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CHIRAL SHIFT REAGENTS FOR NMR-SPECTROSCOPY. A SIMPLE AND IMPROVED ACCESS TO LANTHANIDE-tris-CHELATES OF d-3-TFA-CAMPHOR

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The utility of paramagnetic lanthanide-tris-β-diketonates as pseudo-contact shift reagents in NMR-spectroscopy has first been demonstrated by HINCKLEY (1). More recently, chiral lanthanide-tris-d-3-acyl-camphorates have been applied to the direct determination of enantiomeric compositions (optical purity of enantiomeric substrates) (2-5)

Europium-tris-d-3-trifluoroacetyl-camphorate ($Eu(TFA\text{-}Cam)_3$) has been found to be a most efficient chiral shift reagent (3,5). This compound is synthesized (5,6) from d-3-TFA-camphor (which is purified only with difficulty) and europium(III) nitrate hydrate in the presence of a base according to the general procedure of EISENTRAUT and SIEVERS (7,8) .

However, these shift reagents are much more easily obtained by the quantitative homogeneous exchange reaction of lanthanide nitrates (8) with the barium salt of d-3-TFA-camphor ($Ba(TFA\text{-}Cam)_2$) (9) in ethanol, e.g.:

$$2\ Ln(NO_3)_3 \cdot n\ H_2O + 3\ Ba(TFA\text{-}Cam)_2 \ = \ 2\ Ln(TFA\text{-}Cam)_3 + 3\ Ba(NO_3)_2 + 2\ n\ H_2O$$

(Ln = trivalent lanthanum series ion)

The barium chelate (9) is prepared just as conveniently by the quantitative trapping with barium ions of d-3-TFA-camphor formed from d-3-bromocamphor and ethyl trifluoroacetate in a GRIGNARD reaction (6). The complicated isolation of the free β-diketone and the use of base of definite pH are omitted by this method. The stable barium chelate is insoluble in ether (9) and can thus be easily purified from contaminants of the free ligand, which adversely affect synthesis and use of the shift reagents. The convenient and rapid method provides the desired products in high purity and in excellent overall yield (70% based on starting d-3-bromocamphor). The "barium method" should be applicable also to the syntheses of related lanthanide-β-diketonates (DPM-, FOD-shift reagents).

Working procedure:

Barium-bis-d-3-TFA-camphorate ($Ba(TFA\text{-}Cam)_2$)(9) (1.9 g, 3 mmole) is dissolved in 75 ml boiling 95% ethanol. Lanthanide nitrate hydrate (8) (2 mmole), dissolved in 25 ml ethanol (with addition of little H_2O if necessary), is added to the warm solution with stirring whereby barium nitrate precipitates. The reaction mixture is stirred for 15 min, then filtered, and the solvent removed *in vacuo* with a rotary evaporator. The residue is extracted with warm n-hexane, the extracted solution filtered until clear, and the solvent subsequently removed *in vacuo*. The vacuum is maintained for 90 min in a water bath at 90°C. The resulting glassy chelates are dried with a high vacuum over P_4O_{10} (yield: nearly quantitative) and may be directly used as shift reagents (3, 10) Elemental analyses [Galbraith Laboratories, Knoxville, Tenn., USA] were obtained from sublimed samples (180 - 200°C, $4\cdot10^{-3}$ mm Hg). It is recommended to store the substances over P_4O_{10}. The following lanthanide-tris-d-3-trifluoroacetyl-camphorates ($Ln(TFA\text{-}Cam)_3$) have been prepared by this method:

TABLE:

metal ion	color	elemental analysis C calcd	H calcd	C found	H found
Praseodymium	pale green	48.99	4.80	48.85	4.82
Samarium	yellow	48.47	4.75	48.18	4.66
Europium	dark yellow	48.38	4.74	48.18	4.68
Dysprosium	light pink	47.82	4.68	48.03	4.82
Holmium	beige	47.69	4.67	47.77	4.76
Ytterbium	yellow	47.27	4.63	47.36	4.75

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