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ALICYCLIC COMPOUNDS—III

ACTION OF BASE ON BICYCLIC KETOTOSYLATES: A NOVEL SOLVOLYTIC REARRANGEMENT TO BICYCLO-3:2:0-HEPTENONE DERIVATIVE

P. C. MUKHARJI and A. N. GANGULY*

Department of Chemistry, Presidency College, Calcutta-12, India

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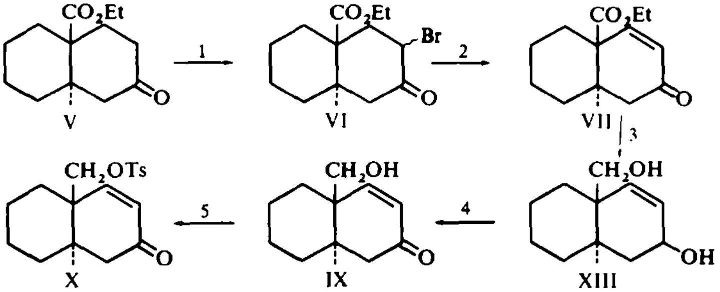
Abstract—The action of $KOBu^t$ on 10-hydromethyl-$\Delta^{3,4}$-2-octalone tosylate (X) furnished the ketone (XVI) containing a bicyclo[3.2.0]heptanone moiety through solvolytic rearrangement of the homoallylic system. The isomeric 10-hydromethyl-$\Delta^{1,9}$-2-octalone tosylate (XX) however, gave the tricyclic ketone (XXI) without rearrangement.†

As DESCRIBED,[1] we found that the *cis* and *trans* decalone tosylates (I and II) yield the corresponding tricyclic ketones (III and IV) through intramolecular displacement in the presence of $KOBu^t$ in hot Bu^tOH. No evidence of fragmentation to a monocyclic dienone could be obtained.

The action of $KOBu^t$ on the octalone tolylate (X) was examined in the expectation that this may suffer fragmentation to the monocyclic trienone (XII) in preference to an intramolecular displacement to the tricyclic ketone (XI) which contains a highly strained bicyclo[3.1.1]heptenone moiety.[1,2]



1. Br_2–dry ether; 2. Collidine; 3. LAH; 4. MnO_2; 5. Tosyl chloride–pyridine.

FIG. 1

The tosylate was prepared as shown in Fig. 1. It reacted with $KOBu^t$ in hot Bu^tOH at a rate faster than the analogous saturated tosylate to yield a fragrant ketone "A"

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(TLC homogeneous) in ca. 50% yield. It did not exhibit any UV absorption maxima in the region 220–260 mμ confirming absence of a conjugated chromophore. It had, however, a low intensity band at 296 mμ and its IR spectrum exhibited a strong CO band at 1725 cm^{-1} (5·79 μ). Catalytic reduction afforded a dihydroketone (ν_{max} 1728 cm^{-1}; λ_{max} 295 mμ) confirming the presence of one double bond in the ketone "A".

Oxidation of the dihydroketone with perbenzoic acid[1,3] followed by successive saponification, esterification and chromic acid oxidation gave a ketoester which showed IR absorption bands at 1775 cm^{-1} (5·63 μ) and 1730 cm^{-1} (5·76 μ) characteristic of the cyclobutanone esters described.[1] The dihydroketone must, therefore, contain the grouping XIV which alone is compatible with the above degradation to a cyclobutanone ester.

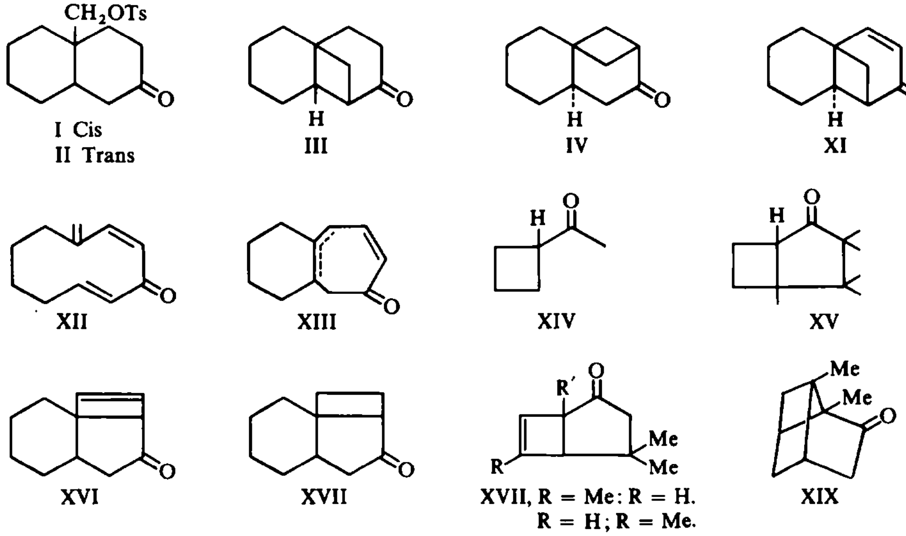

FIG. 2

From the UV and IR spectra of the ketone "A" and its dihydroderivative, the structure XI, XII and XIII can be readily eliminated for "A". The IR CO band of the ketone "A" and its dihydro derivative combined with the low intensity maxima at 295 mμ in their UV spectra is strongly indicative of the presence of a cyclopentanone[4] ring. In fact their CO absorption bands compare favourably with the band at 1730 cm^{-1} reported for the bicyclo[3.2.0]heptenones[5a] (XVIII) and at 1727 cm^{-1} for carvone-camphor (XIX),[5b] where a cyclopentanone is similarly conjugated with a cyclobutane ring.

The spectral considerations and the transformations thus point to the presence of the part structure XV in the dihydroketone. The formation of its precursor, the nonconjugated unsaturated ketone "A" from the octalone tosylate (X) therefore involves a molecular rearrangement with ring contraction during formation of the cyclobutane ring.

Mechanistic reasonings involving the solvolytic rearrangement of the neopentyl type homoallylic tosylate (X) lead to the tentative formulation (XVI) for the unsaturated ketone "A" and (XVII) and its dihydro derivative. These formulations are in agreement with the observed spectral and chemical properties of the compounds. The formation of the unsaturated ketone "A" can be rationalized on sound mechanistic grounds involving Wagner type rearrangements during the solvolysis of a neopentyl homoallylic tosylate.

The solvolytic rearrangements of neopentyl homallylic tosylates have been described.[6–8] In the octalone tosylate (X) the presence of a CO group, however, considerably alters the character of this homoallylic system compared to the example reported. Here the carbonium ion intermediate corresponding to the cyclopropane carbinyl carbonium ion would involve the energetically unfavourable intermediate (1) with a carbonium ion at the α-position of a CO group and the formation of such an intermediate cannot, therefore, be involved in stabilising the neopentyl carbonium ion. On the contrary the π-electrons of the double bond can assist in the solvolysis to give the cyclobutonium carbonium ion (2) where the above unfavourable situation is not present. The observed formation of such cyclobutyl ketones in high yield from the corresponding decalone tosylates[1] demonstrates that such a cyclobutonium ion is sterically feasible. Steric and electronic factors would thus favour the intermediate (2). Subsequent Wagner type rearrangement of this species can then lead to the final product (XVI) as depicted in Fig. 3.

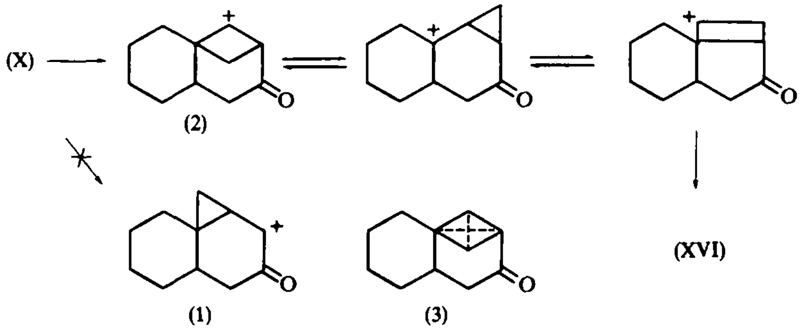

Fig. 3

Whether the rearrangement proceeds through a rapidly equilibriating set of classical carbonium ions as depicted in Fig. 3 or involves a nonclassical tricyclobutonium ion[9] (3) is unknown, but the proposed intermediates are all sterically and electronically feasible.

The stereochemistry of the ketone (XVII) has not been determined. The *cis* ring junction is anticipated from its genesis.

The formation of the bicyclo[3.2.0]heptenone skeleton through a solvolytic rearrangement is novel and provides a new entry to this system which so far have been obtained through photochemical transformation of cycloheptadienones.[10]

In view of the above results, we examined the isomeric tosylate (XX)[4b] which under identical conditions gave the unsaturated ketone (XXI) derived through intramolecular alkylation at the vinylogous γ-position of the conjugated CO group without any structural rearrangement.

The unsaturated ketone (XXI) formed a disemicarbazone and with 2,4-dinitrophenylhydrazine furnished a derivative that analysed for $C_{23}H_{24}N_8O_8$ corresponding to a *bis* product (XXV).

The formation of the unsaturated ketone (XXI) is of interest. Intermolecular alkylation of αβ-unsaturated cyclic ketones are known to occur exclusively at the α-position giving αα-dialkyl derivatives with shift of the double bond in presence of excess of reagents.[11]

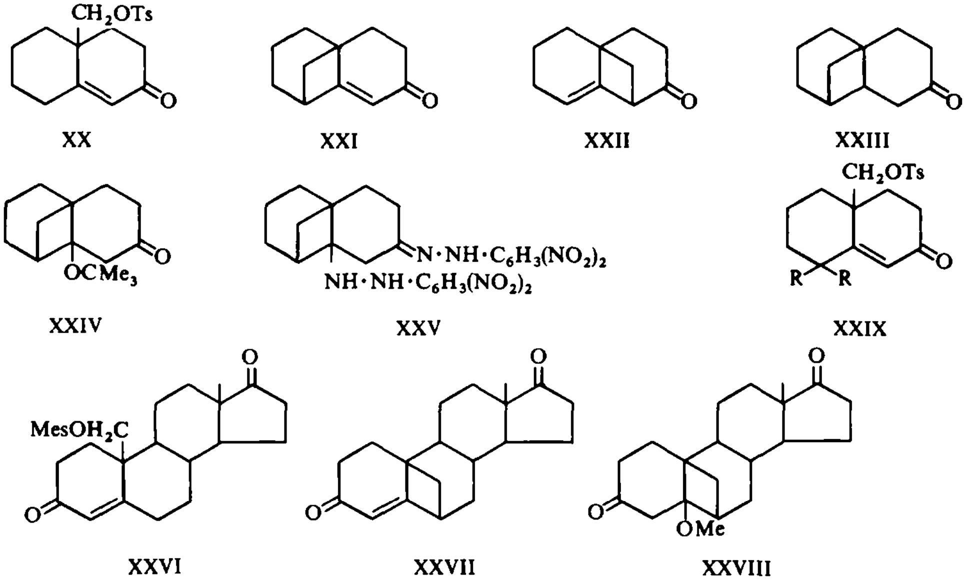

FIG. 4

Our results in the bicyclic series find a parallel in the work of Bonet *et al.*[12] They found that the steroid mesylate (XXVI) in presence of NaOMe gave the pentacyclic ketone (XXVII) contaminated with a small amount of the methanol adduct (XXVIII). Of particular interest, is the ease of addition[12] of the elements of alcohol on the pentacyclic ketone (XXVI). In this context the formation of the *bis* dinitrophenylhydrazone (XXV) is not unusual. The presence of a weak band at 5·84 μ in the IR spectrum of our product which indicates the presence of traces of a saturated ketone might conceivably be due to the presence of the alcohol adduct XXIV rather than the isomer XXII.

The different behaviour of the two isomeric homoallylic tosylates (X and XX) is remarkable. Whereas the former gave a product involving molecular rearrangement, the latter gave one with an unrearranged skeleton through straightforward intramolecular alkylation. Presumably in XX solvolysis involves the heteroannular enolate ion or something equivalent to it which collapses to the tricyclic conjugated ketone (XXI) in preference to the isomeric non-conjugated ketone (XXII) because of the increased resonance energy of the former. In X the somewhat more strained homoannular enolate ion (or its equivalent) cannot effectively participate in the like manner and it is probably this difference which accounts for the observed results. It thus seems logical to expect that tosylates of the type XXIX where the γ-C atom is fully substituted would undergo solvolytic rearrangement of the type exhibited by X. Our work in this direction is in progress and will be reported later.

EXPERIMENTAL

The m.ps and b.ps are uncorrected. Solvent extracts were dried over Na_2SO_4. Alumina used for chromatography was E. Merck aluminium oxide standardized according to Brockmann. Pet. ether indicates the fraction, b.p. 40–60°. The UV spectra were taken in 95% EtOH on Unicam Spectrophotometer SP 500. The IR spectra were taken in thin films unless otherwise stated in Perkin–Elmer Infrachord model 137 E or model 237.

10-Ethoxycarbonyl-2-oxo-Δ^{3-4}*-*trans*-octalin* (VII). Dry Br_2 (7·1 g) was added with swirling to a soln of V (9 g) in dry ether (300 ml) cooled in ice. The mixture was well chilled and the crystalline VI (8 g) was filtered off. The ether soln was washed acid free, dried and concentrated to yield an additional quantity of the bromoketone (1·5 g). Two crystallisations from pet. ether gave the pure material, m.p. 110°. (Found: C, 51·54; H, 6·07. $C_{13}H_{19}O_3Br$ requires: C, 51·48; H, 6·27%).

The above bromoketone (12·5 g) was heated under reflux (170–180°) with 2.4.6-collidine (16·3 ml) under N_2 for 45 min.[13] The mixture was cooled, decomposed with iced HCl and extracted with ether. Usual work up gave VII (6 g) b.p. 125°/2·5 mm, λ_{max} 5·76 and 5·9 μ; λ_{max} 222 mμ (ε, 9600). The *2,4-dinitrophenylhydrazone* was crystallized from EtOH–EtOAc; brick red, m.p. 190°, $\lambda_{max}^{CHCl_3}$ 374 mμ (ε, 25,400). (Found: N, 14·07. $C_{19}H_{22}N_4O_6$ requires: N, 13·93%). The *semicarbazone* crystallized from EtOH m.p. 208°. (Found: C, 59·91; H, 7·11. $C_{14}H_{21}N_3O_3$ requires: C, 60·21; H, 7·52%).

10-Hydroxymethyl-2-hydroxy-Δ^{3-4}*-*trans*-decalin* (VIII). The octalone VII (6·6 g) was stirred with LAH (1·8 g) in dry ether (250 ml) at room temp for 24 hr and decomposed with saturated Na_2SO_4aq. The ether layer was separated, dried and concentrated. The residue after trituration with pet. ether afforded the crystalline diol (4·5 g) which after two crystallizations from acetone–pet. ether had m.p. 126°. (Found: C, 72·77; H, 9·73. $C_{11}H_{18}O_2$ requires: C, 72·93; H, 9·39%).

10-Hydroxymethyl-2-oxo-Δ^{3-4}*-*trans*-decalin* (IX). The diol VIII (9·39 g) in $CHCl_3$ (900 ml) was stirred for 12 hr at room temp with freshly precipitated MnO_2 (70 g)[14] and then worked up in the usual way to give IX (6·9 g) as a viscous oil, b.p. 141°/0·3 mm, λ_{max} 228 mμ (ε, 12,000), λ_{max} 2·6 and 6·02 μ. The *2,4-dinitrophenylhydrazone* was crystallized from EtOH–$CHCl_3$: deep red, m.p. 164°, $\lambda_{max}^{CHCl_3}$ 380 mμ (ε, 29,400). (Found: C, 56·89 H, 5·58. $C_{17}H_{20}N_4O_5$ requires: C, 56·66; H, 5·55%).

Oxidation of this allylic alcohol was found to be extremely sensitive to the quality of MnO_2 as well as to the period of contact with the catalyst. Prolonged contact resulted in an inferior yield of a product which showed weak IR absorption band at 5·8 μ that presumably could be due to oxidation of the homoallylic alcohol.

10. *Hydroxymethyl-2-oxo-*Δ^{3-4}*-*trans*-octalin tosylate* (X). A soln of X (5 g) in anhyd pyridine (9 ml) was treated at −5° with *p*-toluenesulphonyl chloride (6 g) in anhyd pyridine (9 ml) and left at 5° for 48 hrs after which it was worked up in the usual way to give XI (8 g) as a viscous oil which solidified on keeping. Trituration with pet. ether afforded a pale yellow crystalline solid, m.p. 72–74°, λ_{max} 227 mμ (ε, 25,700). This decomposed on storage and was used as such for the next step.

5-Oxo-tricyclo($5.4.0^{1-4}.0^{1-7}$)*undecene* (XVI). The ketotosylate X (16 g) in Bu^{t}OH (200 ml) was added with stirring to the warm KOBu^t (from 1·9 g K and 600 ml Bu^{t}OH) under N_2, and the mixture refluxed on a steam-bath for 4½ hr. It was then cooled, diluted with water and extracted with ether. Usual work up left a brown oil (7 g) which was dissolved in the minimum quantity of pet. ether and left overnight at 5°. The clear soln was separated from the precipitated tar, concentrated and the residue chromatographed over alumina (100 g). Pet. ether eluted a mobile oil which on distillation afforded a colourless liquid (2·5 g) with a very characteristic smell, b.p. 88–92°/0·4 mm, λ_{max} 296 mμ (small inflection), ν_{max} 1725 cm^{-1} (5·79 μ). It formed an oily red 2,4-dinitrophenylhydrazone which was not amenable to easy crystallization.

5-Oxo-tricyclo[$5.4.0^{1-4}.0^{1-7}$]*undecane* (XVII). The unsaturated ketone XVI (1·0 g) in EtOH (20 ml) over 10% Pd on C (0·1 g) absorbed one mole equiv of H_2 at room temp and atm press. Usual work up furnished the saturated ketone (0·9 g), b.p. 95–100° (bath)/0·5 mm; λ_{max} 295 mμ (ε, 45), ν_{max} 1728 cm^{-1} (5·78 μ). (Found: C, 79·97; H, 9·52. $C_{11}H_{16}O$ requires: C, 80·48; H, 9·75%). The *2,4-dinitrophenylhydrazone* was crystallized from MeOH–EtOAc; yellow, m.p. 204°. (Found: C, 59·34; H, 5·92. $C_{17}H_{20}N_4O_4$ requires: C, 59·30; H, 5·81%).

4-Methoxycarbonylmethyl-3-oxo-spiro[5.3]*nonane*. A soln of XVII (1.1 g) in dry $CHCl_3$ (22 ml) was treated at 0° with perbenzoic acid (1·1 g) in dry $CHCl_3$ (22 ml) and a trace of PTSA. The mixture was left at 5° for 15 days, after which it was worked up to give the crude lactone which was saponified with hot 0·5 N methanolic KOH. Usual work up gave an acid which was esterified with diazomethane to furnish hydroxyester (0·55 g) which anhyd pyridine (8 ml) was oxidized with pyridine CrO_3 couples prepared from CrO_3 (0·8 g) and anhyd pyridine (6 ml) at room temp overnight. Usual work up furnished the cyclobutanone ester (0·15 g), b.p. 130–135° (bath)/0·3 mm, ν_{max} 1775 and 1735 cm^{-1}. The 2,4-*dinitrophenylhydrazone* was crystallized from MeOH; yellow, m.p. 178°. (Found: C, 55·68; H, 5·30. $C_{18}H_{22}N_4O_6$ requires: C, 55·38; H, 5·64%).

Better results were obtained by titrimetric oxidation of the hydroxyester with Jones reagent.[15] The hydroxyester (0·8 g) in acetone cooled in ice was oxidized by dropwise addition of the chromic acid soln until the yellow colour persisted, and worked up to give the ketoester (0·4 g) whose IR spectrum was identical in all respects with the above product.

4-*Oxo-tricyclo*[4.4.1$^{1-7}$.0]*undec-5-ene* (XXI). The ketotosylate[14b] XX (5 g) was added with stirring to warm KOBu^t (from 0·6 g K and 275 ml Bu^{t}OH) under N_2, and the mixture was refluxed on a steam bath for 6 hr. Usual work up gave XXI (1 g) b.p. 125°/9 mm, λ_{max} 244 mμ (ε, 13,200), λ_{max} 6·0 μ and inflection at 5·84 μ. The 2,4-*dinitrophenylhydrazone*(*bis*) was crystallized from EtOH–$CHCl_3$; pale yellow, m.p. 196°, $\lambda_{max}^{CHCl_3}$ 352 mμ (ε, 22,700). (Found: C, 51·29; H, 4·14. $C_{23}H_{24}N_8O_8$ requires: C, 51·11; H, 4·44%). The *semicarbazone* was insoluble in alcohol and other common solvents. It was repeatedly boiled with EtOH and filtered hot to remove the soluble impurities to get a pure specimen, m.p. 226°. (Found: C, 53·29; H, 7·04. $C_{13}H_{22}N_6O_2$ requires: C, 53·06; H, 7·49%).

4-*Oxo-tricyclo*[4.4.1$^{1-7}$.0]*undecane* (XXIII). The unsaturated ketone XXIV (0·85 g) in EtOH (15 ml) over 10% Pd on C (0·1 g) absorbed 1 mole equiv of H_2 at room temp and atm press during 30 min. Usual work up furnished XXV (0·7 g), b.p. 140° (bath)/10 mm, λ_{max} 282 mμ (ε, 31), λ_{max} 5·84 μ. The 2,4-*dinitrophenylhydrazone* was crystallized from EtOH–$CHCl_3$; yellow; m.p. 122°, $\lambda_{max}^{CHCl_3}$ 368 mμ (ε, 23,700). (Found: C, 58·97; H, 5·77. $C_{17}H_{20}N_4O_4$ requires: C, 59·30; H, 5·81%). The *semicarbazone* crystallized from MeOH had m.p. 194°. (Found: N, 18·81. $C_{12}H_{19}N_3O$ requires: N, 19·00%).

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