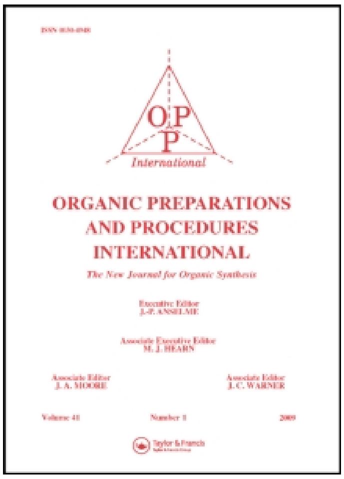


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

AN EFFICIENT, GENERAL SYNTHESIS OF SPIROALKENES AND RELATED DERIVATIVES

Nicholas R. Natale[a]; Robert O. Hutchins[a]
[a] Department of Chemistry, Drexel University, Philadelphia, PA

To cite this Article Natale, Nicholas R. and Hutchins, Robert O.(1977) 'AN EFFICIENT, GENERAL SYNTHESIS OF SPIROALKENES AND RELATED DERIVATIVES', Organic Preparations and Procedures International, 9: 3, 103 — 108
To link to this Article: DOI: 10.1080/00304947709356865
URL: http://dx.doi.org/10.1080/00304947709356865

ORGANIC PREPARATIONS AND PROCEDURES INT. 9(3), 103-108 (1977)

AN EFFICIENT, GENERAL SYNTHESIS OF SPIROALKENES AND RELATED DERIVATIVES[1]

Nicholas R. Natale and Robert O. Hutchins*

Department of Chemistry, Drexel University, Philadelphia, PA 19104

A convenient and general synthetic procedure for procuring spiro [4.5] decene and spiro [5.5] undecene derivatives which could be readily functionalized at various positions, was desired. However, a literature search revealed that while several elegant strategies have been developed to specific members of these classes,[2,3] there remains a need for general approaches to simple examples of these systems. Consequently, we successfully explored the general route outlined below based on the spiro annelation procedure developed by Christol[4b] and modified by Kane[4a] involving conversion of cyclic aldehydes (I) to the corresponding piperidine enamines (II) followed by a Michael-type addition to an α, β-unsaturated ketone and aldol-cyclization to spiro enones (III).[4] Final conversion to spiro-alkenes (V) is accomplished via reductive-migration[5] of intermediate p-tosyl-hydrazones (IV) with catechol borane (see Table I for yields).

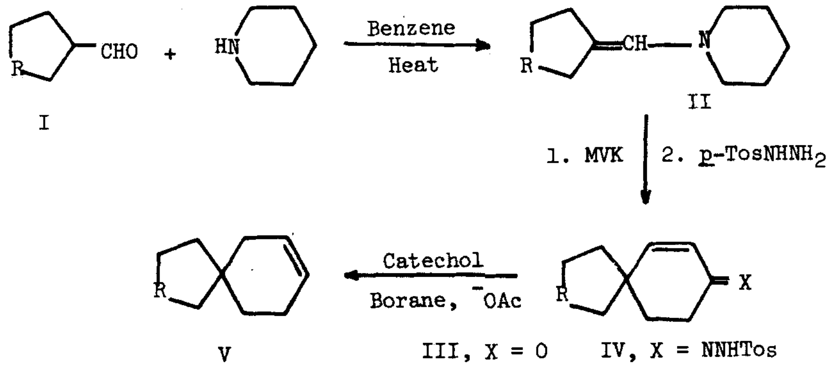
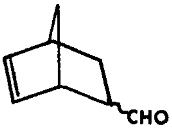


Table I. % Yield in Conversion of Aldehydes to Spiroalkenes

R of ALDEHYDE (I)	II	III	IV	V
(a) $-CH_2-$	83	76	63	59
(b) $-(CH_2)_2-$	83	46	64	70
(c) $-(CH_2)_4-$	82	46	76	85
(d) $-CH=CH-$	90	50	69	62
(e) 	85	35	56	71

EXPERIMENTAL

Preparation of Spiroalkenes. General Procedure.

The general synthetic approach is described in the text and presented below for the preparation of spiro [4.5] dec-7-ene. The yields and major characterization data are presented in Tables I, II and III. In all cases, the spectral data was in complete accord with the assigned structures. The instability of the enamines precluded obtaining combustion analyses; characterization of the spiro enones was accomplished via the corresponding p-toluenesulfonyl hydrazones.

1-Cyclopentylidene-piperidine (IIa). A solution of cyclopentyl methanal (10g, 0.10mole) and piperidine (18g, 0.25mole) in benzene was heated to reflux for 5 hrs. during which time water was removed with a Dean-Stark apparatus. The solvent was then removed with a rotary evaporator and the residue distilled to afford 14.6g(83%) of colorless product, bp. 54-55°/ 0.1 mm. Glpc analysis (180°) indicated the material to be ca. 94% pure and it was used without further treatment.

Spiro [4.5]dec-6-en-8-one (IIIa). A solution of 1-(cyclopentylidene)-piperidine (10g, 0.066mole) and methyl vinyl ketone (4.5g, 0.064mole) in absolute ethanol was heated to reflux for 24 hrs. under a nitrogen atmosphere. Water (17ml), glacial acetic acid (13ml) and sodium acetate (7g) were then added and reflux continued for 24 hrs. The reaction mixture was cooled, the pH adjusted to 9 with aqueous sodium hydroxide and reflux continued for an additional 24 hrs. The mixture was diluted with

Table II. Physical Data for II-V

Compound	bp.(mp.)	nmr, δ (integration)	ir
IIa	54-55°/0.01mm	5.5(1)^a	1660^a
IIb	64-66°/0.1mm^b	5.3(1)^a	
IIc	101-103°/0.6mm	5.3(1)^a	1650^a
IId	83-85°/0.3mm	5.3(1)^a, 5.8(2)^a	1645^a
IIe	66-70°/0.02mm	5.3, 5.58(1)^a, 5.91(2)	1670^a
IIIa		6.7(1)^c, 5.7(1)^d	1683^e
IIIb (f)	83°/0.2mm	6.9(1)^c, 5.9(1)^d	1680^e
IIIc	86°/0.01mm	6.83(1)^c, 5.82(1)^d	1675^e
IIId	95-96°/0.3mm^g	6.75(1)^c, 5.83(1)^d	1686^e
IIIe	94-98°/0.1mm	6.52(1)^{c,h} 5.76(1)^d	1686^e
IVa	(170-172°, dec.)	5.99(2)^i	3231^j
IVb	(188-190°, dec.)	6.05(2)^i	3215^j
IVc	(175-177°, dec.)	6.0(2)^i	3225^j
IVd	(180-182°, dec.)	6.06(2)^i	3225^j
IVe	(179-181°, dec.)	5.8(2)^i	3236^j
Va		5.7(2)^k	1660^m
Vb	n_D1.490^l	5.61(2)^k	1658^m
Vc		5.54(2)^k	1663^m
Vd		5.6(4)^k	1660^m
Ve		5.6(2)^k, 6.02(2)^k	1658^m,1567^m

a) C=CHN b) lit^{4a}bp 66-68/0.1mm c) COCH=CH d) COCH=C e) C=O st.

f) Spiroenones IIIb-IIIe were characterized as the *p*-tosylhydrazones IVb-IVe (see Table III) g) lit.^{4a} bp. 81-83°/0.1mm h) For the major isomer (ca. 70%); other showed 6.92, 5.85 i) CH=CHC=N j) NH st. k) C$\underline{H}$=C$\underline{H}$ l) lit.^{7} n_D 1.4919; m) C=C st.

250 ml of water, cooled and extracted with three 100 ml portions of ether. The ether extract was dried, concentrated on a rotary evaporator and the resulting oil was flash distilled at reduced pressure in a Kugelrohr apparatus to afford 7.8g (76%) of clear product.

p-Toluenesulfonyl Hydrazide of spiro [4.5] dec-6-en-8-one (IVa). A mixture of spiro [4.5]dec-6-en-8-one (4.6g, 0.031 mole) and p-toluenesulfonylhydrazine (6.1g, 0.032 mole) in 50 ml of ethanol was heated until a solution was obtained. The mixture was then cooled and the resulting yellow precipitate collected and recrystallized from aqueous ethanol to afford 5.7 g (63%) of off-white crystals, mp. 170-72^{o} (dec.).

Spiro [4.5]dec-7-ene (Va). Catechol borane (0.70 ml, 5.8 mmoles) was added to a solution of IVa (1.6g, 4.9 mmole) in 25 ml of dry chloroform kept at 0-5^{o} under nitrogen. The reaction was stirred for 1 hr., 2.1g of sodium acetate trihydrate was added and the mixture brought to gentle reflux for 1 hr. The mixture was then cooled, 50 ml of saturated aqueous

Table III. Elemental Analysis Data of Spiro Derivatives

Compound	Analysis C % Calculated (% Found)	H
IIIa	79.95 (79.61)	9.39 (9.57)
IVa	64.12 (64.38)	6.96 (7.14)
IVb	65.03 (64.90)	7.28 (7.15)
IVc	66.63 (66.51)	7.83 (7.82)
IVd	65.42 (65.41)	6.71 (6.76)
IVe	66.64 (66.33)	6.48 (6.63)
Va	88.16 (88.09)	11.83 (12.01)
Vc	87.56 (87.57)	12.43 (12.27)
Vd	89.12 (89.40)	10.87 (10.55)
Ve	89.93 (90.10)	10.06 (10.26)

Acknowledgements.- The authors wish to thank Michael J. Pacana and Reginald Brown for technical assistance and the Donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.

sodium bicarbonate was added and the mixture extracted with two 50 ml portions of chloroform. The chloroform was washed successively with aqueous sodium bicarbonate and water, dried, concentrated on a rotary evaporator and flash distilled under reduced pressure (Kugelrohr) to yield 0.41 g (60%) of colorless liquid which was homogeneous by glpc (OV-1 column, 65°).

REFERENCES

1. Presented in part at the 10th Middle Atlantic Regional Meeting of the American Chemical Society, Philadelphia, PA, Feb. 25, 1976.

2. a) For a recent review of synthetic approaches to carbocyclic spiro compounds see A. P. Krapcho, Synthesis, 383 (1974); b) An excellent account of the chemistry of natural occurring spiro derivatives is provided by J. A. Marshall, St. F. Brady and N. H. Andersen, Fortsch. Chem. Org. Nat., 31, 283 (1974).

3. Examples include: a) B-vetivone. W. G. Dauben and D. J. Hart, J. Am. Chem. Soc., 97, 1622 (1975) and references cited; b) vetispirene. D. Caine, A. A. Boucugnami, S. T. Chao, J. B. Dawson and P. F. Ingwalson, J. Org. Chem. 41, 1539 (1976) and included references; c) hinesol: J. A. Marshall and S. F. Brady. Tetrahedron Lett. 1387 (1969); J. A. Marshall and S. F. Brady, J. Org. Chem., 35, 4068 (1970) and cited references; d) agarospirol: M. Mongrain, J. Lafontaine, A. Belanger, and P. Deslongchamps, Can. J. Chem., 48, 3273 (1970) and references cited.

4. a) V. V. Kane, Syn. Commun., 6, 237 (1976); this procedure represents a modification of one provided by Christol and coworkers using pyrrolidine enamines and, in most cases, gives higher overall yields of the spiro enone reported for the pyrrolidine procedure, see: b) H. Christol, F. Plenat and J. Salancon, Bull. Soc. Chim. Fr., 4468

(1970); c) An alternative approach to the enamine intermediates II has recently been described; see S. F. Martin, J. Org. Chem., 41, 3337 (1976); this procedure utilizes the reaction of diethyl lithiomorpholinomethylphosphonate with cyclic ketones to generate morpholino enamines of type II. d) Sulfonium cycloprophylides are also useful for the construction of spirocyclic rings, see B. M. Trost, Acc. Chem. Res., 7, 85 (1974).

5. a) G. W. Kabalka, D. T. C. Yang and J. D. Baker, Jr., ibid., 41, 574 (1976); b) Reduction of the intermediate p-tosylhydrazones with sodium cyanoborohydride[6] afforded mixtures composed primarily of the saturated spiro alkanes with lesser amounts of the desired alkenes (V).
6. R. O. Hutchins, M. Kacher and L. Rua, J. Org. Chem., 40, 923 (1975).
7. J. A. Dixon and P. A. Naro, ibid., 25, 2094 (1960).

(Received April 11, 1977; in revised form July 18, 1977)