Tetrahedron Vol. 42, No. 14, pp. 3891 to 3898, 1986
Printed in Great Britain.

0040-4020/86 $3.00+.00
Pergamon Journals Ltd.

UNUSUAL ACETONE SOLVATION OF A LONGIBORNANE-BASED C-3 CARBONYL IN NEIGHBOURING GROUP PARTICIPATION: UNIQUE REACTIVITY OF 12-BROMO-LONGIBORNANE-3,4-DIONE†

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(*Received in UK* 10 *April* 1986)

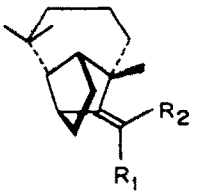
ABSTRACT: When 12-bromolongibornane-3,4-dione 6/12-oxytosyl-longibornane-3,4-dione 15 are exposed to aqueous alkali in acetone, a unique solvolysis-anhydroacetonebenzil type of aldol condensation takes place generating the novel longi-bornane-based cyclopentenone diol 8; the assigned structure has been confirmed by X-ray analysis of its monoacetate 9. Reaction of 6 in dioxane with aqueous alkali results in 12-hydroxylongibornane-3,4-dione 12 while methanolysis of 6 (NaOMe-MeOH) generates the hemiketal 14. The carbonyl solvation concept in neighbouring group participation has been invoked in a common mechanistic pathway for genesis of 8/12/14. On dehydration of 9 with $BF_3.OEt_2$, the heteroannular dienone 25 is formed.

THE CLEAVAGE of cyclic α-diketones/α-ketols with alkaline hydrogen peroxide generating carboxylic acids is a useful reaction[1] which has been exploited[2] by us recently in the transformation of the bridged tricyclic longifolene 1 to the bicyclic azulene 5 via longidione 3 → α-longiforic acid 4. In a proposed synthetic venture, when a similar cleavage was attempted on 12-bromolongibornane-3,4-dione 6, the expected bromodiacid 7 was not formed at all. Instead, structure 8 of the isolated neutral crystalline compound has proved to be quite unprecedented and has been finally confirmed by X-ray analysis.

† NCL Communication No.3915.

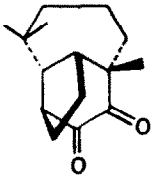
ω-Bromolongifolene 2 (prepared[3] from 1 by action of pyridine perbromide) was exposed to trifluroacetic acid in dichloromethane at room temperature, the resulting trifluoroacetate hydrolysed with alkali and the prodouct oxidized with excess of Jones reagent to furnish[4] the bromodiketone 6. Attempted oxidation of 6 in acetone with alkaline hydrogen peroxide in the usual fashion[5] failed to give any acid but afforded a crystalline, bromine-free, sparingly soluble, high-melting neutral compound ($C_{18}H_{26}O_3$) in good yield. It was thus clear that an unusual reaction in which hydrogen peroxide had not participated but involved only acetone, had taken place. This was proved to be so by omitting hdyrogen peroxide and just treating bromodiketone 6 in acetone with aqueous sodium hydroxide at ambient temperature when the same crystalline compound was again formed (54% yield). In its IR spectrum bands at 3490, 1690, 1585 cm^{-1} indicated hydroxyl and conjugated keto groups; on derivatization under mild conditions, it gave a crystalline hydroxy monoacetate ($C_{20}H_{28}O_4$) and a hydroxymonotosylate ($C_{25}H_{32}O_5S$) suggesting the parent compound to be a diol in which one of the hydroxyl groups is tertiary. On mechanistic considerations (vide infra, Scheme 1), structure 8 was derived for the compound in question which satisfied all the observed spectral/chemical data. At this stage, a direct X-ray diffraction study[6] of the acetylated compound dictated its structure as 9, thus vindicating the proposed mechanistic rationale.

That in 12-bromolongibornane 10, the placement of a keto group at C-3 i.e. 11, confers special reactivity to the molecule in terms of anchimeric assistance by the carbonyl moiety, was borne out by other reactions also. Thus, when bromodiketone 6 in dioxane was stirred with aqueous sodium hydroxide for only three minutes solvolysis was complete affording 12; a similar reaction with 12-bromolongibornane-4-one (devoid of 3-keto group) was a failure. This suggests that a neighbouring group participation of the type indicated in Scheme 1 is not operative for steric reasons in the case of 13 (unfavourable 6-membered ring). On the other hand, exposure of 6 to sodium methoxide in methanol at ambient temperature gave a compound characterized as the cyclic ketal 14. The presence of two carbonyl groups in 12 and only one in 14 was confirmed by their CMR spectral data: two singlets at 205.6 and 217.2 ppm in the former case and only one singlet at 202.1 ppm in the latter. Carbon bearing two oxygen atoms in 14 appeared downfield at 104.4 ppm as a singlet in the off-resonance CMR spectrum of the compound. As expected, the cyclic ketal 14 (which had survived in the alkaline medium of its genesis, unlike in the case of hemiketal 18 which suffers hydrolysis to 12) was smoothly transformed



1 : $R_1 = R_2 = H$

2 : $R_1 = Br$; $R_2 = H$



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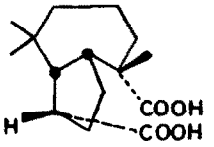

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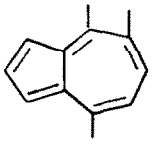

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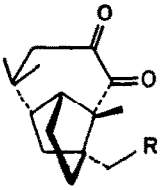
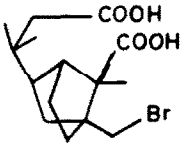


6 : R = Br

12 : R = OH

15 : R = OTs



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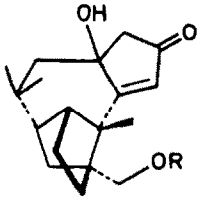
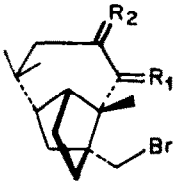


8 : R = H

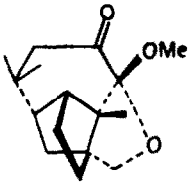
9 : R = Ac



10 : $R_1 = R_2 = H$, H

11 : $R_1 = O$; $R_2 = H$, H

13 : $R_1 = H$, H ; $R_2 = O$



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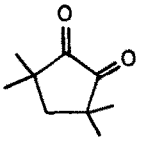

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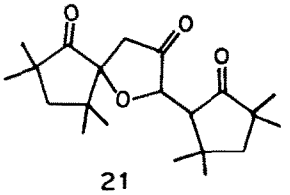

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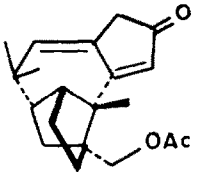

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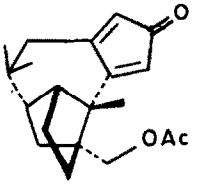

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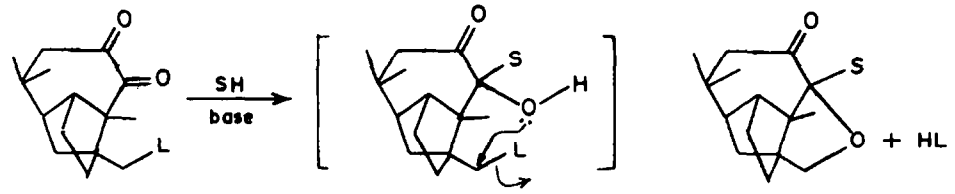
to 12 on exposure to an acid (p-TsOH). The formation of 8/12/14 can be rationalized by a common mechanism based on the carbonyl solvation[7] concept in neighbouring group participation[8]. While generation of 12/14 involves precedented hydroxylic solvents (H_2O/MeOH), the participation of a nonhydroxylic ketonic solvent (Me_2CO) is an interesting new feature of the present work. The solvated species 16 (S=OMe/OH/CH_2COCH_3), undergoes neighbouring group participation generating 14/18/17 which then give the final isolated products as shown in Scheme 1. While 14 remains unchanged, 18 gets hydrolyzed to 12. In the alkaline medium, the aldol reactivity of acetone residue in 17 is responsible for the observed product 8 as shown in Scheme 1 and also discussed below.

In base-catalyzed aldol condensation, enolizable[9] aliphatic and alicyclic 1,2-dicarbonyl compounds have been shown to furnish 1:2 adducts with a monoketone; non-enolizable[10] 1,2-dicarbonyl compounds under similar conditions generally afford 1:1 adducts. A 1-oxaspiro [4.4] nonane derivative 21 (formed through a 1:2 aldol-type adduct from reaction of 3,3,5,5-tetramethylcyclopentane-1,2-dione 20 with acetone in alkaline medium) reported[11] recently is however quite unusual among aldol-type adducts generated via reactions of enolizable or non-enolizable 1,2-diketones in that two molecules of the diketone are utilized in the formation of 21.

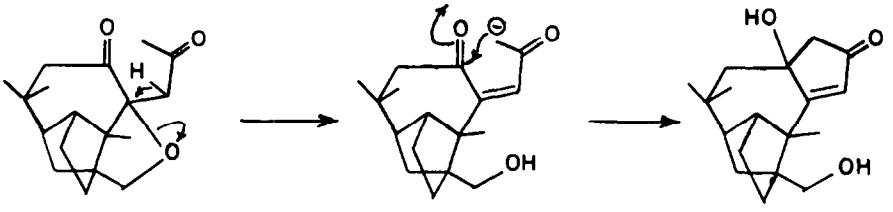
Base-catalyzed aldol[12] condensation of the aromatic 1,2-diketone, benzil 22, with acetone is known[13] to yield the interesting cyclopentenone ketol, anhydroacetonebenzil 23, which does not dehydrate to the stable cyclopentadienone[14] 24 (Scheme 2). The anhydroacetonebenzil type of bisaldol reaction now observed in the case of the alicyclic bromodiketone 6 is however unprecedented in non-aromatic α-diketone chemistry; the special reactivity observed in the case of 6 must be attributed to the presence of a sterically well-disposed bromine at C-12 in the compact longibornane framework functioning as a good leaving group in a highly efficient neighbouring group participation by the acetone-solvated C-3 carbonyl moiety (Scheme 1). When the tosylate 15 was exposed to acetone in aqueous alkali, a mechanistically similar reaction took place resulting in the isolation of the same product i.e. 8. Dehydration of the tertiary hydroxyl in 9 with BF_3-etherate in refluxing benzene gave a dienone for which the heteroannular structure 25 (and not 26) has been assigned on the basis of its PMR signal at δ 2.93 - a 2H singlet assignable to a methylene sandwiched between a double bond and a carbonyl group, present only in 25; the non-formation of cross-conjugated



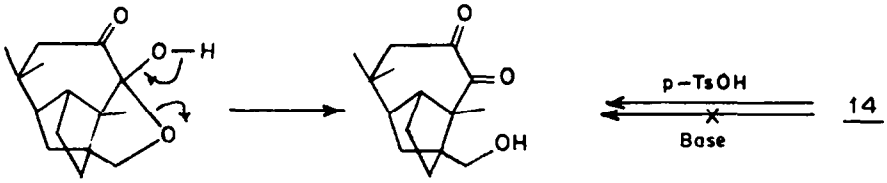
6 : L = Br
15 : L = OTs

16

17 : S = CH_2COCH_3
18 : S = OH
14 : S = OMe

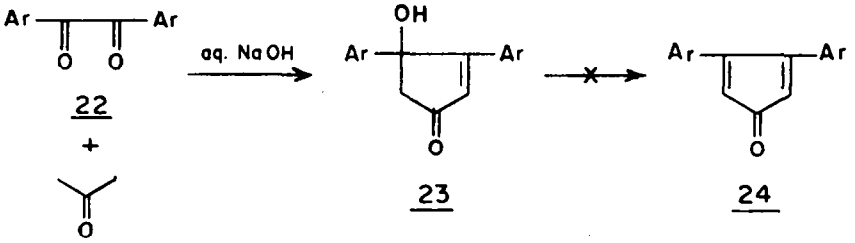


17 19 8



18 12

SCHEME – 1



22 + 23 24

SCHEME – 2

dienone 26 from 9 has analogy in 23 not dehydrating to 24.

EXPERIMENTAL

Light petroleum refers to fraction b.p.60-80°. Solvents extracts were dried over anhydrous Na_2SO_4. Melting and boiling points are uncorrected. IR spectrum (ν_{max} in cm^{-1} were recorded as smears (liquids) or nujol mulls (solids on a Pye-Unicam SP-3 IR spectrometer. PMR spectra were obtained on a Varian T-60/FT-80A/Brucker WH-90 spectrometer. CMR spectra were recorded on the Brucker instrument and mass spectra on a CEC spectrometer model 21-110B, using an ionising voltage of 70 eV and a direct inlet system. The X-ray data for compound 9 were collected on a Enraf-Nonius CAD4-11M diffractometer.

Action of alkaline H_2O_2 on bromodiketone 6 in acetone: Formation of 8

To a stirred mixture of 6 (5 g), acetone (50 ml) and 2N aqueous NaOH (50 ml) was added dropwise 30% H_2O_2 (15 ml) during 10 min. The mixture was further stirred for 4 hr, diluted with water, extracted with ethyl acetate, washed with brine, dried, solvent removed and the solid residue recrystallized from ethyl acetate to furnish colourless prisms of the cyclopentenone diol 8, m.p. 225° (3.1 g, 66%). IR (nujol): 3490, 3300, 1690, 1585, 1020. PMR(pyridine). δ 5.68 (s, 1H, C=CH-C=O); 4.33 (unresolved q, 2H, CH_2OH); 3.20 (s, 2H, O=C-CH_2-C-OH); 1.98 (q, 2H, CH_2-C-OH, J=16 Hz); 0.73 (s, 9H, three tertiary methyls). MS: m/z 290 (M^+). (Found: C, 74.9; H, 9.1. $C_{18}H_{26}O_3$ requires: C, 74.9; H, 9.0%).

The aqueous alkaline portion, on acidification and extraction, gave only a negligible amount of acid.

Action of aqueous NaOH-acetone on 6: Formation of 8

To a stirred solution of 6 (2 g) in acetone (20 ml) was added 2N aqueous NaOH (20 ml) and stirred for 4 hr at room temperature. The mixture was diluted with water, extracted with ethyl acetate, washed with brine, dried, solvent removed and the crude solid recrystallized from ethyl acetate to furnish pure 8 (identified by m.p., m.m.p., IR and PMR).

On acetylation of 8 with acetic anhydride-pyridine at 28°, the monoacetate 9 crystallized from methanol in colourless needles, m.p. 187°. X-ray: Data were collected by using the $\omega/2\theta$ scan technique upto $2\theta = 48°$. Three standard reflections were monitored after every 2000 seconds of exposure time to check for crystal decay, if any. The structure was refined using full matrix least square technique with anisotropic temperature factors for non-hydrogen atoms. Hydrogen atoms were fixed based on stereochemical considerations and their positions verified by difference Fourier synthesis. UV: λ_{max} 235 nm (MeOH, 11590). IR (nujol): 3430, 1730, 1685, 1585, 1250, 1030. PMR (CCl_4):δ5.95 (s, 1H, C=CH-C=O);4.16 (q, 2H, CH_2OAc, J=10 Hz); 2.93 (C-OH, does not exchange with D_2O); 2.53 (s, 2H, O=C-CH_2-C-OH); 2.10 (s, 3H, OCOCH_3); 1.30, 1.26, 0.80 (3H each, tertiary Me singlets). MS: m/z 332 (M^+). (Found: C, 72.5; H, 8.5. $C_{20}H_{28}O_4$ requires: C, 72.3; H, 8.5%).

On tosylation of 8 (R=H) with tosyl chloride in pyridine at 0°, the monotosylate 8 (R=Ts) recrystallized from benzene-light petroleum in colourless microprisms, m.p. 163°. IR (nujol): 3440, 1685, 1580, 1195, 1170, 850. PMR ($CDCl_3$):δ7.90, 7.45 (two d, 2H each, ar-H, J=9 Hz); 5.62 (s, 1H, C=CH-C=O); 4.11 (s, 2H, CHOTs); 2.48 (s, 3H, ar-CH_3); 2.47 (bs, 2H, HO-C-CH_2-C=O); 1.25, 1.16, 0.73 (three tertiary Me singlets). (Found: C, 67.1; H, 7.3. $C_{25}H_{32}O_5S$ requires: C, 67.6; H, 7.3%).

Dehydration of 9 with $BF_3.OEt_2$; Formation of 25

A mixture of 9 (1 g), dry benzene (50 ml) and $BF_3.OEt_2$ (3 drops) was refluxed on a waterbath for 3 hr, washed with 5% aqueous $NaHCO_3$, brine, dried, solvent removed and the crude solid recrystallized from light petroleum to furnish colourless needles of 25, m.p. 102° (0.39 g, 41%). UV: λ_{max} 293 nm (MeOH; ε, 18140). IR (nujol): 1730, 1690, 1550, 1245. PMR (CCl_4): δ 6.3 (s, 1H, HC=C-C=CH-C=O); 5.33 (bs, 1H, C=CH-C=O); 4.10

(s, 2H, CH_2-OAc), 2.93 (s, 2H, C=C-CH_2-C=O); 1.96 (s, 3H, OCO-CH_3); 1.26, 1.20, 1.00 (three tertiary Me singlets). Off-resonance CMR ($CDCl_3$; in ppm); 204.7 (s), 177.2 (s), 171. 1 (s), 136.7 (d), 134.2 (d), 133.5 (s). (Found: C, 76.2; H, 8.5. $C_{20}H_{26}O_3$ requires: C, 76.4; H, 8.3%).

Solvolysis of 6 with aqueous NaOH: Formation of 12

To a stirred solution of 6 (1 g) in dioxane (10 ml) was added 2N aqueous NaOH (10 ml)at room temperature. After 3 min, the mixture was diluted with water, extracted with ethyl acetate, washed with brine, dried, solvent removed and the crude solid recrystallized from light petroleum to afford colourless crystals of 12, m.p. 83-84° (0.5 g, 62%). IR (nujol): 3400, 1700, 1020. PMR (CCl_4): δ 3.68 (q, 2H, CH_2-OH, J=11 Hz); 2.38 (q, 2H, CH_2-CO, J=12 Hz); 1.16 x 2, 1.06 (three tertiary methyl singlets). Off-resonance CMR ($CDCl_3$; in ppm); 205.6 and 217.2 (two singlets; 2 x C=O); 63.0 (t, CH_2OH). MS: m/z 250 (M^+). (Found: C, 71.7; H, 9.0. $C_{15}H_{22}O_3$ requires: C, 72.0; H, 8.9%).

On tosylation of 12 and recrystallization from benzene-light petroleum 15 was obtained as colourless needles, m.p.104°. PMR (CCl_4): δ 7.55, 7.13 (two d, 2H each, ar-H, J=8 Hz); 4.03 (bs, 2H, CH_2OTs); 2.43 (s, 3H, ar-CH_3); 1.06 (3H x 2), 0.90 (three tertiary methyl singlets). (Found: C, 64.7; H, 6.8; $C_{22}H_{28}O_5S$ requires: C, 65.3; H, 7.0%).

The tosylate 15 (0.5 g) in acetone (5 ml) was stirred with 2N aqueous NaOH (5 ml) at room temp for 4 hr. The isolated product, after acetylation, was identified as 9 (m.p., m.mp, IR/PMR).

Sovolysis of 6 with NaOMe in MeOH: Formation of 14

To a stirred solution of NaOMe (50 mg) in dry MeOH (15 ml) was added bromodiketone 6 (1 g) and stirred at room temperature for 15 min. The mixture was diluted with water, extracted with ethyl acetate, washed with brine, dried, solvent removed and the residue distilled to furnish 14 as a colourless liquid b.p. 190°(bath)/1 mm (0.75 g, 89%) which solidified slowly; m.p. 86-88° (light peteroleum). IR (nujol): 1720, 1080, 1020, 990. PMR (CCl_4): δ 3.66 (s, 2H, CH_2O-C); 3.08 (s, 3H, OCH_3); 2.39 (q, 2H, CH_2-CO, J=10 Hz); 1.10 x 2, 0.86 (three tertiary methyl singelts). Off-resonance CMR ($CDCl_3$; in ppm): 202.1 (s, 1 x C=O); 104.4 (s, O-C-OMe); 69.1 (s, -CH_2-O-C). MS: m/z 264 (M^+). (Found: C, 72.0; H, 9.2. $C_{16}H_{24}O_3$ requires: C, 72.7; H, 9.2%).

Action of p-TsOH on cyclic ketal 14: Formation of 12

A mixture of 14 (0.2 g), p-TsOH (0.1 g) and water (5 ml) was stirred at room temperature (17 hr). Usual workup with ether gave a crude solid which, after recrystallisation from light petroleum, was identified as 12 (m.p., mixed m.p., IR and PMR).

Acknowledgement

Financial assistance from CSIR (New Delhi) in the form of a contingency grant and a Senior Research Fellowship (to SPV) is gratefully acknowledged. Thanks are also due to Dr. T.N. Guru Row of this laboratory for the X-ray structure analysis of compound 9.

REFERENCES

1. a) E. Kyburz, B. Riniker, H.R. Schenk, H. Heusser and O. Jeger, Helv. Chem. Acta 36, 1891 (1953).

b) Y. Ogata, Y. Sawaki and M. Shiroyama, J.Org.Chem. 42, 4061 (1977).

2. R.P. Deshpande, P.K. Jadhav and U.R. Nayak, Indian J.Chem. 17B, 266 (1979).

3. S.N. Suryawanshi and U.R. Nayak, Indian J.Chem. 17B, 304 (1979).

4. a) G. Mehta and S.K. Kapoor, J.Org.Chem. 39, 2618 (1974).

4. b) G. Mehta, S.K. Kapoor, T.N. Guru Row and K. Venkatesan, Tetrahedron Lett. 2653 (1974).

c) S.P. Vaidya, S.N. Suryawanshi, P.K. Jadhav and U.R. Nayak, Indian J.Chem. (in press).

5. R.P. Deshpande, S.N. Suryawanshi and U.R. Nayak, Indian J.Chem., 17B, 617 (1979).

6. K.R. Acharya, S.S. Tavale and T.N. Guru Row, Proc.Indian Acad.Sci. (Chem.Sci.) 93, 271 (1984).

7. H. Tanida, T. Nishiya and T. Irie, J.Org.Chem. 44, 3337 (1979).

8. a) B. Capon and S.P. McManus "Neighbouring Group Participation" Vol. 1, Plenum Press, New York (1976).

b) W.J. le Noble, "Highlights of Organic Chemistry", p.690, Marcel Dekker, New York (1974).

9. S. Yang-Lan, M. Muller-Johnson, J. Oelhdrich, D. Wichman, J.M. Cook and U.J. Weiss , J.Org.Chem. 41, 4053 (1976).

10. C.F.H. Allen and J.A. VanAllan, J.Org.Chem. 17, 845 (1952).

11. R. Kivekas and T. Simonen, Acta Chem. Scand. B, 33, 627 (1979).

12. a) A.T. Nielsen and W.J. Houlihan, Organic Reactions 16, 1 (1968).

b) T. Mukaiyama, Organic Reactions 28, 203 (1982).

13. a) F.R. Japp and C.I. Burton, J.Chem.Soc. 51, 431 (1887).

b) F.R. Japp and T.S. Murray, J.Chem.Soc. 71, 144 (1897).

c) C.F.H. Allen and J.A. VanAllan, J.Am.Chem.Soc. 72, 5165 (1950).

14, M.A. Ogliaruso, M.G. Romanelli and E.I. Becker, Chem.Rev. 65, 261 (1965).