The conformation of some *ortho*-bromoarylaldehydes

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X-Ray crystallographic studies have shown that an *ortho*-bromo substituent has less effect on the plane of rotation of an aryl carbonyl group than on an adjacent nitro group.

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The physico-chemical properties of aromatic carbonyl compounds are affected by steric interactions with *ortho* substituents which rotate the plane of the carbonyl group away from co-planarity with the aromatic ring. The diminution in the ultraviolet absorption intensity of *ortho*-substituted benzaldehydes and acetophenones has been associated[1] with transitions between non-planar ground states and near-planar excited states. The values that were obtained were used to estimate an interplanar angle of *ca* 20° for 2- and 2,6-dimethylbenzaldehyde and 35° or 60° for 2-methyl and *2,6*-dimethylacetophenone respectively.

Although there is some dispute[2] concerning the magnitude of the barrier to rotation of the aryl–carbonyl bond of an arylaldehyde, the calculated and experimentally determined barrier to rotation of the aldehyde group in benzaldehyde in the gas phase is about 7.7 kcal mol^{-1}. The plane of the aldehyde of the hindered arylaldehyde, 9-anthraldehyde, has been shown[3] by X-ray crystallography to be rotated by about 27° with respect to the central ring. A bromine atom in the *ortho* position to a nitro group provides sufficient steric compression for the nitro group to be rotated significantly from co-planarity with the aromatic ring.[4,5] Molecular models indicate that there is the potential for steric crowding of the aldehyde group by an adjacent bromine. In this paper, we consider the conformation of some *ortho*-bromoarylaldehydes in the solid state.

In the first group of compounds (Figs 1–4) we examined the structures of an aldehyde without an adjacent bromine and then with one and two adjacent bromine atoms and finally an *ortho*-bromoacetophenone in which the formyl hydrogen had been replaced by a methyl group.

The conformation of an aldehyde with no *ortho*-substituent was considered first. Bromination of vanillin (4-hydroxy-3-methoxybenzaldehyde) gave[6] 5-bromo-4-hydroxy-3-methoxy-benzaldehyde in which the bromine atom is not adjacent to the formyl group. The X-ray crystal structure (Fig. 1) showed that the formyl group is almost co-planar with the aromatic ring (rotation of the plane of the formyl group relative to the aromatic ring 0.7°). The effects of first one and then two bromine atoms adjacent to the formyl group were then studied. Bromination of 3,5-dimethoxybenzaldehyde gave 2-bromo-3,5-dimethoxybenzaldehyde and under more prolonged conditions, 2,6-dibromo-3,5-dimethoxybenzaldehyde.[7] The X-ray crystal structures (Figs 2 and 3) showed that the planes of the formyl groups were rotated to the extent of 6° and 49° with respect to the aromatic ring.

The effect of replacing the hydrogen atom of the formyl group by a larger methyl group was then studied. 6-Bromo-4-hydroxy-3-methoxyacetophenone was prepared by acetylation of 4-hydroxy-3-methoxyacetophenone (apocyanin),[8] bromination and hydrolysis. The plane of the acetyl group (see Fig. 4) was rotated by 15° with respect to the plane of the aromatic ring. The presence of the extra methyl group in place of the hydrogen atom has made a relatively small difference.

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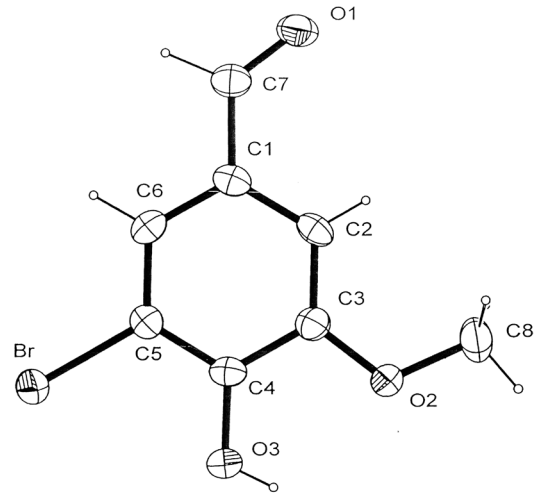

Fig.1 X-ray crystal structure of 5-bromo-4-hydroxy-3-methoxybenzaldehyde formyl:aryl interplanar angle 0.7°.

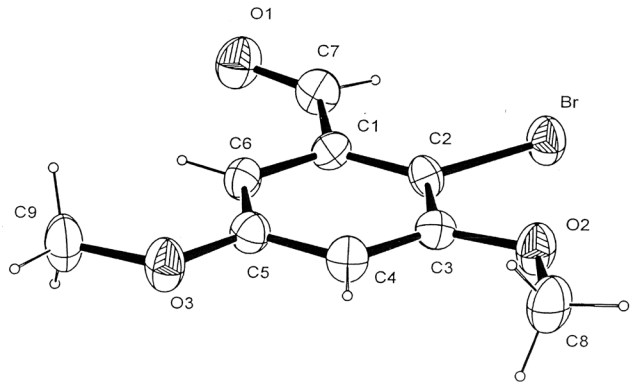

Fig. 2 X-ray crystal structure of 2-bromo-3,5-dimethoxy-benzaldehyde formyl:aryl interplanar angle 6°.

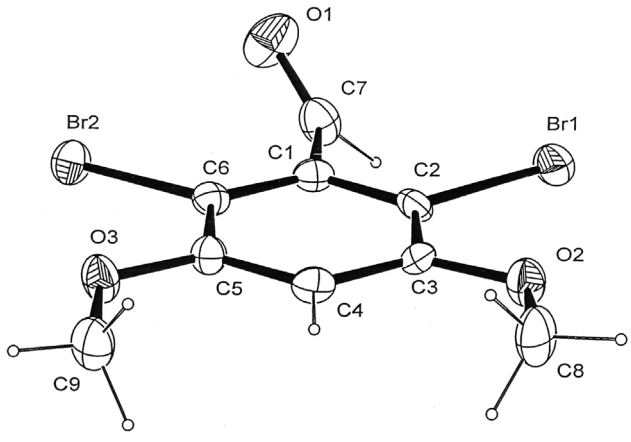

Fig. 3 X-ray crystal structure of 2,6-dibromo-3,5-dimethoxybenzaldehyde formyl : aryl interplanar angle 49°.

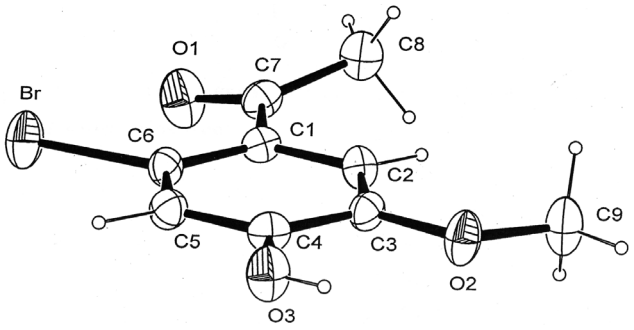

Fig. 4 X-ray crystal structure of 6-bromo-4-hydroxy-3-methoxyacetophenone acetyl:aryl interplanar angle 15°.

The rotamer which existed was that in which the bromine atom interacted with the carbonyl group rather than with the methyl group.

These results contrast with the far greater effect of an adjacent bromine on an aryl nitro group. Thus in 1,3-dibromo-2,4,6-trinitrobenzene,[9] the torsion angle O–N–C–C(Br) for the 2-nitro substituent (two adjacent bromine atoms) is 85.3° and for the 4-nitro group (one adjacent bromine), it is 29.9°. In 2,4-dinitrobromobenzene,[10] the torsion angle for the 2-nitro group is 44.4°.

In a study of the reactions of bromovanillins with amines, Raiford and Stoesser noted[11] that the presence of one *ortho* substituent appeared to cause no noticeable hindrance and even when both *ortho* positions were substituted, the effect was less pronounced than they had expected. We, therefore, examined the conformation of 2-bromo-3-hydroxy-4-methoxybenzaldehyde[12] and 6-bromo-4-hydroxy-3-methoxybenzaldehyde[13] which were obtained by brominating isovanillin and 4-acetoxyvanillin respectively. In each case (Figs 5 and 6), the formyl group remained co-planar with the aromatic ring (rotation of the planes of the formyl groups relative to the aromatic ring 1° and 6° respectively).

Since the presence of two bromine atoms adjacent to the formyl group had been sufficient to produce a significant rotation (49°)(Fig. 3), the effect of replacing one of the bromine atoms by a hydroxyl group which might hydrogen bond to the carbonyl group, was examined. 6-Bromo-2-hydroxy-3-methoxybenzaldehyde was obtained[14] by brominating the

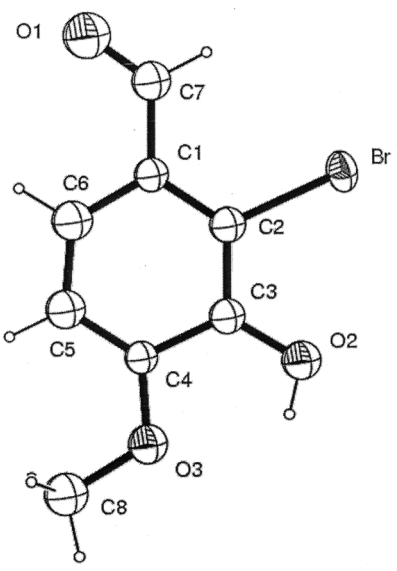

Fig. 5 X-ray crystal structure of 2-bromo-3-hydroxy-4-methoxybenzaldehyde formyl:aryl interplanar angle 1°.

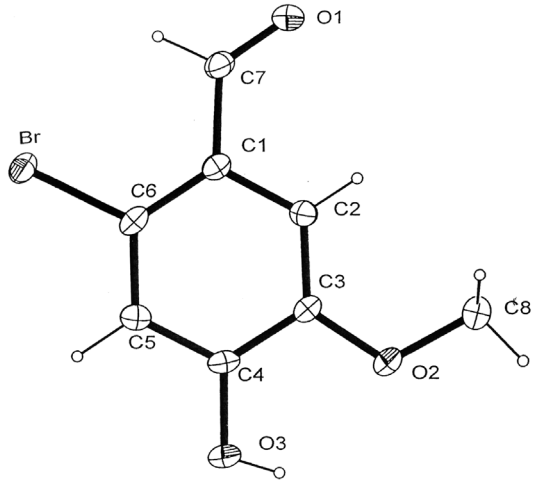

Fig. 6 X-ray crystal structure of 6-bromo-4-hydroxy-3-methoxybenzaldehyde formyl:aryl interplanar angle 6°.

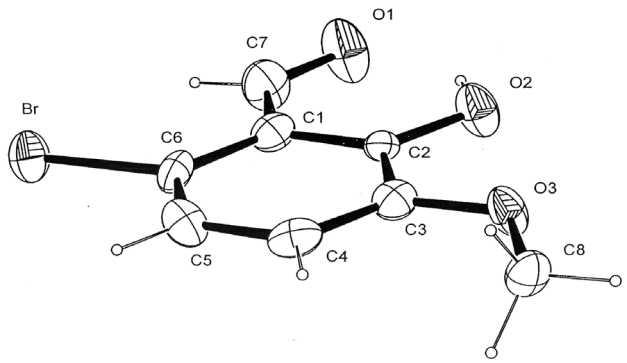

Fig. 7 X-ray crystal structure of 6-bromo-2-hydroxy-3-methoxybenzaldehyde formyl:aryl interplanar angle 5°.

arylsulfonate of *o*-vanillin and hydrolysis of the sulfonate. The X-ray crystal structure (Fig. 7) showed that there is an internal hydrogen bond to the aldehyde carbonyl group and that the formyl group was almost co-planar with the aromatic ring (rotation of the planes 5°).

In conclusion we have shown that in the crystal structure, an *ortho* bromine atom has a smaller effect on the plane of rotation of an aryl carbonyl group, relative to the aromatic ring, than on a nitro compound.

Experimental

General procedure

^{1}H NMR spectra were determined at 300 MHz; for solutions in deuteriochloroform. IR spectra were determined as nujol mulls. Mass spectra were determined on a Bruker Daltonics Apex III electrospray mass spectrometer. The bromobenzaldehydes were prepared by literature methods. 5-Bromo-4-hydroxy-3-methoxybenzaldehyde had m.p. 161°C (lit.,[6] 160–161°C); 2-bromo-3,5-dimethoxybenzaldehyde had m.p. 107°C (lit.,[7] 107°C); 2,6-dibromo-3,5-dimethoxybenzaldehyde had m.p. 221–222°C (lit.,[7] 222–223°C); 2-bromo-3-hydroxy-4-methoxybenzaldehyde had m.p. 209°C (lit.,[12] 211–212°C); 6-bromo-4-hydroxy-3-methoxybenzaldehyde had m.p. l78°C (lit.,[13] 178°C); 6-bromo-2-hydroxy-3-methoxybenzaldehyde had m.p. 125–126°C (lit.,[14] 129°C).

Bromination of 4-acetoxy-3-methoxyacetophenone: The acetate (m.p. 53°C, lit.,[8] 54°C) (1.5 g) in glacial acetic acid (40 cm^3) containing sodium acetate (4 g) was treated with a 25% solution of bromine in glacial acetic acid (8 cm^3) for 45 min at room temperature. The mixture was poured into an ice:water mixture containing sodium sulfite. The product was filtered and recrystallised from aqueous methanol to give 4-acetoxy-6-bromo-3-methoxyacetophenone, m.p. 75°C; ν_{max}/cm^{-1} 1762, 1704, 1596, 1575; δ_H 2.30 (3H, s, OAc), 2.65

(3H, s, ArCOMe), 3.80 (3H, s, OMe), 7.05 (lH, s, Ar–H), 7.35(lH, s, Ar–H). Found M^+ 308.9727, $C_{11}H_{11}BrO_4Na$ requires 308.9733.

Hydrolysis of the acetate: 4-Acetoxy-6-bromo-3-methoxyacetophenone (1.5 g) was suspended in aqueous sodium hydroxide (2 M, 10 cm^3). The solution was heated on a boiling water bath for 5 min. It was then cooled and acidified with 2 M hydrochloric acid. The product (1 g) was collected and crystallised from aqueous methanol to give 6-bromo-4-hydroxy-3-methoxyacetophenone, m.p. 115°C; ν_{max}/cm^{-1} 3303, 1678, 1564; δ_H 2.65 (3H, s, ArCOMe), 3.90 (3H, s, 0Me), 7.10 (lH, s, ArH), 7.15(lH, s, ArH); Found M^+ 266.9620, $C_9H_9BrO_3Na$ requires 266.9627.

X-Ray crystal data and structure determinations: Data were collected using a Kappa CCD diffractometer. Absorption corrections were applied using MULTISCAN. Structures were solved by direct methods and refined using SHELXL-97. The drawings used ORTEP-3 for Windows. The CCDC Numbers given below contain the supplementary crystallographic data for this paper. The data can be obtained free of charge from the Cambridge Crystallographic Centre via www.ccdc.cam.ac.uk/data_request.cif. The data for 2-bromo-3-hydroxy-4-methoxybenzaldehyde and 6-bromo-2-hydroxy-3-methoxybenzaldehyde were of a rather poor quality but were sufficient to determine the angles described in the text.

(i) 5-bromo-4-hydroxy-3-methoxybenzaldehyde, $C_8H_7BrO_3$, M_r 231.05, tetragonal, space group $P4_2/n$ (No.86), a = 13.5896(3), b = 13.5896(3), c = 17.9201(5) Å, $\alpha = \beta = \gamma = 90°$, V = 3309.43(14) Å^3, Z = 16, D_{calc} = 1.86 g cm^{-3}, μ = 4.93 mm^{-1}, F(000) = 1824. Crystal size 0.20 × 0.20 × 0.15 mm. A total of 19586 reflections were collected for $3.54 < \theta < 26.01°$ and $-16 \le h \le 16$, $-15 \le k \le 15$ and $-21 \le l \le 22$. There were 3247 independent reflections and 2647 reflections with $I > 2\sigma(I)$ were used in the refinement. The final R indices were $[I > 2\sigma(I)]$ $R^1 = 0.042$, $wR^2 = 0.087$ and (all data) $R^1 = 0.065$, $wR^2 = 0.093$. The largest difference peak and hole were 0.60 eÅ^{-3} and –0.65 eÅ^{-3}. There were two independent molecules in the unit cell. CCDC No. 267845.

(ii) 2-bromo-3,5-dimethoxybenzaldehyde, $C_9H_9BrO_3$, M_r 245.07, monoclinic, space group $P2_1/c$ (No.14), a = 4.0282(2), b = 17.2047(8), c = 13.2356(8) Å, $\alpha = \gamma = 90°$, β = 92.751(3)°, V = 916.22(8) Å^3, Z = 4, D_{calc} = 1.78 g cm^{-3}, μ = 4.46 mm^{-1}, F(000) = 488. Crystal size 0.25 × 0.20 × 0.15 mm. A total of 5938 reflections were collected for $3.87 < \theta < 26.14°$ and $-4 \le h \le 4$, $-21 \le k \le 19$ and $-11 \le l \le 16$. There were 1778 independent reflections and 1501 reflections with $I > 2\sigma(I)$ were used in the refinement. The final R indices were $[I > 2\sigma(I)]$ $R^1 = 0.048$, $wR^2 = 0.117$ and (all data) $R^1 = 0.058$, $wR^2 = 0.123$. The largest difference peak and hole were 0.97 eÅ^{-3} and –0.56 eA^{-3}. CCDC No. 276704.

(iii) 2,6-dibromo-3,5-dimethoxybenzaldehyde, $C_9H_8Br_2O_3$, M_r 323.97, orthorhombic, space group $P2_12_12_1$ (No.19), a = 4.1198(2), b = 14.3152(6), c = 17.1201(6) Å, $\alpha = \beta = \gamma = 90°$, V = 1009.67(7) A^3, Z = 4, D_{calc} = 2.13 g cm^{-3}, μ = 8.01 mm^{-1}, F(000) = 624. Crystal size 0.20 × 0.15 × 0.05 mm. A total of 11371 reflections were collected for $3.71 < \theta < 26.02°$ and $-5 \le h \le 5$, $-17 \le k \le 17$ and $-21 \le l \le 21$. There were 1972 independent reflections and 1780 reflections with $I > 2\sigma(I)$ were used in the refinement. The final R indices were $[I > 2\sigma(I)]$ $R^1 = 0.030$, $wR^2 = 0.053$ and (all data) $R^1 = 0.038$, $wR^2 = 0.056$. The largest difference peak and hole were 0.34 eÅ^{-3} and –0.41 eÅ^{-3}. CCDC No, 276705.

(iv) 6-bromo-4-hydroxy-3-methoxyacetophenone, $C_9H_9BrO_3$, M_r 245.07, monoclinic, space group $P2_1/c$ (No.14), a = 8.5726(5), b = 15.4522(6), c = 7.6171(4) Å, $\alpha = \gamma = 90°$, β = 114.936(2)°, V = 914.94(8) Å^3, Z = 4, D_{calc} = 1.78 g cm^{-3}, μ = 4.46 mm^{-1}, F(000) = 488. Crystal size 0.10 × 0.10 × 0.05 mm. A total of 15084 reflections were collected for $3.72 < \theta < 26.02°$ and $-10 \le h \le 10$, $-19 \le k \le 19$ and $-9 \le l \le 9$. There were 1800 independent reflections and 1421 reflections with $I > 2\sigma(I)$ were used in the refinement. The final R indices were $[I > 2\sigma(I)]$ $R^1 = 0.037$, $wR^2 = 0.077$ and (all data) $R^1 = 0.059$, $wR^2 = 0.077$. The largest difference peak and hole were 0.493 eÅ^{-3} and –0.570 eA^{-3}. CCDC No. 276706.

(v) 2-bromo-3-hydroxy-4-methoxybenzaldehyde, $C_8H_7BrO_3$, M_r 231.05, monoclinic, space group $P2_1$ (No.4), a = 3.9170(4), b = 12.8183(11), c = 16.4160(14) Å, $\alpha = \gamma = 90°$, β = 95.243(6)°, V = 820.79(13) Å^3, Z = 4, D_{calc} = 1.87 g cm^{-3}, μ = 4.97 mm^{-1}, F(000) = 456. Crystal size 0.20 × 0.10 × 0.10 mm. A total of 4901 reflections were collected for $3.41 < \theta < 26.07°$ and $-4 \le h \le 4$, $-15 \le k \le 15$ and $-19 \le l \le 20$. There were 2770 independent reflections and 2416 reflections with $I > 2\sigma(I)$ were used in the refinement. The final R indices were $[I > 2\sigma(I)]$ $R^1 = 0.093$, $wR^2 = 0.256$ and (all data) $R^1 = 0.105$, $wR^2 = 0.269$. The largest difference peak and hole were 4.32 eÅ^{-3} and –1.17 eÅ^{-3}. The crystals were hollow rods and the data were collected on a fragment from one wall giving rather poor results which are reflected in the R factors. CCDC No. 267847.

(vi) 6-bromo-4-hydroxy-3-methoxybenzaldehyde, $C_9H_7BrO_3$, M_r 231.05, monoclinic, space group $P2_1/c$ (No.14), a = 13.4979(5), b = 3.9038(1), c = 16.1968(6) Å, $\alpha = \gamma = 90°$, β = 110.181(1)° V = 801.06(5) Å^3, Z = 4, D_{calc} = 1.92 g cm^{-3}, μ = 5.09 mm^{-1}, F(000) = 456. Crystal size 0.25 × 0.20 × 0.10 mm. A total of 10347 reflections were collected for $3.40 < \theta < 25.98°$ and $-16 \le h \le 16$, $-4 \le k \le 4$ and $-19 \le l \le 19$. There were 1568 independent reflections and 1449 reflections with $I > 2\sigma(I)$ were used in the refinement. The final R indices were $[I > 2\sigma(I)]$ $R^1 = 0.035$, $wR^2 = 0.094$ and (all data) $R^1 = 0.039$, $wR^2 = 0.095$. The largest difference peak, and hole were 0.82 eÅ^{-3} and –1.71 eA^{-3}. CCDC No. 267846.

(vii) 6-bromo-2-hydroxy-3-methoxybenzaldehyde, $C_8H_7BrO_3$, M_r 231.05, monoclinic, space group $P2_1/n$ (No.14), a = 4.0051(3), b = 11.9662(9), c = 16.8397(14) Å, $\alpha = \gamma = 90°$, β = 91.582(5)°, V = 806.75(11) Å^3, Z = 4, D_{calc} = 1.90 g cm^{-3}, μ = 5.05 mm^{-1}, F(000) = 456. Crystal of size 0.40 × 0.10 × 0.10 mm. A total of 4779 reflections were collected for $3.41 < \theta < 25.97°$ and $-4 \le h \le 4$, $-14 \le k \le 14$ and $-12 \le l \le 20$. There were 1551 independent reflections and 1274 reflections with $I > 2\sigma(I)$ were used in the refinement. The data were rather weak. The final R indices were $[I > 2\sigma(I)]$ $R^1 = 0.101$, $wR^2 = 0.227$ and (all data) $R^1 = 0.118$, $wR^2 = 0.236$. The largest difference peak and hole were 3.95 eÅ^{-3} and –1.21 eA^{-3}. CCDC No. 267848.

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References

1 E.A. Braude and F. Sondheimer, *J. Chem. Soc.,* 1955, 3754.
2 L.D. Speakman, B.N. Papas, H.L. Woodcock and H.F. Schaefer, *J. Chem. Phys.,* 2004, **120**, 4247.
3 J. Trotter, *Acta Crystallogr.*, 1959, **12**, 922.
4 R.J. Butcher, R. Gilgardi, J.L. Flippen-Andersen and C. George, *Nouv. J. Chem.,* 1992, **16**, 679.
5 T. Fricke, A. Dickmans, U. Jena, M. Zabel, F.G. Jones, I. Dix, B. Konig and R. Herges, *Z. Naturforsch., B: Chem. Sci.,* 2002, **57**, 937.
6 F. Tiemann and W. Haarmann, *Ber.*, 1874, **7**, 608.
7 M. Lock and C. Nottes, *Monatsch. fur Chemie,* 1936, **68**, 51.
8 H. Finnemore, *J. Chem. Soc.*, 1908, **93**, 1513.
9 P.K. Thallapally, G.R. Desiraju, M. Bagieu-Beucher, C. Bourgogne and J.F. Nicoud, *Chem. Commun.,* 2002, 1052.
10 R. Kruszynski and W. Czestkowski, *Acta Cryst.*, *Sect. E.,* 2002, **58**, 0481.
11 L.C. Raiford and W.C. Stoesser, *J. Am. Chem. Soc.*, 1928, **50**, 2556.
12 S.E. Hazlett and R.J. Brotherton, *J. Org. Chem.*, 1962, **27**, 3253.
13 L.C. Raiford and W.C. Stoesser, *J. Am. Chem. Soc.,* 1927, **49**, 1077.
14 M. Brink, *Acta Univ. Lund,* 1967, **36**, 12 *(Chem. Abstr.,* 1968, **69**, 76823).