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'PREFERENTIAL SPONTANEOUS RESOLUTION' OF p-ANISYL α-METHYLBENZYL KETONE

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The title compound has been obtained in optically-active form without using any chiral influence, by 'preferential spontaneous resolution'.

'Preferential Spontaneous Resolution' results in the formation of optically-active compounds without any chiral intervention whatsoever[1-7]. However, its potential in asymmetric synthesis has remained unexploited largely because the very few compounds that do show the phenomenon are synthetically uninteresting. We report herein preliminary studies aimed at filling this lacuna.

It is believed that, for a compound to show 'preferential spontaneous resolution', it should be a conglomerate. A list of presently-known conglomerates is available[2] and its study led us to choose p-anisyl α-methylbenzyl ketone (1) for the following reasons: Firstly, we hoped that the enantiomers of (1) would be interconvertible in solution, via the enol or enolate, by basic or acidic catalysts; and secondly, we hoped that the ketone functionality would help in transformations to synthetically useful, optically-active derivatives.

Indeed, when solutions of (1), containing the strong base 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as catalyst, were cooled, crystals of optically-active (1) were obtained. Either of the enantiomers was obtained in each trial, often in high enantiomeric excess (up to 72%). Also, the process could be controlled to produce any desired enantiomer by seeding[8].

Results of various trials are summarised in the table overleaf. The use of methanesulfonic acid as catalyst, instead of DBU, was less successful, producing (1) of only low optical purity. No optically-active material was obtained by crystallising (1) without catalyst.

Finally, we wish to mention a crucially important advantage of (1) over most other compounds known to show[2,6] 'preferential spontaneous resolution': It does not racemise spontaneously in solution (i.e. in the absence of catalysts). This is obviously important for synthetic transformation, efforts at which are in progress.

'Preferential Spontaneous Resolution' of p-(MeO)-C_6H_4-CO-CH(Me)(Ph).

Trial	Yield of crystals(%)	Rotation	E.e.(%)
1.	44	(+)	57.7
2.	44	(-)	67.3
3.	35	(-)	72.0

N.B.: 'Enantiomeric excess' (E.e) values calculated using the reported specific rotation of (1), $\alpha_D = 117^\circ$. Mother liquors racemic in all cases. The Pasteur-type resolution of (1) has been described[3].

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References:

(1) We propose 'Preferential Spontaneous Resolution' for the spontaneous, crystallisation-driven conversion of any racemic solution (or melt) of interconverting enantiomers, preferentially (i.e. > 50%) into either enantiomer. Cf. 'Total Spontaneous Resolution' (100% conversion into either enantiomer), and 'Spontaneous Resolution' (conglomerate formation). (2) J. Jacques, A. Collet, and S.H. Wilen, 'Enantiomers, Racemates and Resolutions', Wiley, New York, 1981, pp 371-373. (3) Ref.2, pp 58-79; A. Collet, M.J. Brienne, and J. Jacques, Bull. Soc. Chim. Fr., 1972, 336. (4) J.D. Morrison, 'Asymmetric Synthesis', Vol.1, ed. J.D. Morrison, Academic Press, New York, 1983, pp 3-6. (5) E.L. Eliel, 'Stereochemistry of Carbon Compounds', McGraw-Hill, New York, 1962, p 79. (6) W.A. Bonner, Top. Stereochem., 1988, 18, 8-10. (7) E. Havinga, Biochim. Biophys. Acta, 1954, 13, 171; A.P. Downings, W.D. Ollis, and I.O. Sutherland, J. Chem. Soc. (B), 1970, 24; K.R. Wilson and R.E. Pincock, Can. J. Chem., 1977, 55 889; W.J. Boyle, Jr., S. Sifniades, and J.F. Van Peppen, J. Org. Chem., 1979, 44, 4841; Y. Okada, T. Takebayashi, and S. Sato, Chem. Pharm. Bull., 1989, 37, 5. (8) A solution of (1) (0.18M) and DBU (0.03M) in 10% CH_2Cl_2-hexane, cooled to $0^\circ C$ for one week. Crystals collected and washed with cold hexane.

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