Journal of Chromatography, 160 (1978) 280–284

CHROM. 11,075

Note

Gas chromatographic investigation of the synthesis of pentafluorophenacylated ketones

SERGIO DILLI and KEVIN ROBARDS
School of Chemistry, University of New South Wales, P.O. Box 1, Kensington, N.S.W. 2033 (Australia)
(Received April 3rd, 1978)

The use of β-diketones in gas chromatography (GC)[1,2] has stimulated continued interest in this class of compound. Although it has been recognised for some time that the introduction of fluorine[2] into such ligands can substantially increase the volatility of the corresponding chelates, there has been no investigation of the effects of fluorination, or extensive substitution by other atoms or groups, upon the volatility and thermal stability of aryl-β-diketonates despite the exceptional thermal stability[3] of these compounds. The main reason for this appears to lie in the fact that studies of the effects of fluorine substitution in aryl-β-diketones are hampered by problems of synthesis when this involves the pentafluorophenyl group and, because of the formation of a variety of products, inevitably lead to low yields of these expensive diketones. Yet, in existing methods of preparation[4–6] of perfluoroaryl-β-diketones, involving the Claisen condensation of ketone and ester, no reasons are given for the low yields of the β-diketones (as low as 25–30%).

It is clear from our observations that these poor yields are associated with the reactivity of the fluorinated ketones and, in turn, related to the ability of the condensing agent to engage in displacement of fluorine from the ring of the aryl group. In this regard, too, temperature and time are important factors in achieving efficient conversions to β-diketones, in addition to promoting the consumption and loss of the product due to over-exposure to a nucleophile, the condensing agent itself.

With the support of GC evidence for identifying the unfavourable reaction conditions, this paper presents details for the synthesis of the two rare β-diketones, 1-(pentafluorophenyl)-4,4,4-trifluorobutane-1,3-dione (Hpptb) and 1-(pentafluorophenyl)-4,4,5,5,5-pentafluoropentane-1,3-dione (Hpppp), in good yields (>80%).

EXPERIMENTAL

General

All materials were commercially available and used directly, without further treatment other than drying.

Reactions monitored by GC were examined on an SE-30 column (6 ft. × ¼ in. glass coils packed with 10% stationary phase on 80–100 mesh, acid-washed, DMCS-treated Chromosorb W HP) programmed between 80 and 220° at 5°/min. Carrier gas (nitrogen) flow-rate was 40 ml/min.

Mass spectra were recorded at 70 eV on an A.E.I. MS12 spectrometer, or an MS9 for chemical-ionization (CI) mass spectra.

Syntheses

1-(Pentafluorophenyl)-4,4,4-trifluorobutane-1,3-dione. (i) The customary procedure[7] which does not recognise the effect of reaction time and temperature on the yield is illustrated by the following example of a synthesis at 15°. To the free-flowing sodium methoxide (prepared from 0.3 g sodium and 8 ml methanol from which excess alcohol was then removed under streaming nitrogen) was added ether (150 ml) and ethyl trifluoroacetate (1.4 g, 0.01 mole) followed by the slow addition (30 min) of the acetylpentafluorobenzene (2.1 g, 0.01 mole) in ether. After reaction (2 h) the mixture was cooled in ice and acidified with cold hydrochloric acid. The crude product (2,4 g, 79%) was found by GC to comprise approximately 70% Hpptb.

(ii) Sodium hydride (10 g of 50% dispersion in oil, 0.21 moles) was washed with hexane (3 × 100 ml) and ether (20 ml), then suspended in ether (200 ml). *tert.*-Butanol (15 g, 0.2 mole) was slowly added, with constant stirring, to this suspension together with sufficient additional ether to prevent solidification of the swelling mass as reaction proceeded. When reaction was complete, the flask was immersed in an ice bath (desirable but not essential), the ester (24 g, 0.17 mole) added rapidly followed by the dropwise addition over 30 min of the ketone (30 g, 0.14 mole in 40 ml ether) and continued stirring (20 min). A slurry of ice in hydrochloric acid was added rapidly to the mixture and the organic phase removed. Yield of the diketone after vacuum distillation was 36 g (82%), and the product showed a single major peak by GC. B.p. was 71–72° at 1.4 mm Hg. Quantitative analysis, found: C, 39.1; H, 0.7; calculated: for $C_{10}H_2F_8O_2$: C, 39.2; H, 0.7%. Mass spectrum: EI, 306 [M^+, 45%]; 286 [$(M-HF)^+$, 100%]; 237 [$(M-CF_3)^+$, 55%]; 209 [$(M-COCF_3)^+$, 31%]; 195 [$(M-CH_2COCF_3)^+$, 59%]; CI, 307 [$(M+1)^+$].

1-(Pentafluorophenyl)-4,4,5,5,5-pentafluoropentane-1,3-dione. This compound was prepared with sodium *tert.*-butoxide as in (ii) above using ethyl pentafluoropropionate (32 g, 0.17 mole). The pure product (40.2 g, 79%) gave a single major peak by GC, b.p. 84–85° at 6.8 mm Hg. Quantitative analysis, found: C, 37.4; H, 0.5; calculated for $C_{11}H_2F_{10}O_2$: C, 37.1; H, 0.6%].

RESULTS AND DISCUSSION

The synthesis of the two β-diketones Hpptb and Hpppp, using sodium methoxide as condensing agent, cannot be considered satisfactory because of poor yields. The reason for this situation lies in the number of by-products which can be formed, depending on the choice of reaction conditions. Commonly these include lengthy periods of standing (16–20 h) with no indication of the consequences of such procedures. While this is desirable and beneficial in some instances (for example, in the preparation[8] of 1,3-alkanediones) prolonged reaction is distinctly undesirable in the synthesis of Hpptb and Hpppp.

The optimal conditions, and a better appreciation of the course of the reaction, can be readily determined when the reaction is monitored by temperature-programmed GC. Information of this type is shown in the chromatograms of Fig. 1 for the preparation of Hpptb using sodium methoxide. Thus, Fig. 1a shows that after 10 min reaction

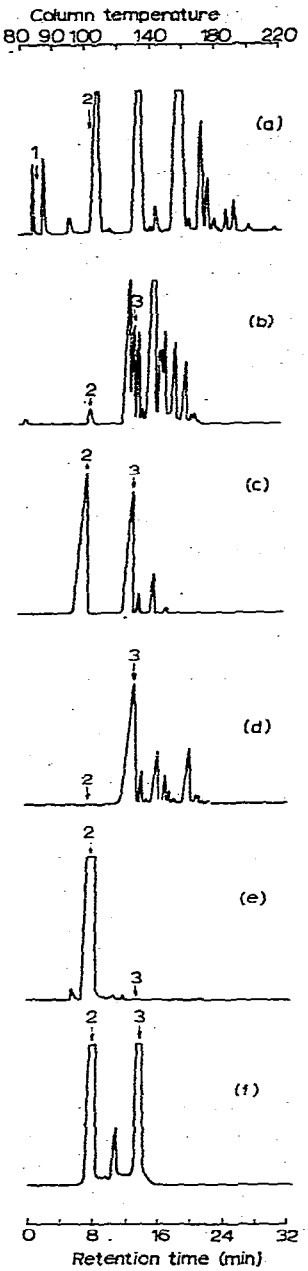
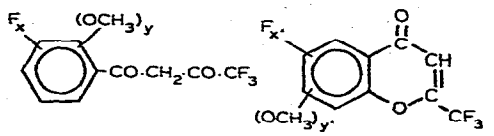


Fig. 1. Products in the reaction involving ethyl trifluoroacetate and acetylpentafluorobenzene in the presence of sodium methoxide. Chromatograms shown are (a) ketone and methoxide at 25° for 10 min; (b) ketone, ester (on 0.01-mole basis) and methoxide at 25° for 2 h; (c) reactants as in (b) at 0° for 2 h; (d) product of (c) after standing 18 h; (e) reactants as in (b) at −16° for 1 h; (f) reactants as in (b) on a 0.35-mole basis at −16° for 1 h. The products are identified (by numbered arrows and retention times) as: 1, acetylpentafluorobenzene (3.6 min); 2, Hpptb (7.7 min); 3, compound II (13.5 min).

of an equimolar mixture of acetylpentafluorobenzene and sodium methoxide, no ketone remains. Indeed, the self-condensation of the ketone in the presence of either sodium hydride or sodium methoxide is so rapid that it is the limiting factor in the condensation reaction. However, methoxide remains the slower reacting and preferred condensing agent. In contrast, ethyl trifluoroacetate is stable to alkoxides for periods exceeding 1 h (at 25°) and for this reason the order of addition to the base was ester, then ketone. The influence of temperature and time is shown in Figs. 1b–d. In Figs. 1b and c, neither of the initial reagents is present after 2 h reaction; however at the higher temperature (see Fig. 1b) no diketone is observed also. As seen in Fig. 1d, protracted exposure of the product to the basic environment, even at low temperature, promotes complete destruction of the diketone. Maximum yield of the diketone can be obtained by reducing further the reaction time and temperature (see Fig. 1e) however a reduced yield (*ca.* 60%) resulted when the scale of the synthesis was increased (see Fig. 1f) from 0.01 to 0.35 mole of ester. As the reaction is exothermic, it appears that the reaction temperature cannot be controlled adequately by the use of an ice bath and in addition to the desired product, nucleophilic attack by the methoxide ion leads to formation of a second β-diketone, that is, 1-(tetrafluoromethoxyphenyl)-4,4,4-trifluorobutane-1,3-dione (compound II).



I : x=3, y=2
II : x=4, y=1
III : x'=y'=2
IV: x'=3, y'=1

In all, four compounds (I–IV) were recovered from the product represented in Fig. 1d and result from nucleophilic displacement of fluorine from the aromatic ring. Although the ring substitution pattern has not been elucidated, their existence has been confirmed by CI–MS. The ligands I and II are formed by substitution of one or two fluorines by methoxyl groups and yield copper chelates giving molecular ions at *m/e* 721 and 723 (relative intensities 100 and 42%, respectively) with I, and at *m/e* 697 and 699 (relative intensities 38 and 17%, respectively) with II. Compound III and IV are evidently the result of intramolecular displacement of fluorine at an *ortho* position in the ring under the influence of an intermediate enolate ion[4], or the enolate ion of Hpptb[9], with the nucleophilic attack by methoxide ions as an additional effect.

Therefore, although sodium methoxide, when compared with sodium hydride, is preferable from kinetic considerations, its nucleophilicity makes it unsuitable for reactions involving the pentafluorophenyl group which is predisposed to nucleophilic attack[10] because of the accumulation of the five fluorine atoms in the aromatic ring.

The use of sodium *tert.*-butoxide as the basic condensing agent, however, gives excellent yields without the need for any of the undue precautions indicated in Fig. 1. GC examination of the crude β-diketones prepared with this condensing agent revealed a single major component only, and when allowed to stand in its presence at ambient temperatures (20 h, 25°) showed no adverse effects on the yield or quality of the crude product.

Despite this success with *tert.*-butoxide, the method appears most useful in reactions with perfluoroalkyl esters. It has proved ineffective in the preparation of 1-(pentafluorophenyl)butane-1,3-dione (for which sodium hydride is preferred) or 1,3-bis(pentafluorophenyl)propane-1,3-dione due evidently, in this case, to the ease of attack[11,12] of benzoate esters by alkoxides. Because of rapid, efficient conversions, it can be recommended for the synthesis of other analogues[13] of 1-phenyl-4,4,4-trifluorobutane-1,3-dione where ring substituents are one or more halogens (F, Cl, Br) or methyl groups.

ACKNOWLEDGEMENTS

Grateful acknowledgement is expressed to Mr. J. Sussman for microanalyses and to Dr. J. Brophy and Mr. D. Nelson for mass spectra.

REFERENCES

1 J. A. Rodriguez-Vasquez, *Anal. Chim. Acta*, 73 (1974) 1.
2 R. W. Moshier and R. E. Sievers, *Gas Chromatography of Metal Chelates*, Pergamon, New York, 1965.
3 E. W. Berg and K. P. Reed, *Anal. Chim. Acta*, 22 (1968) 207.
4 R. Filler, Y. S. Rao, A. Biezois, F. N. Miller and V. D. Beaucaire, *J. Org. Chem.*, 35 (1970) 930.
5 J. F. Engel and C. C. Chappelow, *J. Chem. Eng. Data*, 16 (1971) 381.
6 Y. S. Rao and R. Filler, *J. Org. Chem.*, 36 (1971) 1447.
7 R. Belcher, J. R. Majer, W. J. Stephen, I. J. Thompson and P. C. Uden, *Anal. Chim. Acta*, 56 (1970) 423.
8 S. Dilli and A. M. Maitra, unpublished results.
9 S. Dilli and K. Robards, *Aust. J. Chem.*, 31 (1978) 1833.
10 W. A. Sheppard and C. M. Sharts, *Organic Fluorine Chemistry*, Benjamin, New York, 1969.
11 A. Magnani and S. M. McElvain, *J. Amer. Chem. Soc.*, 60 (1938) 813.
12 S. M. McElvain and K. H. Weber, *J. Amer. Chem. Soc.*, 63 (1941) 2192.
13 S. Dilli and K. Robards, unpublished results.