J. Org. Chem. 1984, 49, 3416-3419

Table I. Product Yields after Photolysis of Samples I-III[a]

	reactants, M			products, mM					
	[t-BuOOBu-t]	[c-C_6H_{12}]	[CCl_4]	[t-BuOH]	[$(CH_3)_2\overline{CCH_2O}$]	[c-$C_6H_{11}Cl$]	[C_2Cl_6]	[$HCCl_3$]	[CH_3Cl]
I	2.71	4.62		25 ± 1					
II	2.71	2.78	2.07	27 ± 2		45 ± 2	14 ± 1	15 ± 1	
III	2.71		5.18	67 ± 3	72 ± 3		8 ± 1		10 ± 2[b]

[a] Based on the results of duplicate or triplicate experiments. [b] Acetone was a complementary product, but its low yield and poor GC response (flame ionization) precluded accurate analysis.

plication of the normal kinetic expression[13] for a chain reaction combined with the value obtained for R_i (vide supra) and the data in Table I gave k_8 = 50 M^{-1} s^{-1} at 35 °C in excellent agreement with gas-phase values of 16 M^{-1} s^{-1}[16] and 60 M^{-1} s^{-1}.[17]

Sample III contained no cyclohexane but gave approximately 3 times more *tert*-butyl alcohol than the other samples, together with an essentially equal yield of isobutylene oxide.[18] This observation is consistent with a chain reaction involving reactions 9 and 10 as the propagation steps.

$$t\text{-BuO}\cdot + t\text{-BuOOBu-}t \rightarrow t\text{-BuOH} + \dot{C}H_2C(CH_3)_2OOBu\text{-}t \qquad (9)$$

$$\dot{C}H_2C(CH_3)_2OOBu\text{-}t \rightarrow t\text{-BuO}\cdot + (CH_3)_2\overline{COCH_2} \qquad (10)$$

The formation of hexachloroethane and chloromethane implies that the squence of reactions 2, 11,

$$\cdot CH_3 + CCl_4 \rightarrow CH_3Cl + \dot{C}Cl_3 \qquad (11)$$

and 7 was partly responsible for chain termination. In addition, the fact that the yield of hexachloroethane was smaller in III than II suggests that some termination was taking place via other processes.

The above results show that the photolysis of di-*tert*-butyl peroxide is not quenched by carbon tetrachloride and that the observation by EPR of trichloromethyl radicals[3] was almost certainly due to reactions 1, 2, and 11.

Two corollaries follows: First, k_{11} must be >10^2 M^{-1} s^{-1} at 25 °C and not 9 M^{-1} s^{-1}[5] for EPR observation of ·CCl$_3$ to have been possible.[19,20] Second, the results imply that the normal rate of thermolysis of the peroxide at 25 °C[21] would be sufficient to initiate its decomposition via reactions 9 and 10. This would proceed with a chain length of ca. 10^6 and a rate of ca. 10^{-5} M^{-1} s^{-1} which would lead to substantial degradation of the peroxide within a few weeks.[22] The reason that this does not normally occur is presumably that dissolved oxygen, hydroperoxide impurities, and especially isobutylene oxide itself, which are all highly reactive toward *tert*-butoxyl radicals,[26] function as chain-breaking inhibitors.

Experimental Section

With the exception of di-*tert*-butyl peroxide, all of the materials used in this work were commercially available in high purity and were used as received. Di-*tert*-butyl peroxide was treated with aqueous silver nitrate solution so as to remove olefinic impurities. It was then washed with water and was dried over magnesium sulfate. It was finally passed through a column of alumina to remove hydroperoxide impurities.

Photolyses were carried out in a merry-go-round reactor, under conditions where the peroxide was the only light absorbing reactant. Thus, the reactor was fitted with 350-nm lamps and their relatively broad spectral output was reduced by the use of filters which had only 15% transmission at 330 nm.

Products were identified by GC/MS (Hewlett-Packard 5995). They were quantified by GC analysis (20 ft, 12% OV-101 column; Varian 3700 instrument); see text for further details.

Acknowledgment. We thank Drs. J. C. Scaiano (NRCC) and P. Engel (Rice University) for helpful discussions and suggestions.

Registry No. Di-*tert*-butyl peroxide, 110-05-4; carbon tetrachloride, 56-23-5; cyclohexane, 110-82-7; trichloromethyl, 3170-80-7.

---

[13] d[HCCl$_3$]/dt = k_8[c-C$_6$H$_{12}$](R_i/2k_7)$^{1/2}$. A value of 2k_7 = 5 × 10^9 M^{-1} s^{-1} was taken for this calculation on the basis of literature data for 2k_7 at −40 °C[14] combined with data for the temperature dependence of diffusion-controlled reactions.[15]

[14] Paul, H. *Int. J. Chem. Kinet.* **1979**, *11*, 495.

[15] Schuh, H.-H.; Fischer, H. *Helv. Chim. Acta* **1978**, *61*, 2130.

[16] White, M. L.; Kuntz, R. R. *Int. J. Chem. Kinet.* **1971**, *3*, 127.

[17] Currie, J. L.; Sidebottom, H. W.; Tedder, J. M. *Int. J. Chem. Kinet.* **1974**, *6*, 481.

[18] Bell, E. R.; Rust, F. F.; Vaughan, W. E. *J. Am. Chem. Soc.* **1950**, *72*, 337. Bloodworth, A. J.; Davies, A. G.; Griffin, I. M.; Muggleton, B.; Roberts, B. P. *Ibid.* **1974**, *96*, 7599.

[19] Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 193.

[20] Recent gas-phase data support this conclusion and give k_{11} = 75 M^{-1} s^{-1} at 25 °C, see: Matheson, I. A.; Tedder, J. M.; Sidebottom, H. W. *Int. J. Chem. Kinet.* **1982**, *14*, 1033.

[21] Koenig, T. In "Free Radicals"; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. I, p 122.

[22] Obtained by application of the normal expression for chain reactions, cf.: ref 13. Reaction 9 must be rate determining since $k_9 \simeq$ 5 × 10^4 M^{-1} s^{-1}[23] while k_{10} = 1.1 × 10^6 s^{-1}.[18,24] The termination step should therefore be 2t-BuO· → products, for which the rate constant is 1.3 × 10^9 M^{-1} s^{-1}.[25]

[23] Estimated from the rate constant for hydrogen abstraction from the methyl groups of pentane; Griller, D.; Ingold, K. U.; Jackson, R. A.; Nazran, A. S., unpublished results.

[24] Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 7739.

[25] Wong, S. K. *Int. J. Chem. Kinet.* **1981**, *13*, 433.

[26] By analogy with ethylene oxide,[27] the rate constant for hydrogen abstraction from isobutylene oxide must be ca. 1 × 10^6 M^{-1} s^{-1}.

[27] Maltesta, V.; Scaiano, J. C. *J. Org. Chem.* **1982**, *47*, 1455.

Metal-Mediated Concomitant Silyl Ether Cleavage/Cyclization Reactions To Construct Bicyclic Piperazinediones and a New Polymer-Supported Mercury(II) Perchlorate

Jen-Sen Dung, Robert W. Armstrong, and
Robert M. Williams*

*Department of Chemistry, Colorado State University,
Fort Collins, Colorado 80523*

Received March 16, 1984

Recently, we developed[1] a short and efficient cyclization reaction to construct the bicyclic piperazinedione ring system present in the novel antibiotic bicyclomycin.[2] The bicyclic piperazinediones 2 have proven to be versatile intermediates for elaboration into structurally diverse bicyclomycin analogues[3] as well as potential intermediates for the total synthesis of the natural product.[4] During the

---

[1] Williams, R. M.; Anderson, O. P.; Armstrong, R. W.; Josey, J.; Meyers, H.; Eriksson, C. *J. Am. Chem. Soc.* **1982**, *104*, 6092.

[2] See the citations in ref 1 and 3 for biological activity, structure elucidation, isolation, and synthetic approaches to bicyclomycin (bicozamycin, aizumycin, The Merck Index, 10th ed., 1983, p 1213).

[3] Williams, R. M.; Dung, J-S.; Josey, J.; Armstrong, R. W.; Meyers, H. *J. Am. Chem. Soc.* **1983**, *105*, 3214.

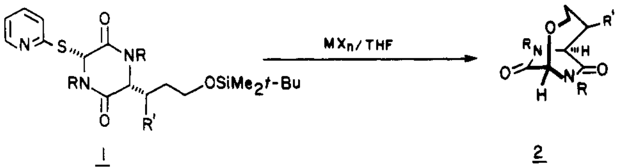
0022-3263/84/1949-3416$01.50/0

Table I. One-Step Conversions of 1 → 2

entry	reagent	equivalents	reaction conditions[a]	substrate 1	isolated yield of 2,[h] %
1	$Cu(ClO_4)_2$[c]	1	25 °C, 18 h	R = CH_2Ph-*p*-OCH_3; R′ = H	95.4
2	$Cu(ClO_4)_2 \cdot 6H_2O$[d]	1	25 °C, 60 h		72.6
3	$AgClO_4$[c]	1	25 °C, 24 h		88.4
4	$Hg(ClO_4)_2$[c]	3	25 °C, 60 h		88
5	$Fe(ClO_4)_3$[c]	2	25 °C, 120 h		59.4
6	$Ni(ClO_4)_2$[c]	2	25 °C, 24 h		84
7	$Pb(ClO_4)_2$[c]	2	reflux, 120 h		87.3
8	$PhHgClO_4$[e]	2	25 °C, 19 h		98
9	$Tl(ClO_4)_3 \cdot 6H_2O$[d]	0.9	25 °C, 24 h		56.6
10	Ⓟ$PhHgClO_4$[b]	2–7.3[b]	25 °C, 46–144 h[b]		70–86
11	$PhHgClO_4$	2	25 °C, 2 min	R = CH_3; R′ = H[f]	90
12	$PhHgClO_4$	3	25 °C, 0.5 h	R = CH_2Ph; R′ = CH_2OMs[g]	78
13	$PhHgClO_4$	3	25 °C, 2 h	R = Ph-*p*-Ome; R′ = H[g]	82.2
14	$Cu(ClO_4)_2$	1	25 °C, 12 h	R = CH_2Ph-*p*-OCH_3; R′ = CH_2OMs[g]	83

[a] All reactions were carried out in distilled THF. [b] See Experimental Section. [c] Azeotropically dried by evaporation from acetonitrile/toluene. [d] Used directly as sold commercially. [e] Freshly prepared as described in ref 3. [f] See ref. 1. [g] See supplementary material section. [h] Yields not optimized.

course of our ongoing investigations in this area, we observed the remarkably efficient one-step[1] conversion of the silyl-protected (pyridylthio)piperazinediones 1 into the bicyclic derivatives 2 by treatment with 2 molar equiv of phenyl mercuric perchlorate in THF at 25 °C. We felt that this reaction was of sufficient inherent and practical interest to warrant a more detailed study regarding the possible metal salts that could bring about this concomitant silyl ether cleavage/cyclization reaction. Herein, we present the results we have obtained from "screening" a variety of commercially available thiophilic metal salts. In addition, we have prepared the polymer-supported phenyl mercuric perchlorate reagent 5 and demonstrate the utility of such a solid-phase metal salt.



1 2

Results and Discussion

The substrates 1 were prepared according to the procedure described in ref 1.[5] Table I provides the isolated yields and reaction conditions for each salt that was examined.[6] As discussed previously, the relative stereochemistry of the pyridylthio and (*tert*-butyldimethylsiloxy)propyl residues is syn, requiring that iminium species such as 3 are plausible intermediates prior to cyclization.

3

Thus, a reagent capable of effecting this transformation must be capable of (1) removing the pyridylthio residue from the piperazinedione nucleus through coordination and (2) cleaving the silicon–oxygen bond via nucleophilic interception by the counterion. Examination of the data in Table I reveals that the metal cations Cu^{2+}, Ag^+, Hg^{2+}, Tl^{3+}, Pb^{2+}, Fe^{3+}, and Ni^{2+} as their perchlorate salts effect the cyclization reactions; only Mg^{2+} failed to produce product.[6] Most of the commercially available perchlorate salts are sold as hydrates with the exception of silver(I) perchlorate. The hydrated salts were azeotropically dried[7] from toluene/acetonitrile; we have subsequently found that this is not critical since the hydrated reagents such as $Tl(ClO_4)_3 \cdot 6H_2O$ and $Cu(ClO_4)_2 \cdot 6H_2O$ (Table I, entries 2 and 9) efficiently effect cyclization *without significant competing hydrolysis at C-6 of the piperazinedione.* The most economical reagent for this type of reaction is $Cu(ClO_4)_2$ (Table I, entry 1) which is available for ca. $0.10 per gram and cleanly effects the concomitant deprotection/cyclization efficiently. Of the counterions we screened, perchlorate is by far the best; triflate, hexafluoroantimonate, and tosylate (as their Ag^+ salts) work with modest efficiency;[6] fluoborate and sulfate do not provide any detectable amount of bicyclic products, leaving only unreacted starting material.[6]

Operationally, these reactions are very simple to perform, requiring no specialized equipment and no extraordinary precautions other than the use of distilled solvents. Standard aqueous isolation and chromatographic separation of the bicyclic product from the 2-mercaptopyridine byproducts[8] is required.

In an effort to circumvent the need to chromatographically separate the bicyclic product from the 2-mercaptopyridine byproducts and the potentially toxic metals, we have prepared the novel and potentially versatile mercurial polymer reagent 5. We chose -$ArHg^+$, due to the known stability[9] of the C–Hg bond; the observed stability[1] of soluble PhHgSpy; and the ease of preparation of the me-

---

(4) (a) Armstrong, R. W.; Dung, J-S.; Williams, R. M. "Abstracts of Papers", 185th National Meeting of the American Chemical Society, Division of Organic Chemistry, Seattle, Wa, March 1983; American Chemical Society: Washington, D.C., 1983; Abstr. 10. (b) For a recently reported total syntheses, see: Nakatsuka, S.; Yamada, K.; Yoshida, K.; Asano, O. *Tetrahedron Lett.* **1983**, *24*, 5627. Williams, R. M.; Armstrong, R. W.; Dung, J.-S. *J. Am. Chem. Soc.*, in press.

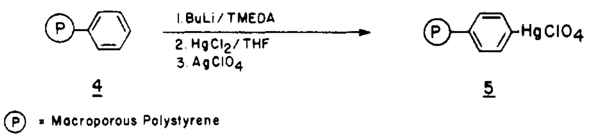
(5) The preparation of 1,4-bis(*p*-methoxybenzyl)-2,5-piperazinedione from glycine anhydride and *p*-methoxybenzyl chloride in the presence of NaH in DMF proceeds in 87% yield. The sequential enolate alkylation and enolate sulfenylation (affording 1) of this compound is performed according to the procedure described in ref 1 (see Experimental Section). The preparation of substrates 1 (R = CH_2Ph, R′ = CH_2OMs; and R = CH_2Ph-*p*-OCH_3, R′ = CH_2OMS) shall be reported as part of a full account regarding these compounds elsewhere; see also ref 4.

(6) See supplementary material section for a more extensive table.

(7) We have not experienced any safety hazards in handling and/or drying these perchlorate salts. The dangers pointed out by Professor K. N. Raymond (*Chem. Eng. News*, Dec 5, **1983**) and L. Bretherick (*Chem. Eng. News*, Dec 12, **1983**) with heavy-metal perchlorates as their acetonitrile and Me_2SO solvates suggests that the use of the commercially sold hydrates is preferable.

(8) In general, the 2-mercaptopyridine byproducts were not characterized other than as faster moving bands on TLC; only in the case of $PhHgClO_4$, was the PhHgSpy byproduct isolated and identified.

(9) See Ei-ichi Negishi in "Organometallics in Organic Synthesis", Wiley: New York, 1980; Vol. I, Chapter 7.



tallopolymer. Commercially available macroporous polystyrene was lithiated[10,11] and transmetalated with $HgCl_2$. Anion exchange with $AgClO_4$ followed by thorough agitative washings produced the resin **5**. Exposure of **1** to this resin in THF at room temperature for several days afforded the expected product **2** (Table I, entry 10). Filtration and thorough washing of the insoluble resin with THF followed by evaporation of the solvent from the filtrate and examination of the "crude" residue by ^1H NMR and TLC indicated clean formation of **2** that was uncontaminated by starting material. Furthermore, no evidence (^1H NMR, TLC) could be obtained for 2-mercaptopyridine byproducts leaching from the resin into the crude filtrate. Based on our experience with the soluble PhHgSpy,[1] it is reasonable that all of the 2-mercaptopyridine remains covalently attached to the polymer support as the stable ⓅPhHgSpy species; the "crude" filtrate only contains bicyclic product that needs only a simple recrystallization. In addition, the polymer can be regenerated after use by (1) conversion back to the ⓅPhHgCl by treatment with HCl and (2) counterion exchange as described above (see Experimental Section). We expect that this polymer-supported mercury salt shall find useful applications in other areas of synthesis such as macrolide formation,[12] glycoside-forming reactions,[13] and other thio–acetal exchanges; work is in progress to elucidate the versatility of this material.

Thus, we have demonstrated that a variety of metal perchlorates in at least stoichiometric proportion[14] efficiently effect cleavage of the Si–O bond with concomitant O–C bond formation and removal of the thiopyridine residue to afford the bicyclic piperazinediones. Application of these reagents to other ring-forming reactions and synthetic problems are under study in these laboratories.

Experimental Section[15]

1,4-Bis(*p*-methoxybenzyl)-3-[3-[(*tert*-butyldimethylsilyl)oxy]propyl]-6-(2-pyridylthio)-2,5-piperazinedione (1). This substrate was prepared according to the procedures described in ref 1 in 35% overall yield from N,N′-di-*p*-methoxybenzyl-2,5-piperazinedione (oil): ^1H NMR (270 MHz) ($CDCl_3$) (Me_4Si) δ 0.092 (6 H, s), 0.942 (9 H, s), 1.679–1.725 (2 H, m), 1.994–1.110 (2 H, m), 3.677 (2 H, t, J = 10.4 Hz), 3.803 (6 H, s), 3.940 (1 H, t, J = 4 Hz), 4.010 (1 H, $^1/_2$ AB q, J = 15.5 Hz), 4.013 (1 H, $^1/_2$ AB q, J = 14 Hz), 5.169 (1 H, $^1/_2$ AB q, J = 14 Hz), 5.170 (1 H, $^1/_2$ AB q, J = 15.5 Hz), 6.623 (1 H, s), 6.809–7.624 (11 H, m), 8.497 (1 H, d, J = 4.9 Hz); IR (NaCl, neat) 1680, 1610, 1580, 1515, 1460, 1250, 1180, 1110, 1035, 840, 730 cm^{-1}.

8,10-Bis(*p*-methoxybenzyl)-8,10-diaza-2-oxabicyclo[4.2.2]decane-7,9-dione (2). A representative procedure for the conversion of **1** → **2** (R = *p*-methoxybenzyl; R′ = H) is given below employing $Cu(ClO_4)_2$[7] (Table I, entry 2). The reaction conditions for the other metal salts are given in Table I.

To a stirred solution of **1** (R = *p*-methoxybenzyl; R′ = H) (44 mg, 0.07 mmol, 1.0 equiv) in THF (1.5 mL) was added $Cu(ClO_4)_2$[7] (18.2 mg, 0.07 mmol, 1.0 equiv) at room temperature. The mixture was allowed to stir for 18 h at room temperature, evaporated, and separated on a small silica gel column (eluted with Et_2O) to afford 27 mg (95.4%) of pure bicyclic **2**: (on larger scales, an aqueous isolation procedure involving 0.1 N $NaOH/CH_2Cl_2$ extraction is employed), mp 147–147.5 °C (recrystallized from Et_2O/CH_2Cl_2); ^1H NMR (270 MHz) ($CDCl_3$) (Me_4Si) 1.508–1.750 (2 H, m), 1.912–1.953 (2 H, m), 3.315–3.397 (1 H, m), 3.733–3.858 (1 H, m), 3.797 (6 H, s), 4.082 (1 H, dd, J = 5.32 Hz, J = 2.77 Hz), 4.082 (1 H, $^1/_2$ AB q, J = 14.426 Hz), 4.306 (1 H, $^1/_2$ AB q, J = 14.507 Hz), 4.715 (1 H, $^1/_2$ AB q, J = 14.507 Hz), 4.978 (1 H, $^1/_2$ AB q, J = 14.426 Hz), 5.174 (1 H, s), 6.827–7.273 (8 H, m); IR (NaCl, neat) 1665, 1615, 1515, 1470, 1250, 1100, 1035, 830, 775, 730 cm^{-1}; mass spectrum, *m/e* (relative intensity) 410 (M^+, 7.3), 289 (3.2), 274 (8.7), 121 (100). Anal. ($C_{23}H_{26}N_2O_5$) C, H, N.

Synthesis of the Resin-Bound $Hg^{II}ClO_4$. To a stirred, room temperature suspension of washed polystyrene[16] (2.8 g, 27 m equiv) in dry cyclohexane (20 mL), containing 4 mL (25 mmol) of tetramethylethylenediamine, was added *n*-BuLi (16.9 mL, 2.0M in hexane, 33.75 mmol). After 10 min at room temperature, the reaction mixture was heated at 65 °C for 4 h and cooled to room temperature, the liquid phase was removed, and the reddish brown resin was rinsed 3 times with dry cyclohexane. This lithiated resin was immediately used for the following transmetalation reaction.

To a stirred, room temperature suspension of the freshly prepared lithiated resin (~27 mequiv) in THF (65 mL) was added $HgCl_2$ (12.24 g, 45 mmol). After stirring 17 h at room temperature, the liquid layer was removed and the grey polymer beads were exhaustively washed with THF, ether, THF–H_2O (1:1), THF, and MeOH. The resin[17] was collected on a filter paper and washed successively with THF, THF/H_2O (1:1), THF, benzene, and MeOH and then dried at room temperature under vacuum. Anal. C, 61.46; H, 5.20; Hg, 28.55; Cl, 5.12. IR (KBr) 1600, 1585, 1495, 1450, 750, 690, 525 cm^{-1}.

To a stirred, room temperature suspension of ⓅPhHgCl[17] (1.26 g, ca. 1.8 mequiv) in THF (10 mL) was added a solution of $AgClO_4$[7] (518 mg, 2.5 mmol) in THF (10 mL). The reaction mixture was stirred for 2 days and filtered. The bone-white polymer was collected on a filter paper and washed with THF (20 mL × 12) before using. Anal. C, 60.59; H, 5.86; Hg, 13.93; Cl, 5.06 (ca. 0.7 mequiv per g).[18] IR (KBr) 1600, 1580, 1500, 1450, 1060, 1020, 900, 750, 690, 605, 525 cm^{-1}.

Cyclization of 1 Employing Resin 4. To a stirred solution of **1** (R = CH_2Ph-*p*-OCH_3; R′ = H) (79 mg, 0.12 mmol, 1.0 equiv) in THF (3 mL) was added the resin **4** (1.2 g, ca 7.0 mequiv) at 25 °C. The suspension was gently stirred for 46 h and filtered, and the resin was washed extensively with THF. The combined

---

[10] See: Hodge, P., Sherrington, D. C., Eds. "Polymer-Supported Reactions in Organic Synthesis"; Wiley: New York, 1980.

[11] Farrall, J. M.; Frechet, M. J. *J. Org. Chem.* **1976**, *41*, 3877.

[12] See (a) Corey, E. J.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1974**, *96*, 5614. (b) Gerlach, H.; Thalmann, A. *Helv. Chim. Acta* **1974**, *57*, 2661. (c) Masamune, S.; Kamata, S.; Schilling, W. *J. Am. Chem. Soc.* **1975**, *97*, 3715.

[13] Williams, R. M.; Stewart, A. O. *Tetrahedron Lett.* **1983**, *24*, 2715 and references cited therein.

[14] We have carefully examined the stoichiometry of the Hg^{2+} and Cu^{2+} reactions and find that at least 1 molar equiv of metal salt is needed to obtain high yields.

[15] Microanalyses are within ±0.3% of the calculated values. Anhydrous AgOTf, $AgClO_4$, $Mg(ClO_4)_2$, $AgSbF_6$, $AgBF_4$, AgOTs, and Ag_2SO_4 were used as obtained from Ventron. All other metal perchlorates were dissolved in 50% acetonitrile/toluene, evaporated to dryness several times, and dried under high vacuum for 24 h (*CAUTION*, see ref 7). The hydrated perchlorates were used as furnished commercially by Ventron. The following abbreviations are used throughout: Et_2O = diethyl ether; THF = tetrahydrofuran; LDA = lithium diisopropylamide; MeOH = methanol; Spy = 2-mercaptopyridine. Preparative silica gel TLC was carried out on a Harrison Research Chromatotron using 1.0-, 2.0-, and 4.0-mm layer thickness silica gel adsorbents. All solvents and reagents were purified according to standard protocol. Polystyrene beads were commercial, macroporous material (Aldrich), 22–50 mesh, average pore diameter of 800 Å (cross-linked with DVB).

[16] The polystyrene used was washed routinely to remove surface impurities. The following solutions were used at 60–80 °C with, in each case, a contact time of 1 h with the resin: 1 N NaOH, 1 N HCl, 2 N NaOH–dioxane (1:2), 2 N HCl–dioxane (1:2), H_2O, dimethylformamide. The resins were then washed at room temperature with the following solutions (1 h in each case): 2 N HCl in methanol, H_2O, methanol, methanol–CH_2Cl_2 (C1:3), MeOH–CH_2Cl_2 (1:10). The resins were then dried under vacuum for 3 days.

[17] For other preparations of polymer-bound HgCl, see: (a) Taylor, R. T.; Flood, L. A. *J. Org. Chem.* **1983**, *48*, 5161. (b) Burlitch, J. M.; Winterton, R. C. *J. Organomet. Chem.* **1978**, *159*, 299 and references cited therein.

[18] The elemental analysis indicates more Cl relative to Hg than the formula $ⓅHgClO_4$ requires. This is due to AgCl trapped in the resin matrix that cannot be completely expelled from the polymer through washing. This material is inocuous for the reaction and the regenerated resin does not lose activity after several cycles (same mequiv/g stoichiometry).

filtrate was evaporated, diluted with CH_2Cl_2, poured into H_2O, and extracted several times with CH_2Cl_2. The combined extracts were dried over anhydrous sodium sulfate, filtered, and evaporated from MeOH to afford pure bicyclic **2** (35.3 mg, 70%; crystallized from Et_2O/CH_2Cl_2). An additional 5.1 mg of **2** was recovered from the mother liquors (total yield 80%). The yields for this reaction reproducibly varied between 70% with 2 mequiv of **4** (96 h, 25 °C) to 86% with 7.3 mequiv (144 h, 25 °C).

Regeneration of Resin 4. The resin (1.3 gm) obtained after cyclization of **1** and washing was suspended in 1 N HCl in MeOH and stirred at 25 °C for 3 h. The polymer was filtered and washed successively with CH_2Cl_2, MeOH, THF, THF/H_2O (1:1), THF, MeOH, THF, THF/H_2O (1:1), THF, benzene, and MeOH and dried in vacuo to afford 1.30 g of resino mercury(II) chloride; IR (KBr, pellet) 1600, 1585, 1495, 1450, 750, 690, 525 cm^{-1}. This resin (1.08 g) was suspended in THF, and $AgClO_4$[7] (320 mg, 2.0 equiv) was added and the suspension stirred for 48 h at 25 °C. Successive agitative washing with THF (10 × 20 mL) afforded 1.3 g of **4**; IR (KBr) 1600, 1580, 1500, 1450, 1060, 1020, 900, 750, 690, 605, 525 cm^{-1}. The regenerated resin obtained above effected the deprotection/cyclization of **1** → **2** (R = CH_2Ph-*p*-OMe; R′ = H) in 80–85.6% yields.

Acknowledgment. We gratefully acknowledge financial support for this work from the National Institutes of Health, Grants 1R01AIGM18957-02 and 1R01HL30888-01. NMR measurements at 360 MHz were obtained at the Colorado State University Regional NMR Center, funded by the National Science Foundation Grant CHE78-18581.

Registry No. **1** (R = *p*-$MeOC_6H_4CH_2$; R′ = H), 91238-03-8; **1** (R = CH_3; R′ = H), 91238-04-9; **1** (R = $PhCH_2$: R′ = CH_2OMs), 91238-05-0; **1** (R = *p*-$MeOC_6H_4$; R′ = H), 91238-06-1; **1** (R = *p*-$MeOC_6H_4CH_2$; R′ = CH_2OMs), 91238-07-2; **1** (R = $PhCH_2$; R′ = H), 91238-08-3; **2** (R = MeO-*p*-$C_6H_4CH_2$; R′ = H), 91238-09-4; **2** (R = Me; R′ = H), 78877-97-1; **2** (R = $PhCH_2$; R′ = CH_2OMs), 90301-46-5; **2** (R = *p*-$MeOC_6H_4$; R′ = H), 91238-10-7; **2** (R = *p*-$MeOC_6H_4CH_2$; R′ = CHOMs), 91238-11-8; **2** (R = $PhCH_2$; R′ = H), 91238-12-9; iii, 29182-87-4; iv, 21535-05-7; v, 91238-13-0; $Cu(ClO_4)_2$, 13770-18-8; $AgClO_4$, 7783-93-9; $Hg(ClO_4)_2$, 7616-83-3; $Fe(ClO_4)_3$, 13537-24-1; $Ni(ClO_4)_2$, 13637-71-3; $Pb(ClO_4)_2$, 13637-76-8; $PhHgClO_4$, 49804-95-7; AgOTf, 2923-28-6; $AgSbF_6$, 26042-64-8; *t*-$BuMe_2SiO(CH_2)_3I$, 78878-05-4; *p*-anisidine, 104-94-9; bromoacetyl bromide, 598-21-0; 2,2′-dipyridyl disulfide, 2127-03-9.

Supplementary Material Available: Detailed experimental procedure for the preparation of 8,10-bis(*p*-methoxyphenyl)-8,10-diaza-2-oxabicyclo[4.2.2]decane-7,9-dione (**2**, R = Ph-*p*-OCH_3; R′ = H) and spectral data for compounds **2** (R = CH_2Ph, R′ = CH_2OMs; R = CH_2Ph-*p*-OCH_3, R′ = CH_2OMs); complete table of reagents examined for the conversion of **1** → **2** (27 entries) (6 pages). Ordering information is given on any current masthead page.

Electrolytic Side-Chain Oxidation of Alkylbenzenes Using Polymeric Electron Carrier

Jun-ichi Yoshida, Keiji Ogura, and Nariyoshi Kawabata*

Department of Chemistry, Faculty of Polytechnic Science,
Kyoto Institute of Technology, Matsugasaki, Sakyo-ku,
Kyoto 606, Japan

Received December 29, 1983

The utility of indirect electrochemical reactions using a catalytic electron carrier (mediator) has been recognized by synthetic organic chemists in the last decade (Scheme I).[1] Use of electron carrier makes it possible to perform electrochemical oxidations at lower potentials than those required for direct anodic reactions. Although various inorganic and organic carriers have been employed so far, recent development of polymeric electron carriers[2] opens an intriguing aspect of indirect electrochemical reactions. Such polymeric electron carriers enable simple workup of the reaction as well as easy recovery and repeated use of the reagent. Previously we have reported polymer-mediated oxidation of alcohols[2a] and sulfides[2c] and epoxidation of olefins.[2b] In this paper we describe the use of a polymeric electron carrier to effect electrochemical side-chain oxidation of alkylbenzenes[3] (eq 1).

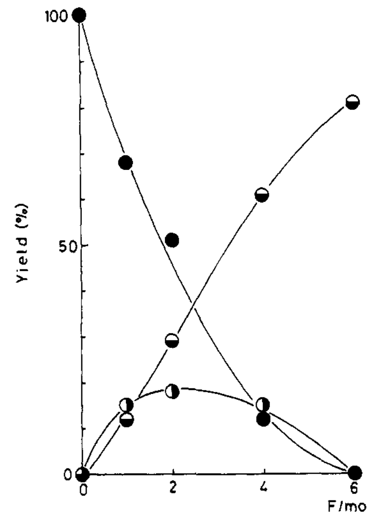
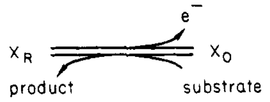


Figure 1. Electrolytic oxidation of diphenylmethane using PVP·HBr (0.50 g) and PVP·H_2SO_4 (0.50 g) in a mixture of acetonitrile (2.7 mL) and acetic acid (0.3 mL). Dependence of yields of benzophenone (◒), diphenylmethanol (◑), and unchanged diphenylmethane (●) on the passed electricity.

Scheme I



X_R : reduced form of electron carrier
X_O : oxidized form of electron carrier

$$ArCH_2R + H_2O \xrightarrow[\substack{\text{PVP·HBr} \\ \text{PVP·H}_2\text{SO}_4}]{-e^-} ArC(O)R \qquad (1)$$

Diphenylmethane was chosen as a simple model to explore reaction conditions. Constant electric current was passed through a cell containing platinum electrodes, polymer beads, diphenylmethane, water, and solvent with slow stirring, and the reaction was monitored by GLC analysis. The initial question of what kind of polymer best effects the side-chain oxidation of alkylbenzenes was answered by the observation that a 1:1 mixture of cross-linked poly(vinylpyridinium bromide) (hereafter abbreviated as PVP·HBr) and cross-linked poly(vinylpyridinium sulfate) (PVP·H_2SO_4) efficiently catalyzed the reaction to give benzophenone in 81% yield (6.0 F/mol) (eq 2). In the early stage of the reaction both benzophenone and

---

[1] For example: (a) Semmelhack, M. F.; Chou, C. S.; Cortes, D. A. *J. Am. Chem. Soc.* **1983**, *105*, 4492. (b) Masui, M.; Ueshima, T.; Ozaki, S. *J. Chem. Soc., Chem. Commun.* **1983**, 479. (c) Moyer, B. A.; Thompson, M. S.; Meyer, T. J. *J. Am. Chem. Soc.* **1980**, *102*, 2310. (d) Shono, T.; Matsumura, Y.; Hayashi, J.; Mizoguchi, M. *Tetrahedron Lett.* **1980**, *21*, 1867. (e) Shono, T.; Matsumura, Y.; Mizoguchi, M.; Hayashi, J. *Ibid.* **1979**, 3861.

[2] (a) Yoshida, J.; Nakai, R.; Kawabata, N. *J. Org. Chem.* **1980**, *45*, 5269. (b) Yoshida, J.; Hashimoto, J.; Kawabata, N. *Ibid.* **1982**, *47*, 3575. (c) Yoshida, J.; Sofuku, H.; Kawabata, N. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1243.

[3] (a) Matsue, T.; Fujihira, M.; Osa, T. *J. Electrochem. Soc.* **1981**, *128*, 2565. (b) Torii, S.; Tanaka, H.; Siroi, T.; Akada, M. *J. Org. Chem.* **1979**, *44*, 3305. (c) Ramaswamy, R.; Venkatachalapathy, M. S.; Udupa, H. V. K. *Bull. Chem. Soc. Jpn.* **1962**, *35*, 1751. (d) Ramaswamy, R.; Venkatachalapathy, M. S.; Udupa, H. V. K. *J. Electrochem. Soc.* **1963**, *110*, 202.

0022-3263/84/1949-3419$01.50/0 © 1984 American Chemical Society