## Enantiomerically Pure 2-Bromoalkyl Aryl Ketones

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The non-conventional hydrolysis of mixtures of diastereoisomeric α-bromo acetals, available in high yields, high diastereomeric excesses, and in large amounts, allows the synthesis and the full characterization of enantiomerically pure (2*S*)- and (2*R*)-bromoalkyl aryl ketones. The developed methodology represents the first route to enantiomerically pure 2-bromoalkyl aryl ketones of (2*R*) and (2*S*) configurations.

2-Bromoalkyl aryl ketones are important intermediates in organic synthesis thanks to the presence of two functional groups each of which can be easily converted, in a controlled fashion, to a variety of other functionalities.[1] Accordingly, enantiomerically pure 2-bromoalkyl aryl ketones can be expected to be interesting bifunctional intermediates in the synthesis of enantiomerically pure compounds (EPC).[2]

To the best of our knowledge, enantiomerically pure 2-bromoalkyl aryl ketones have not yet been described,[3] while optically active 2-bromoalkyl aryl ketones are reported in the patent literature,[4] in which, however, enantiomeric purity as well as spectroscopic and analytical data are not given.

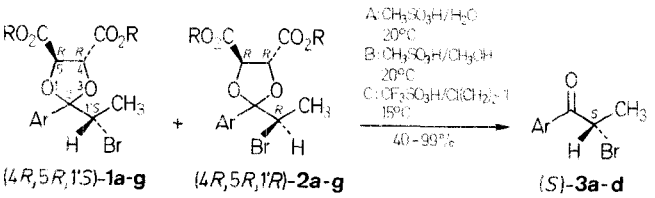
As part of our study on the synthesis of optically active 2-arylalkanoic acids, we now report on the conversion of diastereoisomeric mixtures of α-bromo acetals **1** and **2** [available in high yields, high diastereomeric excess (**1** > **2**), and in large amounts from the corresponding alkyl aryl ketones[5,6]] into optically active 2-bromoalkyl aryl ketones **3**.

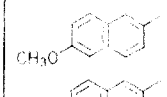
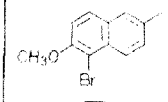
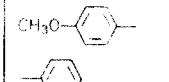
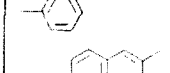
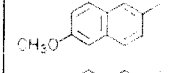
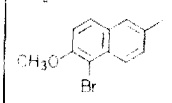
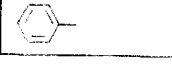
The new method allows, for the first time, the preparation and full characterization of enantiomerically pure 2-bromoalkyl aryl ketones **3**.

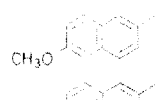
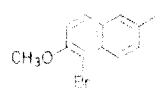
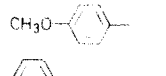
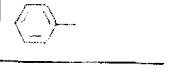
α-Bromo acetals **1a–d; 2a–d** were prepared by bromination of alkyl aryl acetals obtained from (2*R*, 3*R*)-tartaric acid dimethyl ester.[5,6] α-Bromo acetals **1e, f, g; 2e, f, g** (R = H) were prepared from the corresponding dimethyl esters (**1a, b, d; 2a, b, d**) by hydrolysis of the two methoxycarbonyl groups.[7]

The attempted conversion of mixtures of **1** and **2** into **3** under conventional aqueous acidic conditions was unsuccessful. Mild conditions did not hydrolize the α-bromo acetals, while more drastic aqueous conditions caused **1** and **2** to rearrange to 2-arylalkanoic acids.[7]

We now report that diastereoisomer mixtures of **1** and **2**, in which the epimer **1** having *S*-configuration at C-1′ predominates, are converted, in high yields and in high enantiomeric excess, into optically active (*S*)-2-bromoalkyl aryl ketones **3** and into (2*R*, 3*R*)-tartaric acid. Thus, treatment at 15–20 °C of mixtures of α-bromoacetals **1** and **2** (**1** > **2**) with an excess of methanesulfonic acid in the presence of water (Method A) or of methanol (Method B), or with an excess of trifluoromethanesulfonic acid in 1,2-dichloroethane (Method C) provided **3** (Table 2).




| 1,2 | Ar | R |
|---|---|---|
| a |  | $CH_3$ |
| b |  | $CH_3$ |
| c |  | $CH_3$ |
| d |  | $CH_3$ |
| e |  | H |
| f |  | H |
| g |  | H |

| 3 | Ar |
|---|---|
| a |  |
| b |  |
| c |  |
| d |  |

Method C is particularly suitable for the hydrolysis of substrates **1g** and **2g**.

**Table 1.** Mixtures of Diastereoisomeric α-Bromo Acetals **1e–g** and **2e–g** Prepared[a]

| **1 : 2** (ratio **1 : 2**)[b] | Yield[c] (%) | m.p. (°C) (solvent) | Molecular Formula[d] | IR ($CHCl_3$) (C=O) $\nu$ ($cm^{-1}$) | $^1$H-NMR (acetone-$d_6$/TMS) $\delta$, $J$(Hz) |
|---|---|---|---|---|---|
| **1e : 2e** (89 : 11) | 95 | – | $C_{18}H_{17}BrO_7$ (425.2) | 1745 | **1e:** 1.66 (d, 3H, $J$ = 7); 3.93 (s, 3H); 4.66 (q, 1H, $J$ = 7); 5.01 (2H, ABq, $\Delta\nu$ = 56.2, $J$ = 6.6); 7.15–8.10 (m, 6H)<br>**2e:** 1.68 (d, $J$ = 7) |
| **1f : 2f** (90 : 10) | 97 | – | $C_{18}H_{16}Br_2O_7$ (504.1) | 1745 | **1f:** 1.69 (d, 3H, $J$ = 7); 4.06 (s, 3H); 4.69 (q, 1H, $J$ = 7); 4.95 (2H, ABq, $\Delta\nu$ = 52.3, $J$ = 6.6); 7.45–8.20 (m, 5H)<br>**2f:** 1.67 (d, $J$ = 7) |
| **1f** | 90 | 184–186 ($CH_2Cl_2$) | $C_{18}H_{16}Br_2O_7$ (504.1) | 1745 | **1f:** as reported above |
| **1g : 2g** (90 : 10) | 96 | – | $C_{13}H_{13}BrO_6$ (345.15) | 1750 | **1g:** 1.64 (d, 3H, $J$ = 7.1); 4.57 (q, 1H, $J$ = 7.1); 4.86 (2H, ABq, $\Delta\nu$ = 65.2, $J$ = 6.9); 7.35–7.60 (m, 5H)<br>**2g:** 1.60 (d, $J$ = 7.1) |

[a] The mixtures of diastereoisomers **1e–g** and **2e–g** were prepared according to the Typical Procedure given for the preparation of **1f**. The preparations of mixtures of diastereoisomers **1a–d** and **2a–d** (R = $CH_3$) are given in Ref. 6.
[b] Determined by $^1$H-NMR (300 MHz) using the $CH_3$(CHBr) resonances and by HPLC carried out with the corresponding dimethyl esters obtained by reaction with diazomethane in $Et_2O$.
[c] Yield of isolated products based on dimethyl esters.
[d] Satisfactory microanalyses obtained: C ±0.2, H ±0.2, Br ±0.3.

**Table 2.** Preparation of 2-Bromoalkyl Aryl Ketones **3**

| Substrate **1 : 2** (ratio **1 : 2**) | Method[a] | Reaction Conditions Temp. (°C) Time (h) | Product | Yield (%)[b] | Enantiomeric Ratio $S$ : $R$[c] | Crystallized **3** Yield (%)[d] | Enantiomeric Ratio $S$ : $R$[c] |
|---|---|---|---|---|---|---|---|
| **1a : 2a**[e] (88 : 12) | A | 20, 2[f] | **3a** | 94 | 79 : 21 | 59 | > 99 : 1 |
| **1e : 2e** (89 : 11) | A | 20, 18[f] | **3a** | 94 | 89 : 11 | – | – |
| **1b : 2b** (90 : 10) | A | 20, 18[f] | **3b** | 99 | 91 : 9 | 75 | > 99 : 1 |
| **1f : 2f** (90 : 10) | B | 20, 18[f] | **3b** | 95 | 90 : 10 | – | – |
| **1f** | B | 20, 18[f] | **3b** | 96 | 99 : 1 | – | – |
| **1c : 2c** (90 : 10) | A | 15, 4 | **3c** | 96 | 80 : 20 | 46 | > 99 : 1 |
| **1d : 2d** (90 : 10) | A | 20, 18 | **3d** | 92 | 50 : 50 | – | – |
| **1g : 2g** (90 : 10) | C | 15, 2 | **3d** | 40 | 80 : 20 | – | – |

[a] See Typical Procedures.
[b] Yields of isolated products based on α-bromoacetals **1** + **2**.
[c] Determined by $^1$H-NMR (see Experimental Section).
[d] Yields of crystallized **3** are based on α-bromo acetals **1** + **2**.
[e] Hydrolysis of the mixture of the diastereoisomeric (1′*R*, 4*S*, 5*S*)- and (1′*S*, 4*S*, 5*S*)-2-(1-bromoethyl)-2-(6-methoxy-2-naphthyl)-1,3-dioxolane-4,5-dicarboxylic acid dimethyl esters, prepared by bromination of alkyl aryl acetals obtained from (2*S*, 3*S*)-tartaric acid, provided (*R*)-**3a** in the same yield and enantiomeric purity.
[f] Heterogeneous reaction conditions.

Substrates **1** and **2** with R = H are preferred to those with R = $CH_3$ because they allow the acid-base separation of the α-bromoketone from impurities and from the unreacted starting material, if any.

Generally, 2-bromoalkyl aryl ketones racemize under the reaction conditions: for this reason, in the case of **3d** the reaction has to be stopped at low conversions in order to obtain the desired enantiomeric purity. Racemization does not occur in the cases of **3a** and **3b** because of their low solubility in the reaction medium. Compound **3c** is found to be only slightly racemized at complete conversion of the corresponding α-bromo acetals.

The enantiomeric purity of the crude 2-bromoalkyl aryl ketones **3** reflects the diastereomeric excess of the starting α-bromo acetals; crystallization of crude 2-bromoalkyl aryl ketones leads to the enantiomerically pure ketones **3** (Table 2).

The *S*-configuration was assigned to **3a** by comparing its chiroptical properties with those of the known 2(*S*)-bromo-1-(6-methoxy-2-naphthyl)-1-propanone.[8] Compound **3a** has the same absolute configuration at C-1′ as the major epimer **1a** of the starting diastereoisomer mixture. The *S*-configuration is assigned to **3b–d** because these compounds are obtained from diastereoisomer mixtures of α-bromo acetals in which the major epimer **1** has the *S*-configuration at C-1′ (Table 2) and because the major epimer **1** remains prevalent during the hydrolysis.

All compounds **3** were fully characterized by C, H, Br analyses, IR, UV, and $^1$H-NMR spectra, optical rotation, and CD spectra (Table 3). The enantiomeric purity was determined by $^1$H-NMR analysis carried out in the presence of the optically active shift reagent Europium(III) tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorate], Eu(hfc)$_3$.

As expected, hydrolysis of the diastereoisomer mixtures of α-bromo acetals prepared by bromination of alkyl aryl acetals obtained from (2*S*, 3*S*)-tartaric acid provides 2-bromoalkyl aryl ketones of *R*-configuration.

**Table 3.** Analytical Data of Compounds **3**

| Product | m.p. (°C)[a] (solvent) | Racemic **3** Lit. m.p. (°C) bp (°C/mmHg) | $[\alpha]_D^{20}$ (c = 1, $CHCl_3$) | Molecular Formula[b] | UV ($CH_2Cl_2$) $\lambda_{max}$, nm ($\varepsilon$, $M^{-1}cm^{-1}$) | CD ($CH_2Cl_2$) $\lambda_{max}$, nm ($\Delta\varepsilon$, $M^{-1}cm^{-1}$) | $^1$H-NMR ($CDCl_3$/TMS) $CH_3(CHBr)$ resonance[c] $\delta$ (Hz) | $\Delta\delta$ (Hz) | $\Delta\Delta\delta$ (Hz) |
|---|---|---|---|---|---|---|---|---|---|
| (*S*)-**3a** | 107–108 (MeOH) | m.p. 78–80[10] | +205.9° | $C_{14}H_{13}BrO_2$ (293.2) | 355 sh (4900), 322 (12800), 267 (18700), 250 (17300) | 348 (+5.29), 338 (+5.60), 308 (−2.80), 270 (+1.80), 252 (+5.29) | 586 | 133 | 24 |
| (*R*)-**3a** | 99–100 (MeOH) | m.p. 78–80[10] | −202.7° | $C_{14}H_{13}BrO_2$ (293.2) | 355 sh (5200), 321 (13800), 265 (20000), 250 (18700) | 348 (−5.55), 338 (−5.65), 309 (+3.25), 272 (−1.68), 253 (−5.45) | 586 | 157 | 24 |
| (*S*)-**3b** | 163 (1,2-dichloroethane/MeOH) | m.p. 160–162[10] | +162.25° | $C_{14}H_{13}Br_2O_2$ (372.1) | 360 sh (4800), 327 (9350), 271 (29500) | 357 (+3.88), 340 (+4.06), 310 (−1.21), 280 (+0.73), 273 (−0.36), 255 (+4.61) | 589 | 56 | 10 |
| (*S*)-**3c** | 82–83 (MeOH) | m.p. 66–67[11] | + 88.28° | $C_{10}H_{11}BrO_2$ (243.1) | 291 (14300), 255 (8400) | 359 (−0.45), 348 sh (−0.31), 315 (+2.11), 282 (−2.65), 255 sh (+1.15), 233 (+12.35) | 568 | 181 | 30 |
| (*S*)-**3d**[d] | – | b.p. 134–136/20[12] | | $C_{10}H_9BrO_2$ (213.1) | 324 (170), 290 sh (800), 253 (4050) | 335 br (−0.16), 308 sh (−0.06), 288 (+0.19), 258 (+0.25), 240 sh (+0.20) | 574 | 81 | 12 |

[a] Uncorrected and measured with a Koefler apparatus.

[b] Satisfactory microanalyses obtained: C ±0.2, H ±0.2, Br ±0.3.

[c] $\Delta\delta$ represents the difference between the reported resonance of the *S* or the *R* enantiomer in the presence of $Eu(hfc)_3$ and in the absence of $Eu(hfc)_3$. $\Delta\Delta\delta$ represents the difference between the reported resonance of the *S* enantiomer and that of the *R* enantiomer in the presence of $Eu(hfc)_3$. $\Delta\delta$ and $\Delta\Delta\delta$ are calculated by taking $^1$H-NMR spectra at 300 MHz for equimolar solutions of $Eu(hfc)_3$ and of **3**.

[d] UV and CD spectra of (*S*)-**3d** with 60% ee (see Table 1).

The CD spectra of (*R*)- and (*S*)-**3a** show mirror image behavior throughout the spectral range (Table 3). There is no apparent general correlation between the naphthalene **(3a, b)** and the benzene series **(3c, d)**. The lowest energy (CD band, which is attributed to the carbonyl n → π* transition, is in fact negative for (*S*)-**3c** and (*S*)-**3d** but positive for (*S*)-**3a** and (*S*)-**3b**.

The developed methodology represents the first asymmetric synthesis of enantiomerically pure 2-bromoalkyl aryl ketones of *S* and *R*-configurations starting from alkyl aryl ketones.

Melting points were measured on a Kofler apparatus and were not corrected. Microanylses were obtained by using a Hewlett-Packard instrument. HPLC analyses were carried out on a Hewlett-Packard 1090 Liquid Chromatograph equipped with a Merck 50329 lichrospher (5 μ, 250 mm × 4 mm) column (eluent $H_2O$/MeOH 40:60, flow 1.5 mL/min, oven temperature 50 °C; wavelenght 254 nm). Analytical TLC analyses were performed by using precoated silica gel 60 F254 plates supplied by Merck: visualization was accomplished under UV light (254, 366 nm). Optical rotations were measured at the sodium D-line in a 1 dm cell on a Perkin-Elmer 241 polarimeter. IR spectra were taken on a Perkin-Elmer 1420 instrument: positions of interesting absorptions are quoted to be ± 2.5 $cm^{-1}$. UV and CD spectra were obtained on a Perkin-Elmer Lambda 5 spectrophotometer and on a Jasco J 500 C dichrograph, respectively. $^1$H-NMR spectra were taken at 300 MHz on a Varian XL-300. Enantiomeric purities of compounds **3** were evaluated by taking $^1$H-NMR spectra of 0.025 molar solutions in $CDCl_3$ in the presence of an equimolar amount of the optically active shift reagent $Eu(hfc)_3$ (see Table 3).

All solvents and reagents were commercially available (reagent grade) and were used without further purification. Evaporation of solvents in the workup procedures was done with a Büchi rotary evaporator. α-Bromo acetals **1a–d; 2a–d** were prepared as described in Ref. 5,6. α-Bromo acetals **1e, g; 2e, g** were prepared according to the procedure given for α-bromo acetal **1f**.

**(1′*S*,4*R*,5*R*)-2-(1-Bromoethyl)-2-(5-bromo-6-methoxy-2-naphthyl)-1,3-dioxolane-4,5-dicarboxylic Acid (1f); Typical Procedure** (Table 1):

A solution of NaOH (8.4 g, 0.21 mol) in $H_2O$ (70 mL) is added, over 1 h, to a stirred mixture of α-bromo acetal **1b**[6] (53.2 g, 0.1 mol) and MeOH (250 mL) at 20 °C. The mixture is kept at 20 °C for 2 h, then MeOH is distilled off while keeping the volume constant by addition of $H_2O$. The aqueous solution is extracted with $CH_2Cl_2$ (2 × 100 mL) and acidified with conc. HCl to pH 1. The mixture is extracted with $Et_2O$ (3 × 100 mL). The combined organic extracts are washed with $H_2O$ (3 × 50 mL), dried ($Na_2SO_4$), and filtered. Evaporation of the solvent at 20 Torr leads crude **1f**, which is crystallized from $CH_2Cl_2$; yield: 45.4 g, 0.09 mol, 90%; m.p. 184–186 °C; $[\alpha]_D^{20}$ +39.73° (*c* = 1, acetone).

| | | | | |
|---|---|---|---|---|
| $C_{18}H_{16}Br_2O_7$ (504.1) | calc. | C 42.88 | H 3.20 | Br 31.70 |
| | found | 43.01 | 3.18 | 31.67 |

$^1$H-NMR (300 MHz, acetone-$d_6$/TMS): δ = 1.69 (d, 3H, *J* = 7 Hz); 4.06 (s, 3H); 4.69 (q, 1H, *J* = 7 Hz); 4.95 (2H, ABq, Δν = 52.33 Hz, *J* = 6.6 Hz); 7.45–8.20 (m, 5H).

**2-Bromo-1-aryl-1-propanones (3); Typical Procedures:**

Method A, using excess methanesulfonic acid in the presence of water:

*(2S)-2-Bromo-1-(6-methoxy-2-naphthyl)-1-propanone* **(3a)**: A mixture of the diastereoisomeric α-bromo acetals **1a** and **2a** (ratio 88:12; 4.53 g, 10 mmol) is added all at once, with stirring at 20 °C, to a solution of $H_2O$ (0.5 g, 27.7 mmol) in methanesulfonic acid (20 mL). The mixture is kept at 20 °C for 2 h and is then slowly poured into a mixture of $Et_2O$ (20 mL) and crushed ice (10 g). The organic phase is washed with $H_2O$ (2 × 5 mL), dried ($Na_2SO_4$), and filtered. Evaporation of the solvent at 20 Torr gives the crude optically active product **3a**; yield: 2.75 g, 9.4 mmol, 94%); enantiomeric excess: 58% [according to $^1$H-NMR analyses using the optically active shift reagent $Eu(hfc)_3$]. Crystalliza-

tion of crude **3a** from MeOH affords enantiomerically pure (*S*)-**3a**; yield: 1.73 g (5.9 mmol, 59%); m.p. 107–108°C; $[\alpha]_D^{20} + 205.9°$ ($c = 1$, $CHCl_3$).

| | | | | |
|---|---|---|---|---|
| $C_{14}H_{13}BrO_2$ | calc. | C 57.36 | H 4.47 | Br 27.25 |
| (293.2) | found | 57.28 | 4.43 | 27.31 |

IR (Nujol): $\nu_{(C=O)} = 1680\ cm^{-1}$.

$^1$H-NMR (300 MHz, $CDCl_3$/TMS): $\delta = 1.96$ (d, 3H, $J = 6.6$ Hz); 3.96 (s, 3H); 5.48 (1q, 1H, $J = 6.6$ Hz); 7.15–8.50 (m, 6H).

Method B, using excess methanesulfonic acid in the presence of methanol:

*(2S)-2-Bromo-1-(5-bromo-6-methoxy-2-naphthyl)-1-propanone* (**3b**): The α-bromo acetal **1f** (5.04 g, 10 mmol) is added all at once, with stirring at 20°C, to a solution of MeOH (5 mL, 3.95 g, 123 mmol) in methanesulfonic acid (20 mL). The mixture is kept at 20°C for 18 h and is then slowly poured into a mixture of $Et_2O$ (20 mL) and crushed ice (10 g). The organic phase is washed successively with $H_2O$ (2 × 5 mL), and 2% aqueous $NaHCO_3$ solution (2 × 5 mL), dried ($Na_2SO_4$), and filtered. Evaporation of the solvent at 20 Torr gives the enantiomerically pure product (*S*)-**3b**; yield: 3.57 g (9.6 mmol, 96%); m.p. 161°C; $[\alpha]_D^{20} + 161.3°$ ($c = 1$, $CHCl_3$).

An analytically pure sample is obtained by crystallization from MeOH/1,2-dichloroethane (the minimum amount to solubilize the product at reflux); m.p. 163°C; $[\alpha]_D^{20} + 162.25°$ ($c = 1$, $CHCl_3$).

| | | | | |
|---|---|---|---|---|
| $C_{14}H_{13}Br_2O_2$ | calc. | C 45.20 | H 3.52 | Br 42.95 |
| (372.1) | found | 45.22 | 3.47 | 42.93 |

IR (Nujol): $\nu_{(C=O)} = 1670\ cm^{-1}$.

$^1$H-NMR (300 MHz, $CDCl_3$/TMS): $\delta = 1.97$ (d, 3H, $J = 6.6$ Hz); 4.08 (s, 3H); 5.43 (q, 1H, $J = 6.6$ Hz); 7.30–8.50 (m, 5H).

Method C, using excess trifluoromethanesulfonic acid in 1,2-dichloroethane:

*(2S)-Bromo-1-phenyl-1-propanone* (**3d**): Trifluoromethanesulfonic acid (3 g, 1.76 mL, 20 mmol) is added within 5 min, with stirring at 15°C, to a solution of a mixture of the diastereoisomeric α-bromo acetals **1g** and **2g** (ratio 9:1; 3.89 g, 10 mmol) in 1,2-dichloroethane (20 mL). The reaction mixture is kept at 15°C for 2 h and is then slowly poured into a mixture of $Et_2O$ (20 mL) and crushed ice (10 g). The organic phase is washed with $H_2O$ (5 mL), with a 2% aqueous $NaHCO_3$ solution (2 × 5 mL), dried ($Na_2SO_4$), and filtered. Evaporation of the solvent at 20 Torr gives the optically active product **3d** as an oil; yield: 0.852 g (40 mmol, 40%); enantiomeric excess: 60% [according to $^1$H-NMR analysis using the optically active shift reagent Eu(hfc)$_3$].

| | | | | |
|---|---|---|---|---|
| $C_9H_9BrO_2$ | calc. | C 56.37 | H 4.26 | Br 37.50 |
| (213.1) | found | 56.28 | 4.24 | 37.48 |

IR (neat): $\nu_{(C=O)} = 1680\ cm^{-1}$.

$^1$H-NMR (300 MHz, $CDCl_3$/TMS): $\delta = 1.91$ (d, 3H, $J = 6.6$ Hz); 5.30 (q, 1H, $J = 6.6$ Hz); 7.45–8.05 (m, 5H).

**Recovery of Dimethyl Tartrate:**

The product mixture obtained as described for Method A [preparation of **3a** starting from **1f** (504 mg, 1 mmol)] is worked up at complete conversion of **1f** (reaction time: 18 h) as follows: the mixture is slowly diluted with MeOH (3 mL) and treated at 0°C with diazomethane in $Et_2O$. The solvent is removed under reduced pressure and the excess of methyl methanesulfonate distilled off at 1 Torr. The residue is diluted with $H_2O$ (3 mL) and extracted with $Et_2O$ (2 × 5 mL). The aqueous solution is evaporated to dryness under reduced pressure and $CHCl_3$ (2 mL) is added. The insoluble material is filtered off and evaporation of the solvent at 20 Torr affords tartaric acid dimethylester; yield: 80 mg (0.45 mmol, 45%); m.p. 45–47°C; $[\alpha]_D^{20} + 21.7°$ ($c = 2.5$, $H_2O$) (Lit.[9] m.p. 48–49°C; $[\alpha]_D^{20} + 21.0$, $c = 2.5$, $H_2O$).

$^1$H-NMR (300 MHz, $CDCl_3$/TMS): $\delta = 3.66$ (s, 2H); 3.87 (s, 6H); 4.56 (s, 2H).

*The authors thank Mr. L. Arbizzani for technical assistance and Prof. L. Casella, University of Milano, for UV and CD spectra.*

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(1) For the reviews on the reactivity of α-halo ketones see:
Verhè, R., De Kimpe, N., in: *The Chemistry of Halides, Pseudo-halides and Azides*, Patai, S., Rappoport, Z. (eds.), 2nd ed., Supplement D, Part 1, John Wiley & Sons, New York, 1983, Chap. 19, pp. 813–931.
Rappe, C., in: *The Chemistry of Carbon-Halogen-Bond*, Patai, S. (ed.), Part 2, John Wiley & Sons, New York, 1973, Chap. 17, pp. 1071–1114.
Charpentier-Morize, M. *Bull. Soc. Chim. Fr.* **1974**, 343.
Giordano, C., Castaldi, G., Uggeri, F. *Angew. Chem.* **1984**, *46*, 413; *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 413.
For articles on the reactivity of α-halo ketones see:
Giordano, C., Castaldi, G., Uggeri, F., Gurzoni, F. *Synthesis* **1985**, 436.
De Kimpe, N., De Buyck, L., Verhè, R., Schamp, N. *Chem. Ber.* **1983**, *116*, 3631.
Castaldi, G., Giordano, C., Uggeri, F. *Synthesis* **1985**, 505.

(2) Seebach, D., Imwinkelried, R., Weber, T. *Modern Synthetic Methods*, Vol. 4, Springer Verlag, Berlin, 1986, pp. 128–248.
Seebach, D. Hungerbühler, H., in: *Modern Synthetic Methods*, Sheffold, R. (ed.), Vol. 2, Verlag Salle-Sauerländer, Aarau, 1980, pp. 91–171.

(3) Asymmetric syntheses of optically active 2-bromocycloalkanones have been reported:
Hiroi, K., Yamada, S. *Chem. Pharm. Bull.* **1973**, *21*, 54.
Simpkins, N.S. *J. Chem. Soc. Chem. Commun.* **1986**, 88.

(4) Schloemer, G.C. *European Patent. Appl.* EP 81, 993 (1983): *C.A.* **1983**, *99*, 175386; the patent reports only the preparation of one optically active 2-bromoalkyl aryl ketone (see Ref. 8).

(5) Castaldi, G., Cavicchioli, S., Giordano, C., Uggeri, F. *Angew. Chem.* **1986**, *98*, 273; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 259.

(6) Castaldi, G., Cavicchioli, S., Giordano, C., Uggeri, F. *J. Org. Chem.* **1987**, *52*, 3018; see also "Corrections", in press.

(7) Castaldi, G., Cavicchioli, S., Giordano, C., Uggeri, F. *European Patent Appl.* EP 158913; EP 158255 (1985); *C.A.* **1986**, *104*, 14566, 168205.

(8) The preparation of (*S*)-**3a** was accomplished starting from (6-methoxy-2-naphthyl)magnesium bromide and 2(*S*)-bromopropanoyl chloride as reported in Ref. 6.

(9) Kocienski, P., Street, S.D.A. *Synth. Commun.* **1984**, 1087.

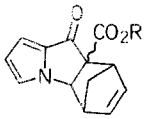
(10) Marquet, A., Jacques, J. *Bull. Soc. Chim. Fr.* **1962**, 90.

(11) Dombrovskii, A.V., Shevchuk, M.I., Kravets, V.P. *Zh. Obshch. Khim.* **1962**, *32*, 2278; *C.A.* **1963**, *58*, 7857.

(12) Armani, E., Dossena, A., Marchelli, R., Casnati, G. *Tetrahedron* **1984**, *40*, 2035.

# Errata and Addenda 1987

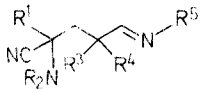
**Hall, G., Sugden, J.K., Waghela, M.B.**
Page 10. Line 3 of the Abstract should read: dropyrolizines ...
Page 14. The first word of Section 3.11. should be: Benzo[*b*]pyrrolizines.
Page 15. Formula **27** should be:



**27**

Page 15. The product referred to in Section 4.6., lines 4–5, should be: 10*H*-pyrrolizino[1,2-*b*]quinoline
Page 17. In Section 7., line 4 of the second paragraph should read: **34**.[182] ...

**Ahlbrecht, H., von Daacke, A.**
Page 24. Formula **8** should be:



**8**

**Costisella, B., Keitel, I.**
Page 45. In the heading of the experimental procedure, **6** should read **3** and **8** should read **7**.

**Stoss, P., Merrath, P., Schlüter, G.**
Page 174. Numbers 1 and 3 should be exhanged in formula **2a–f**.

**Singh, G., Deb, B., Ila, H., Junjappa, H.**
Page 286. Compounds **1** are 2-aroyl-2-arylthioketene dithioacetals.

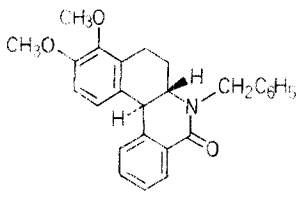
**Asaad, F.M., Becher, J., Møller, J., Varma, K.S.**
Page 301. Under the reaction scheme, the X group in compounds **3b,d** and **4b,d** should be $CO_2C_2H_5$.

**Legrel, P., Baudy-Floc'h, M., Robert, A.**
Page 306. The title should read: A One-Pot Synthesis of α-Halohydrazides from 2,2-Dicyanooxiranes.
Page 306. In the table under the reaction scheme, the second heading $R^1$ should be $R^2$.

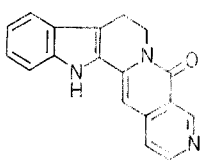
**van der Goorbergh, J.A.M., van der Steeg, M., van der Gen, A.**
Pages 314–317. The systematic names for the heterocycles involved are: 4,5-dioxo-3,4-dihydro-2*H*,5*H*-thiopyrano[3,2-*c*][1]benzopyrans **4** (RF 24756), 4,5-dioxo-2*H*,5*H*-thiopyrano[3,2-*c*][1]benzopyrans **7** (RF 24756), and 4,5-dioxo-1,3,4,4a,5,10b-hexahydro-2*H*-[1]benzopyrano[4,3-*b*]pyridines **8** (RF 24539).

**Attanasi, O.A., Filippone, P., Santensanio, S., Serra-Zanetti, F.**
Page 382. In the table under the reaction scheme, $R^3$ for **1b** should be $CO_2C_2H_5$ and $R^3$ for **1c** should be $CO_2CH_3$.

**Campbell, A.L., Lenz, G.R.**
Pages 428 and 446. Formulae **95** and **298** should be:



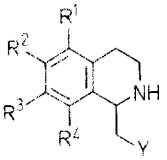
**95**



**298**

Page 437. The heading for Table 3 should be: Intermolecular ...

**Pelletier, J.C., Cava, M.P.**
Page 476. Formula **1a–m** should be:



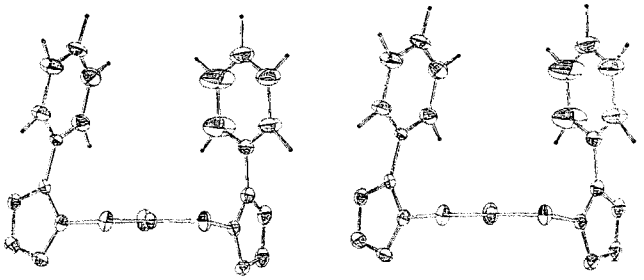
**1a-m**

**L'abbé, G.**
Page 528. Compound **45** should be named: 3-(2-pyridyl)-2,4-dithioxo-3,4-dihydro-2*H*-pyrido[1,2-*a*][1,3,5]triazine (RF 9177).

**Evans, R.D., Schauble, J.H.**
Page 551. Compounds **10** and **11** are tricyclo[2.2.1.0$^{2,6}$]heptane derivatives.

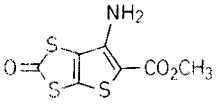
**Takeda, K., Tsuboyama, K., Hoshino, M., Kishino, M., Ogura, H.**
Page 559. The Y-group for **2g** and **2j** should be furfuryloxy.

**Takeda, K., Tsuboyama, K., Takayanagi, H., Ogura, H.**
Page 560. The following figure should appear after the 4th paragraph:



**Eicher, T., Stapperfenne, U.**
Page 625. Compounds **13a,b** are 6,7-dihydrofuro[2,3-*b*]pyridines (RF 7431), and compounds **15a,b** are 1,4-dihydrocyclopentimidazoles (RF 5892).

**Dölling, W., Augustin, M., Ihrke, R.**
Page 655. Formula **6** should be:



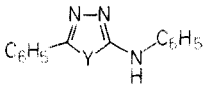
**6**

**Mikołajczyk, M., Bałczewski, P.**
Page 661. The second paragraph of ref. 21 should be ref. 22; refs. 22 and 23 should be 23 and 24, respectively.

**Rösch, W., Regitz, M.**
Page 692. Compounds **21a,b** are 2*H*-1,2,3-diazaphospholes.

**Tietze, L.-F., Brumby, T., Pretor, M.**
Page 702. Compounds **8** and **9** are 4a,10b-dihydro-4*H*,5*H*-pyrano[3,4-*c*][1]benzopyran-2-carboxylic esters.

**Wamhoff, H., Zahran, M.**
Page 877. Formula **18a,b** should be:



**18a,b**

**Castaldi, G., Giordano, C.**
Page 1039. The target compounds **3** are 1-bromoalkyl aryl ketones.