# Bamford–Stevens Reaction of (+)-1,3,3-Trimethyl-2-oxabicyclo[2.2.2]-octan-6-one p-Tolylsulphonylhydrazone

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The Bamford–Stevens reaction of (+)-1,3,3-trimethyl-2-oxabicyclo[2.2.2]octan-6-one tosylhydrazone in protic conditions (sodium dissolved in ethylene glycol) at 115—120 or 135—140° gave 1-[3-(2-hydroxyisopropyl)cyclopentyl]ethanone as the major product, together with pinolone and pinol. In aprotic conditions (sodium methoxide in diglyme or DMF) at 135—140°, the major component was the Δ¹-1.2-diazetine (12), followed by the azine of (+)-1,3,3-trimethyl-2-oxabicyclo[2.2.2]octan-6-one, transoid and cisoid 1,3,3-trimethyl-6-(1,3,3-trimethyl-2-oxabicyclo[2.2.2]oct-6-ylidene)-2-oxabicyclo[2.2.2]octane, 1,3,3-trimethyl-2-oxabicyclo[2.2.2]oct-5-ene, and p-cymene. Besides these products, 1-[3-(2-hydroxyisopropyl)cyclopentyl]ethanone was found with diglyme, and pinol with DMF. The structures of the new compounds reported are consistent with u.v., i.r., n.m.r., and mass spectral data.

THE basic decomposition of tosylhydrazones of aliphatic ketones (Bamford–Stevens reaction) is sometimes a useful method for the synthesis of alkenes,[1] but very often different products are obtained by carrying out the reaction in protic or aprotic media.[2]

In pursuing our work on rearrangements of 1,8-

(12%) and pinol (6) (2%), whereas the unknown polar products (probably arising from interaction with the solvent) were 10% overall. At 135—140° there was a decrease in the yield of (8) (53%) and (7) (7%), and an increase in that of (6) (31%), whereas the amount of unknown polar products was nearly constant (9%).



(1)

a; X = NNHSO₂C₆H₄CH₃ -4
b; X = O

(2a)        (2b)        (2c)

(3)        (4)        (5)

(6)        (7)        (8)        (9)
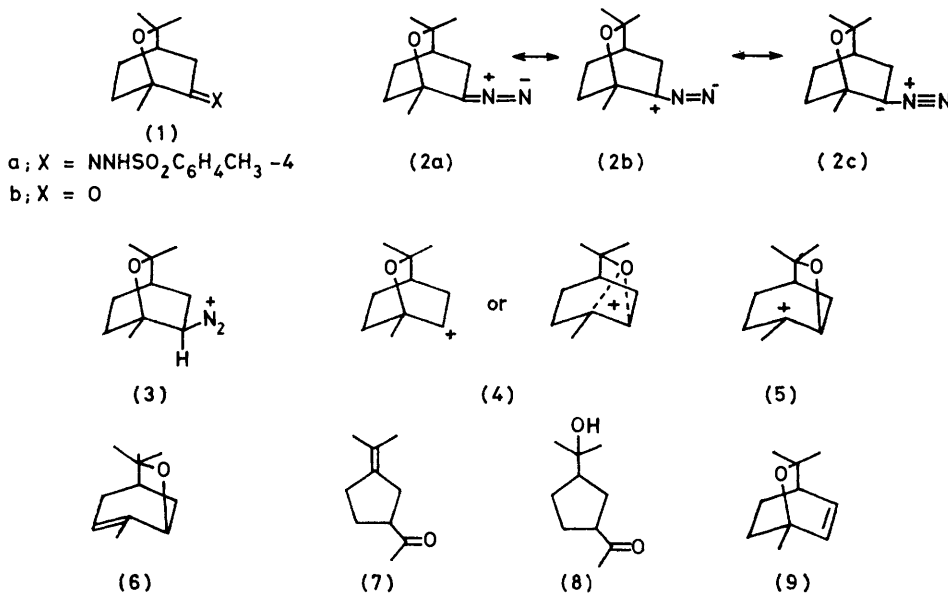
cineole derivatives,[3,4] we decided to try the Bamford–Stevens reaction on (+)-1,3,3-trimethyl-2-oxabicyclo-[2.2.2]octan-6-one tosylhydrazone (1a), both in ethylene glycol containing previously dissolved sodium (protic conditions) and in diglyme (diethylene glycol dimethyl ether) or DMF (NN-dimethylformamide) containing sodium methoxide (aprotic conditions). In the case of the protic medium, the reaction was carried out for 1 h over two different temperature ranges, 115—120 and 135—140°, with an excess of base.

At 115—120° the major component of the reaction mixture (g.l.c.) was 1-[3-(2-hydroxyisopropyl)cyclo-pentyl]ethanone (8) (76%), followed by pinolone (7)

These results can be interpreted as due to protonation of the intermediate diazo compound (2c) from the less hindered endo-side to give the exo-diazonium cation (3), whose stereospecific decomposition is known to give exclusively the cyclopentane derivative (8);[4] in the present circumstance, some pinolone (7) was also formed by basic deprotonation of the common carbocation intermediate. It is noteworthy that (7) plus (8) account for 88% of all products found in the reaction mixture.

The rise of temperature to 135—140° probably increased the decomposition of (3) prior to the rear attack by C-7, thus giving rise to more carbocation (4) which can rearrange to (5), the parent ion of (6). Thus the results

obtained in the protic Bamford–Stevens reaction of (1a) are in good agreement with our previous findings on the rearrangements of 1,8-cineole derivatives [4] and with the currently accepted mechanisms for the above-mentioned reaction.[2]

Interestingly, different results were found in aprotic conditions, which are likely to afford chiefly carbene intermediates. Actually, in the reaction of (1a) with excess of sodium methoxide in diglyme for 1 h at 135—140°, the major component of the reaction mixture (t.l.c.) was the $\Delta^1$-1,2-diazetine (12) (*ca.* 30%). G.l.c. of the reaction mixture also showed the presence of the azine (11), transoid and cisoid 1,3,3-trimethyl-6-(1,3,3-trimethyl-2-oxabicyclo[2.2.2]oct-6-ylidene)-2-oxabicyclo-[2.2.2]octane (13a and b), 1,3,3-trimethyl-2-oxabicyclo-[2.2.2]oct-5-ene (9), 1-[3-(2-hydroxyisopropyl)cyclo-



(11)

+(2a)

(10) +(2b) ⟶ (12) ⟶ -N₂ (13a)

+(10)

(13a) + (13b)
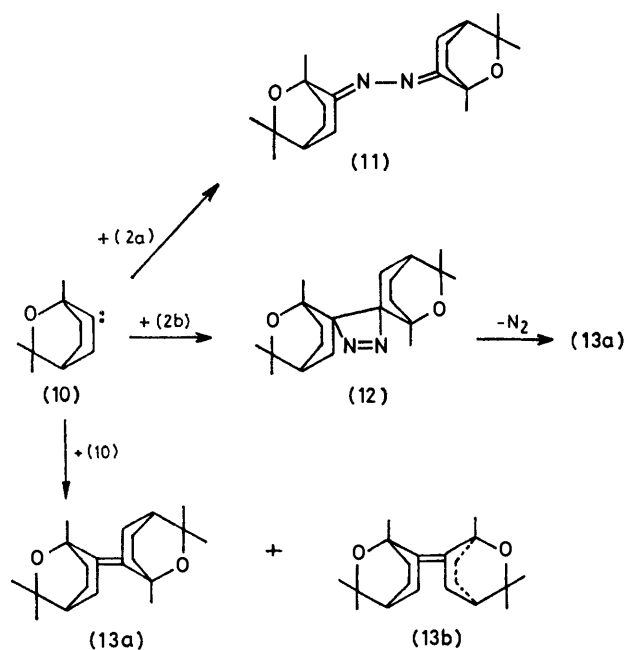
SCHEME

pentyl]ethanone (8), and *p*-cymene, whereas the unknown products ranged to *ca.* 18% overall.

Under the same conditions, but with the more polar DMF as solvent,[5] the percentages of compounds (9), (11), (12), (13a and b), and *p*-cymene were near constant, (8) was found only in small amount and pinol (6) was formed, whereas the unknown products decreased to 9%.

Compounds (11), (12), and (13a) were isolated by chromatography on silica gel. Qualitative differences for (8) and (6) could be explained by a protonation side reaction, where the proton source is given by methanol formed in the reaction and/or by the tosylhydrazone.[2] Cationic species such as (3) and (4), which could be preferentially stabilized depending on the solvent polarity, could give (8) or (6), respectively. Because in protic conditions (9) is wholly absent, we believe that this compound arises from the carbene (10) (*cf.* ref. 6),

and *p*-cymene from opening of the ether bridge of (10), followed by dehydration and aromatisation.

Carbene (10) can react with (2a and b) in two different ways to give the azine (11) and the $\Delta^1$-1,2-diazetine (12), respectively (see Scheme). The structure of (11), which was easily synthesized starting from hydrazine and (1b), was further supported by u.v., i.r., n.m.r., and mass spectral data (see Experimental section).

The $\Delta^1$-1,2-diazetine structure was attributed to (12) on the following basis. Compound (12) decomposes slowly on standing at room temperature; at the m.p. evolution of gas was clearly observed, and t.l.c. of the melt revealed the presence of (13a).[7] The mass spectrum of (12) showed a peak of appreciable intensity at $m/e$ 304, corresponding to loss of nitrogen from the molecular ion, and the subsequent fragmentation was the same as for (13a), but different from that of (11). In the n.m.r. spectrum no downfield proton signal was found in the region $\delta$ >3, thus excluding CH=C and CH–N=N functions; the u.v. and i.r. spectra exhibited typical absorptions for an N=N group. Moreover, the general patterns of the n.m.r. and i.r. spectra were quite similar to those of (11). Chemical evidence for the presence of a cyclic diazo group was also found from the positive test with copper(I) chloride.[8] All these data are in agreement with those found for known $\Delta^1$-1,2-diazetines.[9]

Other products could also be derived from the carbene (10). First, this intermediate could give (13a and b) by reacting with itself. The structure of (13a) was confirmed both by spectral data [double bond i.r. stretching; no olefinic proton signal in the n.m.r. spectrum; $m/e$ 304 $(M^+)$ and 152 in the mass spectrum] and chemical tests (discharge of the bromine colour of a tetrachloromethane solution and positive Baeyer test). The transoid configuration was tentatively attributed to (13a) owing to the presence of C–H stretching at 3 050 cm$^{-1}$, which could be due to two separate methylene and methyl groups brought very close together in space in the transoid form, as was revealed by molecular models (*cf.* ref. 10). Moreover, the u.v. spectrum (see Experimental section) was comparable with that of transoid 2-bornanylidenebornane (214 and 218 nm).[11]

Compound (13b) was not isolated, but its g.l.c.–mass spectrum was identical with that of (13a), and therefore we propose the cisoid configuration for it. Due to its thermal instability, (12) is another source of (13a), as was shown by repeating the reaction in diglyme at reflux temperature (165°), whereupon the yield of (12) strongly decreased in favour of (13a), and the percentage composition (g.l.c.) of the other components was little affected.

Starting from (1b), we were unable to synthesize (13a and/or b) by a recently described procedure for reductive coupling of carbonyl groups to alkenes,[12] because (1b) decomposes rapidly under the reaction conditions. In conclusion, whereas the protic Bamford–Stevens reaction of (1a) confirmed the ability of the 1,8-cineole ring to rearrange in conditions whereby a potential carbocation in position 2 could be formed, the aprotic

reaction gave less rearrangement products and a low yield of alkene (9), but a fair yield of the rather exceptional $\Delta^1$-1,2-diazetine (12).

### EXPERIMENTAL

U.v. spectra were measured with a Hitachi–Perkin-Elmer EPS-3T spectrophotometer, and i.r. spectra with a Perkin-Elmer 257 spectrometer. N.m.r. spectra were recorded with a Perkin-Elmer R12 instrument (60 MHz; tetramethylsilane as internal standard), and mass spectra with a GC/MS Varian Mat 111 spectrometer. G.l.c. was performed on a Fractovap GI instrument (C. Erba; 2 000 × 3 dual column differential system, packed with 3% SE 30 on silanized Chromosorb W; injection port 290 °C; linear temperature programming 80—110 °C over 10 min, and 110—250 °C over 20 min; helium flow rate 100 ml min$^{-1}$). T.l.c. was carried out on silica gel plates, with cyclohexane–benzene–ethyl acetate (1 : 1 : 3) as developer. M.p.s were determined with a Fisher–Johns apparatus.

*Reaction of Compound* (1a) *with Sodium in Ethylene Glycol.*—Tosylhydrazone (1a)[3] (3.36 g, 10 mmol) was added to a solution of sodium (1.15 g, 50 mmol) in ethylene glycol (25 ml). The mixture was heated with stirring at 115—120 °C for 1 h, cooled, poured into ice–water (100 ml), and extracted with ether. The combined extracts were washed with 1M-hydrochloric acid and brine, dried (Na$_2$SO$_4$), filtered, and evaporated. G.l.c. of the oily residue (2.10 g) showed five components, according to their increasing retention times: A 2, B 12, C 4, D 76, E 6%. A, B, and D were recognized as (6)—(8), respectively, by superimposition with authentic samples and by their g.l.c.–mass spectra,[3,4] but we were unable to identify C and E. The major component (8) was isolated by distillation *in vacuo* as a liquid, b.p. 83—85° at 0.2 mmHg; i.r. and n.m.r. spectra were identical with those already described.[4] The same reaction carried out at 135—140 °C showed the same components in the ratio 31 : 7 : 3 : 53 : 6.

*Reaction of Compound* (1a) *with Sodium Methoxide in Diglyme.*—Tosylhydrazone (1a) (10.10 g, 30 mmol) was added to a solution of sodium methoxide (2.43 g, 45 mmol) in dry diglyme (150 ml). The mixture was heated with stirring at 135—140 °C for 1 h, cooled, poured into ice–water (300 ml), and extracted with light petroleum (b.p. 40—70°). The combined extracts were washed with water, dried (Na$_2$SO$_4$), filtered, and evaporated. G.l.c. of the oily residue (5.0 g) showed ten components: A 8, B 3, C 2, D 1, E 5, F 14, G 36, H 12, I 14, J 6%. Components A—E were recognized as (9), *p*-cymene, (1b), (7), and (8), respectively, by superimposition with authentic samples and by their g.l.c.–mass spectra,[3,4] whereas G resulted from a superimposition of (12) and (13a). Component F was tentatively recognized as (13b) by its g.l.c.–mass spectrum, *m/e* 304, 289, 261, 243, 221, 203, 177, 151, 135, 109, 93, 69, and 43 (base peak) [*cf.* the mass spectrum of (13a)], but H and J were not identified. T.l.c. of the mixture showed that (12) was the major component (*ca.* 30%).

Chromatography on silica gel gave, with pentane–ether (4 : 1) as eluant, a product identified as 1,3,3-*trimethyl*-6-(1,3,3-*trimethyl*-2-*oxabicyclo*[2.2.2]*oct*-6-*ylidene*)-2-*oxabicyclo*-[2.2.2]*octane* (13a), b.p. 120—123° at 0.3 mmHg, solidified on cooling, m.p. 55—56° (Found: C, 78.7; H, 10.5. C$_{20}$H$_{32}$O$_2$ requires C, 78.9; H, 10.6%); $\lambda_{max.}$ (n-hexane) 213 ($\varepsilon$ 550) and 218sh nm (280); $\nu_{max.}$ (neat) 3 050 and 1 640 cm$^{-1}$; $\delta$(CCl$_4$) 1.12 (3 H, s, CH$_3$), 1.17 (3 H, s, CH$_3$), 1.23 (6 H, s, 2CH$_3$), 1.28 (6 H, s, 2CH$_3$), 1.5—2.3 (14 H, m,

6CH$_2$ + 2CH); *m/e* 304, 289, 261, 243, 221, 203, 177, 151, 135, 109, 93, 69, and 43 (base peak).

With pentane–ether (3 : 1) as eluant, component I was obtained and identified as (+)-1,3,3-*trimethyl*-2-*oxabicyclo*-[2.2.2]*octan*-6-*one azine* (11), m.p. 177° (from light petroleum) (Found: C, 72.4; H, 9.3; N, 8.5. C$_{20}$H$_{32}$N$_2$O$_2$ requires C, 72.3; H, 9.7; N, 8.4%); $\lambda_{max.}$(n-hexane) 223 ($\varepsilon$ 6 200), 234 (5 700), and 240 nm (5 200); $\nu_{max.}$(KBr) 1 650 cm$^{-1}$; $\delta$(CCl$_4$) 1.15 (6 H, s, 2CH$_3$), 1.25 (6 H, s, 2CH$_3$), 1.33 (6 H, s, 2CH$_3$), 1.5—2.5 (14 H, m, 6CH$_2$ + 2CH); *m/e* 332, 317, 289, 206, 166, 148, 139, 124, 109, 108, 107, 81, 71, and 43 (base peak).

With pentane–ether (2 : 1) as eluant, 1,3,3-*trimethyl*-2-*oxabicyclo*[2.2.2]*octane*-6-*spiro*-3′-$\Delta^1$-1,2-*diazetine*-4′-*spiro*-6″-1,3,3-*trimethyl*-2-*oxabicyclo*[2.2.2]*octane* (12) was obtained, m.p. 159—160° (decomp., gas evolved) (from light petroleum) (Found: C, 72.4; H, 9.8; N, 8.4. C$_{20}$H$_{32}$N$_2$O$_2$ requires C, 72.3; H, 9.7; N, 8.4%); $\lambda_{max.}$ (95% EtOH) 340 nm ($\varepsilon$ 120); $\nu_{max.}$(KBr) 3 020, 1 640, and 1 560 cm$^{-1}$; $\delta$(CCl$_4$) 1.05 (3 H, s, CH$_3$), 1.15 (3 H, s, CH$_3$), 1.23 (6 H, s, 2CH$_3$), 1.28 (6 H, s, 2CH$_3$), and 1.3—2.5 (14 H, m, 6CH$_2$ + 2CH); *m/e* 332, 317, 304, 289, 261, 243, 221, 203, 177, 151, 135, 109, 93, 69, and 43 (base peak). Compound (12) decomposes slowly on standing at room temperature, becoming pale yellow. The mixture obtained by carrying out the same reaction at reflux temperature (*ca.* 165°) showed (t.l.c.) only traces of (12) and an increased yield of (13a) (*ca.* 35%).

*Azine* (11).—A synthetic sample was prepared by refluxing for 2 h under nitrogen a solution of (1b) (1.68 g, 10 mmol) and anhydrous hydrazine (0.16 g, 5 mmol) in anhydrous ethanol (3 ml) containing acetic acid (1 drop). After cooling, the precipitate (1.55 g, 93%) was recrystallized from light petroleum. A pure sample showed m.p. 177° and had u.v., i.r., and n.m.r. spectral data identical with those of component I.

*Reaction of Compound* (1a) *with Sodium Methoxide in DMF.*—This reaction was carried out as in the case of diglyme, starting from (1a) (3.36 g, 10 mmol), sodium methoxide (0.81 g, 15 mmol), and anhydrous DMF (20 ml). G.l.c. of the oily residue (2.20 g) showed eleven components: (9) 6, *p*-cymene 2, (6) 14, (1b) 4, (7) 1, (8) 1, (13b) 12, (12) + (13a) 35, X 5, (11) 16, and Y 4%. All the components, with the exception of X and Y which remained unknown, were identified by g.l.c. superimposition with authentic samples and by their g.l.c.–mass spectra.[3,4]

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