Synthesis and Some Reactions of 3,3,6-Trisubstituted Tricyclo[3.2.0.0^{1,4}]heptan-2-ones

Harry Finch,[a] Rona M. Highcock,[b] Stanley M. Roberts,[c] Kevin M. Short,[c] and Vladimir Sik[c]

[a] Department of Chemical Research, Glaxo Group Research, Ware, Herts SG12 0DP, U.K.
[b] Chemical Analysis Department, Glaxo Group Research, Greenford, Middlesex UB6 0HE, U.K.
[c] Department of Chemistry, Exeter University, Exeter, Devon EX4 4QD, U.K.

Electrophiles and most nucleophiles react with tricyclo[3.2.0.0^{1,4}]heptan-2-ones with preferential cleavage of the C(1)–C(4) or C(1)–C(5) bond; X-ray data show the highly strained tricycloheptanone (14) has a bond angle of 149.2(9)° at a tetravalent carbon atom.

The tricyclo[3.3.0.0^{1,4}]octan-2-ones (1)—(3) are readily prepared and react with the softer nucleophiles such as azide, iodide, cyanide, and thiolate ion as shown.[1] In later studies we found that attack by the harder methoxide ion on compound (1) gave the esters (4) and (5) (95%, ratio 4.3:1 respectively) as the only identifiable products.
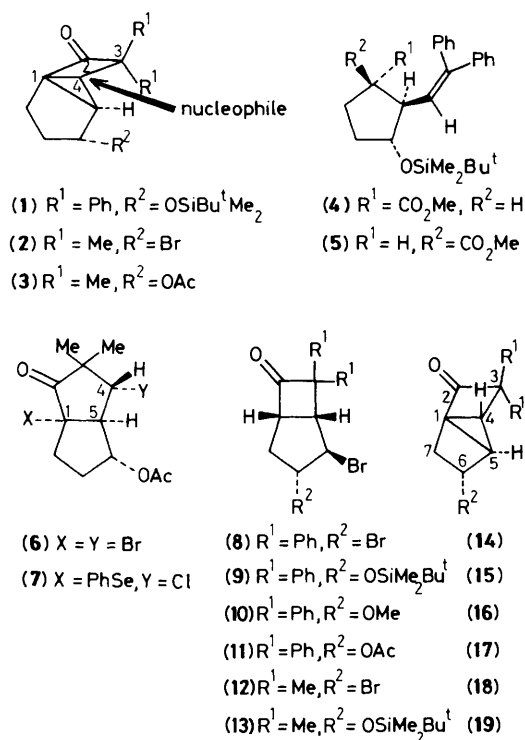
More recent work showed that electrophilic attack on the tricyclo[3.3.0.0^{1,4}]octan-2-one ring system leads to fracture of the C(1)–C(4) bond. Thus bromination of the tricyclic ketone (3) gave the dihalo-compound (6) (78%), while reaction of (3)

with phenylselenenyl chloride furnished the addition product (7) (86%). Attachment of the selenium atom to the quaternary carbon centre was established by the observation of the appropriate ^{13}C–^{77}Se coupling.[2] The assignment of stereochemistry to compound (7) was aided by nuclear Overhauser enhancement (n.O.e.) measurements. Through-space interactions were observed between the aromatic ring protons, the low-field C(3)-methyl group, and H–C(5) as well as between the high field C(3)-methyl group and H–C(4).

Treatment of the bicyclic ketones (8)—(13)[3] with potassium

Table 1. Reactions of 3,3,6-trisubstituted tricycloheptan-2-ones with nucleophiles.

		Reaction conditions		Product
Substrate	Nucleophile (solvent)	Temp.	Time/h	(% yield)
(15)	NH₄Cl, Fe (MeOH)	Room temp.	4	(21) (93)
(16)	PhCH₂NH₂ (CH₂Cl₂)	Room temp.	48	(22) (100)
(17)	Li(ButO)₃AlH (THF)ᵃ	−78 → 0 °C	12	(23) (89)
(17)	Et₃N·3HF (CH₂Cl₂)	Reflux	24	(24) (64)

ᵃ THF = tetrahydrofuran.

(1) R^1 = Ph, R^2 = OSiBu^{t}Me$_2$

(2) R^1 = Me, R^2 = Br

(3) R^1 = Me, R^2 = OAc

(4) R^1 = CO$_2$Me, R^2 = H

(5) R^1 = H, R^2 = CO$_2$Me

(6) X = Y = Br

(7) X = PhSe, Y = Cl

(8) R^1 = Ph, R^2 = Br   (14)

(9) R^1 = Ph, R^2 = OSiMe$_2$Bu^t (15)

(10) R^1 = Ph, R^2 = OMe   (16)

(11) R^1 = Ph, R^2 = OAc   (17)

(12) R^1 = Me, R^2 = Br   (18)

(13) R^1 = Me, R^2 = OSiMe$_2$Bu^t (19)

Figure 1

(20) R^1 = SCH$_2$Ph, R^2 = Br

(21) R^1 = Cl, R^2 = OSiMe$_2$Bu^t

(22) R^1 = NHCH$_2$Ph, R^2 = OMe

(23) R^1 = H, R^2 = OAc

(24) R^1 = F, R^2 = OAc

(25)   (26)
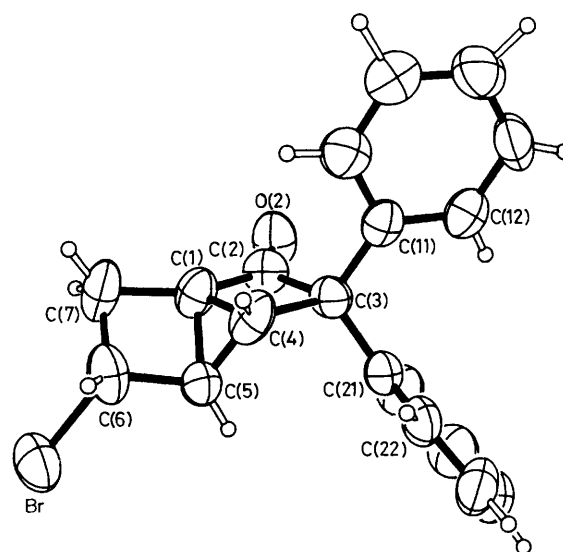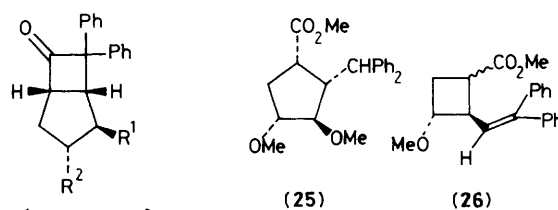
t-butoxide gave the corresponding highly strained tricyclo[3.2.0.0¹·⁴]heptan-2-ones (14)—(19). The ketone (14) was crystalline and X-ray data show that the molecule accommodates most of the intense strain by a remarkable widening of the C(2)–C(1)–C(7) bond angle to 149.2(9)° (Figure 1).† A
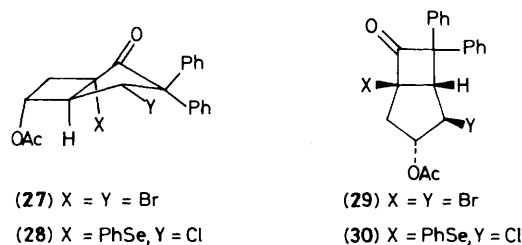
† *Crystal data* for (14): C₁₉H₁₅OBr, M = 339.2, monoclinic, space group $P2_1/n$, Z = 4, a = 8.787(3), b = 18.231(7), c = 10.355(5) Å, β = 110.19(3)°; U = 1557(1) Å³, $F(000)$ = 688. The structure was solved by direct methods from data collected at 295 K to 2θ = 115° on a Nicolet R3m/V diffractometer with monochromatised Cu-K_α X-radiation. For the 1081 observed reflections [I > 3.0 σ(I)], and with anisotropic thermal parameters for all non-hydrogen atoms, R = 0.060, R_w = 0.063, goodness-of-fit = 1.49.

Crystal data for (27): C₂₁H₁₈O₃Br₂, M = 398.3, triclinic, space group $P\bar{1}$, Z = 2, a = 9.241(4), b = 10.039(3), c = 11.350(4) Å, α = 87.68(3), β = 79.00(3), γ = 69.18(3)°; U = 966(1) Å³, $F(000)$ = 476. The structure was solved by direct methods from data collected at 295 K to 2θ = 115° on a Nicolet R3m/V diffractometer with monochromatised Cu-K_α X-radiation. For the 2494 observed reflections [I > 3.0 σ(I)], and with anisotropic thermal parameters for all non-hydrogen atoms, R = 0.064, R_w = 0.075, goodness-of-fit = 1.64.

Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue 1.

(27) X = Y = Br

(28) X = PhSe, Y = Cl

(29) X = Y = Br

(30) X = PhSe, Y = Cl

search of the Cambridge Structural Database[4] shows this to be the largest interatomic angle yet recorded at a tetracoordinate carbon atom in a crystalline compound at ambient temperature.
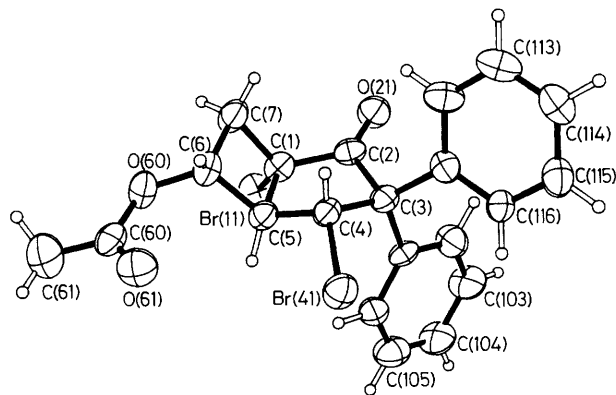
Figure 2

The 3,3-diphenyltricycloheptanones (**14**)—(**17**) generally react with soft nucleophiles through exclusive attack at C(5) to give 2,3,7,7-tetrasubstituted bicyclo[3.2.0]heptan-6-ones. For example the tricyclic compound (**14**) reacted with benzylthiolate ion to give the ketone (**20**). A selection of other results are described in Table 1. Methoxide ion, in contrast, reacted with the ketone (**16**) to give the cyclopentane derivative (**25**) (38%) and the cyclobutane derivatives (**26**) (27%).

As expected from previous work[5] the 3,3-dimethyltricycloheptanone (**19**) is attacked by azide ion or methoxide ion at C(5) *and* C(4) (70—80% yield) with the products formed in the ratio 1 : 5—10 respectively. The protection offered to C(4)

by the adjacent phenyl group in compounds (**14**)—(**17**) is underlined.

Addition of bromine to the tricyclic ketone (**17**) gave products of '*cis*'-addition to the cyclopropyl unit; thus the major product obtained was the ketone (**27**) (49%); the other product was the dibromo-compound (**29**) (17%). The detailed structure of the highly substituted bicycloheptan-2-one (**27**) was clearly seen from X-ray data (Figure 2).[†] Addition of phenylselenenyl chloride gave the bicycloheptan-2-one (**28**) (56%) and the bicycloheptan-6-one (**30**) (13%). Thus this strategy may provide a general method for the synthesis of highly substituted bicyclo[3.2.0]heptan-2-ones.

References

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