

## NOTES

## Synthesis of 2-, 3- and 4-Carboxyphenoxyacetic Acid: A Necessary Modification

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Selective esterification of aliphatic primary carboxy groups over the aromatic ones within the same framework of a molecule needed 2-, 3- and 4-carboxyphenoxyacetic acids which were synthesised in very good yield, by slight modification of the method introduced hundred years back. Condensed product from chloroacetic acid and corresponding hydroxybenzaldehyde was separated from the mixture as methyl or ethyl ester and subsequently oxidised by alkaline  $\text{KMnO}_4$ . Acidification and usual work up generated the desired products in good quality.

Tests for applicability of the method of selective esterification<sup>1</sup> of aliphatic primary carboxylic groups over the aromatic ones within the same framework of a molecule needed 2-, 3- and 4-carboxyphenoxyacetic acids (I, II and III respectively). Synthesis of these compounds were made a century ago by condensing chloroacetic acid with corresponding hydroxybenzoic acid in presence of alkali<sup>2</sup>. Since the details of the experiments are not adequate, reproducibility of the said method could not be challenged. Attempts to synthesise the acids in that way failed to generate the desired acids in appreciable yields and should not be practiced for preparative purpose.

Preparation of acid I was made by condensation of salicylaldehyde and chloroacetic acid in presence of alkali, unreacted salicylaldehyde was removed by steam-distillation and on acidification of the reaction mixture 2-formylphenoxyacetic acid<sup>3</sup>(A) was obtained as solid precipitate which was subsequently oxidised by alkaline  $\text{KMnO}_4$  (described later). Experiments with *meta* and *para*-isomers in a similar way posed a problem of separation of the unreacted hydroxyaldehydes (since they are not steam-volatile as the *ortho*-isomer). In these cases, after the condensation was over, the whole alkaline mixture was evaporated to dryness and acidified with conc. HCl. The precipitated material was filtered, washed and dried ( $110^\circ$ ) for 6 hrs. The dried material was dissolved in dry alcohol (10 ml per gram of the material) and was heated under reflux for 16 hrs in presence of conc.  $\text{H}_2\text{SO}_4$  (1 ml per 10 ml of alcohol) under moisture-free condition. The reaction mixture was worked up with a mixture of ether and benzene in the usual

way. The organic extract was washed thoroughly with NaOH (4 N) solution. The alkaline extract, thus obtained, was acidified to recover unreacted hydroxybenzaldehyde as solid precipitate.

The neutral part, on distillation, produced the corresponding esters of 3- and 4-formylphenoxyacetic acid, (B) and (C), respectively, and they were oxidised by alkaline  $\text{KMnO}_4$  in the following way.

To a hot mixture of the substrate (A/B/C, 5 gm) and NaOH solution (4 N, 50 ml) contained in a beaker was added dropwise a saturated solution of  $\text{KMnO}_4$  (4 gm) till the purple colour persisted while the solution remained alkaline and it was kept hot for 15 min. more. Finally the brown muddy precipitate of  $\text{MnO}_2$  was decomposed by alternate and portionwise addition of conc. HCl and  $\text{Na}_2\text{SO}_3$  to the hot reaction mixture until the muddy appearance was completely destroyed and the mixture became colourless. Solid organic acid was precipitated which was filtered cold, washed and dried at  $110^\circ\text{C}$  to give desired dicarboxylic acids I, II and III.

### Substrates oxidised

(i) *2-Formylphenoxyacetic acid* (A): m.pt.  $133^\circ$ , N.E.  $178 \pm 3$ .

(ii) *Methyl 3-formylphenoxyacetate* (B): colourless thick liquid, b.pt.  $168\text{--}174^\circ/10\text{--}12$  mm, yield 70%,

IR:  $\nu_{\text{max}}$  (film) 1755, 1700, 1590, 1485,  $\text{cm}^{-1}$  etc.

PMR:  $\delta(\text{CDCl}_3)$  3.80 (3H, s,  $-\text{COOCH}_3$ ), 4.70 (2H, s,  $-\text{O}-\text{CH}_2-\text{CO}-$ ), 7.3–7.5 (4H, m, aromatic protons) and 9.95 (1H, s,  $-\text{CHO}$ ) ppm.

(iii) *Ethyl 4-formylphenoxyacetate* (C): brown thick liquid, b.pt.  $194\text{--}196^\circ/20\text{--}22$  mm, yield 60%.

IR:  $\nu_{\text{max}}$  (film) 1750, 1690, 1600, 1580, 1510,  $\text{cm}^{-1}$  etc.

PMR:  $\delta(\text{CDCl}_3)$  1.29 (3H, t,  $-\text{COOCH}_2-\text{CH}_3$ ), 4.27 (2H, q,  $-\text{COOCH}_2-\text{CH}_3$ ), 4.70 (2H, s,  $-\text{O}-\text{CH}_2-\text{COO}-$ ), 6.95 and 7.90 (4H, d, d, aromatic protons) and 9.89 (1H, s,  $-\text{CHO}$ ) ppm.

### Products obtained

(i) *2-Carboxyphenoxyacetic acid*<sup>2</sup> (I): colourless needles, m.pt.  $191^\circ$ , yield 79%, N.E.  $100 \pm 3$ .

IR:  $\nu_{\text{max}}$  (Nujol) 3180, 1740, 1680,  $1600\text{ cm}^{-1}$  etc.

PMR:  $\delta(\text{CDCl}_3)$  4.85 (2H, s,  $-\text{O}-\text{CH}_2-\text{COO}-$ ), 7.0–8.2 (4H, m, aromatic protons) and 11.0 (2H, s, b; exchangeable with  $\text{D}_2\text{O}$ , two  $\text{COOH}$  groups) ppm.

UV:  $\lambda_{\text{max}}$  (EtOH) 233 (log  $\epsilon$  3.972) and 289 (log  $\epsilon$  3.185) nm which shifted to 229 and 280 nm, respectively, on addition of a drop of alkali.

(ii) *3-Carboxyphenoxyacetic acid*<sup>2</sup> (II): colourless crystals, m.pt.  $208^\circ$ , yield 95%, N.E.  $105 \pm 5$ .

IR:  $\nu_{\max}$  (Nujol) 3360, 1700, 1610, 1590  $\text{cm}^{-1}$  etc.

PMR:  $\delta(\text{CDCl}_3)$  4.80 (2H, s,  $-\text{O}-\underline{\text{CH}_2}-\text{COO}-$ ), 6.5–8.0 (4H, m, aromatic protons) ppm and carboxy protons did not appear.

UV:  $\lambda_{\max}$  (EtOH) 232 ( $\log \epsilon$  3.812) and 292 ( $\log \epsilon$  3.292) nm which shifted below 220 and 287 nm respectively, on addition of a drop of alkali.

(iii) 4-Carboxyphenoxyacetic acid<sup>2</sup> (III): colourless crystals, m.pt. 280°, yield 80%, N.E.  $98 \pm 5$ .

IR:  $\nu_{\max}$  (Nujol) 1700, 1660, 1600, 1570  $\text{cm}^{-1}$  etc.

PMR:  $\delta(\text{CDCl}_3)$  4.70 (2H, s,  $-\text{O}-\underline{\text{CH}_2}-\text{COO}-$ ), 6.5–9.5 (6H, m, 2H's exchangeable with  $\text{D}_2\text{O}$  when 2H, d at 7.0 to 7.10 and 2H, d at 7.95–8.0 appeared) ppm.

UV:  $\lambda_{\max}$  (EtOH) 213 ( $\log \epsilon$  3.765) and 252 ( $\log \epsilon$  4.088) nm which shifted to 214 and 257 nm, respectively, on addition of a drop of alkali.

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### REFERENCES

1. A. Banerjee, M.M. Adak, S. Das, S. Banerjee and S. Sengupta, *J. Indian Chem. Soc.*, **64**, 34 (1987); M.M. Adak, Ph.D. Dissertation, Part II, Jadavpur University, Calcutta 700 032, India (1985)
2. A. Rossing, *Ber.*, **17**, 2988 (1884); Th. Elkan, *Ber.*, **19**, 3041 (1886).
3. A.W. Burgtähler and L.R. Worden, *Org. Synth.*, **46**, 28 (1966).

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