

Are all charge-repulsed carbocations really unstable? Dramatic difference in reactivities of benzyl- and *p*-methoxybenzyl halides in benzene

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Abstract. Two distinct reaction mechanisms are proposed for the reactions of **1**, **5** and **6** with nucleophiles as against those of **11**, **12** and **16**. The former set undergoes the reactions through carbocation type intermediates **2** and **3** as efficiently as the stable carbocation **4** does, even under similar and very mild conditions. The compounds from the latter group do not form the carbocations under the same conditions and undergo only direct substitution by strong nucleophiles.

Keywords. Charge-repulsed carbocations; benzyl halide; *p*-methoxybenzyl halide.

1. Introduction

Intimate ion pair hypothesis (Shiner 1970; Snee 1973) in unification of S_N1 and S_N2 reaction mechanism has been studied in great detail (Bentley and Schleyer 1976; Schadt *et al* 1976; Bentley *et al* 1981). It has been suggested that in less nucleophilic solvents having good ionising capacity, substrates such as 1- or 2-adamantyl tosylate undergo solvolysis through intermediates having considerable carbocation character. Considering the solvolysis of 2-adamantyl tosylate in various hydroxy solvents as a limiting case of S_N1 reaction, all other simple secondary substrates involving neighbouring group participation undergoing solvolysis were placed in the ' $S_N1 - S_N2$ (intermediate) - S_N2 (classical)' spectrum. The slower rate or no reactions in case of some substrates were explained by the terms 'internal return' (Snee 1973) or by involving a 'tight' ion pair (Bentley and Schleyer 1976; Schadt *et al* 1976; Bentley *et al* 1981).

In these studies, however, only such solvents were used which would support or stabilise a carbocation. Substrates such as 1- or 2-adamantyl tosylate would form the carbenium ions stabilised mainly by solvent support. Converse of this, would be to study the reaction of substrates which would intrinsically support the carbocation through resonance or other factors, in non-ionising and non-nucleophilic hydrocarbon solvents.

Recently we reported (Kulkarni *et al* 1988) reactions of haloketones **1** under very mild conditions, indicating the intermediacy of α -acylcarbenium ions **2** - an area of

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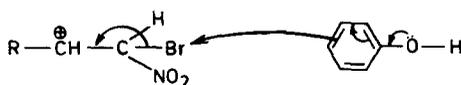
halides 6 and 5 respectively would be an index of the relative stabilities of these three cations (2, 3 and 4).

2. Results and discussion

We have now observed that halide 5 reacts with phenol in benzene without any catalyst at room temperature to give two products, identified (IR, PMR, CMR) as the C-alkylated products 7 and 8. This is parallel to our earlier report of formation of 9 from 1 under identical conditions. Compound 7 (soluble in 2N NaOH, positive FeCl₃ reaction) has been reported (Binley *et al* 1956) earlier, only from acid catalysed reaction of 5 in polar solvents. As against this, 8 (insoluble in 2N NaOH, negative FeCl₃ reaction) is so far unknown. In this reaction, there was no trace of O-alkylated product 10, which could otherwise be obtained from 5 by reaction with phenol in the presence of K₂CO₃/acetone. The structure of 8 was confirmed by converting it into its acetyl derivative and also by its formation as the exclusive product in the reaction of 7 with 5 in benzene at room temperature. It was interesting to note that under identical conditions, 12 was recovered unchanged. These results along with those obtained earlier with 1, suggested that either the uncatalysed reaction had different mechanism than the K₂CO₃ catalysed one, or that the halides 1 and 5 react through the corresponding cations 2 and 4 in both the catalysed and uncatalysed reactions, while 11 and 12 undergo displacement with K₂CO₃ and phenol in acetone, but do not undergo the reaction in benzene due to the much lower stability of the corresponding cations 13 and 14. This means that under the mild conditions such as benzene at room temperature, cations 2 and 4 have similar ease of formation and cations 13 and 14 are not formed at all. In case of reaction of 1 with phenols, when a rod dipped in ammonia was brought nearer to the reaction flask, intense fumes of ammonium chloride were observed during the initial hours. This was not observed in case of reaction of 11.

Reaction of erythro isomer 6 (prepared by addition of bromine to the solution of (E)-3,4-dimethoxynitrostyrene 15 (Karmarkar 1978) in benzene at room temperature and identified from its PMR and CMR) with phenol in benzene at room temperature afforded 15 and *p*-bromophenol. Under identical conditions 16 was recovered unreacted. These reactions also suggest that the conversion of 6 to 15 also involved formation of ion 3 as the first step. This is further confirmed as 16 does not undergo similar elimination under same conditions. This means that phenol prefers to attack bromine (scheme 1) rather than the proton, to neutralise the positive charge.

In order to check this hypothesis, reaction of 6 with methanol was planned. With no chance of attack on the bromine, the reaction should yield 17 as the only product. In agreement with this, the reaction of 6 with 50% methanol in benzene at room temperature, provided a product, identified as an exclusive erythro isomer of hitherto unknown 17, identified by its IR, PMR and CMR spectra. The stereospecificity of this reaction could be explained only by visualising a carbocation undergoing a rotation around C-C bond to afford the thermodynamically stable product. The



alternate structure **18** could be ruled out by calculation of CMR values for C₁ and C₂ (calculated for **17**, C₁ 79.2, C₂ 97.6, for **18**, C₁ 48.2, C₂ 128.6; observed, C₁ 80.1, C₂ 84.6) and by the expected upfield shift of C₁-H and C₂-H in the PMR of **17** as compared to the corresponding values in that of **6** (observed for **17**, C₁-H 4.8, C₂-H 5.9; for **6**, C₁-H 5.54, C₂-H 6.4). Reaction of **6** with 50% ethanol in benzene yielded **19** as the only product. Under identical conditions **16** was recovered unreacted in both reactions. However, **20** and **21** were also formed in high yields by reaction of corresponding dibromonitrostyrenes with 50% methanol in benzene at room temperature.

The reaction of **6** with phenol, methanol and ethanol then indicated that a common cation **3** is obtained in all reactions, which undergoes elimination of Br⁺ in first case and nucleophilic capture in others. Failure of reaction of **16** with same reagents under identical conditions suggests that **3** is not only more stable than **22**, but has similar stability as **2** and **4**.

A reaction of **23** with methanol catalysed by thallium nitrate giving **24** as major product along with elimination product **25** in 5–10% yield is reported (Nagao *et al* 1976). In this study the presence of carbocation intermediate was ruled out by the authors. However, the reaction in absence of catalyst was not carried out during the above study.

3. Experimental

All melting points are uncorrected. All substances and solvents were properly purified by crystallisation or distilled and dried prior to use. Elemental analyses were obtained using Hosli's rapid carbon-hydrogen analyser. IR spectra were recorded in cm⁻¹ on a Perkin-Elmer infracord model 337. The PMR and CMR are recorded in δ units with CDCl₃ as solvent and TMS as internal standard on JEOL FX 90.

Reaction of 4-methoxybenzyl chloride 1 with phenol: Phenol (2.82 g, 0.03 mol) was added to the solution of 4-methoxybenzyl chloride **1** (4.68 g, 0.03 mol) in dry benzene (50 ml). The reaction mixture was kept at room temperature for 36 hours. After completion of the reaction (tlc), the solvent was removed under reduced pressure. The crude product was extracted with ether (50 ml) and the ether extract with 2N NaOH (2 \times 15 ml). The aqueous and the ether extracts were collected separately.

Isolation of 7: The aqueous layer was acidified with 2N HCl and extracted with ether (25 ml). The ether layer was washed with water and dried over Na₂SO₄ and evaporated. Petroleum-ether was added to the residue to get a solid (3.3 g), identified as **7**, m.p. 79°, Lit. m.p. 80–1° (Binkley *et al* 1955). Unreacted phenol could not be isolated.

Isolation of 8: The ether layer of the original extract was washed with water and dried. Solvent was removed under reduced pressure to get gummy liquid (1.35 g). It was further purified by passing through a column of silica gel with hexane as eluent. IR: 3550–3200 (broad), PMR: 3.8 (s, 6H, Ar-OCH₃), 3.9 (s, 4H, Ar-CH₂), 4.6 (s, 1H, exchanges with D₂O, Ar-OH), 6.8–7.4 (m, 11H, Ar-H), CMR: 35.55, 40.25, 55.33, 55.4, 114.06 (4C), 115.78, 127.21, 127.5 (2C), 129.54 (4C), 131.28, 131.5, 133.77, 152.14, 158.15, 158.3, Found: C, 78.86; H, 6.7; C₂₂H₂₂O₃ requires C, 79.01; H, 6.63%.

Acetate of 8: A mixture of **8** (0.33 g), acetic anhydride (2 ml) and sodium acetate (0.1 g) was refluxed in oil bath for 90 min. After usual workup a gummy liquid (0.26 g) was obtained, identified as the acetyl derivative of **8**. IR: 1770, 1600, 1500 cm^{-1} , PMR: 2.23 (s, 3H, Ar-O-CO-CH₃), 3.8 (s, 6H, 2 × Ar-OCH₃), 3.9 (s, 4H, Ar-CH₂-Ar), 6.8-7.4 (m, 11H, Ar-H), Found: C, 76.46; H, 6.44; C₂₄H₂₄O₄ requires C, 76.57; H, 6.43%.

Reaction of 6 with phenol: A mixture of **6** (0.369 g, 1 mmol) and phenol (0.094 g, 1 mmol) in dry benzene (5 ml) was kept at room temperature for 96 hours. After removal of the solvent under the reduced pressure, the mixture was treated with ether and extracted with 2N NaOH (3 × 3 ml). The aqueous and the ether layer were collected separately.

The ether layer was washed with water, after drying (anhydrous Na₂SO₄) and removal of solvent, a solid product (0.16 g) was obtained identical in all respects with nitrostyrene **15** (m.p., mixed m.p., superposable IR).

The aqueous layer was acidified with HCl and extracted with ether. After drying and evaporation of the solvent a liquid (0.13 g) was obtained which was found to be identical (IR, NMR) with *p*-bromophenol.

Reaction of dibromonitrostyrene 6 with methanol: Compound **6** (0.369 g) was dissolved in 1:1 (v/v) methanol: benzene and the mixture was kept at room temperature for 96 hours. Solvent was removed under reduced pressure and the product crystallised from 1:1 ether: petroleum-ether mixture to yield **17**. m.p. 92-94°, yield 75%. IR: 1530, 1340, 1150 cm^{-1} , NMR: 3.30 (s, 3H, -OCH₃), 3.9 (s, 6H, 2 × Ar-OCH₃), 4.8 (d, *J* = 11Hz, 1H, Ar-CH-), 5.9 (d, *J* = 11Hz, 1H, Ar-CH-CH-), 6.8-7.4 (m, 3H, Ar-H), Found C, 41.5; H, 4.6; C₁₁H₁₄O₅NBr requires C, 41.25; H, 4.38%.

Compounds **20** and **21** were prepared using the same procedure and **19** was prepared by using ethanol instead of methanol.

Compound **20**: m.p. 76-78°C, yield 75%, PMR: 3.3 (s, 3H, -OCH₃), 4.8 (d, *J* = 11Hz, 1H, Ar-CH-CH), 5.9 (d, *J* = 11Hz, 1H, Ar-CH-CH-), 6.1 (s, 2H, -O-CH₂-O), 7.0 (s, 3H, Ar-Hs), Found C, 39.27; H, 3.47; C₁₀H₁₀O₅NBr requires C, 39.47; H, 3.29%.

Compound **21**: Gummy liquid, yield 65%, PMR: 3.3 (s, 3H, -OCH₃), 3.9 (s, 3H, Ar-OCH₃), 4.8 (d, *J* = 12Hz, 1H, Ar-CH-), 5.9 (d, *J* = 12Hz, 1H, Ar-CH-CH-), 7.0 and 7.4 (d, *J* = 8Hz, 2H each, Ar-Hs), Found: C, 41.59; H, 4.31; C₁₀H₁₂O₄NBr requires C, 41.38; H, 4.14%.

Compound **19**: m.p. 92-94°, yield 75%, IR: 1530, 1340, 1150 cm^{-1} , PMR: 0.9 (t, 3H, -O-CH₂-CH₃), 3.3 (q, *J* = 8Hz, 2H, -O-CH₂-CH₃), 3.9 (s, 6H, 2 × Ar-OCH₃), 4.77 (d, *J* = 11Hz, 1H, Ar-CH-CH-), 5.8 (d, *J* = 11Hz, 1H, Ar-CH-CH-), 6.7-7.2 (m, 3H, Ar-Hs), CMR: 14.91, 55.81 (2C), 65.67, 80.46, 82.90, 110.47, 111.02, 121.31, 126.78, 149.37, 150.08, Found C, 43.47; H, 4.85; C₁₂H₁₆O₅NBr requires C, 43.11; H, 4.79%.

4. Conclusions

Based on our studies, it is now concluded that-

(1) Carbocation type intermediates such as **2**, **3**, and **4**, could be formed under very mild conditions, such as in benzene at room temperature, but cations such as **13**, **14** and **22** are not formed under similar circumstances.

(2) The similar ease of formation of 2, 3 and 4 suggest that they do not have significant differences in their stabilities.

(3) The stable carbocation type intermediates 2 and 4 yield thermodynamically stable C-alkylated products on reactions with phenols in benzene without any catalyst.

We certainly foresee a good synthetic utility of the C-alkylation reaction. Work on these lines is in progress. The preliminary study on kinetics of reaction of 2 indicated that it is of the unique oscillatory type (Cook 1979). This will be reported later.

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