Tetrahedron Letters No. 45, pp 4033 - 4036, 1976. Pergamon Press. Printed in Great Britain.

A METHOD FOR THE BENZOANNULATION OF KETONES

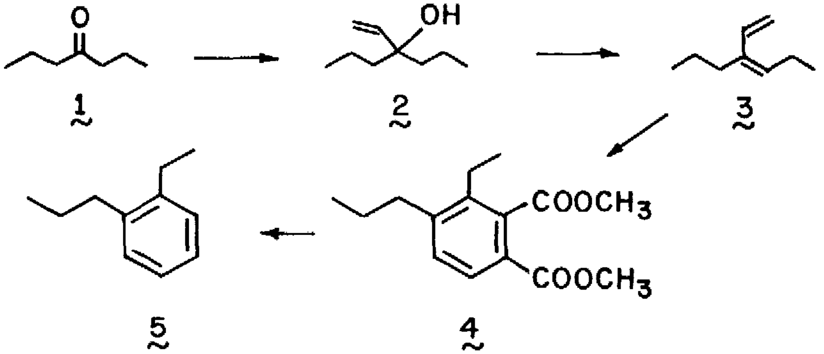
Leo A. Paquette,* William P. Melega,[1a] and James D. Kramer[1b]

Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210

(Received in USA 9 August 1976; received in UK for publication 21 September 1976)

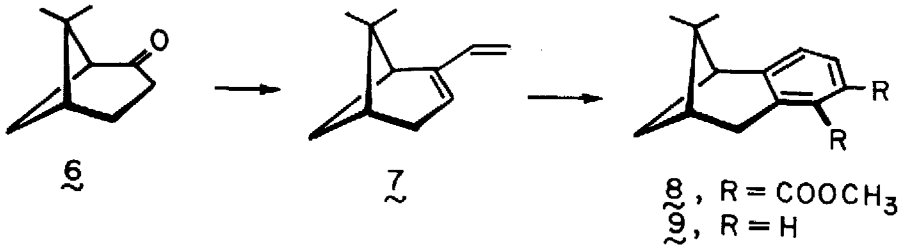
The importance to organic synthesis of the varied annulation reactions which result in fusion of a cyclohexenone ring to a preexisting carbonyl compound has recently been underscored.[2] Despite the widespread utilization of this particular transformation, there has appeared to our knowledge no satisfactory method for the benzoannulation of a ketone having an adjacent methylene group. Because the need for such a synthetic transformation arose in these laboratories, we were led to develop a convenient procedure whose utilitarian nature is now described in the form of several adaptations.

Reaction of 4-heptanone (1)with 2 equiv of vinylmagnesium bromide in refluxing tetrahydrofuran for 5 hr followed by quenching with saturated NH_4Cl solution produced alcohol 2 (93%), from which diene 3 was obtained in 74% yield by iodine-catalyzed dehydration (95°, 3 hr).[3] Diels-Alder cycloaddition of dimethyl acetylenedicarboxylate (DMAD) to 3 followed by direct dehydrogenation with DDQ (C_6H_6, 25°, 20 hr) gave diester 4 (66%). Saponification of 4 and subsequent decarboxylation with copper powder in quinoline (reflux, 20 hr) afforded *o*-(*n*-propyl)ethylbenzene (5, 45%).[4]

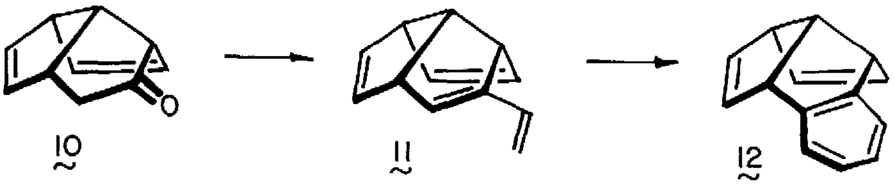


Benzopinane (9) was obtained as follows. Sequential treatment of nopinone (6) with vinylmagnesium bromide and iodine in the predescribed fashion gave nopadiene (7) free of isomeric contaminants[5] in 65% overall yield. Subsequent condensation with DMAD produced 8

(75%). This diester underwent ready saponification and decarboxylation to deliver exclusively the desired hydrocarbon (74%).

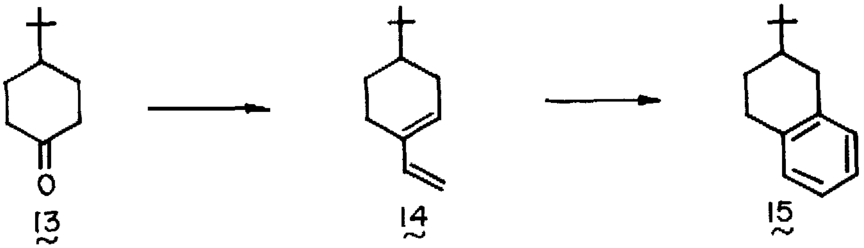


Of interest is the comparison of these results with those obtained in the case of 2,3-dihydrotriquinacen-2-one (10),[6] where vinylmagnesium chloride addition occurred with >98% exo stereoselectivity (85% isolated). Diene 11 resulted (90%) when this alcohol was dehydrated with thionyl chloride and powdered Na_2CO_3 in ether (25°, 36 hr). The further elaboration of benzotriquinacene (12), achieved in comparable fashion (30% overall from 11), demonstrated the successful application of this procedure to polyolefinic systems.



For simple cyclohexanone derivatives such as 13, the two-carbon homologation, dehydration, and cycloaddition steps proceed with particular efficiency (80-95%). When aromatization of the DMAD adduct is conducted at room temperature, selective aromatization of the 1,4-cyclohexadiene ring can again be accomplished without difficulty. The preparation of 2-*tert*-butyl-1,2,3,4-tetrahydronaphthalene (15)[7] was thereby successfully realized (25% overall from 14). Suitable experimental conditions are given below. However, by conducting the DDQ reactions at more elevated temperatures, direct conversion to the respective naphthalenes can be achieved. Thus, the sequence may be extended to the preparation of polycyclic aromatics if desired.[8]

Although our yields are not maximized, numerous variations in reaction conditions are conceivable, particularly as regards the initial steps, which might lead to enhanced efficiency. For example, one might favorably effect introduction of the vinyl group by making recourse instead to vinyllithium.[9] By this expedient, the level of 1,2 addition might be



enhanced at the expense of simple enolization. Also, several alternative modes of dehydration of the intermediate vinyl alcohols could be employed. While iodine in catalytic quantities is generally preferred because of the intrinsic mildness of this reagent,[10] the use of more forcing conditions is not precluded in those cases where this reagent may prove ineffective.

Conversion of 4-*tert*-Butylcyclohexanone (13) to 1,2,3,4-Tetrahydronaphthalene 15. A solution of 13 (4.0 g, 25.9 mmol) in dry tetrahydrofuran was added dropwise to a solution of vinylmagnesium bromide (prepared from 5.5 ml of vinyl bromide and 1.57 g of magnesium in 80 ml of the same solvent). This mixture was heated at reflux for 15 hr, cooled, and hydrolyzed with saturated ammonium chloride solution. The tetrahydrofuran was evaporated and the residual aqueous solution was extracted with ether. Concentration and molecular distillation of the dried organic phases gave 4.15 g (88.3%) of vinyl alcohol.

A mixture of 6.0 g (33 mmol) of this alcohol and 225 mg of sublimed iodine crystals was heated at 95° for 2 hr under nitrogen, diluted with hexane (50 ml), washed with water, and dried. The solvent was removed and the crude product chromatographed on silica gel to give 4.4 g (82%) of 14 as a colorless liquid; $\delta^{CDCl_3}_{TMS}$ 6.8 - 4.8 (series of m, 4), 2.6 - 1.8 (m, 7), and 0.95 (s, 9).

A mixture of 14 (340 mg) and dimethyl acetylenedicarboxylate (290 mg) was heated with stirring at 90° under nitrogen for 20 hr. Anhydrous benzene (20 ml) and DDQ (470 mg) were added and this solution was stirred for 18 hr at room temperature. The benzene was removed and the residue chromatographed on alumina (ether elution). There was obtained 550 mg (85%) of the singly aromatized diester as a viscous pale yellow oil; $\delta^{CDCl_3}_{TMS}$ 7.6 (d, J = 7 Hz, 1), 7.08 (d, J = 7 Hz, 1), 3.9 (s, 3), 3.82 (s, 3), 3.1 - 2.7 (m, 4), 1.8 - 1.1 (m, 3), and 0.95 (s, 9); *m/e* 304.1680 (calcd 304.1674).

A 2.0 g (6.58 mmol) sample of the diester was treated with 4 equiv of aqueous sodium hydroxide solution and stirred at 55° under nitrogen for 36 hr. The homogenous solution was acidified with 5% hydrochloric acid and extracted with dichloromethane. The combined organic layers were dried and evaporated to furnish 1.1 g (60%) of crystalline diacid.

A mixture of the diacid (1.0 g) and copper powder (2.54 g) in freshly distilled quinoline (50 ml) was heated at reflux under nitrogen for 10 hr, cooled, diluted with hexane, filtered, and washed thoroughly with 3 *N* hydrochloric acid, water, and saturated $NaHCO_3$ and NaCl solutions. The dried concentrate was purified by preparative gas chromatography to give a 38% isolated yield of 15 which proved identical to the authentic sample.[7]

Acknowledgment. The authors thank the National Institutes of Health (AI-11490) for financial support.

References

(1)(a) Undergraduate research participant, 1975-1976; (b) National Institutes of Health Postdoctoral Fellow, 1974-1975.

(2) M. E. Jung, *Tetrahedron*, **32**, 3 (1976).

(3) B. A. Arbusow and W. S. Abramow, *Chem. Ber.*, **67**, 1942 (1934); W. L. Mosby, *J. Am. Chem. Soc.*, **74**, 2564 (1952); Y. -R. Naves and F. Bondavalli, *Helv. Chim. Acta*, **48**, 563 (1965); B. A. Nagasampagi, S. Dev, C. Rai, and K. L. Murthy, *Tetrahedron*, **22**, 1949 (1966).

(4) R. A. Benkeser, T. E. Johnston, and W.-H. Tong, *J. Org. Chem.*, **33**, 2203 (1968).

(5)(a) L. J. Kitchen, *J. Am. Chem. Soc.*, **73**, 2368 (1951); (b) G. Ohloff and G. Schade, *Angew. Chem.*, **67**, 427 (1955); G. Ohloff, *Ann.*, **627**, 79 (1959); G. Ohloff, H. Farnow, and G. Schade, *Chem. Ber.*, **89**, 1549 (1956); G. Ohloff, *ibid.*, **90**, 1554 (1957); (c) C. A. Cupas and W. A. Roach, *J. Org. Chem.*, **34**, 742 (1969); (d) B. Bochwic and S. W. Markowicz, *Roczniki Chem.*, **47**, 1083 (1973); **50**, 87 (1976).

(6) R. C. Kelly, Ph.D. Thesis, Harvard University, 1965; L. A. Paquette, G. V. Meehan, and S. J. Marshall, *J. Am. Chem. Soc.*, **91**, 6779 (1969); R. Russo, Y. Lambert, and P. Deslongchamps, *Can. J. Chem.*, **49**, 531 (1971); L. A. Paquette, W. B. Farnham, and S. V. Ley, *J. Am. Chem. Soc.*, **97**, 7273 (1975); L. A. Paquette, I. Itoh, and W. B. Farnham, *ibid.*, **97**, 7280 (1975).

(7) W. P. Duncan, J. W. Burnham, E. J. Eisenbraun, M. C. Hamming, and G. W. Keen, *Synth. Commun.*, **3**, 89 (1973).

(8) As examples of other possible dienophiles, see L. A. Paquette, R. E. Wingard, Jr., J. C. Philips, G. L. Thompson, L. K. Read, and J. Clardy, *J. Am. Chem. Soc.*, **93**, 4508 (1971).

(9) E. C. Juenge and D. Seyferth, *J. Org. Chem.*, **26**, 563 (1961); R. West and W. H. Glaze, *ibid.*, **26**, 2096 (1961); D. Seyferth and M. A. Weiner, *J. Am. Chem. Soc.*, **83**, 3583 (1961).

(10) R. P. Thummel, *J. Am. Chem. Soc.*, **98**, 628 (1976).