was analyzed by gas chromatography on a 10% tris(cyanoethoxy)-propane column (80–100 mesh Chromosorb C-AW-DCMS support in a stainless steel, 2.4 mm inside diameter, 2.7 m column). Peak identifications were established as described in ref 2. The same procedure was followed for damsylate solvolyses, but only 0.06 g of damsylate was used for each solvolysis.

Registry No.—1a·trifluoromethanesulfonate, 68854-29-5; **1b**, 68854-30-8; **4**, 13395-76-1; **5**, 1601-00-9; **6**, 24395-07-1; sodium *p*-(dimethylamino)benzenesulfonate, 2244-40-8; sulfanilic acid, 121-57-3.

References and Notes

(1) P. E. Peterson and R. J. Kamat, *J. Am. Chem. Soc.*, **88**, 3152 (1966).
(2) P. E. Peterson and R. J. Kamat, *J. Am. Chem. Soc.*, **91**, 4521 (1969).
(3) (a) M. Hanack, J. Häffner, and I. Herterich, *Tetrahedron Lett.*, 875 (1965); (b) W. D. Clossen and S. A. Roman, *ibid.*, 6015 (1966).
(4) (a) W. S. Johnson, S. Escher, and B. W. Metcalf, *J. Am. Chem. Soc.*, **98**, 1040 (1976); (b) W. S. Johnson, R. S. Brinkmeyer, V. M. Kapoor, and T. M. Yarnell, *ibid.*, **99**, 8341 (1977); (c) M. B. Gravestock, W. S. Johnson, R. F. Meyers, T. A. Bryson, and B. E. Ratcliff, *ibid.*, **100**, 4268 (1978).
(5) (a) K. A. Parker and W. S. Johnson, *J. Am. Chem. Soc.*, **96**, 2556 (1974); (b) W. S. Johnson and L. A. Bunes, *ibid.*, **98**, 5597 (1976).
(6) (a) C. N. Sukenik and R. G. Bergman, *J. Am. Chem. Soc.*, **98**, 6613 (1976); (b) C. N. Sukenik, J. A. P. Bonapace, N. S. Mandel, P-Y. Lau, G. Wood, and R. G. Bergman, *ibid.*, **99**, 851 (1977).
(7) F. L. Schadt, T. W. Bentley, and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **98**, 7667 (1976), and references cited therein.
(8) (a) P. E. Peterson and F. J. Waller, *J. Am. Chem. Soc.*, **94**, 991 (1972); (b) P. E. Peterson, D. W. Vidrine, F. J. Waller, P. M. Henrichs, S. Magaha, and B. Stevens, *ibid.*, **99**, 7968 (1977).
(9) E. E. van Tamelin and T. J. Curphey, *Tetrahedron Lett.*, 121 (1962).
(10) W. F. Giauque, E. W. Horning, J. E. Kunzler, and T. R. Rubin, *J. Am. Chem. Soc.*, **82**, 62 (1960).
(11) P. C. Myhre and E. Evans, *J. Am. Chem. Soc.*, **91**, 5641 (1969).
(12) J. Meisenheimer and H. Denner, *Ber. Dtsch. Chem. Ges.*, **65**, 1803 (1932).

Direct Fractionation Procedure, an Improved Technique for the Quantitative Isolation of Highly Purified Chromate(VI) Oxidation Products by Utilizing Porous Styrene–Divinylbenzene Copolymer Gel–Liquid Chromatography

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For the isolation of the products from synthetic reaction mixtures, multiple and discontinuous separation techniques such as extraction, distillation, recrystallization, or sublimation have been generally adopted. Such separation procedures are not only tedious and time consuming but also inefficient, causing a significant loss of products and in many cases leading to contamination of the products. Because each process is carried out manually, experimental results often depend heavily on the technical skill of the laboratory worker himself. Also, these methods are not generalizable, and the details of an isolation procedure must be tailored to fit the conditions met within a particular synthesis.[1]

One of the authors (Hara) has been trying to generalize and to systematize the separation procedures in organic synthesis in order to do away with tedious traditional experimental techniques.[2,3] To achieve this, a direct fractionation technique using high-performance liquid chromatography has been developed.[3] The procedure was designed to simplify and speed up isolation procedures, while providing for quantitative isolation of a highly purified product. We wish to report here an improved technique for the isolation of chromate oxidation products as an example of this scheme.

Chromate(VI) oxidation has been used very often as an important synthetic method. However, the isolation procedure used in this reaction is troublesome. Multiple extraction is required in the first stage to insure complete removal of the chromate and other polar substances. This often results in loss of products. In order to fundamentally improve the separation procedure, a single-step resolution of the polar inorganic and less polar organic substances in the chromate oxidation products has been extensively investigated. In a model experiment, the individual components of a crude reaction mixture were directly injected into a column packed with various materials and retention behaviors of the compounds were experimentally determined. A reversed phase column[4] packed with a porous styrene–divinylbenzene copolymer gel was found to exclude inorganic salts such as chromates(III and VI) by using methanol/water as an eluent. For example, the capacity factor of chromate(VI) in the case of the methanol/water (9:1 v/v) system was nearly equal to zero. On the other hand, organic compounds were retained and could be separated from each other. Retention of the solutes on the column was intensified when the water content in the mobile phase increased. The retention was also strengthened when the polarity of functional groups in the organic solutes decreased or the number of carbons in the solutes increased.[5]

These results suggest that the clean up of crude reaction mixtures and separation of the organic products can be accomplished in a single step by using liquid chromatography

Table I. Application Examples of Direct Liquid Chromatographic Isolation Procedure for Chromate(VI) Oxidation Products

ref	substrate	registry no.	reagent	methanol water (v/v)[i]	*j*	g of substrate[k]	product yield %	product yield lit. %	recovered %
6	cholesterol	57-88-5	$Na_2Cr_2O_7$, CH_3CO_2H, C_6H_6	1:0	4-choletene-3,6-dione,[c] 6.1; cholesterol, 10.3; CH_3CO_2H, 0.1	3.5	71	39–40	
7	*p*-nitrotoluene	99-99-0	CrO_3, H_2SO_4, $(CH_3CO)_2O$	4:1	*p*-nitrobenzal diacetate,[d] 5.4; *p*-nitrotoluene, 8.3	6.4	95	65–66	
8	naphthalene	91-20-3	CrO_3, CH_3CO_2H	9:1	1,4-naphthoquinone,[a,e] 3.8; naphthalene, 7.3	1.6	35	18–22	62
9	1-decanol	112-30-1	$CrO_3(C_5H_5N)_2$, CH_2Cl_2	4:1	decanal,[f] 2.5; 1-decanol, 1.9	0.5	94	63–66	
10	indene	95-13-6	$K_2Cr_2O_7$, H_2SO_4	9:1	homophthalic acid,[g] 2.5; indene, 7.8	6.3	81	66–77	
11	2-acetylfluorene[b]	781-73-7	$Na_2Cr_2O_7$, CH_3CO_2H	20:1	9-oxo-2-fluorenecarboxylic acid,[h] 1.8; 2-acetylfluorene, 2.3	5.8	78	67–74	

[a] Colorless crystals. Yellow needles were obtained in the literature.[8] [b] Starting material was synthesized from fluorene by the procedure described in "Organic Syntheses", Collect. Vol. III, Wiley, New York, 1952, p 23. [c] Registry no. 984-84-9. [d] Registry no. 2929-91-1. [e] Registry no. 130-15-4. [f] Registry no. 112-31-2. [g] Registry no. 89-51-0. [h] Registry no. 784-50-9. [i] Solvent system for polystyrene gel LC. [j] Capacity factor of products, substrate, and medium solvent. [k] Quantity injected.

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with an optimized column and solvent system.

At first, oxidation of cholesterol was selected as a model reaction from "Organic Syntheses".[6] Chromatographic retention data of the components in the reaction mixture were obtained by using an analytical column. The solvent system for the reversed phase column was optimized experimentally. Acetic acid used for the reaction medium was removed at the same time as the chromates. The loading capacity of the polystyrene gel packed column was large enough to retain and to separate the crude reaction products from a large amount of reagents and reaction medium solvents. The crude reaction mixture, which was directly injected into the preparative column, was separated into its constituents. The colorless crystalline product obtained by evaporation of the eluent was identified as 4-cholestene-3,6-dione by its spectroscopic data. The high purity of the sample was demonstrated by its showing a single peak on an analytical high-resolution column. On the other hand, the specimen obtained by extraction and recrystallization of the product following the procedure described in the literature was a pale yellow crystalline substance which showed several minor peaks on an analytical liquid column chromatography due to impurities. The yield of the reaction was increased from 40% in the literature to 71% in this experiment. These results seem to be due to not only high efficiency fractionation of the main product, but also the removal of chromates at the beginning, which prevents inorganic impurities from contaminating the product during the evaporation under heat. Such contamination is common in conventional separation.

The direct fractionation procedure using reversed phase liquid chromatography was applied further to several typical chromate oxidation reactions described in "Organic Syntheses".[7-11] A few results are shown in Table I. In every case, the purity and yield of these reactions were improved over conventional isolation procedures. Quantitative recovery of the starting material was possible, for instance in the case of the oxidation of naphthalene.[8] Fractions of low purity such as second crop crystals or mother liquors are always given by the traditional techniques. However, with the direct fractionation procedures, only a single, pure fraction is obtained. In a series of these experiments, the same packed column has been used repeatedly to examine the lifetime of the column material. No deterioration of the column function was observed.

The direct fractionation procedure with no pretreatment, which was described above, is simple and fast. It can be automated and waste materials can be minimized by recovering the inorganic and organic reagents, starting materials, and mobile phase solvents. The characteristics of this method are the high purity of the products and the quantitative yield of the reaction products, which are obtainable only by direct fractionation using a high-resolution column. This method can be useful as a general separation procedure for chromate oxidation reaction and as a substitute for the conventional procedure which is now widely utilized.

Experimental Section

General. Starting materials and reagents employed were technical grade chemicals obtained from Wako Pure Chemicals Co., Osaka. Packing material was TSK-gel 110, Toyo Soda Co., Tokyo, spherical porous polymer, diameter of 10 μm for analytical and 30 μm for preparative high performance liquid chromatography. Glass columns (CIG column system,[2] Kusano Scientific Co., Tokyo) packed with a slurry of polystyrene gel–methanol (inter diameter of 4 mm, length of 10 cm for analytical, inter diameter of 15 mm, length of 30 cm for preparative work) were connected with a sample injector valve made of PTFE or glass. The crude reaction mixture obtained was directly injected into the top of the column. The flow rates of the mobile phase consisting of methanol (technical grade, Wako Pure Chemicals Co.) and water were 1 mL/min under pressure of 30 kg/cm^2 for analytical work, and 3 mL/min under pressure of 10 kg/cm^2 for preparative purpose. Chromatographic equipment was assembled from a reciprocating pumping system, KP-9H, Kusano Scientific Co., a 254 nm UV detector, UVILOG, Kusano Scientific Co., and a RI detector, Waters Associates, Mass. Capacity factors in Table I were calculated by $k' = (V_R - V_0)/V_0$ where V_R is the elution volume for the chromatographic peak and V_0 is the column void volume which was measured by *p*-toluenesulfonic acid in water (V_0: 0.8 mL for analytical column, 18 mL for preparative column). The resolution factor of the products was always larger than 1. Yield of the main product shown in Table I was calculated from the weight of the residue obtained by evaporation of the separated fraction. Polar side products which were highly oxidized were eluted from the column with chromates and were not examined precisely in this experiment.

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References and Notes

(1) An example is the series "Organic Syntheses" which deals with standard and reliable procedures. About half of the book is taken up by detailed description of isolation procedures.
(2) S. Hara, *J. Chromatogr.*, **137**, 41 (1977).
(3) S. Hara and M. Nakahata, *J. Liq. Chromatogr.*, **1**, 43 (1978).
(4) Octadecylsilylated silica (ODS) packing is available as a common reversed phase stationary; however, it is deteriorated by the adsorption of chromates on the surface of the remaining silanol groups.
(5) Correlation between retention behavior and solute molecular structure has been systematically investigated in our laboratory. Details will be reported in the future. Cf. D. J. Pietrzyk and Chi-Hung Chu, *Anal. Chem.*, **49**, 757 (1977).
(6) "Organic Syntheses", Collect. Vol. IV, Wiley, New York, 1962, p 189.
(7) "Organic Syntheses", Collect. Vol. IV, Wiley, New York, 1962, p 713.
(8) "Organic Syntheses", Collect. Vol. IV, Wiley, New York, 1962, p 698.
(9) *Org. Synth.*, **55**, 84 (1976).
(10) "Organic Syntheses", Collect. Vol. III, Wiley, New York, 1952, p 449.
(11) "Organic Syntheses", Collect. Vol. III, Wiley, New York, 1952, p 420.

Synthesis and Photochemistry of 2,4,6-Tri-*tert*-butylacetophenone

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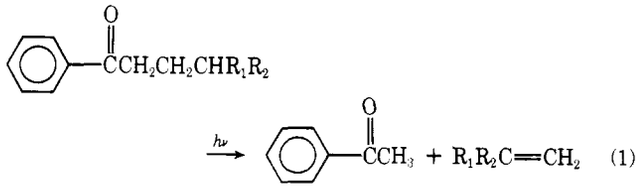
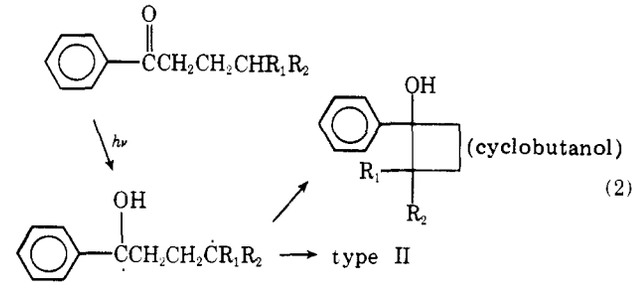
Hydrogen abstraction reactions by excited aromatic carbonyl compounds are generally triplet reactions,[1] and in the case of the Norrish type II reaction of arylalkanones they occur intramolecularly from the γ position of the attached alkyl group. Scission follows and the products are an alkene and a lower molecular weight aryl ketone (eq 1). The type II process



(1)

is accompanied by cyclobutanol formation[2] in the general case (eq 2), and the reaction is known to proceed through biradical intermediates.[2]



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