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NITRODESTANNYLATION.
A NEW SYNTHESIS OF CONJUGATED NITRO CYCLO OLEFINS

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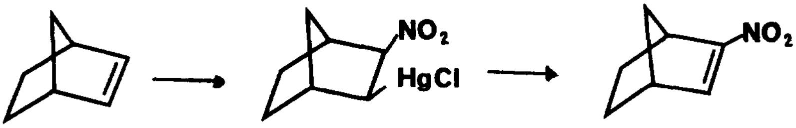
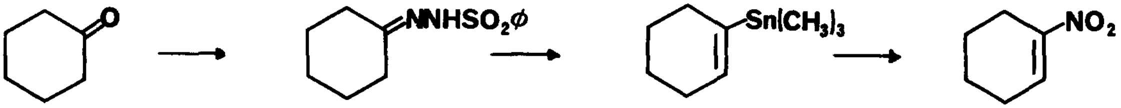
Summary. A new process for the conversion of cyclic ketones to 1-nitro olefins, as outlined in eq. 2 below, is described.

We have recently described a synthesis of conjugated cyclic nitro olefins from cyclic olefins under extremely mild conditions as exemplified in eq. 1.[1] In addition the versatility of such products was demonstrated by conversion to a wide variety of new structures by annulation, appendage addition, functionalization, etc.[2] The utility of cyclic nitro olefins in synthesis made it apparent that routes to these substances from other types of precursors would be highly desirable. One of the most fruitful processes would be a route for the transformation of cyclic ketones to cyclic nitro olefins.[3] We now describe a new method which responds to this need. The process is illustrated in eq. 2.



eq. 1



eq. 2

Modification of procedures described by Bond and Chamberlin[4] permits the efficient conversion of ketones to vinylsilanes or vinylstannanes via arylhydrazone intermediates, especially in the case of 2,4,6-triisopropylbenzenesulfonyl (trisyl) hydrazones. The problem of synthesis according to this line of analysis then reduces to the replacement of a tin or silicon substituent by nitro. In practice this was found to be unexpectedly difficult to achieve. The vinylsilanes were so unreactive that nitration under mild conditions was not possible. In the case of vinylstannanes a number of reagents and reaction conditions which seemed reasonable were found to be inapplicable. For example, N-nitro-2,6-lutadinium fluoroborate in acetonitrile or nitromethane at 25° was totally without effect. On the other hand, nitronium fluoroborate at -78° in solvents such as acetonitrile-methylene chloride, methylene chloride, ethyl acetate or ether reacted indiscriminately to afford complex mixtures of products. Other commonly used mild nitrating reagents were no more successful.

It was discovered, however, that a new reagent, tetranitromethane in dimethyl sulfoxide (DMSO), was highly effective in replacing tin by nitro at unsaturated carbon. The solvent was found to be critical; acetonitrile, tetrahydrofuran, methanol and chloroform were unsatisfactory since little or no reaction occurred. Dimethylformamide did yield some of the product, but reaction rates were inconveniently slow. Hexamethylphosphoric amide could be used successfully, but offers no advantage to compensate for cost and toxicity problems.

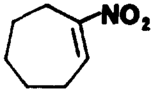
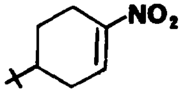
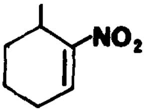
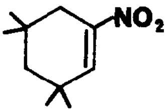
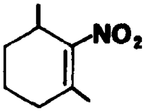
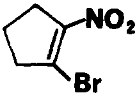
Reaction of vinylstannanes with tetranitromethane was carried out in DMSO at 25° until analysis of the reaction mixture (by TLC or PMR) indicated complete consumption of starting material (2-24 hr). Aqueous workup followed by silica column chromatography afforded the pure product.[5] The results of several experiments with a variety of substrates are summarized in the accompanying table. The experimental procedure which follows is illustrative.

1-Nitrocycloheptene. A solution of the trisyl hydrazone[6] (38.3 mmole, 15.0g) in 200 ml of TMEDA-hexanes (1:1)[7] was metalated with exactly 2.0 equivalents of sec-butyllithium/cyclohexane (76.6 mmole s-Bu Li, -80°C) and allowed to warm to -10°C until N_2 evolution ceased (40 min). A solution of freshly sublimed trimethyltin chloride (50 mmole, 9.97g, 1.3 equiv) in 30 ml hexanes was added all at once. Aqueous workup was followed by distillation through a short path apparatus at reduced pressure (85°C, aspirator) to give 1-trimethylstannylcycloheptene (8.3 g, 84%).

To a solution of the vinylstannane (3.8mmole, 991mg) and dry DMSO (4.0 ml) was added tetranitromethane (4.4 mmole, 863 mg, 1.1 equiv) over ca. 2 min. The resulting deep orange homogeneous solution was stirred at 18°C under argon for 2.5 hr. The reaction mixture was poured into 100 ml of water and extracted with pentane (5 x 15 ml). The pentane layer was washed with water (5 x 5 ml) until the organic layer was colorless. Filtration of the residue through a short column of silica (75 g SiO_2, 2% acetone-hexanes eluant) afforded 466 mg (87%) of pure nitrocycloheptene, pmr ($CDCl_3$, ppm): 7.42 (1H, t, J=6Hz, vinylic), 2.9 (2H, m, allylic CH_2), 2.4 (2H, m, allylic CH_2), 1.8 (6H, m, satd. CH_2); ir (CCl_4) 1663 (w, C=C), 1513 (s, unsatd. NO_2), 1337 (s, unsatd. NO_2).

The method for the conversion of cyclic ketones to nitro cycloolefins[9] which is disclosed herein makes available unsaturated nitro compounds which are not accessible by previously described reactions. This fact coupled with the utility of such compounds and the efficiency of the transformations involved in the present preparation should contribute to further development and future application.[10]

Table

Carbonyl Compound	Hydrazone,[a,b] % yield	Vinylstannane,[e] % yield	Nitroolefin	% yield,[g,h] Reaction, Time
cycloheptanone	99%	84%		87%, 2.5 hr.
4-t-butylcyclohexanone	89%	79%		94%,[i]
2-methylcyclohexanone	90%	91%		82%, 17 hr.
3,3,5,5-tetramethylcyclohexanone	90%	94%		77%,[j] 23 hr.
2,6-dimethylcyclohexanone	74%[c]	66%[f]		90%, 27 hr.
1,2-dibromocyclopentene	-	91%, d		92%, 5.8 hr.

[a] All hydrazones were prepared by treatment of the ketone in THF or CH_3CN with 1.0 equiv. of 2,4,6 triisopropylbenzenesulfonyl hydrazide at 23° (2-24 hr).

[b] Yields of hydrazone formation were not maximized.

[c] In CH_3CN containing 1 mole% conc. HCl at 23° for 21.3 hr.

[d] Prepared from 1-lithio-2-bromocyclopentene.[8]

[e] All vinylstannanes were purified by distillation at reduced pressure.

[f] Dropwise addition of s-BuLi/cyclohexane (3.2 equiv) to a finely divided suspension of the hydrazone in tetramethylethylenediamine at 0°C. Reaction at 23° for 6.4 hr, cooling to -45°C, followed by treatment with Me_3SnCl (2.4 equiv) for 3 hr.

[g] Tetranitromethane was stirred over CaH_2 (25°C, 12 hr) and distilled directly into a precooled flask (25°C, 0.5 mm).

[h] Treatment of the vinylstannane in dry DMSO (1M) with tetranitromethane (1.1 equiv) at r.t.

[i] Reaction in CCl_4 at reflux for 5.75 hr.

[j] HMPA used as solvent.

References and Notes

1. E. J. Corey and H. Estreicher, *J. Am. Chem. Soc.*, **100**, 6294 (1978).
2. For a recent review on the synthesis and chemistry of nitro compounds, see D. Seebach, E. W. Colvin, F. Lehr, and T. Weller, *Chimia*, **33**, 1 (1979).
3. This process, which represents a retro vinyl Nef reaction, is unprecedented.
4. A. R. Chamberlin, J. E. Stemke, and F. T. Bond, *J. Org. Chem.*, **43**, 147 (1978).
5. For a discussion of the mechanism of tetranitromethane nitrations, see, (a) C. Lagercrantz, *Acta Chem. Scand.*, **18**, 382 (1964), (b) R. W. Bradshaw, *Tetrahedron Lett.*, 5711 (1966).
6. N. J. Cusack, C. B. Reese, A. C. Risius, and B. Roozpeikar, *Tetrahedron*, **32**, 2157 (1976).
7. THF can be used as solvent as long as the alkenyllithium solution is recooled to −78°C prior to addition of Me_3SnCl.
8. G. Wittig et al., *Chem. Ber.* **98**, 458 (1965).
9. The above described nitration conditions can also be used in the preparation of allyl nitro compounds. Thus treatment of allyl trimethylstannane with 1.0 equiv of $C(NO_2)_4$ in DMSO at 17°C leads to isolation of the corresponding allyl nitro in 56% yield.
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