Tetrahedron Letters No. 22, pp 2255 - 2257, 1972. Pergamon Press. Printed in Great Britain.

SYNTHESIS OF 1.1.2-TRISUBSTITUTED SPIRO-[2.5]-OCTANES

Hans Johan Storesund and Per Kolsaker

Department of Chemistry, University of Oslo, Blindern, Oslo 3, Norway

(Received in UK 20 March 1972; accepted for publication 27 April 1972)

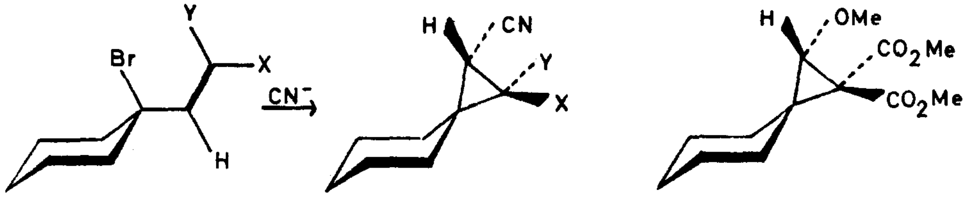
The usual way of preparing spiro-[2.5]-octanes described in the literature has been the addition of suitable carbene generating systems to methylene cyclohexanes.[1]

Based on our recent report[2] on cyclopropane formation from reactions between selected nucleophiles and dimethyl 2-bromo-2-methylpropylidenemalonate, attempts to extend this reaction to include systems where analogous pathways would lead to spiro compounds would be appropriate.

We now wish to report the preparation of 1.1.2-trisubstituted spiro-[2.5]-octanes formed by reactions of dimethyl (1-bromocyclohexyl)methylidenemalonate (Ia), methyl (1-bromocyclohexyl)methylidenecyanoacetate (Ib) and (1-bromocyclohexyl)methylidenemalonitrile (Ic) with potassium cyanide in methanol.

The starting olefins were made in excellent yields by Knoevenagel condensation of hexahydrobenzaldehyde and the respective methylene compounds using Amberlite IR-45 as basic catalyst.[3] The condensation of the aldehyde and methyl cyanoacetate yielded isomerically pure trans olefin (cyclohexyl and ester group in trans position) as shown by photochemical isomerisation experiments. The olefins were brominated in the allylic position with N-bromosuccinimide, the ease of bromination being in the order of (Ia)>(Ib)>>(Ic). An attempt to prepare a cis/trans mixture of (Ib) by bromination of the corresponding olefin mixture obtained by irradiation (CCl_4/benzophenone) of the trans compound, failed due to a complete isomerisation to the trans isomer under bromination conditions, the rate of isomerisation being much faster than the rate of substitution.

After treatment of the bromides (Ia-c) with equivalent amounts of potassium cyanide in 78% methanol at 30 °C for 2 hrs., the nucleophile had been completely consumed which was indicated by the neutral reaction of the reaction mixture. This was verified by n.m.r. and i.r. analyses of the crude products which strongly indicated spiro compounds (II) as the sole products. The assumingly more reactive bromide (Ic), however, produced in the reaction also 1.1-dicyano-2-methoxyspiro-[2.5]-octane in ca. 60% yield as compared with a yield of ca. 40% of the expected cyano compound (IIc). Separation of the two spiro compounds could not be effected satisfactorily by fractional destillation. Pure samples of (IIc) were obtained by column chromatography on neutral aluminium oxide (activity I) as the methoxy analog was absorbed and probably decomposed on the column. (Ia) and (Ib) produced only minor amounts of the methoxy compound in their reaction with methanolic potassium cyanide, the cyano products (IIa,b) being isolated in high yields using the purification method mentioned above.



I II III

a) $X = Y = CO_2Me$
b) $X = CO_2Me$
$Y = CN$
c) $X = Y = CN$

Regardless of the direction of attack by the incoming nucleophile on the β-carbon of the trans bromide (Ib) the reaction will lead to the cis-configuration of (IIb) provided that no inversion takes place in the intermediate γ-carbanion. N.m.r. studies of the $Eu(DPM)_3$ complex of (IIb) indicated the presence of a single isomer as no splitting of the methine proton in the 2-position could be observed.

The ready formation of spiro compounds under the given conditions is demonstrated by the observation of no elimination products being formed when (Ia) is treated with sodium methoxide in methanol; only (III) was formed in high yield.

Table

Physical and spectral properties of spiro- [2.5]-octanes (II)[a]

	B.p./M.p.(°C)	IR(cm^{-1})[b]	MS(m/e)	NMR(δ in p.p.m)[c]
IIa	177-8/10mm	1730(C=O) 2240(C≡N) 3010(cycloprop.)	251(M^+)	1.1-2.1, 10H,m 2.33, 1H, s 3.74, 3H, s 3.79, 3H, s
IIb	86-86.5	1735(C=O) 2240(C≡N) 3010(cycloprop.)	218(M^+)	1.2-2.0, 10H,m 2.64, 1H, s 3.85, 3H, s
IIc	106-106.5	2240(C≡N) 3010(cycloprop.)	185(M^+)	1.4-2.0, 10H,m 2.37, 1H, s

[a] Elemental analyses were satisfactory

[b] CCl_4 solutions

[c] 100 Mhz, $CDCl_3$ solutions, tetramethylsilane as internal standard

References

1. Houben Weyl, Die Methoden der Organischen Chemie. IV/3-1971
2. P. Kolsaker, H.J. Storesund. Chem. Comm., in press
3. M.J. Astle, J.A. Zaslowsky. Ind. Eng. Chem. 44, 2867 (1952)