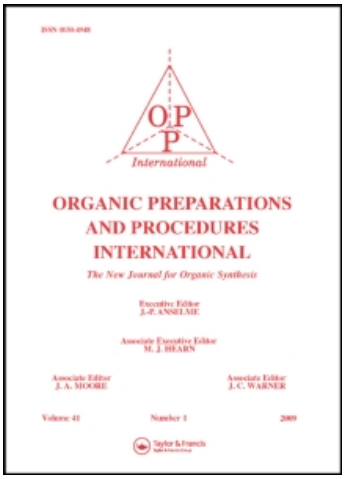


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# A VERY MILD AND EFFICIENT PREPARATION OF δ-VALEROLACTONE

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# A VERY MILD AND EFFICIENT PREPARATION OF δ-VALEROLACTONE

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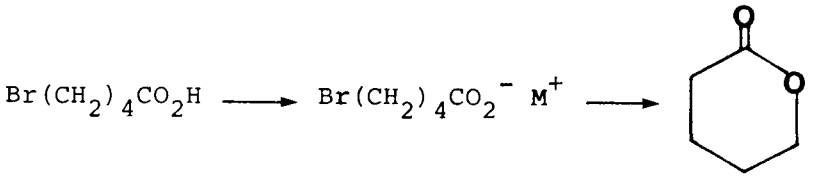
We describe herein a very simple and efficient procedure for preparing δ-valerolactone under solid-liquid phase transfer catalysis conditions without any solvent, a method which has been improved for many alkylations.[1] Our experiments involve the use of Aliquat 336[2] to allow the intramolecular alkylation of the carboxylate anion of 5-bromovaleric acid formed in situ by addition of a base.




1 2 3

The main results are given in the Table. A quantitative yield of 3 is obtained when the cyclization of 1 is performed in the presence of one equivalent potassium carbonate and 2% Aliquat 336 under very mild conditions (2 hrs at 40°) without any solvent. This yield and these conditions compare very favourably with those of classical homogeneous cyclizations carried out under high dilution condition with cesium salts in DMF[3] (yield 70%) or from 2-pyridinethiol ester in benzene at reflux.[4] Among the bases tested, potassium carbonate proves to be the best as it is the less basic one; more basic species such as potassium t-butylate promote ring opening of the lactone and the yields decrease with increased reaction time. This method complements that described by Kimura and Regen,[5] which requires the preformed potassium salt of the ω-bromoacid followed by

cyclization in toluene at 90° in the presence of catalytic amounts of tetraalkylammonium salts. This high dilution *via* solid-liquid phase-transfer catalysis is very efficient for the synthesis of lactones with ring size $\geqslant 7$ but rather unsuitable for smaller rings. In our hands, the Kimura and Regen procedure afforded only a 27% yield of pure lactone 3; however, their procedure is superior to ours for 7-member lactone synthesis as a 92% yield was obtained against only a 30% yield by our method.

TABLE. Cyclization of 5-Bromovaleric Acid (1)

| Base | Time (hrs) | Temp (°C) | Isolated Yield of 3 (%) No Aliquat | 2% Aliquat |
|---|---|---|---|---|
| NaOMe | 2 | 60 | 29 | 35 |
| | 2 | 85 | 44 | 57 |
| | 2 | 20 | 32 | 46 |
| KOBu-t | 5 | 20 | 21 | 25 |
| | 2 | 40 | 13 | 32 |
| $K_2CO_3$ | 2 | 20 | 50 | 55 |
| | 2 | 40 | 81 | 98 |
| | 2 | 60 | 10 | 36 |



## EXPERIMENTAL SECTION

To 25 mmol. of 5-bromovaleric acid 1 were added 25 mmol. of finely ground NaOMe, KOBu-t or $K_2CO_3$ and occasionally 2% mol. of tetraalkylammonium salt (Aliquat 336). After 5 min. stirring, the mixture was left to stand for the required time and temperature. The lactone 3 was then removed by simple addition of 50 ml diethyl ether, then filtration through 3 g of Florisil (to trap mineral salts and Aliquat 336). Under

these conditions, none of the possible dilactones (derived from intermolecular reactions) was found. The products were characterized by IR and analyzed by VPC (internal standard, octadecane) and then isolated by chromatography on Florisil column. Lactone 3 is rather unstable and very sensitive to both base and acid which induce ring opening[6] [VPC conditions: Carbowax 2 m; $P_{N2}$ = 1.2 kg; retention time 3 = 7.0 min., standard = 5.6 min.].

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## AN IMPROVED SYNTHESIS OF β-TETRALONE

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An urgent need for β-tetralone in quantities larger than commercial sources could supply led us to investigate methods for preparing this compound. The many literature methods of synthesis discussed by Soffer[1]