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STUDIES ON OXYGEN HETEROCYCLES

PART-1 : ACID CATALYSED AND PHOTOCHEMICAL REACTIONS OF SOME ARYLDIAZOKETONES

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ABSTRACT: Trifluoroacetic acid catalysed reaction of 2-methoxyphenyldiazomethylketone (4a), 2-acetoxyphenyldiazomethylketone (4b) and 3-(2-anisyl)-α-diazo-2-propanone (11) leads to the formation of coumaranone (6) and 3-chromanone (12), while 4-(2-anisyl)-α-diazo-2-butanone (16) affords benzo[b]-1-oxepan-3-one (17) and 5-methoxy-2-tetralone (18) in moderate yield. The photochemical decomposition of the said diazoketones (4a, 11 and 16) gave products depending on the length of the side chain present in the substrates.

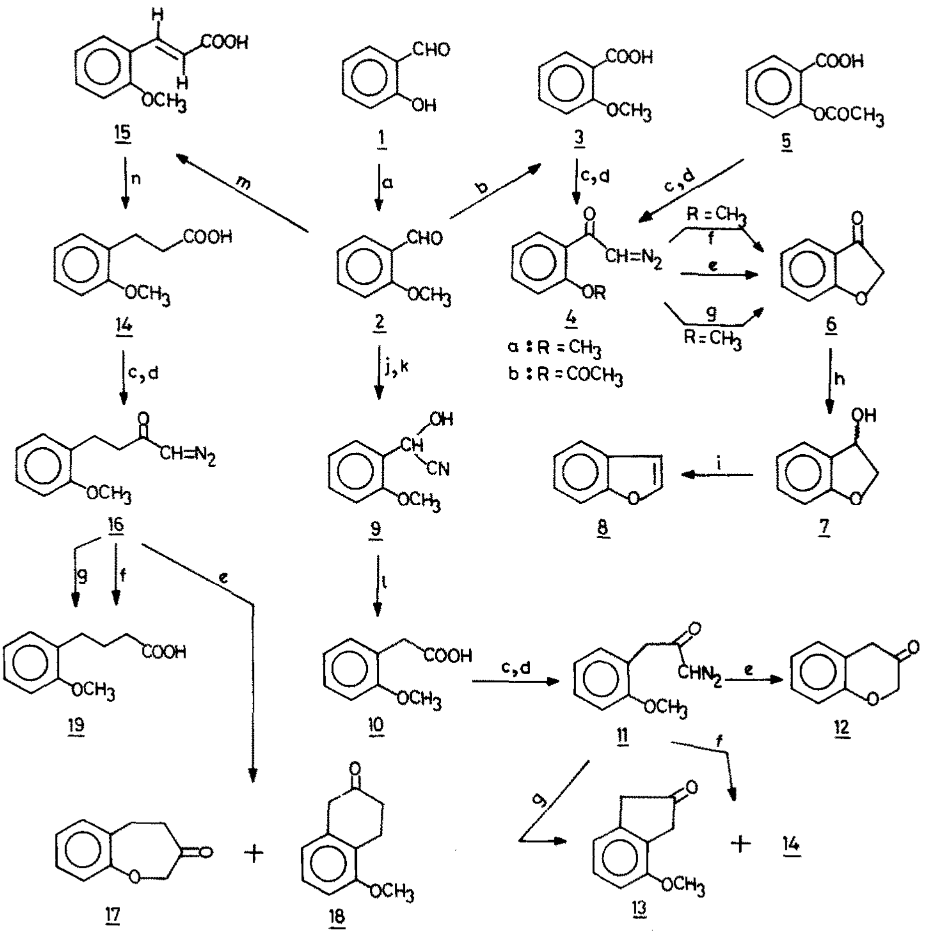
The decomposition of α-diazocarbonyl compounds in the presence of copper-bronze catalyst, as first demonstrated by Stork *et al*[1] in the early sixties, has received wide attention for the last two decades and several elegant methodologies[2-7] involving acid, heat, light and transition metal complexes as catalyst have been developed in recent years for the synthesis of complex carbocyclic and heterocyclic compounds. In connection with our interest for the synthesis of naturally occurring compounds[8-10] and photochemical studies[11] on heterocyclic systems, we wish to report here the acid-catalysed and photochemical decomposition of some 2-substituted aryldiazoketones (4,11 and 16).

Although there are some earlier reports[12-17] of the synthesis of coumaranone (6) and 3-chromanone (12), in the present study we have chosen trifluoroacetic acid (TFA), which has not been used so far, for the acid-catalysed decomposition of 4,11 and 16, whereby we could isolate 6,12 and benzo[b]-1-oxepan-3-one (17) in good yield. It is to be mentioned here that we did not isolate any hydroxymethylketone, as reported earlier[16], because of the poor nucleophilicity of the trifluoroacetate anion. Moreover, the acid catalysis of 16 also afforded for the first time 5-methoxy-2-tetralone (18) in moderate yield (Scheme-1). It is significant to note that this is the first report of the synthesis of 17 through acid catalysed reaction of 16, in contrast to Scheffer's observation[16], where only a fluoroketone was isolated with boron-trifluoride etherate as catalyst. The results of these studies have been assembled in Table-1.

We next endeavoured to investigate the photochemical behaviour of 4,11 and 16, as the same has not been reported so far. While the photolysis of 4a in the presence of dry benzene under nitrogen atmosphere neatly afforded coumaranone (6) in reasonable yield (Table-1) at different wavelengths (Scheme-1), 2-acetoxyphenyldiazomethylketone (4b) failed to yield 6 and instead, some polymeric material was obtained. The latter observation may be attributed to the poor nucleophilicity of the acetoxy group under irradiative condition, while the same substrate (4b) gave a very good yield of 6 (Table-1) in the presence of TFA, possibly through a facile deacetylation initiated by the trifluoroacetate anion in the intermediate reaction step (Scheme-2).

Encouraged by this observation, we carried out the photolysis of 11 in benzene using a low pressure mercury lamp (16W, > 90% 254 nm, Applied Photophysics Ltd., England) and surprisingly, could isolate only 4-methoxy-2-indanone (13) alongwith a small amount of the known acid[18](14). The same result was also obtained by irradiating 11 at 365-366 nm. The formation of 13 could be visualised through a preferential Ar^{1}-2 participation (Scheme-2) over the neighbouring methoxy group on the ketocarbenoid species (20, n=1), followed by a rearrangement of the intermediate spiro-dienone (21); but in the presence of acid, 11 generates the highly reactive carbocation which triggers off a spontaneous participation by the *ortho*-methoxy group. The reaction clearly proceeds through a delicate balance between the participation of the methoxy group and the aromatic ring under two different conditions of

SCHEME-1



a: $(CH_3)_2SO_4/NaOH/\Delta$; b: Dil.HNO_3/Δ; c: $SOCl_2/C_6H_6/\Delta$; d: CH_2N_2/Ether/0°; e: TFA/-15°; f: $h\nu$ (254 nm)/C_6H_6; g: $h\nu$ (365-366 nm)/C_6H_6; h: $NaBH_4/CH_3OH$/0°; i: $KHSO_4/\Delta$; j: Aq.$NaHSO_3$/R.T.; k: Aq.NaCN/Ether/0°; l: $SnCl_2/HI/HCl/HOAc/\Delta$; m: $CH_2(COOH)_2/C_5H_5N/C_5H_{11}N/\Delta$; n: Na(Hg)/Aq.NaOH/R.T.

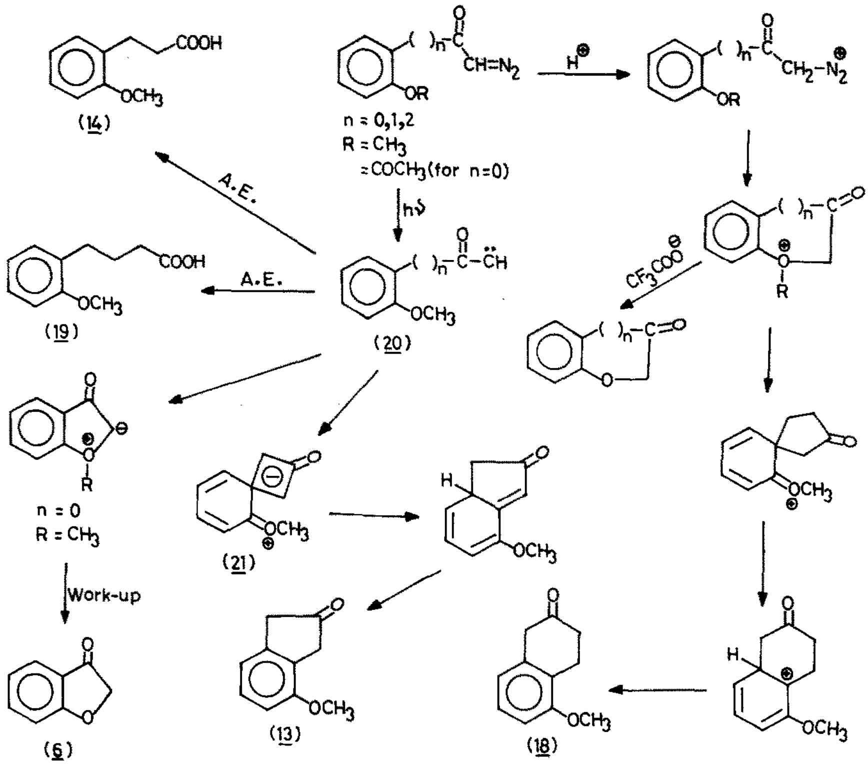
experiment, thereby providing a method for the preparation of oxa-ketone (12) and indanone (13) through the same intermediate. The isolation of a small amount of 14 may be explained by a photo-Arndt-Eistert type of reaction. Table-1 collectively presents an overview of these experiments.

Unfortunately, the reaction of 16 under photolytic conditions failed to afford 17 or 18; instead, the higher homologous acid, 4-(2-anisyl)-butyric acid[19](19) was isolated. The apparent failure of this reaction may be attributed to the greater degree of freedom(entropy factor) of the diazocarbonyl functionality in 16, which renders aryl or methoxy participation on 20(n=2)(Scheme-2) a less favourable process. On the other hand, the ketocarbocation produced from 16 by TFA leads to a facile participation (thermodynamic control) of the methoxy group and aromatic ring to furnish 17 and 18 in reasonable yield.

It is also of paramount importance to observe the behaviour of 4a under photochemical condition, the structural features of which compel the methoxy group to participate on the ketocarbenoid species (20, n=0) to generate the five-membered ring in preference to the aryl participation.

Finally, we have also elaborated the conversion of 6 to benzofuran (8) with a view to synthesising some naturally occurring 2-substituted benzofurans.

SCHEME-2



A.E.:ARNDT-EISTERT

Thus, we conclude that the acid catalysis of 4,11 and 16 offers a good method for the synthesis of the corresponding oxa-ketones, whereas the photolysis of the same substrates affords neatly 6 (from 4a) and 13 (from 11).

EXPERIMENTAL :

The melting points, recorded in a Kofler block or boiling points (bath temperature) are uncorrected. The IR spectra were obtained in a Perkin-Elmer 297 Infrared spectrophotometer and ^{1}H NMR spectra, unless otherwise stated, in a Varian XL 200 MHz spectrometer in $CDCl_3$ with TMS as internal standard. The solvent abbreviations are: A - Acetone; B - Benzene; C - Chloroform; E - Ether; P' - Light Petrol (40-60°) and P - Petroleum ether (60-80°) with the subscripts referring to the proportions of the solvent used for chromatography. The yield denotes the combined amounts of crystallised or sublimed material obtained after chromatography.

2-Methoxybenzaldehyde (2) : To a mechanically stirred solution of salicylaldehyde (1) (25.0 g; 200 mmol) in sodium hydroxide (92 ml; 8.5%) was added alternately dimethyl sulphate (DMS)(16 ml) keeping the temperature at 40-45°, followed by addition of sodium hydroxide solution (46 ml; 8.5%) and DMS (11 ml). The solution was cooled and worked up in the usual way to yield 2-methoxybenzaldehyde (22.3 g; 80%), bp.240°/30 mm Hg.

IR (Neat) : ν_{max} 1690, 1600, 1485, 1245, 1025 and 760 cm^{-1}.

2-Methoxybenzoic acid (3): 2-Methoxybenzaldehyde (2) (17.6 g; 130 mmol) and dil.HNO_3 (200 ml) was heated on a steam-bath for 2 hr with occasional stirring. The reaction mixture was then poured in ice-cold water to obtain 2-methoxybenzoic acid (14.2 g; 72%) which was crystallised to yield pure 3, mp.101° (E-P) (lit.[20] mp.99-101°).

2-Methoxyphenyldiazomethylketone (4a): To a suspension of 3 (5.4 g; 36 mmol) in dry

TABLE-1: RESULTS OF ACID CATALYSED AND PHOTOCHEMICAL REACTION OF DIAZOKETONES(4,11 AND 16)

Sub-strate	IR(cm^{-1});^{1}H NMR(δ)	Reagent	Product Yield mg(%)	MP.(Solvent) BP./mm Hg Eluent	IR(cm^{-1});^{1}H NMR(δ)
4a (1.0 g; 6 mmol).	2110,1640; 3.83(3H,s), 6.16(1H,s),6.66-7.86 (4H,m)	TFA	6 600(80)	100°(A-P') (lit.[12] mp. 101-101.5°) P_9B_1	1725; 4.62(2H,s),7.12 (2H,m),7.60(2H,m)
(1.0 g; 6 mmol)		$h\nu$ /C_6H_6 16W/10.0 h	6 130(17)	100°(A-P') P_9B_1	
(1.5 g; 8 mmol)		$h\nu$ /C_6H_6 400W/4.5 h	6 140(12)	100°(A-P') P_9B_1	
4b (1.0 g; 4 mmol)	2120,1740,1600; 2.28 (3H,s),5.56(1H,s), 6.83-7.56(4H,m)	TFA	6 400(61)	100°(A-P') P_9B_1	
11 (1.0 g; 5 mmol)	2120,1640; 3.64(2H,s), 3.84(3H,s),5.16(1H,s), 6.86-7.00(2H,m), 7.14-7.32(2H,m)	TFA	12 530(68)	$P+P_9B_1$	1730; 3.60(2H,s),4.38 (2H,s),6.80-7.80(4H,m)
(1.9 g; 10 mmol)		$h\nu$ /C_6H_6 16W/10.0 h	13 180(12)	83°/0.5 (sublimed) $P_9B_1+P_3B_1$	1735; 3.66(2H,s),3.72 (2H,s),3.82(3H,s), 6.93-7.26(3H,m)
			14 60(3)	160-180°/0.6 (sublimed) 84°(A-P') (lit.[18] mp.92°) $P_9B_1+P_3B_1$	1710; 2.60-3.00(4H,m), 3.80(3H,s),6.90-7.22 (4H,m)
(1.2 g; 6 mmol)		$h\nu$ /C_6H_6 400W/9.5 h	13 400(40)	P_3B_1	
			14 30(3)	P_1B_3	
16 (1.28 g; 6 mmol)	2120,1640; 2.30-3.03 (4H,m),3.76(3H,s), 4.96(1H,s),6.53-7.20 (4H,m)	TFA	17 270(27)	P_9B_1	1725; 2.88-3.20(4H,m), 4.52(2H,s),7.04-7.34 (4H,m)
			18 140(13)	P_9B_1	1720; 2.88-3.40(4H,m), 3.70(2H,s),3.84(3H,s), 6.92(3H,m)
(2.2 g; 10 mmol)		$h\nu$ /C_6H_6 16W/9.5 h	19 190(9)	140°/1.0 (sublimed) (lit.[19] mp. 39-39.5°) $P_1B_1+P_1B_3$	1710; 1.70-2.80(6H,m), 3.73(3H,s),6.50-7.16 (4H,m)
(1.4 g; 7 mmol)		$h\nu$ /C_6H_6 400W/3.5 h	19 130(10)	$P_1B_1+P_1B_3$	

benzene (30 ml) was added thionyl chloride (6.0 g; 50 mmol) at room temperature and the mixture was stirred for 1 hr, followed by heating under reflux for another hour. The excess reagent and the solvent was stripped off in vacuo. The acid chloride in dry benzene (30 ml) was added dropwise to a well-stirred ethereal diazomethane solution at 0° and stirring was continued for 2 hr. Excess solvent and diazomethane was distilled off in vacuo to afford 4a as a brown oil (5.3 g; 87%), purified further over neutral alumina (BDH).

2-Acetoxyphenyldiazomethylketone (4b): Acetylsalicylic acid (5) (5.4 g; 30 mmol) was used in the same way as above to yield 4b (6.02 g; 98%), which was crystallised to afford 4b as shining yellow crystals, mp.78°(A-P').(4b was previously reported as an oil[12]).

1-Cyano-(2-methoxy)-benzylalcohol (9): 2-Methoxybenzaldehyde (2) (22.3 g; 160 mmol) was taken and the standard procedure[21] followed, whereby 9 was obtained as colourless crystals (19.7 g; 75%), mp.73°(A-P')(lit.[21] mp.73-74°).

IR(KBr): ν_{max} 3370-3420(b), 2250, 1595, 1460, 1250, 1020, 900 and 750 cm^{-1}.

^{1}H NMR (60 MHz,Hitachi R 600): δ 3.47 (1H,d,J=10.0 Hz), 3.97(3H,s), 5.60(1H,d,J=10.0 Hz), 6.90-7.60(4H,m).

2-Methoxyphenylacetic acid (10): The cyanohydrin (9)(14.0 g; 90 mmol) was converted to the desired acid (10) by the known procedure[21] and the product obtained (10.2 g; 72%) was crystallised to yield pure 10 as granular crystals, mp.122°(A-P)(lit.[21] mp.122-124°).

IR(KBr): ν_{max} 2850-3000(b), 1695, 1600, 1590, 1230, 1020, 930 and 755 cm^{-1}.

^{1}H NMR(60 MHz,Varian EM 360): δ 3.60(2H,s),3.80(3H,s),6.67-7.00(2H,m),7.03-7.30(2H,m).

3-(2-Anisyl)-α-diazo-2-propanone (11): 2-Methoxyphenylacetic acid (10)(5.8 g; 40 mmol) was converted, by the procedure described earlier,to 3-(2-anisyl)-α-diazo-2-propanone (11) as a red oil (5.84 g; 88%) which was purified over neutral alumina (BDH).

2-Methoxycinnamic acid (15): Standard procedure[22] was followed to convert 2-methoxybenzaldehyde (2)(10.0 g; 70 mmol) to crude 15 (10.0 g; 77%), which was crystallised to yield pure 15, mp.184°(A-P)(lit.[18] mp.186°) as colourless, shining, granular crystals.

IR(KBr): ν_{max} 2800-3100(b), 1670, 1620, 1420, 1245, 1020, 930 and 750 cm^{-1}.

^{1}H NMR(100 MHz,Zeol FX): δ 3.84(3H,s), 6.56(1H,d,J=16.0 Hz), 6.94(2H,d,J=8.0 Hz), 7.02 (2H,d,J=8.0 Hz), 8.12(1H,d,J=16.0 Hz).

3-(2-Anisyl)-propanoic acid (14): To a stirred solution of 2-methoxycinnamic acid (15) (9.0 g; 50 mmol) in sodium hydroxide (50 ml; 10%), sodium amalgam (prepared from sodium, 5 g and mercury, 130 g) was added in small portions. The mixture was stirred for 3 hr and allowed to stand overnight. The mercury was filtered off and the reaction mixture, after usual workup, afforded 14 (9.0 g; 99%), crystallised further to give the desired acid (14) as colourless granular crystals, mp.82°(C-P')(lit.[18] mp.92°).

IR(KBr): ν_{max} 2800-3100(b), 1700, 1490, 1435, 1240, 1110, 1030 and 760 cm^{-1}.

^{1}H NMR(100 MHz,Zeol FX): δ 2.66(2H,ddd,J_1=10.0 Hz, J_2=6.0 Hz, J_3=2.0 Hz), 2.96(2H,ddd, J_1=10.0 Hz, J_2=6.0 Hz, J_3=2.0 Hz), 3.76(3H,s), 6.80(1H,d, J=8.0 Hz),7.14(2H,dd,J_1=8.0 Hz, J_2=3.0 Hz),6.90(1H,d,J=8.0 Hz).

4-(2-Anisyl)-α-diazo-2-butanone (16): The acid (14)(5.0 g; 30 mmol) was used according to the method described above to afford the diazoketone (16)(5.32 g; 94%) and purified by chromatography over neutral alumina (BDH).

TFA Cyclisation: A solution of 4 in dry dichloromethane (5 ml) was added dropwise to a well-stirred and well-cooled TFA (-15°) under nitrogen atmosphere. The solution was stirred for 30 min and the solvent and excess TFA were stripped off in vacuo. The residue was purified by chromatography over silica gel (60-120 mesh,BDH) and the results have been given in Table-1.

Similar experiments were performed with 11 and 16 under the same conditions. However,17 and 18, obtained from the TFA catalysed reaction of 16,migrated in P_9B_1 mixture and were further purified over basic alumina(BDH) to yield pure 17 and 18 in $P_{95}B_5$, P_9B_1, $P_{75}B_{25}$, $P_{65}B_{35}$ mixtures and P_1B_1, P_2B_3 mixtures respectively.

Photochemical Reaction of 4a,11 and 16 : The compound 4a was taken in dry benzene(350 ml) and subjected to UV radiation in a quartz vessel (immersion type) using a low pressure mercury lamp (16W) under an atmosphere of nitrogen for 10 hr (monitored by TLC). After the reaction was complete, the solvent was removed in vacuo and the residual mass subjected to chromatography over silica gel (60–120 mesh, BDH).

The diazoketones (11 and 16) too were analogously photolysed and the entire results have been assembled in Table-1.

The same procedure was repeated with a medium pressure mercury lamp (400W, λ_{max} 365–366 nm) and the observations have been recorded (Table-1).

3-Hydroxy-2,3-dihydrobenzofuran (7): To a well-stirred solution of coumaranone(6)(1.92 g; 10 mmol) in AR methanol (45 ml, Merck), sodium borohydride (6.2 g; 160 mmol, Merck) was added pinch by pinch at 0° for a period of 1 hr. The reaction mixture was worked up in the usual way to obtain 7 as an oil (1.4 g; 72%).

IR(Neat): ν_{max} 3300–3400(b), 1610, 1600, 1480, 1320, 1230, 1075, 1015 and 755 cm^{-1}.

^{1}H NMR(100 MHz, Zeol FX): δ 2.26(1H, envelope bs), 4.38(2H, dd, J_1=8.0 Hz, J_2=4.0 Hz), 5.28 (1H, dd, J_1=8.0 Hz, J_2=4.0 Hz), 6.84(2H, m), 7.22(1H, dd, J_1=8.0 Hz, J_2=4.0 Hz), 7.40(1H, dd, J_1=8.0 Hz, J_2=4.0 Hz).

Benzofuran (8): A mixture of 7 (1.40 g; 10 mmol) and fused potassium bisulphate (2.0 g; Johnson and Co) was slowly and carefully sublimed under reduced pressure to obtain benzofuran (800 mg; 67%) at 65°/10–15 mm Hg.

IR(Neat): ν_{max} 1535, 1450, 1250, 1030, 860 and 745 cm^{-1}.

^{1}H NMR(100 MHz, Zeol FX): δ 6.68(1H, dd, J_1=4.0 Hz, J_2=1.0 Hz), 7.08–7.40(4H, m), 7.52(1H, d, J=4.0 Hz).

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REFERENCES :

1. Stork,G.; Ficini,J. J.Am.Chem.Soc. 1961, 83, 4678.
2. Kirmse,W. Prog.Org.Chem. 1964, 6, 164.
3. Davie,V.; Warnhofer,E.W. Org.React. 1970, 18, 217.
4. Kirmse,W. "Carbene Chemistry", 1971, Academic Press, N.Y.
5. Marchand,A.P.; MacBrockway,N. Chem.Rev.1974, 74, 431.
6. Meier,H.; Zeller,K.P. Angew.Chem.Int.Ed.Engl. 1975, 7, 32.
7. Burke,S.D.; Grieco,P.A. Org.React. 1979, 26, 361.
8. Chatterjee,A.; Ghosh,S.N. Synthesis 1981, 818.
9. Banerji,A.; Bandyopadhyay,D.; Sarkar,M.; Siddhanta,A.K.; Pal,S.C.; Ghosh,S.N.; Abrahm,K.; Shoolery,J.N. Phytochemistry 1985, 24, 279.
10. Ghosh,S.N.; Datta,D.B.; Sen,N. Synth.Commun. 1987, 17, 299.
11. Ghosh,S.N.; Das,T.K.; Datta,D.B.; Mehta,S. Tetrahedron Lett. 1987, 4611.
12. Marshall,E.R.; Kuck,J.A.; Elderfield,R.C. J.Org.Chem. 1942, 7, 444.
13. Pfeiffer,P.; Endres,E. Ber. 1951, 84, 247.
14. Bose,A.K.; Yates,P. J.Am.Chem.Soc. 1952, 74, 4703.
15. Bhati,A. J.Org.Chem. 1962, 27, 1183.
16. Scheffer,H.E.; Moore,J.A. J.Org.Chem. 1963, 28, 129.
17. Still Jr.,W.C.; Goldsmith,D.J. J.Org.Chem. 1970, 35, 2282.
18. Frederick,J.; Dippy,J.; Page,J.E. J.Chem.Soc. 1938, 357.
19. Lockett,J.; Short,W.F. J.Chem.Soc. 1939, 787.
20. Cohen,J.B.; Dudley,H.W. J.Chem.Soc. 1910, 1732.
21. Levine,J.; Eble,T.E.; Fischbach,H. J.Am.Chem.Soc. 1948, 70, 1930.
22. Vogel,A.I. "A Textbook of Practical Organic Chemistry including Qualitative Organic Analysis", 1978, 803, ELBS and Longman, London.