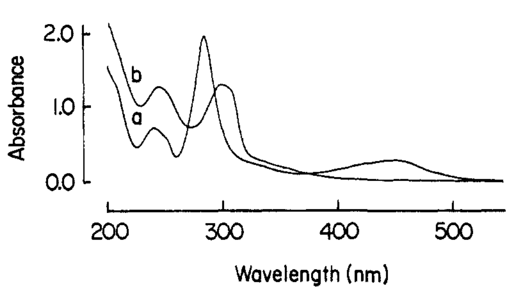
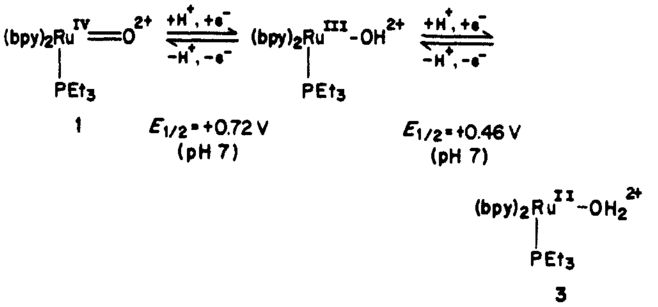


Figure 1. Electronic spectra of (a) $(bpy)_2Ru^{II}(OH_2)(PEt_3)^{2+}$ (4.0×10^{-5} M in H_2O; 1-cm quartz cells) and (b) $(bpy)_2Ru^{IV}(O)(PEt_3)^{2+}$ (8.0×10^{-5} M in H_2O; 1-cm quartz cells).

mograms of **1** and **3** taken in aqueous solution at solution pH values of 1–7 proved to be identical, indicative of the interconversion of $Ru^{IV}{=}O$ to $Ru^{II}{-}OH_2$ through two one-electron, one-proton redox steps:



$$\underset{\mathbf{1}}{\underset{PEt_3}{(bpy)_2Ru^{IV}}{=}O^{2+}} \underset{-H^+,\,-e^-}{\overset{+H^+,\,+e^-}{\rightleftharpoons}} \underset{PEt_3}{(bpy)_2Ru^{III}}{-}OH^{2+} \underset{-H^+,\,-e^-}{\overset{+H^+,\,+e^-}{\rightleftharpoons}} \underset{\mathbf{3}}{\underset{PEt_3}{(bpy)_2Ru^{II}}{-}OH_2^{2+}}$$

$$E_{1/2} = +0.72\ V\ (pH\ 7) \qquad E_{1/2} = +0.46\ V\ (pH\ 7)$$

The redox potentials for the Ru(IV)/Ru(III) and the Ru(III)/Ru(II) couples of complex **1** display potential shifts of 59 mV per pH unit, consistent with one-electron, one-proton transfers. In further cyclic voltammetric studies, when benzyl alcohol was added to an aqueous solution of the $[(bpy)_2Ru(IV)(O)(PEt_3)]^{2+}$ complex, the electrochemical potential for the onset of alcohol oxidation was less positive by 600 mV and appeared at the redox potential of the Ru(IV)/Ru(III) couple of the complex, as evidenced by an enhanced peak current of the anodic wave. This well-behaved, chemically reversible oxidation chemistry of the $[(bpy)_2Ru^{IV}(O)(PEt_3)]^{+2}$ complex is significant, for it suggests the possibility of utilizing such complexes as electron-transfer agents in catalytic organic substrate oxidation applications.

The reactivity of $[(bpy)_2Ru^{IV}(O)(PR_3)]^{2+}$ complexes with organic substrates is very sensitive to the nature of the phosphine ligand. Through spectroscopic monitoring, we have determined that the Ru(IV)–oxo complexes serve as reagents in the oxidation of organic substrates. Upon addition of alcohol to an aqueous solution of a *cis*-phosphine–ruthenium(IV)–oxo complex, spectral changes are observed in which the spectrum of the Ru(IV)–oxo species is converted to the spectrum of the corresponding Ru(II)–aquo species. Notably, there is a marked difference in the rate of alcohol oxidation depending on the phosphine ligand employed. With $[(bpy)_2Ru^{IV}(O)(PPh_3)]^{2+}$ as the catalyst, the oxidation of benzyl alcohol has a second-order rate constant of $1.9 \times 10^{-2}\ M^{-1}\ s^{-1}$, while the reaction involving $[(bpy)_2Ru^{IV}(O)(PEt_3)]^{2+}$ has a second-order rate constant of $1.1 \times 10^{-3}\ M^{-1}\ s^{-1}$. In general, we have determined that $[(bpy)_2Ru^{IV}(O)(PEt_3)]^{2+}$ oxidizes a variety of organic and inorganic substrates, including isopropyl alcohol to acetone, propionaldehyde to propionic acid, and triphenylphosphine to triphenylphosphine oxide.

Acknowledgment. This work was supported in part by the Petroleum Research Fund, administered by the American Chemical Society, the Cottrell Research Corporation, and both the Biomedical Research Support Grant Program and the Research Development Fund of the University of Buffalo, SUNY.

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(12) Electrochemical measurements were made using a glassy carbon electrode vs. saturated sodium chloride calomel electrode (SSCE) in aqueous buffer solutions. $E_{1/2}$ values are equal to $(E_{p,a} + E_{p,c})/2$.

Sequential Michael–Michael–Aldol Additions for Easy, One-Pot, 2 + 2 + 2 Construction of Polyfunctionalized Cyclohexanols

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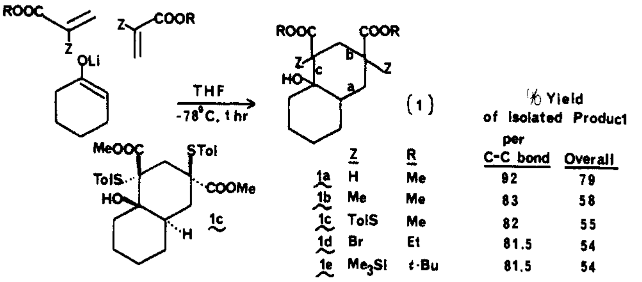
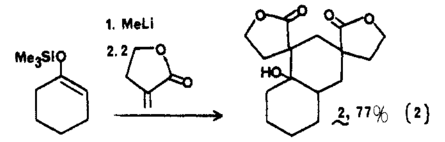
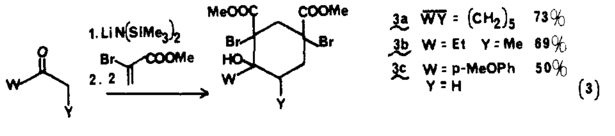
Polymerization of acrylates is an important industrial process.[1] Ketone enolate-initiated polymerization of acrylates, however, is interrupted after only two acrylate units have reacted with one ketone enolate unit (eq 1).[2] This novel process represents sequential, one-pot, three-component,[3] Michael–Michael–aldol additions leading to a very efficient, general, 2 + 2 + 2 synthesis of polyfunctionalized cyclohexanols. We report here on several aspects of this simple and synthetically useful procedure.



	Z	R	% Yield of Isolated Product per C-C bond	Overall
1a	H	Me	92	79
1b	Me	Me	83	58
1c	TolS	Me	82	55
1d	Br	Et	81.5	54
1e	Me_3Si	*t*-Bu	81.5	54

Approximate thermodynamic considerations indicate quite clearly that the overall process represented in eq 1 is very favorable indeed. The average yield for each of the three C–C bonds formed in eq 1 is 82.5–92%. Although methyl acrylate itself gave the best results, various α-substituted acrylates led very effectively to adducts **1b–e**. An X-ray study of adduct **1c**, the only diastereomer formed, revealed its relative stereochemistry to be as shown. Even a cyclic acrylate (i.e., α-methylene γ-butyrolactone) led very efficiently to bis-spiro adduct **2** with an average yield of almost 92% per new C–C bond (eq 2). Acrylonitrile and phenyl vinyl sulfone were not effective in place of an acrylate ester. Besides cyclohexanone lithium enolate, the lithium enolates formed by deprotonation of other representative ketones such as cycloheptanone, 3-pentanone, and *p*-methoxyacetophenone were used in some cases on gram scale very successfully (eq 3).





3a $\overline{WY} = (CH_2)_5$ 73%
3b W = Et Y = Me 69%
3c W = p-MeOPh Y = H 50%

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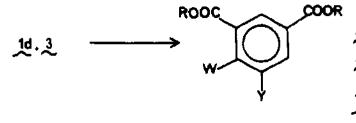
(1) (a) Webster, O. W.; Hertler, W. R.; Sogah, D. Y.; Farnham, W. B.; RajanBabu, J. *J. Am. Chem. Soc.* **1983**, *105*, 5706. (b) Seymour, R. B.; Carraher, C. E., Jr. "Polymer Chemistry—An Introduction"; Marcel Dekker: New York, 1981.

(2) (a) For two isolated examples of this process see: Davis, R.; Untch, K. G. *J. Org. Chem.* **1979**, *44*, 3755. Dionne, G.; Engel, C. R. *Can. J. Chem.* **1978**, *56*, 419. CF.: Wakselman, C.; Mondon, M. *Tetrahedron Lett.* **1973**, 4285. (b) For a report on the trimerization of methyl acrylate in the presence of palladium chloride and sodium acetate, see: Sakakibara, T.; Nishimura, S.; Kimura, K.; Fujioka S.; Odaira, Y. *Tetrahedron Lett.* **1971**, 4719. (c) For reviews on synthetic uses of acrylates, see: Tanimoto, S.; Ikehara, H. *Bull. Inst. Kyoto Univ.* **1983**, *61*, 120; **1984**, *62*, 72. We thank Professor H. Nozaki and Dr. K. Takai for a copy of these reviews.

(3) (a) For a review, see: Posner, G. H. *Chem. Rev.*, in press. (b) For some recent samples of two-component *Mi*chael–*Mi*chael-*r*ing closure (MIMIRC) reactions, see: (a) Danishefsky, S.; Harrison, P.; Silvestri, M.; Segmuller, R. *J. Org. Chem.* **1984**, *49*, 1319. (b) Hagiwara, H., Okano, A., and Uda, H., *J. Chem. Soc. Chem. Commun.*, 1985, 1047.

0002-7863/86/1508-0511$01.50/0

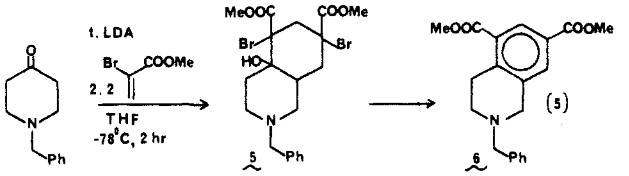
The multifunctionality of the annulated adducts **1c–e** provides much opportunity for many different further chemical manipulations. For example, the two sulfur atoms of bis-α-tolylthio ester **1c** can be oxidized into sulfoxide groups which can be thermally eliminated.[4] In this way, followed by dehydration, we have converted adduct **1c** effectively (55–60% yield) into the corresponding aromatic tetrahydronaphthalene system; dibromocyclohexanol **1d** also was transformed (LiCl/DMF, 100 °C, 12 h) into tetrahydronaphthalene **4a** (eq 4). One-pot dehydration and bisdehydrobromination of dibromocyclohexanols **3a** and **3b** (NaOMe/PhH) and **3c** (pyridinium trifluoroacetate/pyridine, reflux, 12 h) led to the aromatic systems **4** shown in eq 4. This overall process represents a direct, convenient, two-step procedure for annulating a meta-dicarboxylated benzene ring onto the -$COCH_2$- group of a ketone, thereby regiospecifically forming a trisubstituted or tetrasubstituted aromatic system. Recently, considerable effort has been directed at developing new methods for regiospecific synthesis of polyfunctionalized aromatic compounds.[5]



	W	Y	R	% Yield
4a	(CH$_2$)$_4$		Et	56
4b	(CH$_2$)$_5$		H	51
4c	Et	Me	H	55
4d	p-MeOPh	H	Me	57

(4)

The lithium enolate of *N*-benzyl-4-piperidone[6] was annulated into dibromocyclohexanol **5** which was isolated on gram scale in 66% overall yield after purification by short-path chromatography (eq 5). One-pot dehydration and bisdehydrobromination ((dimethylamino)pyridine, triethylamine/pyridine, reflux, 12 h) gave tetrahydroisoquinoline **6** in 35% yield. This two-step sequence represents an unusually direct synthesis of the biologically important isoquinoline alkaloid ring system.[7]



The triply convergent,[8] 2 + 2 + 2, *Mi*chael-*Mi*chael-*r*ing *c*losure (MIMIRC)[9] cyclohexannulations[10] shown in eq 1–3 and 5 represent an extremely useful, mild, easy, and convenient (e.g., no motor-driven syringe technique required)[11] means of transforming relatively simple into structurally much more complex cyclic systems.[12] These one-pot, multiple C–C bond-forming annulations will undoubtedly be of substantial value in organic synthesis. We are actively exploring further applications.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for a research grant (No. 14645) and for a Summer Research Fellowship to Professor Silversmith. We also thank Professor J. Clardy and Dr. C. He (Cornell) for the X-ray study of adduct **1c** and Professor D. Poland of this department for a helpful discussion. Purchase of a 400-MHz NMR spectrometer was made possible by the NSF (DCM 83-03176) and by the NIH (1 S10 RR0934).

Supplementary Material Available: IR, ^1H NMR, mp, and elemental analysis or high resolution mass spectral data for compounds **1–6** (4 pages). Ordering information is given on any current masthead page.

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(4) For a review, see: Trost, B. M. *Acc. Chem. Res.* **1978**, *11*, 453.

(5) (a) Boger, D. L.; Mullican, M. D. *J. Org. Chem.* **1984**, *49*, 4045. (b) Danheiser, R. L.; Gee, S. K. *Ibid.* **1984**, *49*, 1674. (c) Dieter, R. K.; Lin, Y. J. *Tetrahedron Lett.* **1985**, *26*, 39. (d) For reviews, see: Bamfield, P.; Gordon, P. F. *Chem. Soc. Rev.* **1984**, *13*, 441. Dötz, K. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 587.

(6) Boger, D. L.; Mullican, M. D. *J. Org. Chem.* **1984**, *49*, 4033.

(7) For a review of synthetic methods, see: Paquette, L. A. "Principles of Modern Heterocyclic Chemistry"; W. A. Benjamin: New York, 1968; Chapter 8.

(8) For very recent examples of other effective multicomponent C–C bond-forming reactions, see: (a) Knochel, P.; Normant, J. F. *Tetrahedron Lett.* **1985**, *26*, 425. Deshpande, M. N.; Jawdosiuk, M.; Kubiak, G.; Venkatachalam, M.; Weiss, U.; Cook, J. M. *J. Am. Chem. Soc.* **1985**, *107*, 4786.

(9) This notation is due to: Posner, G. H.; Mallamo, J. P.; Black, A. *Tetrahedron* **1981**, *37*, 3921 ("MIMIRC"). Danishefsky, S.; Chakulamannil, S.; Silvestri, M.; Springer, J. *J. Org. Chem.* **1983**, *48*, 3615, ("2 + 2 + 2").

(10) For some recent cyclohexannulation procedures, see: (a) Danheiser, R.; Fink, D. M.; *Tetrahedron Lett.* **1985**, *26*, 2513. (b) Byers, J. H.; Spencer, T. A. *Ibid.* **1985**, *26*, 713. (c) Meyer, W. L.; Brannon, M. J.; Burgos, C. G.; Goodwin, T. E.; Howard R. W. *J. Org. Chem.* **1985**, *50*, 438. (d) Tang, P.-D.; Wulff, W. D. *J. Am. Chem. Soc.* **1984**, *106*, 1132. (e) Pariza, R. J.; Fuchs, P. L. *J. Org. Chem.* **1983**, *48*, 2304. (f) Pietrusiewicz, K. M.; Monkiewicz, J.; Bodalski, R. *Ibid.* **1983**, *48*, 788. (g) Danheiser, R. L.; Martinez-Davila, C.; Sand, H. *Tetrahedron* **1981**, *37*, 3943.

(11) Cf.: Posner, G. H.; Lu, S.-B. *J. Am. Chem. Soc.* **1985**, *107*, 1424.

(12) A typical experimental procedure is as follows: A dry 10-mL flask cooled in an ice bath and fitted with a magnetic stirring bar, an argon inlet, and a serum cap was charged with cyclohexanone enol trimethylsilyl ether (100 mg, 0.59 mmol) in 1 mL of dry THF and treated dropwise via syringe with MeLi in Et_2O (0.59 mL, 1.1 M, 0.65 mmol) over 1 min. After it was warmed to room temperature, the mixture was stirred for 1 h. The reaction flask was then cooled to −78 °C. Ethyl α-bromoacrylate (232 mg, 1.30 mmol) was added without solvent dropwise via syringe over 0.5 min. Stirring was continued for 1 h at −78 °C. Quenching was achieved by the addition of aqueous NH_4Cl (saturated). The organic layer was separated, and the aqueous layer was extracted with Et_2O (3x). The combined organic solution was dried ($MgSO_4$), filtered, concentrated, and subjected to preparative TLC (petroleum ether:ethyl ether = 2:1); 145.6 mg (54.1%) of **1d** was obtained. MIMIRC product **1d** (49 mg, 0.11 mmol) and LiCl (8.6 mg, 0.20 mmol) in 33 μL of dry DMF were stirred at 100 °C overnight under N_2. After cooling the reaction mixture to room temperature, 2 mL of 50% (v/v) of 2.5% sulfuric acid in Et_2O was added. Stirring was continued at room temperature for 4 h. The organic layer was then separated. The aqueous layer was extracted with Et_2O (3x). The combined Et_2O solution was dried over $MgSO_4$, filtered, concentrated, and subjected to preparative TLC. Aromatic **4a** (16.6 mg, 56%) was obtained. Similar results (51% yield) were obtained by dissolving MIMIRC product **1d** in pyridine and refluxing overnight.

Tricyclo[5.5.0.0^{2,8}]dodecatetraene

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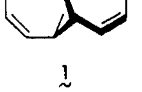
Received October 7, 1985

Considerable attention has been focused on the valence isomers of [12]annulene, approximately 40 of which are now known,[2] because their unusual structural features have proven useful in defining the practical limits of orbital symmetry control. Included among the yet unknown $(CH)_{12}$ hydrocarbons, whose acquisition has been thwarted by serious synthetic complications, are **1–4**.[3]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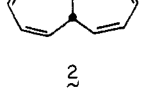
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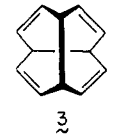
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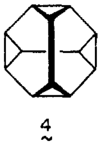
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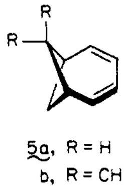

5a, R = H

b, R = CH_3

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(1) Fulbright Scholar, 1982–1983; Evans Fellow, 1985–1986.

(2) Banciu, M.; Popa, C.; Balaban, A. T. *Chem. Scr.* **1984**, *24*, 28.