faced with a pdp-8/m computer. Before analyzing a deuterated sample, the nondeuterated sample was run to determine the exact intensities of P, P + 1, and P + 2 at a voltage which eliminated the P − 1 peak (usually 18–20 eV). The molecular ion region was scanned 10–20 times; the mean and standard deviation are reported.

Spectral grade $CDCl_3$ was supplied by Merck, Sharp, and Dohme, CCl_4 by Mallinckrodt, D_2O by Stohler Isotope Chemicals. Pyruvic acid was purified by distillation in vacuo using a Kugelrohr distillation apparatus.

4-Deuterio-2,4-dimethyl-3-pentanone. CH_3OD was prepared by the general method of Streitwieser.[6] Using carefully dried apparatus, a solution prepared from 15 mL of CH_3OD, 3.0 g (0.026 mol) of ketone, and 0.08 g of Na was stirred for 9 h at room temperature. The solution was then quenched with D_2O, extracted with ether, washed with H_2O, and dried over $MgSO_4$; NMR (CCl_4) δ 2.7 (heptet, 0.9 H, J = 7 Hz), 1.06 (m, 12 H); mass spectrum % D_0 = 27.4 ± 0.6, % D_1 = 49.1 ± 0.6, % D_2 23.5 ± 0.5.

4-Deuterio-2,4-dimethyl-3-pentanone Tosylhydrazone. Ketone (2.2 g, 0.019 mol), tosylhydrazine (3.59 g, 0.019 mol), 40 mL of ethanol (95%), and 1 drop of concentrated HCl were combined and the resulting solution placed on a steam bath for 4 h. The solvent was largely removed by evaporation. Refrigeration produced 3.5 g (65%) of a white crystalline solid which was used without further purification, mp 95–99 °C. An analytical sample of undeuteriated tosylhydrazone had mp 106.9–108.7 °C.

Anal. Calcd for $C_{14}H_{22}N_2O_2S$: C, 59.54; H, 7.85. Found: C, 59.66; H, 7.87.

3-Deuteriocamphor. An adaptation of the procedure of Tidwell[5d] was used. In a dry 250-mL round-bottom flask, 60 mL of reagent grade dioxane and 30 mL of D_2O were combined. The flask was cooled to 0 °C, and 0.08 g of Na was added in three portions. The ice bath was removed and the solution was allowed to come to room temperature. Camphor (2.0 g.) was dissolved in 5 mL of dioxane and then added to the above solution. After 30 h of stirring, the solution was extracted with ether, washed with H_2O, and dried over $MgSO_4$: mass spectrum % D_0 = 7.0 ± 0.4, % D_1 = 79.3 ± 0.4, % D_2 = 13.7 ± 0.3.

The Tosylhydrazone (8a) and the Lithium Salt of the Tosylhydrazone (8b) of *exo*-3-Deuteriocamphor. Tosylhydrazone **8a** was prepared as described above for 2,4-dimethyl-3-pentanone, giving a 75% yield, mp 157–159 °C.[7] The lithium salt of tosylhydrazone **8a** (**8b**) was prepared by treating **8a** (0.2916 g, 0.908 mmol) in 10 mL of THF with 1 equiv of methyllithium (2 M solution in THF). The lithium salt **8b** was then reconverted to tosylhydrazone by neutralization with 0.1 N acetic acid. This mixture was extracted with ether, washed with water, and dried ($MgSO_4$); evaporation of solvent gave an 80% recovery of **8a**.

The Tosylhydrazone to Ketone Conversion Using *N*-Bromosuccinimide. This procedure is an adaptation of the method of Rosini.[4] Tosylhydrazone (10^{-4} mol) and internal standards, if desired, were dissolved in a mixture of 14 mL of acetone and 4 mL of water. When dissolution was complete, the mixture was cooled to 0 °C using an ice/water bath. *N*-Bromosuccinimide (4×10^{-4} mol) was then added. Stirring, using a magnetic stirring bar, was continued for 2 min. (Evolution of N_2 was apparent after 10–15 s, and the resulting solution was yellow.) The reaction was quenched with 1–2 mL of saturated sodium bisulfite. The ice bath was removed and the stirring continued while adding ca. 10 mL of water. The ketone was extracted with ether and the combined organic extracts were washed with water, 10% Na_2CO_3, water, and then dried over $MgSO_4$.

The Tosylhydrazone to Ketone Conversion Using Pyruvic Acid. Tosylhydrazone (10^{-4} mol) was combined with 10^{-4} mol of *p*-cymene (internal standard), 4 mL of glacial acetic acid, 1 mL of water, and 0.5 g of purified pyruvic acid. The solution was heated at reflux for 2 h. After cooling, it was extracted with ether, washed with water, 10% Na_2CO_3, water, and finally dried over $MgSO_4$. Yields were typically ca. 75%.

Registry No.—**6**, 27808-88-4; **7**, 60877-43-2; **8a**, 62930-36-3; **8b**, 62930-37-4; **9**, 62930-38-5; CH_3OD, 1455-13-6; 2,4-dimethyl-3-pentanone, 565-80-0; tosylhydrazine, 1576-35-8; camphor, 76-22-2.

References and Notes

(1) W. Kirmse, "Carbene Chemistry", Academic Press, New York, N.Y., 1971; M. Jones, Jr., and R. A. Moss, "Carbenes", Wiley, New York, N.Y., 1973, Chapter 1.
(2) A. F. Thomas, R. A. Schneider, and J. Meinwald, *J. Am. Chem. Soc.*, **89**, 68 (1967); A. F. Thomas and B. Willhalm, *Tetrahedron Lett.*, 1309 (1965).
(3) E. B. Hershberg, *J. Org. Chem.*, **13**, 542 (1948).
(4) G. Rosini, *J. Org. Chem.*, **39**, 3504 (1974). See also S. R. Maynez, L. Pelavin, and G. Erker, *ibid.*, **40**, 3302 (1975).
(5) (a) G. A. Abad, S. P. Jindal, and T. T. Tidwell, *J. Am. Chem. Soc.*, **95**, 6326 (1973); (b) S. P. Jindal and T. T. Tidwell, *Tetrahedron Lett.*, 783 (1971); (c) S. P. Jindal, S. S. Sohoni, and T. T. Tidwell, *ibid.*, 779 (1971); (d) T. T. Tidwell, *J. Am. Chem. Soc.*, **92**, 1448 (1970); (e) S. Banerjee and N. H. Werstiuk, *Can. J. Chem.*, **53**, 1099 (1975); (f) S. Banerjee and N. H. Werstiuk, *ibid.*, **54**, 678 (1976).
(6) A. Streitweiser, L. Verbet, and P. Stang, *J. Org. Chem.*, **29**, 3706 (1964).
(7) R. H. Shapiro, J. H. Duncan, and J. C. Clopton, *J. Am. Chem. Soc.*, **89**, 471, 1442 (1967).

Gas Chromatographic Analysis of Ortho Esters as a Convenient New General Method for Determining the Enantiomeric Purities of Chiral δ-Lactones

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The rapid developments being made in the area of asymmetric synthesis have increased the demand for methods of measuring enantiomeric purities. The traditional dependence on optical rotation comparisons for this purpose is well recognized to be unreliable at times and techniques permitting enantiomeric excesses to be measured directly are much to be preferred. Determination of optical purities by NMR analysis, either of appropriate diastereomeric derivatives[1] or in the presence of chiral shift reagents,[2] has proven to be the most powerful of the generally applicable approaches to the problem. However, at the present time there are many compounds whose enantiomeric purities cannot be readily evaluated by the NMR techniques because the preferred structural features or functionalities are absent. Lactones of the type **1a,d,e**,[4a]

Scheme I

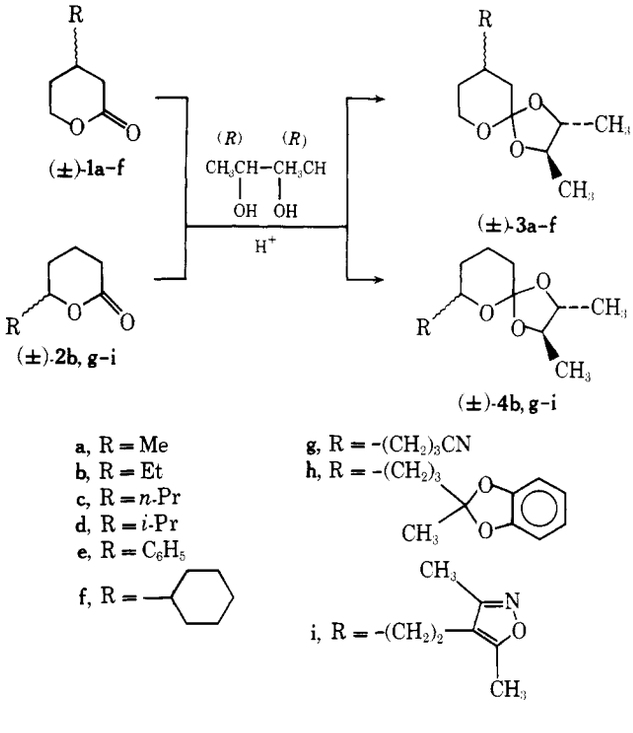

Table I. Diastereomeric Ortho Ester Mixtures

Compd[a]	Method[b]	Yield, %[c]	Formula[d]	GC retention times, min[e]		Column temp, °C
3a	A	52	$C_{10}H_{18}O_3$	6.30	6.89	100
3b	A	73	$C_{11}H_{20}O_3$	8.90	9.55	110
3c	A	57	$C_{12}H_{22}O_3$	9.91	10.69	120
3d	A	50	$C_{12}H_{22}O_3$	8.97	9.82	125
3e	A	54	$C_{15}H_{20}O_3$	17.20	18.50	165
3f	A	43	$C_{15}H_{26}O_3$	16.20	17.30	155
4b	A	60[h]	$C_{11}H_{20}O_3$	2.18[i]	2.47[i]	220
4g	B	62	$C_{13}H_{21}NO_3$	5.25	5.76	220
4h	A	60[h]	$C_{20}H_{28}O_5$	13.08	14.24	220
4i	A	53[h]	$C_{16}H_{25}NO_4$	13.25	14.51	220
4i	B	86[f,h]		84.60[g]	85.60[g]	

[a] All ortho ester mixtures prepared from racemic lactone. [b] See Experimental Section. [c] Data refer to ortho ester mixtures purified by column chromatography. [d] Microanalyses within ±0.3% of theory (C, H) (also N in the case of **4g** and **4i**) were obtained for these compounds. [e] The observed ratios of diastereomers were within 3% of the expected 50:50 relative proportions. [f] Reaction mixture heated for a total of 19 h. [g] Analysis performed on a 3 m, 10% OV-101 column packed on GCQ 100/120 mesh with a temperature program of 2 °C/min over 80–260 °C; N_2 carrier gas flow rate 30 mL/min. [h] Purified by chromatography on alumina (method B) rather than silica gel. [i] Retention times of 37 and 40 min, respectively, observed when analysis was carried out using a 3 m × 0.4 mm (i.d.) column of 10% OV-17, at 130 °C, N_2 carrier gas flow rate of 30 mL/min; these conditions were employed for analyzing the sample derived from (−)-(*S*)-**2b**.

1b,c,f,[4b] **2b,**[3a] **2g,**[3b] **2h,**[3c] and **2i**[3d] are in this category and our interest in developing chemical[3] and enzymic[4] methods for preparing such compounds in optically active form prompted us to seek alternative methods of establishing their enantiomeric purities. In this paper we describe a convenient GC analytical technique which permits enantiomeric excesses of variously substituted chiral δ-lactones to be accurately measured.[5]

The method involves conversion of the lactones to their ortho esters with (−)-(2*R*,3*R*)-2,3-butanediol as shown in Scheme I, followed by GC analysis of each mixture of diastereomers.[6] Of the methods available for effecting this type of condensation,[9-13] *p*-toluenesulfonic acid catalyzed dehydration in refluxing benzene was used first (method B). Subsequently, it was found that the reaction could also be carried out under milder conditions, viz. with sulfuric acid catalysis in tetrahydrofuran at room temperature in the presence of triethyl orthoformate (method A).

Good (~40–85%) yields[14] of the ortho esters were obtained from each of the Scheme I lactones and each pair of diastereomers were easily and quantitatively resolvable by GC. The results are summarized in Table I. From the peak area ratios observed, the accuracy of this method of enantiomeric purity determination is generally ≤±3%. Furthermore, the approach lends itself to preparative scale applications. This was demonstrated by the isolation of both diastereomers of **4g** by preparative GC.

One example of an enantiomerically enriched δ-lactone was examined. Thus, (−)-(*S*)-**2b** of estimated 85% optical purity,[3a] upon reaction with (−)-(2*R*,3*R*)-2,3-butanediol (method A), furnished ortho ester **4b**, whose GC analysis revealed a diastereomer ratio of 94.5:5.5 corresponding to an optical purity of 89% for the starting lactone. The observed peaks were identical with those derived from (±)-**4b** by coinjection, the major diastereomer (*R,R,S*) exhibiting the greater retention time. In order to provide assurance that racemization of the 5-substituted δ-lactones does not occur under the conditions of ortho ester formation, this highly enriched ortho ester sample was hydrolyzed to lactone (dilute H_2SO_4, acetone, room temperature), which was then reconverted to **4b** under vigorous conditions (method B). GC analysis of the ortho ester so obtained revealed a composition virtually identical with that of the initial **4b**, specifically 94.2% (*R,R,S*) and 5.8% (*R,R,R*), indicating that alteration of the initial δ-lactone composition is not observed under the acidic conditions employed for derivatization.

The above method of enantiomeric purity determination is clearly applicable to a broad structural range of chiral δ-lactones[15] and is now in routine use for this purpose in our laboratories.

Experimental Section

D-(−)-(2*R*,3*R*)-2,3-Butanediol was prepared by the method of Watson et al.[17] It is also available from Aldrich. NMR analyses were performed in $CHCl_3$ on Varian A-60, T-60, or HA-100 spectrometers with Me_4Si as internal standard. GC analyses were carried out using an F&M 400 chromatograph equipped with a 4 mm × 1 m glass column of 3% QF-1 on Chromosorb G, 80–100 mesh (for **3a–f**), and a Hewlett-Packard 402 instrument using a 6 mm × 1 m glass column of 10% XE-60 on Chromosorb W, 80–100 mesh (for **4b,g–i**). All GC analytical results are recorded in Table I.

Representative Experimental Procedures. (A) Trimethyl Orthoformate Method. Preparation of (2*R*,3*R*,9(*R*,*S*))-2,3,9-Trimethyl-1,4,6-trioxaspiro[4.5]decane ((±)-3a). To 3-methylvalerolactone[4] [(±)-**1a**, 228 mg, 2 mmol] in dried (with $LiAlH_4$)tetrahydrofuran (5 mL) was added, under nitrogen, D-(−)-2,3-butanediol [$[\alpha]_D$ −12.95° (neat), 270 mg, 3 mmol], trimethyl orthoformate (318 mg, 3 mmol), and 3 drops of concentrated sulfuric acid. The mixture was stirred at room temperature (21 °C) for 24 h and then treated with triethylamine (0.5 mL) and poured into saturated aqueous sodium bicarbonate. (Alternatively, solid sodium bicarbonate may be used.) The mixture was then extracted three times with benzene and the benzene extracts washed first with aqueous sodium bicarbonate, then with brine, and finally dried over anhydrous $MgSO_4$ or Na_2SO_4. Rotary evaporation of the solvent afforded a yellow oil (341 mg) suitable for direct GC analysis. It was purified by passing through silica gel (50 g, 60–200 mesh); elution with hexane–acetone (9:1) followed by evaporative distillation (0.1–0.2 Torr) yielded (±)-**3a** (192 mg, 52%): NMR δ 0.99 (d, 3 H, *J* = 6.0 Hz), 1.10–2.05 (m, 5 H), 1.30 (d, 6 H, *J* = 6.0 Hz), and 3.53–4.25 (m, 4 H).

(B) With *p*-Toluenesulfonic Acid. Preparation of [2*R*,3*R*,7(*R*,*S*)]-7-(3′-Cyanopropyl)-1,4,6-trioxaspiro[4.5]decane ((±)-4g). To a stirring solution of the lactone (±)-**2g**[3b] (3.3 g, 20 mmol) in benzene (85 mL) were added, under nitrogen, D-(−)-2,3-butanediol (2.14 g, 24 mmol) and *p*-toluenesulfonic acid (0.1 g, 0.5 mmol). The mixture was refluxed using a Dean–Stark trap. More *p*-toluenesulfonic acid (0.1 g) and D-(−)-2,3-butanediol (1.05 g, 12 mmol) were added after 1.5 and 2.4 h, respectively. After heating under reflux for a further 2 h the mixture was cooled and neutralized with triethylamine (1 mL) and powdered sodium bicarbonate (0.5 g). It was then poured into saturated aqueous sodium bicarbonate and was extracted three times with benzene. The combined extracts were washed (aqueous sodium bicarbonate followed by brine), dried (Na_2SO_4), and concentrated to give 4.2 g of a light yellow oil. The crude product was purified by passing through a column of alumina (grade III, 125 g). Fractions eluted with 4:1 hexane–ether yielded 2.93 g (62%) of (±)-**4g**, which was evaporatively distilled (0.05–0.2 Torr):

NMR δ 1.26, 1.31 (2d, 6 H, J = 6.0 and 5.5 Hz), 1.41–1.89 (m, 10 H), 2.35 (br t, 2 H), 3.54–4.16 (m, 3 H).

Isolation of the two diastereoisomers was achieved using a Varian Autoprep 705 gas chromatograph with a 9 mm × 2 m aluminum column of KOH-modified 20% polyethylene glycol 20M on Chromosorb W (60–80 mesh). The column temperature was held at 230 °C for 75 min and then was increased to 240 °C. A nitrogen flow rate of 150 mL/min was maintained throughout. The two samples obtained were chromatographed separately on alumina (grade III). Fractions eluted with 2:1 hexane–ether contained the pure products: NMR (diastereomer I) δ 1.28 (2d, 6 H, J = 5.5 Hz), 1.41–1.96 (m, 10 H), 2.33 (br t, 2 H), and 3.55–3.91 (m, 3 H); NMR (diastereomer II) δ 1.26 (d, 6 H, J = 6.0 Hz), 1.42–1.96 (m, 10 H), 2.32 (br t, 2 H), and 3.56–4.21 (m, 3 H).

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Registry No.—(±)-**1a**, 62989-38-2; (±)-**1b**, 62989-39-3; (±)-**1c**, 62948-63-4; (±)-**1d**, 21754-22-3; (±)-**1e**, 61949-75-5; (±)-**1f**, 62948-64-5; (±)-**2b**, 35221-77-3; (±)-**2g**, 35337-27-0; (±)-**2h**, 30665-84-6; (±)-**2i**, 28458-39-1; **3a** isomer 1, 62948-65-6; **3a** isomer 2, 62989-40-6; **3b** isomer 1, 62948-66-7; **3b** isomer 2, 62989-41-7; **3c** isomer 1, 62948-67-8; **3c** isomer 2, 62989-42-8; **3d** isomer 1, 62948-68-9; **3d** isomer 2, 62989-43-9; **3e** isomer 1, 62948-69-0; **3e** isomer 2, 62989-44-0; **3f** isomer 1, 62948-70-3; **3f** isomer 2, 62989-45-1; **4b** isomer 1, 62948-71-4; **4b** isomer 2, 62989-46-2; **4g** isomer 1, 62948-72-5; **4g** isomer 2, 63038-29-9; **4h** isomer 1, 62948-73-6; **4h** isomer 2, 62989-47-3; **4i** isomer 1, 62948-74-7; **4i** isomer 2, 62989-48-4; (−)-(2R,3R)-2,3-butanediol, 24347-58-8.

References and Notes

(1) Cf. J. A. Dale, D. L. Dull, and H. S. Mosher, *J. Am. Chem. Soc.*, **84**, 2543 (1962).
(2) Cf. M. D. McCreary, D. W. Lewis, D. L. Wernick, and G. M. Whitesides, *J. Am. Chem. Soc.*, **96**, 1038 (1974), and references cited therein.
(3) (a) Racemic: H. D. Zook and J. A. Knight, *J. Am. Chem. Soc.*, **76**, 2303 (1954); optically active: G. Saucy and R. Borer, *Helv. Chim. Acta*, **54**, 2121 (1971); (b) N. Cohen, B. Banner, R. Borer, R. Mueller, R. Yang, M. Rosenberger, and G. Saucy, *J. Org. Chem.*, **37**, 3385 (1972); (c) M. Rosenberger, A. J. Duggan, R. Borer, R. Mueller, and G. Saucy, *Helv. Chim. Acta*, **55**, 2663 (1972); (d) J. W. Scott and G. Saucy, *J. Org. Chem.*, **37**, 1659 (1972).
(4) (a) A. J. Irwin and J. B. Jones, *J. Am. Chem. Soc.*, **99**, 556 (1977); (b) J. B. Jones, I. H. Goodwin, and K. P. Lok, unpublished results.
(5) GC analysis of diastereomers has been used extensively for the determination of enantiomeric purity: cf. M. Raban and K. Mislow, *"Top. Stereochem.* **2**, 211–216 (1967). For a more recent example, see D. Valentine, Jr., K.-K. Chan, C. G. Scott, K. Johnson, K. Toth, and G. Saucy, *J. Org. Chem.*, **41**, 62 (1976).
(6) This approach has been used to resolve racemic ketones via separation of their diastereomeric ketals.[7,8] Our attention was drawn to the possibility of extending the technique to chiral δ-lactones by the observation that certain steroid lactones underwent facile ortho ester formation with ethylene glycol.[9]
(7) J. Casanova and E. J. Corey, *Chem. Ind. (London)*, 1664 (1961).
(8) M. Sanz-Burata, J. Irurre-Pérez, and S. Juliá-Arechaga, *Afinidad*, **27**, 693, 705 (1970).
(9) R. A. LeMahieu and R. W. Kierstead, *Tetrahedron Lett.*, 5111 (1970).
(10) H. Meerwein, P. Borner, O. Fuchs, H. J. Sasse, H. Schrodt, and J. Spille, *Chem. Ber.*, **89**, 2060 (1956).
(11) K. Bodenbenner, *Justus Liebigs Ann. Chem.*, **633**, 183 (1959).
(12) P. Deslongchamps, K. Chênevert, R. J. Taillefer, C. Moreau, and J. K. Saunders, *Can. J. Chem.*, **53**, 1601 (1975).
(13) S. Danishefsky, T. Kitahara, P. F. Schuda, and S. J. Etheredge, *J. Am. Chem. Soc.*, **98**, 3028 (1976).
(14) When the yield of any such reaction is less than quantitative, the possibility always exists that rate differences in the reaction of the individual enantiomers may result in the formation of unequal amounts of the diastereomeric products. That this reservation does not apply here is indicated by the fact that the proportions of each diastereomeric pair of ortho esters was within 3% of the 1:1 ratio expected from using racemic lactone precursors. The last entry demonstrates that, if desired, yields very close to quantitative can be attained using method B.
(15) Attempts to extend the analysis to chiral γ-lactones using a variety of ortho ester synthetic methods[9–13] have not been successful.[16] Recently, an NMR method for determination of enantiomeric composition of γ-lactones was published: W. H. Pirkle, D. L. Sikkenga, and M. S. Pavlin, *J. Org. Chem.*, **42**, 384 (1977); W. H. Pirkle and D. L. Sikkenga, *ibid.*, **42**, 1370 (1977).
(16) J. B. Jones and I. J. Jacovac, unpublished results.
(17) (a) R. W. Watson, F. Tamboline, and G. W. Harmsen, *Can. J. Res.*, **27**, 457 (1949); (b) L. J. Rubin, H. A. Lardy, and H. O. L. Fischer, *J. Am. Chem. Soc.*, **74**, 425 (1952).

The Pomeranz–Fritsch Reaction, Isoquinoline vs. Oxazoles

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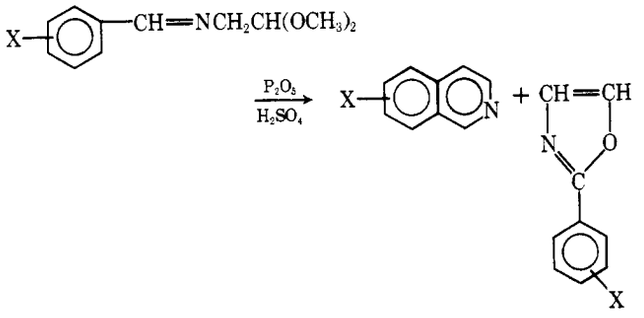
The Pomeranz–Fritsch reaction has been used for the preparation of a number of isoquinolines with varying yields.[1] As ordinarily carried out it involves the condensation of benzal aminoacetal to the isoquinoline. The yield varies from quite good with certain methoxy substituents to zero with nitro groups; in the latter case, the products are oxazoles.[2,3]



In this work we report the percent of oxazole formed with methyl, chloro, and nitro groups present in the original benzaldehyde. The Pomeranz–Fritsch reaction has been run with both o- and p-tolualdehyde. The yield of 8-methylisoquinoline in the first case is 18% and of 6-methylisoquinoline in the second case is 21%. We have also run the reaction with m-tolualdehyde and have obtained a yield of crude mixed 5- and 7-methylisoquinolines of 22%. A very careful search for 2-(tolyl)oxazole by chromatography and mass spectra analysis has shown yields of 3, 1, and 6%, in the cases of o-, m-, and p-tolaldehydes in the crude isolated products.

When acetals of the three chlorobenzaldehydes were subjected to conditions of the Pomeranz–Fritsch reaction, the oxazole production became appreciable. In the case of ortho it was 36% of the crude product isolated, in meta 23%, and in para 61%. The acetals of o-, m-, and p-nitrobenzaldehyde were cyclized and the yields were 54, 50, and 40%, respectively, of oxazole with no evidence for any isoquinoline. The three 2-nitrophenyloxazoles were then reduced and the amino compounds subjected to Sandmeyer[4] reactions to give the corresponding chloro compounds. These were then compared to the chlorophenyloxazoles formed by direct Pomeranz–Fritsch reaction (Table I).

Experimental Section

Separations were carried out on a Hewlett-Packard 5750 chromatograph with a 20 ft × ¼ in. column filled with Carbowax M on Anakrom 50/60 AB.

2-(x-Nitrophenyl)oxazoles. 2-(p-Nitrophenyl)oxazole (mp 163–164 °C) and 2-(o-nitrophenyl)oxazole (mp 43–46 °C) were prepared by the method of Cass and co-workers.[2,3] Heating 100 g (0.67 mol) of m-nitrobenzaldehyde and 70 g (0.67 mol) of dimethyl aminoacetal to 100 °C for 2 h and cooling gave a crude m-nitrobenzal aminoacetal. Twenty grams of this was dissolved in 100 mL of concentrated H_2SO_4, and poured into 40 g of P_2O_5 and 10 mL of H_2SO_4 at 180 °C and heated for 20 min. The solution was cooled and neutralized with NH_4OH to give 9 g (56%) of crude oxazole, mp 96–98 °C. Recrystallization from ethanol gave material with mp 97–98 °C, m/e (M^+) 190. Anal. Calcd for $C_9H_6N_2O_3$: C, 56.84; H, 3.15. Found: C, 56.88; H, 3.20.

2-(x-Aminophenyl)oxazoles. All three of the nitrophenyloxazoles above were hydrogenated in methanol with 10% Pd–C. 2-(o-Aminophenyl)oxazole[2] (mp 32–33 °C), 2-(p-aminophenyl)oxazole[3] (mp 121–123 °C), and the new 2-(m-aminophenyl)oxazole (mp 69–70 °C) were obtained.