}H_{13}Br$: C, 69.90; H, 4.20. Found: C, 69.71; H, 4.40.

---

(17) Hodgson, H. H.; Mahadevan, A. P. *J. Chem. Soc.* **1947**, 173.

Acknowledgment. We are indebted to the National Institutes of Health GM15997 for financial support of this research.

Registry No. **1**, 19821-80-8; **7**, 92-06-8; **8**, 103068-13-9; **9**, 3073-05-0; **10**, 16716-13-5; **11**, 1568-74-7; **12**, 103068-14-0; **13**, 103068-15-1; **14**, 103068-16-2; **15**, 103068-17-3; **18**, 82777-09-1; **19**, 103068-19-5; **20**, 21521-51-7; **21**, 103068-20-8; p-$C_6H_5C_6H_4MgBr$, 3315-91-1; m-$C_6H_5C_6H_4MgBr$, 103068-18-4; o-$CH_3OC_6H_4MgBr$, 16750-63-3; C_6H_5MgBr, 100-58-3; 2,4,6-$(CH_3)_3C_6H_2MgBr$, 2633-66-1; p-$CH_{30}C_6H_4MgBr$, 13139-86-1; 2,5-$(CH_3O)_2C_6H_4MgBr$, 62890-98-6; 2,6-$Br_2C_6H_3NH_2$, 608-30-0; 1,2,3-$(CH_3)3C_6H_3$, 608-21-9; 2,6-$Cl_2C_6H_3I$, 19230-28-5; 2,4,6-$Br_3C_6H_2I$, 21521-51-7; 1-naphthylmagnesium bromide, 703-55-9; 2-naphthylmagnesium bromide, 21473-01-8.

An Improved Method for S_N2-Type Demethoxycarbonylation of Activated Esters with 4-Aminothiophenol and a Cesium Catalyst

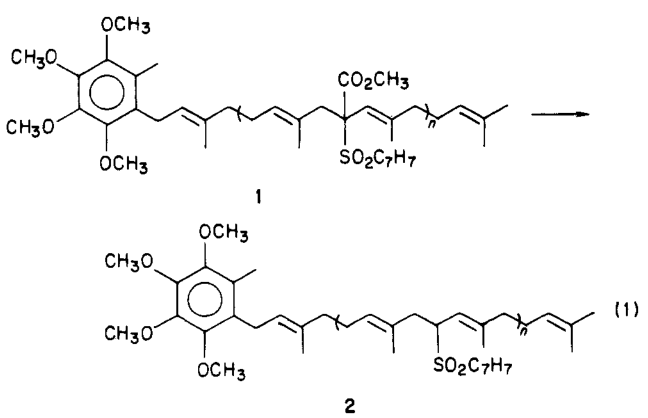
Ehud Keinan*† and Doron Eren

Department of Organic Chemistry, Weizmann Institute of Science, Rehovot 76100, Israel

Received January 27, 1986

A powerful method for demethoxycarbonylation of activated methyl esters was developed, employing stoichiometric amounts of 4-aminothiophenol and catalytic quantities of cesium carbonate in hot (85 °C) DMF. The superiority of this technique over several other methods was demonstrated in a comparative study on linear polyprenoid substrates, in which the thiolate/Cs_2CO_3 approach benefited from shorter reaction times, lower temperatures, higher yields, and simpler workup procedures. The method enabled simultaneous removal of two methoxycarbonyl functions contained in a single molecule, a transformation representing a crucial step in the total synthesis of ubiquinone-10.

The synthesis of linear polyprenoid chains still represents a major challenge in synthetic organic chemistry,[1] particularly when compared to the fairly efficient oligomerization techniques that were developed for other important biopolymers and oligomers, including peptides, polynucleotides, and polysaccharides. We have recently developed a general route for making polyprenoids via a palladium(0)-catalyzed oligomerization of modified monoterpene unit.[2] One of the crucial steps in this approach involves the simultaneous removal of several methoxycarbonyl groups from a large molecule, as shown in the example in eq 1—one of the last steps in the total synthesis of ubiquinone-10.[3]



Demethoxycarbonylation at multiple reaction sites in a rather complex multifunctional molecule requires a highly efficient and yet chemoselective reaction that transforms each site in nearly quantitative yield while preserving all other functionalities.

Dealkoxycarbonylation of active esters via S_N2-type dealkylation[4] is certainly the most attractive one-step process for removal of the methyl ester entity, particularly when sterically hindered. The reaction usually involves heating of the substrate in a dipolar aprotic solvent in the presence of a nucleophile. Following Krapcho's original development of this approach,[5] which employed NaCl in dimethyl sulfoxide (Me_2SO), many other nucleophiles have been found applicable,[4] including halides, thiolates, *tert*-butoxide, thiocyanate, amines, and acetate. By far, the best method is probably that developed by Johnson[6] and modified by Trost and Verhoeven,[7] which employs tetramethylammonium acetate in hot (130 °C) Me_2SO or hex-

---

[†] Incumbent of The Joseph and Madeleine Nash Career Development Chair established by Fondacion Madelon, Zurich, Switzerland.

(1) (a) Britton, G. *Natl. Prod. Rep.* **1984**, *1*, 68. (b) Cainelli, G.; Cardillo, G. *Acc. Chem. Res.* **1981**, *14*, 89. (c) Isler, O.; Schudel, P. *Adv. Org. Chem.* **1973**, *4*, 115.

(2) (a) Keinan, E.; Eren, D., submitted for publication. (b) Keinan, E.; Eren, D. Israel Patent 71 482, 1985.

(3) For general information concerning ubiquinone-10, see: Yammamura, Y.; Folkers, K.; Ito, Y. *Biochemical and Clinical Aspects of Coenzyme Q_{10}*; Elsevier: Amsterdam, 1977(a), 1980(b), 1981(c), 1983(d); Vol. I(a), II(b), III(c), IV(d).

(4) (a) Krapcho, A. P. *Synthesis* **1982**, 805, 893. (b) McMurry, J. *Org. React. (N.Y.)* **1976**, *24*, 187. (c) Stevens, R. V.; Lee, A. W. M. *J. Am. Chem. Soc.* **1979**, *101*, 7032.

(5) (a) Krapcho, A. P.; Glynn, G. A.; Grenon, B. J. *Tetrahedron Lett.* **1967**, *215*. (b) Krapcho, A. P.; Weimaster, J. F.; Eldridge, J. M.; Jahngen, E. G. E., Jr.; Lovey, A. J.; Stephens, W. P. *J. Org. Chem.* **1978**, *43*, 138.

(6) Johnson, W. S.; Harbert, C. A.; Ratcliffe, B. A.; Stipanovic, R. D. *J. Am. Chem. Soc.* **1976**, *98*, 6188.

(7) (a) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4743. (b) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1976**, *98*, 630. (c) Trost, B. M.; Weber, L.; Strege, P.; Fullerton, T. J.; Dietsche, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 3426.

0022-3263/86/1951-3165$01.50/0

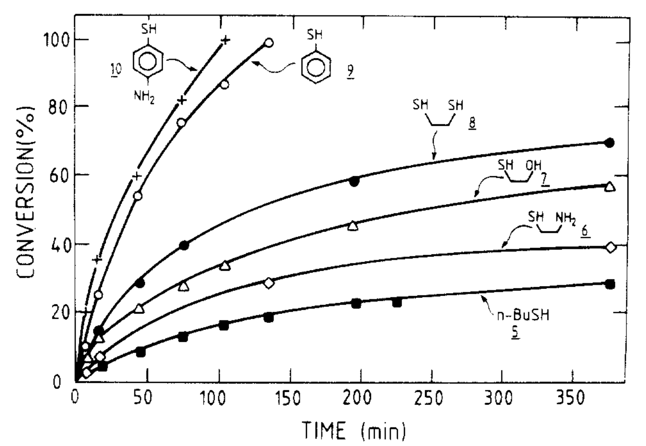


Figure 1. Dependence of demethoxycarbonylation rate on the nature of the thiol. A mixture of 3-carbomethoxy-4-phenyl-2-butanone (206 mg, 1 mmol), cesium carbonate (100 mg, 0.3 mmol), and the appropriate thiol (**5**–**10**) (1.5 mmol) in 5 mL of DMF was stirred at 85 °C and the progress of the reaction was monitored by GC using diphenyl ether as an internal standard.

amethylphosphoramide (HMPA) (at 100 °C). Unfortunately, a number of the above-mentioned procedures, including the tetramethylammonium acetate approach, were not satisfactory for multiple decarboxylation reactions such as that given in eq 1. Only low to moderate yields of the desired products were realized with model substrates **3** and **4** (vide infra, Table II).

In our search for more effective methods, we delved deeper into dealkoxycarbonylation with the thiolate anion. In the literature, this group of weak bases and powerful nucleophiles is employed only infrequently for this purpose, perhaps due to the inconvenience of preparing and storing the required solid sodium or lithium thiolate salts. The procedures described[8] usually require large excesses of thiolate salts which, in addition to their notorious stench, are moisture and oxygen sensitive. In attempting to apply the thiolate approach to the problem at hand, we investigated how four largely neglected factors influence thiolate-promoted dealkoxycarbonylation: (a) the nature of the thiol employed, (b) the procedure for generating the corresponding thiolate anion, (c) the kind of base used for this purpose, and (d) the workup procedure for efficient removal of byproducts, organosulfur compounds in particular.

A systematic study along these lines yielded a powerful demethoxycarbonylation technique, which utilizes stoichiometric amounts of 4-aminothiophenol and catalytic quantities of cesium carbonate.

Results and Discussion

In all of our studies, the solvent of choice was *N*,*N*-dimethylformamide (DMF)—a stable, nontoxic, dipolar medium. In order to avoid problems associated with the preparation and handling of thiolate anion solutions, we employed the required thiol along with catalytic amounts of base, which formed low concentrations of the thiolate anion in situ. For these basic catalysts, we utilized very mild, inexpensive, and readily available alkali metal carbonates. Certainly, the identity and amounts of both the thiol and alkali metal compounds are critical for the course of reaction. The study outlined below enabled us to identify the best choices for these two components.

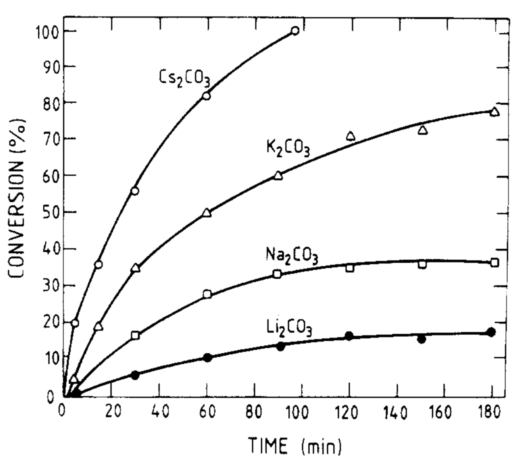
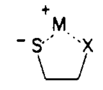


Figure 2. Dependence of demethoxycarbonylation rate on the base employed. A solution of 3-carbomethoxy-4-phenyl-2-butanone (206 mg, 1 mmol), PATP (190 mg, 1.5 mmol), and the appropriate alkali metal carbonate (0.3 mmol) in 5 mL of DMF was stirred at 85 °C, and the reaction was monitored by GC as described above.

The Thiol. Six different thiols were initially studied for their ability to demethoxycarbonylate methyl 2-benzylacetoacetate (Figure 1). Two simple monofunctional thiols, *n*-butanethiol (**5**) and thiophenol (**9**), were chosen as representative aliphatic and aromatic thiols, respectively. Three highly polar β-heterosubstituted ethanethiols—cystamine (**6**), 2-thioethanol (**7**), and 1,2-ethanedithiol (**8**)—were employed with the hope of (a) increasing thiolate nucleophilicity, as expected on the basis of possible chelation to the metal (see structure I), and (b) enabling simple removal of excess reagent and methyl thioether product by either aqueous workup or by washing through silica gel with a nonpolar solvent.



$X = SH, OH, NH_2$

I

Interestingly, of the thiols examined, the simple, aliphatic compound **5**, which has been recommended for ester cleavage,[8a] is, apparently, the least efficient reagent for this reaction. As predicted, the bifunctional aliphatic thiols (**6**–**8**) are significantly more effective than the monofunctional one (**5**). Nevertheless, still faster reactions were achieved with thiophenol. This aromatic thiol, however, has two major drawbacks: the unpleasant odor of both thiophenol and thioanisole and the need to use chromatography to separate the desired product.

In order to solve these problems we increased the water solubility of the thiol by replacing thiophenol with *p*-aminothiophenol (PATP)[9] (**10**). This improvement not only circumvented the inconvenient odor and separation problems but also increased the overall reaction rate (Figure 1). This is due, perhaps, to the enhanced nucleophilicity of the thiolate, which contains an electron-donating substituent. Both 4-aminothiophenol and 4-aminothioanisole are nonvolatile materials that are easily removed from the reaction mixture by aqueous, acidic workup.

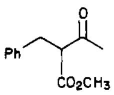
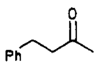
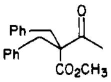
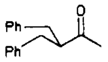
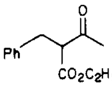
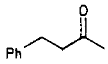
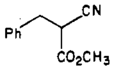
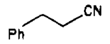
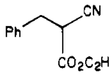
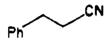
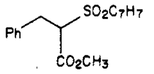
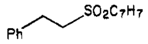
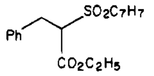
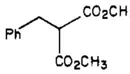
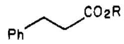
The Catalyst. The relative catalytic activities of lithium, sodium, potassium, and cesium carbonates were compared on two model substrates in order to study

---

[8] (a) Bartlett, P. A.; Johnson, W. S. *Tetrahedron Lett.* **1970**, 4459. (b) Sheehan, J. C.; Daves, G. D., Jr. *J. Org. Chem.* **1964**, *29*, 2006. (c) Corey, E. J.; Brennan, T. M.; Carney, R. L. *J. Am. Chem. Soc.* **1971**, *93*, 7316.

[9] 4-Aminothiophenol is easily prepared in large quantities from 4-nitrochlorobenzene: Gilman, H.; Gainer, G. C. *J. Am. Chem. Soc.* **1949**, *71*, 1747.

Table I. Dealkoxycarbonylation of Activated Esters[a]

entry	substrate	time, h	product	yield,[b] %
1		3		98
2		3		100
3		20		37[c]
4		3		86
5		10		40[d]
6		2		94
7		3		e
8		3		93[b,f]

[a] All reactions were carried out according to the general procedure described in the text. [b] Products were isolated and identified by comparison to authentic samples (NMR, IR, MS). [c] 45% recovered starting material. [d] No starting material left. [e] No reaction. [f] Two products were isolated: 3-phenylpropanoic acid (R = H) and its methyl ester (R = CH_3) in a 1:2 ratio, respectively.

possible regularities in their behavior in this reaction. In the first set of experiments, methyl 2-benzylacetoacetate was treated with 1.5 equiv of PATP in hot (85 °C) DMF in the presence of 10 mol % of each of the four metal carbonates (Figure 2). In the second set, similar demethoxycarbonylation reactions were carried out on a different substrate (methyl 2,2-dibenzylacetoacetate) and with a different thiol (**9**).

The set of experiments presented in Figure 2 clearly indicate an order of reactivity which parallels the increased ionic character and enhanced nucleophilicity of the alkali metal thiolates: Cs > K > Na > Li. A similar trend with the various alkali metal carbonates was also observed in the second set of experiments, where a more acidic thiol, **9** was employed. However, the differences in successive reactivities decrease when moving toward the more ionic salts with very small difference between potassium and cesium. Yet, in both cases the lithium salt is clearly inferior to the heavier alkali metal carbonates. Interestingly, lithium salts are the most widely used nucleophiles in many of the alternative demethoxycarbonylation methods.[2]

The question of optimal base concentration was explored with cesium carbonate. Generally, reaction rates increase with increasing base concentration; however, reactions proceed at satisfactory rates with as little as 5 mol % of Cs_2CO_3, with salt solubility in the reaction medium appearing to be the limiting factor. Maximal decarboxylation rates are achieved with 0.04 M (20 mol %) of this base, under which conditions the mixture is still homogeneous. Additional quantities of cesium carbonate have no further effect.

On the basis of the above-described study, we recommend the following general procedure for demethoxycarbonylation of activated methyl esters. The substrate (1 mmol) is dissolved in freshly distilled DMF (5 mL) along with PATP (1.5–2 mmol) and cesium carbonate (0.3 mmol). The mixture is stirred at 85 °C under an inert atmosphere and monitored by either GC or TLC until reaction is complete (usually between 1 and 3 h). The mixture is then poured into water and extracted with ether. The latter is washed with aqueous HCl (3%) and then with brine and dried over magnesium sulfate. Removing solvent under reduced pressure resulted, in most cases, in a product that does not require further purification. Typical transformations carried out according to this procedure are listed in Table I.

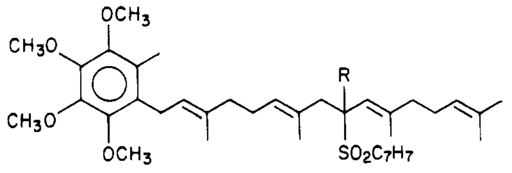
Table II. Comparison of Demethoxycarbonylation Methods

substrate	nucleophilic reagent	solvent	temp, °C	time, h	product (yield, %)
3a	NaCl, H_2O[a]	DMF	153	15	**3b** (26)
3a	NaCN, LiI[b]	DMF	120	15	**3b** (28)
3a	CsOAc	DMF	130	24	**3b** (47)
3a	Me_4NOAc[c]	HMPA	100	24	**3b** (62)[d]
3a	PhSH, Cs_2CO_3	DMF	85	1	**3b** (73)
3a	PATP, Cs_2CO_3	DMF	85	1	**3b** (98)
4a	NaCN, LiI[b]	DMF	120	20	**4b** (58)
4a	Me_4NOAc[c]	HMPA	100	7	**4b** (47)
4a	PATP, Cs_2CO_3	DMF	85	1	**4b** (97)
4c	PATP, Cs_2CO_3	DMF	85	5	**4d** (92)

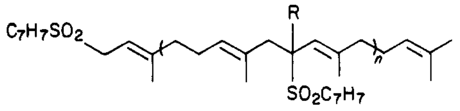
[a] Reaction carried out according to ref 4c. [b] Reaction carried out according to ref 5. [c] Reaction carried out according to ref 7. [d] 10% recovered starting material.

As expected for an S_N2-type process, the reaction is highly selective for methyl esters that are activated by an adjacent ketone, nitrile, sulfone, etc. Higher esters are nearly inert to the reaction conditions, as demonstrated by the sluggish reactivity of ethyl esters (entries 3, 5, and 7). This chemoselectivity, reminiscent of the situation observed in dealkoxycarbonylation with chloride and cyanide anions in polar solvents[5b,10] as well as in ester cleavage with LiI/pyridine or molten thiocyanate,[11] may be taken advantage of in complex syntheses. Additionally, the general reaction conditions that are useful for dealkoxycarbonylation of activated methyl esters are suitable for dealkylation of unactivated methyl esters, as demonstrated by the formation of a free carboxylic acid, shown in entry 8.

The superiority of our technique to several popular demethoxycarbonylation methods is manifested by shorter reaction times, lower temperatures, and higher yields. A comparative study of the various methods (Table II) was carried out with two linear diterpene derivatives, **3** and **4**,



3a, R=CO_2CH_3
b, R=H



4a, R=CO_2CH_3, n=1
b, R=H, n=1
c, R=CO_2CH_3, n=2
d, R=H, n=2

which were prepared during our efforts toward the total synthesis of ubiquinone-10.[2] Essentially quantitative yields were realized when PATP and cesium carbonate were

---

(10) (a) Muller, P.; Siegfried, B. *Tetrahedron Lett* **1973**, 3565. (b) Wilczynski, J. J.; Johnson, H. W., Jr. *J. Org. Chem.* **1974**, *39*, 1909.

employed. With both substrates no side products could be observed by either TLC or NMR, and therefore no chromatographic purification was needed. Conversely, all other methods yielded varying quantities of decomposition products, requiring separation by either flash chromatography or TLC.

As outlined above, the crucial test of this new method is its ability to simultaneously transform multiple methoxycarbonyl functions contained in a single molecule. Indeed, double demethoxycarbonylation of the triterpenoid **4c** was carried out, giving **4d** in 92% isolated yield. Utilization of this technique for multiple demethoxycarbonylation of long-chain polyprenoids, such as **1** (n = 2–4), leading to various ubiquinone precursors, is currently under way in our laboratories.[2]

Conclusion

In this paper we have introduced a selective and relatively mild method for demethoxycarbonylation of activated methyl esters. It is based on employing stoichiometric amounts of PATP and catalytic quantities of cesium carbonate in hot (85 °C) DMF. The superiority of this technique over several other methods was demonstrated in a comparative study on linear polyprenoid substrates, in which the thiolate/Cs_2CO_3 approach benefited from shorter reaction times, lower temperatures, higher yields, and simpler workup procedures. The method is particularly useful for sterically hindered systems, such as α,α-disubstituted active esters. It enabled an efficient simultaneous removal of several methoxycarbonyl functions contained in a single molecule, a transformation representing a crucial step in the total synthesis of ubiquinone-10. A detailed description of that synthesis is to be published.[2]

Experimental Section

General Methods. Melting points (uncorrected) were determined on a Büchi apparatus. Infrared spectra were measured on the neat compounds with a Perkin-Elmer 467 grating spectrometer and are given in cm^{-1} units. ^1H NMR spectra were measured in deuteriochloroform on a Bruker WH-270 NMR spectrometer. All chemical shifts are reported in δ units downfield from Me_4Si, and the J values are given in hertz. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Thin-layer chromatography (TLC) was performed on aluminum sheets precoated with silica gel (Merck, Kieselgel 60, F254, Art 5549). Preparative TLC was performed on glass plates precoated with silica gel (Merck, Kieselgel 60 F-254, Art 5717). GC analyses were performed on a Spectra-Physics 7100 (FI detector) gas chromatograph equipped with a 0.125 in. × 2 ft column packed with 10% SE-30 on Chromosorb W.

Materials. DMF and HMPA were distilled over barium oxide and kept under argon. Commerical lithium, sodium, potassium, and cesium carbonates, potassium cyanide, lithium iodide trihydrate (all purchased from Fluka), and tetramethylammonium acetate (Aldrich) were used without any treatment. p-Aminothiophenol (PATP) was prepared from p-chloronitrobenzene (Aldrich) according to ref 9. 3-Carbomethoxy-4-phenyl-2-butanone, 3-benzyl-3-carbomethoxy-4-phenyl-2-butanone, and 3-carboethoxy-4-phenyl-2-butanone were prepared by reacting methyl or ethyl acetoacetate (BDH) with benzyl chloride and potassium *tert*-butoxide in THF. Cyano ester substrates were prepared in the same way from methyl or ethyl cyanoacetate. α-Sulfone esters were prepared from methyl or ethyl 2-(p-tolylsulfonyl)acetate which in turn were prepared by reacting alkyl-2-bromoacetate (BDH) with sodium p-toluenesulfinate (Merck) in DMF.

Dependence of Demethoxycarbonylation Rate on the Nature of the Thiol. Details are given in Figure 1.

Dependence of Demethoxycarbonylation Rate on the Base Employed. A. A solution of 3-benzyl-3-carbomethoxy-4-phenyl-2-butanone (296 mg, 1 mmol), thiophenol (165 mg, 1.5 mmol), and the appropriate alkali metal carbonate (0.5 mmol) in 5 mL of DMF was stirred at 85 °C. The progress of the reaction was monitored by GC using diphenyl ether as an internal standard. The following conversions were observed:

time, min	Na_2CO_3	K_2CO_3	Cs_2CO_3
30	9	47	49
60	76	88	90
90	91	97	97
120	95	100	100

B. Details are given in Figure 2.

Demethoxycarbonylation of 1-(3,7,11,15-Tetramethyl-9-carbomethoxy-9-(*p*-tolylsulfonyl)-2,6,10,14-hexadecatetraenyl)-2-methyl-3,4,5,6-tetramethoxybenzene (3a). A. With PATP. A solution of **3a**[12] (232 mg, 0.33 mmol), PATP (64 mg), and cesium carbonate (35 mg) in 3 mL of DMF was stirred at 85 °C for 1 h. The mixture was worked up as described in the general procedure, yielding **3b** in the form of a nearly colorless oil, which was found to be pure by TLC, NMR and elemental analysis (206 mg, 98%): NMR 7.70 (d, J = 8 Hz, 2 H), 7.29 (d, J = 8 Hz, 2 H), 5.10 (t, J = 6.5 Mz, 1 H), 5.07–4.94 (m, 2 H), 4.87 (d, J = 13 Hz, 1 H), 3.90 (s, 3 H), 3.89 (s, 3 H), 3.88–3.79 (m, 1 H), 3.78 (s, 3 H), 3.77 (s, 3 H), 3.29 (d, J = 6 Hz, 2 H), 2.43 (s, 3 H), 2.12 (s, 3 H), 2.07–1.80 (m, 10 H), 1.73 (s, 3 H), 1.66 (s, 3 H), 1.56 (s, 3 H), 1.50 (s, 3 H), 1.20 (s, 3 H); IR 2920, 1595, 1410, 1355, 1315, 1300, 1260, 1200, 1140, 1090, 1040, 980, 820, 740, 670 cm^{-1}. Anal. Calcd for $C_{38}H_{54}O_6S$: C, 71.44; H, 8.52. Found: C, 71.22; H, 8.60.

B. With Sodium Chloride. A solution of **3a** (90 mg, 0.13 mmol) and NaCl (7 mg, 0.13 mmol) in 5 mL of DMF was refluxed for 24 h, cooled, and poured into 50 mL of water. The mixture was extracted with ether; the ether solution was washed with water and brine and dried over $MgSO_4$; the solvent was removed under reduced pressure and the oily residue purified by preparative TLC (20% ethyl acetate in hexane), affording **3b** (22 mg, 26%).

C. With Lithium Iodide and Sodium Cyanide. A solution of **3a** (70 mg, 0.10 mmol), lithium iodide trihydrate (176 mg), and NaCN (10 mg) in 5 mL of DMF was stirred at 120 °C for 48 h, cooled, poured into 50 mL of water, and worked up and purified by preparative TLC as described above, affording **3b** (21 mg, 28%).

D. With Cesium Acetate. A solution of **3a** (70 mg, 0.10 mmol) and cesium acetate (76 mg 0.4 mmol) in 5 mL of DMF was stirred at 130 °C for 24 h, cooled, and poured into 50 mL of water. The mixture was worked up and purified as described above, affording **3b** (30 mg, 47%).

E. With Tetramethylammonium Acetate. A solution of **3a** (229 mg, 0.33 mmol) and tetramethylammonium acetate (386 mg) in 3 mL of HMPA was stirred at 95 °C for 24 h, after which no starting material could be observed by TLC. The mixture was worked up and purified as described above, affording 127 mg of **3b** (0.20 mmol, 62% yield).

F. With Thiophenol. A solution of **3a** (206 mg, 0.29 mmol), thiophenol (66 mg, 0.6 mmol), and cesium carbonate (50 mg) in 5 mL of DMF was stirred at 85 °C for 1 h. The solution was poured into water (50 mL) and extracted with ether (3 × 10 mL). The extracts were combined, washed with 5% NaOH, water, and brine, and dried over $MgSO_4$; the solvent was removed under reduced pressure. The oily residue was purified by preparative TLC, affording 143 mg of **3b** (0.22 mmol, 73% yield).

Demethoxycarbonylation of 8-Carbomethoxy-3,7,11,15-tetramethyl-1,9-bis(*p*-tolylsulfonyl)-2,6,10,14-hexadecatetraene (4a). A. With PATP. A solution of **4a**[12] (229 mg, 0.38 mmol), PATP (100 mg), and cesium carbonate (50 mg) in 3 mL of DMF was stirred at 85 °C for 4 h, after which TLC indicated complete conversion. The mixture was poured into water (20 mL) and worked up with ether and diluted HCl as described above, affording 215 mg of nearly colorless oil, which was found (by TLC and NMR) to be pure **4b** (0.37 mmol, 97% yield): NMR 7.77–7.64 (m, 4 H), 7.38–7.25 (m, 4 H), 5.22–4.97 (m, 3 H), 4.90 (t, J = 9

---

(11) (a) Borch, R. F.; Grudzinskas, C. V.; Peterson, D. A.; Weber, L. D. *J. Org. Chem.* **1972**, *37*, 1141. (b) Meinwald, J.; Putzig, D. E. *Ibid.* **1970**, *35*, 1891. (c) Thomas, E. W.; Crowell, T. I. *J. Org. Chem.* **1972**, *37*, 744.

(12) The preparation of compounds **3a**, **4a**, and **4c** are reported in ref 2.

Hz, 1 H), 3.83–3.72 (m, 3 H), 2.44 (s, 6 H), 2.08–1.83 (m, 10 H), 1.68 (s, 3 H), 1.58 (s, 6 H), 1.33 (s, 3 H), 1.17 (s, 3 H); IR 2920, 1735, 1655, 1595, 1495, 1440, 1380, 1305, 1240, 1140, 1090, 1045, 900, 820, 750, 665 cm^{-1}. Anal. Calcd for $C_{34}H_{46}O_4S_2$: C, 70.06; H, 7.95. Found: C, 69.17; H, 7.92.

B. With Lithium Iodide and Sodium Cyanide. A solution of **4a** (211 mg, 0.33 mmol), lithium iodide trihydrate (580 mg), and sodium cyanide (32 mg) in 5 mL of DMF was stirred at 120 °C for 20 h, after which no starting material could be observed by TLC. The solution was worked up as described above, and purification afforded **4b** (101 mg, 0.19 mmol, 58% yield).

C. With Tetramethylammonium Acetate. A solution of **4a** (211 mg, 0.33 mmol) and tetramethylammonium acetate (386 mg) in 3 mL of HMPA was stirred at 95 °C for 7 h. The mixture was worked up as described above, affording 91 mg of **4b** (0.17 mmol, 47% yield).

Demethoxycarbonylation of 9,17-Dicarbomethoxy-3,7,11,15,19,23-hexamethyl-1,9,17-tris(*p*-tolylsulfonyl)-2,6,10,14,18,22-tetracosahexaene (4c). A solution of **4c**[12] (122 mg, 0.12 mmol), PATP (45 mg, 0.4 mmol), and cesium carbonate (50 mg) in 3 mL of DMF was stirred at 85 °C for 5 h. The mixture was poured into water (20 mL) and extracted with ether (3 × 10 mL). The combined extracts were washed twice with 1 M HCl (5 mL), water, and brine and dried over $MgSO_4$. The solvent was removed under reduced pressure to yield 95 mg of pale yellow oil, which was found (by TLC and NMR) to be pure **4d** (0.11 mmol, 92% yield): NMR 7.83–7.63 (m, 6 H), 7.40–7.23 (m, 6 H), 5.25–4.82 (m, 6 H), 3.95–3.72 (m, 4 H), 2.44 (s, 3 H), 2.43 (s, 6 H), 2.07–1.77 (m, 16 H), 1.68 (s, 3 H), 1.58 (s, 6 H), 1.50 (s, 6 H), 1.33 (s, 3 H), 1.20 (s, 3 H); IR 2920, 1660, 1595, 1495, 1440, 1380, 1305, 1240, 1180, 1140, 1090, 1025, 910, 820, 735, 670 cm^{-1}. Anal. Calcd for $C_{51}H_{68}O_6S_3$: C, 70.15; H, 7.85. Found: C, 68.78; H, 7.85.

Acknowledgment. We thank the Schmidt Foundation for Applied Research for their generous financial support.

Registry No. **3a**, 102779-87-3; **3b**, 102745-41-5; **4a**, 102779-88-4; **4b**, 68690-58-4; **4c**, 102745-40-4; **4d**, 66958-23-4; Cs_2CO_3, 534-17-8; 4-aminothiophenol, 1193-02-8; ubiquinone-10, 303-98-0; methyl 2-benzyl-3-oxobutanoate, 3666-82-8; dimethyl dibenzylpropanedioate, 3666-83-9; ethyl 2-benzyl-3-oxobutanoate, 620-79-1; methyl α-cyanobenzenepropanoate, 57519-78-5; ethyl α-cyanobenzenepropanoate, 6731-58-4; methyl α-tosylbenzenepropanoate, 94143-11-0; dimethyl benzylpropanedioate, 49769-78-0; 4-phenyl-2-butanone, 2550-26-7; 3-benzyl-4-phenyl-2-butanone, 3506-88-5; benzenepropanenitrile, 645-59-0; phenethyl *p*-tolyl sulfone, 19719-87-0; 3-phenylpropanoic acid, 501-52-0; methyl 3-phenylpropanoate, 103-25-3.

Electron Transfer in the Decomposition of Hexaalkylhydrazine Dications

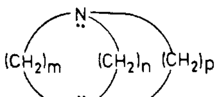
Stephen F. Nelsen* and J. Thomas Ippoliti

McElvain Laboratories of Organic Chemistry, Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706

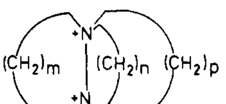
Received April 22, 1986

Rearrangements of hexaalkylhydrazine dications [$R_3N^+N^+R_3$] to α-amino ammonium cations [$R_3N^+CHR'NR_2$] derived by Hofmann-like degradation (loss of an α proton and NN bond cleavage to give an amino immonium cation, followed by addition of the amino group to the $C{=}N^+$ bond) are investigated. Tricyclic dications $\mathbf{6}^{2+}$ and $\mathbf{10}^{2+}$ give $\mathbf{14}^{+}$ and $\mathbf{8}^{+}$, respectively, showing high selectivity for hydrogen loss from the methylenes in the bicyclo[2.2.2]octyl rings which can have CH bonds aligned with the NN bond over the three other types of methylene groups as well as the methyl group. Selectivity for hydrogen loss from the methyl and methylene carbons of the bicyclic dication $\mathbf{3}^{2+}$ proves to be sensitive to the reaction conditions. $NC\mathit{H}_3/NC\mathit{H}_2$ attack ratios from 4 to 10 were observed for carbonate and chloride in acetonitrile (chloride in water failed to react), but a ratio of about 1 was observed for iodide in both acetonitrile and water. It is argued that iodide decomposes the dications by an electron-transfer mechanism in which the key step is hydrogen atom abstraction from the 3e-σ-bonded cation radical. This is consistent with the observed even higher selectivity to HC,NN bond alignment than occurs for base attack on the dication.

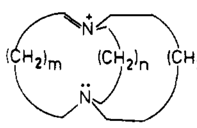
Alder and co-workers have intensively studied the chemistry of medium-ring tricyclic diamines 1[*mnp*], which they have shown to have very unusual electron- and proton-transfer properties.[1] Most notably for this work, 1[333] and 1[444] are oxidized to cation radicals having three electron σ bonds and to tetracyclic diazoniapropellane dications $\mathbf{1}^{2+}$. Their first route to these compounds grew out of work on alkylation of 1,8-diaminonaphthalene with 1,3-dibromopropane[2] and involved bicyclo-bis-alkylation of bicyclic hydrazines to bridgehead diazoniapropellanes $\mathbf{1}^{2+}$, which were reduced to the diamines. This route has been used to prepare 1[332], 1[333], 1[433], 1[433], and 1[444].[3-5] Other members of the 1[*mnp*] series have been prepared by reduction of α-amino ammonium ions generated from bicyclic amidines and α,ω-dihaloalkanes (used for 1[433], 1[432], and 1[633])[6] and by reaction of ω-chloroalkanals with cyclic medium-ring diamines (11 examples).[7] Not surprisingly, $\mathbf{1}^{2+}$ is sensitive



1[mnp]



1^{2+}



2

---

[1] For a review, see: Alder, R. W.; Sessions, R. B. *Chemistry of Amino, Nitroso, and Nitro Compounds and their Derivatives*, Shvo, Y., Ed.; J. Wiley and Sons: New York, 1982; Part 2, Chapter 18, pp 782–804.

[2] (a) Alder, R. W.; Goode, N. C.; King, T. J.; Mellor, J. M.; Miller, D. W. *J. Chem. Soc., Chem. Commun.* **1976**, 173. (b) Alder, R. W.; Gill, R.; Goode, N. C. *Ibid.* **1976**, 973.

[3] Alder, R. W.; Sessions, R. B.; Mellor, J. M.; Rawlins, M. F. *J. Chem. Soc., Chem. Commun.* **1977**, 747.

[4] Alder, R. W.; Sessions, R. B. *J. Am. Chem. Soc.* **1979**, *101*, 3651.

[5] Alder, R. W.; Sessions, R. B.; Bennett, A. J.; Moss, R. E. *J. Chem. Soc., Perkin Trans. 1* **1982**, 603.

[6] Alder, R. W.; Sessions, R. B. *Tetrahedron Lett.* **1982**, *23*, 121.

0022-3263/86/1951-3169$01.50/0