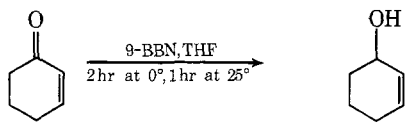
Table I
Reduction of 2-Cyclopentenone with Various Reducing Agents

Reagent	Product composition,[a] % O	OH	O	OH
$LiAlH_4$, THF, 0°[b]	0.0	14.0	2.5	83.5
$LiAlH(O\text{-}tert\text{-}Bu)_3$, THF, 0°[b]	0.0	0.0	11.2	88.8
$NaBH_4$, EtOH, 78°[b]	0.0	0.0	0.0	100.0
AlH_3, THF, 0°[b]	0.0	90.0	6.1	3.9
$i\text{-}Bu_2AlH$, C_6H_6, 0°[c]	0.5	99.0	0.0	0.5
9-BBN, THF, 0°[d]	0.0	100.0	0.0	0.0

[a] Analysis by GLC. [b] Reference 7. [c] Reference 9a. [d] Present work.

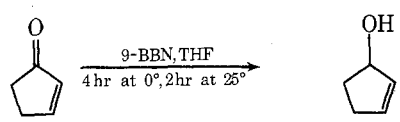
2-Cyclohexenone is converted to 2-cyclohexenol in quantitative yield (eq 3).



(3)

100% (84% isolated)

Even 2-cyclopentenone, known for it's susceptibility to undergo conjugate addition with hydride reducing agents,[7] is cleanly converted to the desired 2-cyclopentenol in essentially quantitative yield (eq 4).

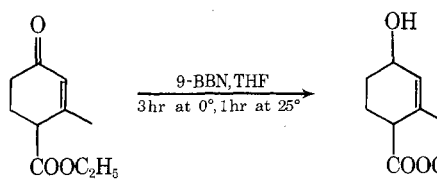


(4)

100% (85% isolated)

Results summarized in Table I clearly reveals the superiority of 9-BBN over previously available reagents, such as lithium aluminum hydride, lithium tri-*tert*-butoxyaluminohydride, sodium borohydride, and aluminum hydride.

Further, the results of the competition experiments involving 2-cyclohexenone and organic compounds containing representative functional groups toward 9-BBN and of other research underway[5] indicate that the present reaction can tolerate the presence of a large variety of functional groups, such as nitro, halogen, epoxide, carboxylic acid, ester, amide, nitrile, sulfide, disulfide, sulfoxide, sulfone, tosylate, azo, etc. This is a major advantage of 9-BBN over other reagents such as diisobutylaluminum hydride.[9] The remarkable utility of 9-BBN for such selective reductions involving polyfunctional substrates is confirmed by the selective conversion of 4-carbethoxy-3-methyl-2-cyclohexenone to 4-carbethoxy-3-methyl-2-cyclohexenol and *o*-nitrocinnamaldehyde to *o*-nitrocinnamyl alcohol in yields of 95 and 76%, respectively (eq 5).



(5)

95% (86% isolated)

The following preparative procedure for the reduction of 2-cyclopentenone to 2-cyclopentenol is representative. An oven-dried 500-ml three-necked flask, equipped with a side arm fitted with a silicone rubber stopple, egg-shaped stirring bar, and pressure equalizing dropping funnel connected to a mercury bubbler through a connecting tube, was flame dried and cooled to room temperature under a dry stream of nitrogen. The flask was charged with 25 ml of dry THF and 8.35 ml (8.21 g, 100 mmol) of 2-cyclopentenone ($n^{20}D$ 1.4814) and cooled to 0° with an ice bath. Then, 171.7 ml (103 mmol) of a 0.6 *M* 9-BBN solution in THF was added dropwise over a period of 2 hr with vigorous stirring. After 4 hr at 0°, the solution was stirred for 2 hr at 25°. Then 0.5 ml of methanol was added to destroy excess 9-BBN. THF was removed under reduced pressure and dry *n*-pentane (100 ml) added, followed by 6.4 ml (6.3 g, 103 mmol) of 2-aminoethanol. Immediately the ethanolamine derivative of 9-BBN precipitated. The mixture was centrifuged and the clean pentane layer decanted. The precipitate was washed with three 30-ml portions of *n*-pentane and centrifuged, and the decantates were added to the main fraction. Pentane was distilled off and the residue on vacuum distillation gave 7.12 g (85%) of 2-cyclopentenol as a colorless liquid, bp 78° (59 mm), $n^{20}D$ 1.4716 [lit.[10] bp 52° (12 mm), $n^{20}D$ 1.4717], >99% pure by GLC.

In conclusion, it should be pointed out that 9-BBN possesses certain major advantages over other reagents for this transformation. It reduces 2-enones, normally highly susceptible to conjugate reduction, cleanly to the allylic alcohols. Yet it is a very mild reducing agent, similar to sodium borohydride and lithium tri-*tert*-butoxyaluminohydride in its selectivity.

References and Notes

(1) Presented at the 169th National Meeting of the American Chemical Society, Philadelphia, Pa., April 1975.
(2) E. F. Knights and H. C. Brown, *J. Amer. Chem. Soc.*, **90**, 5280, 5281 (1968).
(3) C. G. Scouten and H. C. Brown, *J. Org. Chem.*, **38**, 4092 (1973); H. C. Brown, E. F. Knights, and C. G. Scouten, *J. Amer. Chem. Soc.*, **96**, 7765 (1974).
(4) 9-BBN is now available commercially from the Aldrich Chemical Co., Milwaukee, Wis., both as the solid and the solution in tetrahydrofuran.
(5) An extensive study by Drs. S. Krishnamurthy and N. M. Yoon is underway.
(6) For a recent detailed and critical discussion, see M. R. Johnson and B. Rickborn, *J. Org. Chem.*, **35**, 1041 (1970).
(7) H. C. Brown and H. M. Hess, *J. Org. Chem.*, **34**, 2206 (1969).
(8) This convenient precipitation of the 9-BBN–ethanolamine adduct was developed by Gary W. Kramer of our laboratory for a related application.
(9) (a) K. E. Wilson, R. T. Seidner, and S. Masamune, *J. Chem. Soc., Chem. Commun.*, 213 (1970); (b) "The Use of Aluminum Alkyls in Organic Synthesis", Ethyl Corporation, 1970 and 1973; (c) "Specialty Reducing Agents", Texas Alkyls Inc.
(10) K. Alder and F. H. Flock, *Chem. Ber.*, **89**, 1732 (1956).
(11) Postdoctoral Research Associate on Grant No. DA-ARO-D-31-124-73G148, supported by the U.S. Army Research Office (Durham).

Richard B. Wetherill Laboratory **S. Krishnamurthy**[11]
Purdue University **Herbert C. Brown***
West Lafayette, Indiana 47907

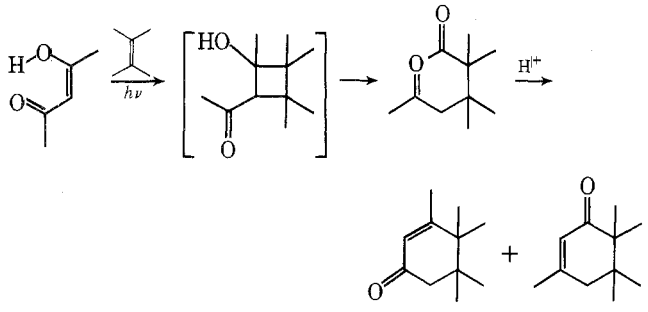
Received March 5, 1975

Photoannelations with α-Formyl Ketones. Enol Specificity in the Reaction of Acyclic α-Formyl Ketones with Alkenes[1]

Summary: The irradiation of several acyclic α-formyl ketones in the presence of alkenes gives rise to photoproducts derived exclusively from that tautomer enolized toward the aldehyde carbonyl, which can then be cyclized to provide a new cyclohexenone annelation sequence.

Sir: The photochemical cycloaddition of β diketones to alkenes[2a,b] is well documented and has been adequately reviewed.[3a-e] In general this reaction can be viewed as pro-

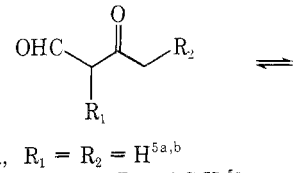
ceeding through one of two possible enols to give a substituted 2-acylcyclobutanol which then suffers ring fragmentation yielding a 1,5 diketone. Subsequent aldol cyclization of the photoproduct affords various cyclohexenones. Al-



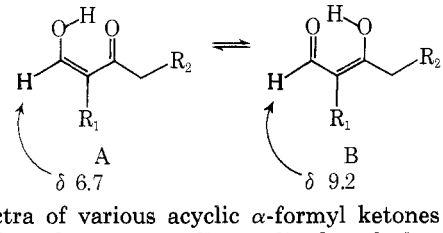
though the material yields are generally good, the considerable synthetic potential of this two-step sequence has not been totally realized. In significant measure this is due to the large number of products which often results. For example, the reaction between an *unsymmetrical* β diketone and an *unsymmetrical* alkene followed by aldolization can give eight structurally different cyclohexenones, neglecting stereoisomers. This multiplicity arises because there are (a) *two* reactive enol tautomers per diketone, (b) *two* alkene orientations per enol, and (c) *two* aldol products per photoproduct. Such mixtures have often restricted the preparative value of the process.[3f]

We now wish to report that the analogous reaction with α-formyl ketones leads to a significant reduction in product complexity and renders the process generally useful.

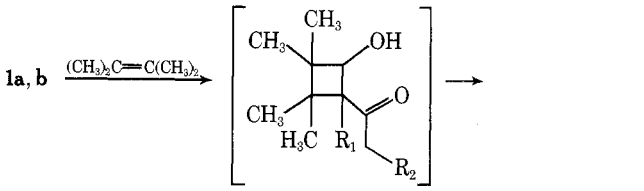
It occurred to us some time ago that acyclic α-formyl ketones might be attractive partners in photochemical annelations. We reasoned that their use could result in significant simplification of the photochemical annelation sequence, as compared to β diketones. For instance, a twofold simplification arises directly because the ketoaldehyde photoproduct can only undergo a single aldol cyclization. We hoped that additional simplification would result if the two enol tautomers were sufficiently different, either in reactivity or concentration, to permit preferential reaction of one tautomer in the photochemical cycloaddition step. It is the purpose of this paper to report that our preliminary findings are in complete accord with these expectations and that a potentially general and useful annelation process has emerged. To date there have been no reports of such reactions with α-formyl ketones, although two groups have employed a dialdehyde in ingenious syntheses of loganin.[4]



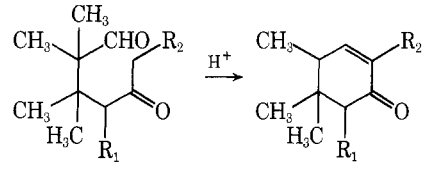
1a, $R_1 = R_2 = H$[5a,b]
b, $R_1 = H$, $R_2 = i\text{-}C_3H_7$[5c]
c, $R_1 = R_2 = CH_3$[5d]



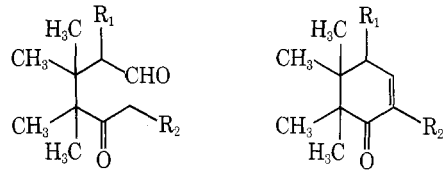
The NMR spectra of various acyclic α-formyl ketones clearly indicate that they are totally enolized and that there is an appreciable concentration of both enols in all cases.[6,7] In fact the relative amounts of the two enols are rather insensitive to substitution patterns, in contrast to the formyl derivatives of cyclic ketones.[6a] It was thus somewhat surprising when irradiation of various symmetrical alkenes with α-formyl ketones provided products which were exclusively derived from tautomer A. For instance formylacetone and tetramethylethylene afforded keto aldehyde **3a** in quantitative yield. Particularly diagnostic was the aldehyde singlet at 9.64. There was no trace of an additional aldehyde proton absorption (triplet) for the alternative photoproduct **5a,** ruling out the intervention of tautomer B in the photocycloaddition. Acid-catalyzed cyclization of **3a** then yielded cyclohexenone **4a** (69%)[8] as a single homogeneous substance.[9] Similar results were obtained with 4-isopropylformylacetone (**1b**) which was smoothly converted to keto aldehyde **3b.**[8] In no instance were we able to detect even trace quantities of **5b** which would arise from the alternate enol tautomer B.



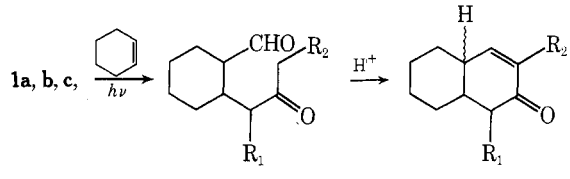
2a, b



3a, b **4a, b**



5a, b **6a, b**



7a, b, c **8a, b, c**

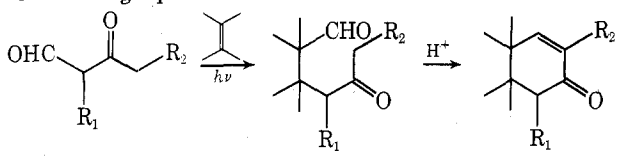
1a–8a, $R_1 = R_2 = H$; **1b–8b**, $R_1 = H$, $R_2 = i\text{-}C_3H_7$;
1c–8c, $R_1 = R_2 = CH_3$

We have also caused formyl ketones **1a–c** to react with cyclohexene and again the results indicate a specific reaction with tautomer A. For example, formylacetone (**1a**) reacted with cyclohexene at −20° to −30° to give ketoaldehyde **7a** which was then directly cyclized to octalone **8a** (mixture of stereoisomers).[8,10] In a similar fashion, formyl ketones **1b** and **1c** were specifically converted to the substituted octalones **8b** and **8c**[8,11]

An explanation for the selective enol reactivity observed in this study is difficult to advance at this time. We have made the *qualitative* observation that formyl ketone **1b** affords more product than does acetylacetone in a competitive reaction for excess cyclohexene. However, the reversible formation of intermediates in this reaction[12] does not permit us to determine the relative rates of reaction.

Taken together, the experiments that we have reported here indicate that alkenes can be expected to react preferentially, if not exclusively, with that tautomer of a simple

acyclic α-formyl ketone which is enolized toward the aldehyde carbonyl. Because the photoproducts can only undergo aldolization in a single sense, a fourfold simplification in the overall annelation sequence has resulted, compared with the analogous reactions with β diketones. In terms of net structural change, the reaction can be summarized by the following equation.



The single remaining point of ambiguity, orientation of the photoaddition with unsymmetrical alkenes, is currently under investigation. Based on preliminary findings we expect our studies to result in a general cyclohexenone synthesis which complements existing methods.[13]

References and Notes

(1) (a) We wish to thank the U.S. Public Health Service for financial support (Grant No. 1 R01 GM20780-01). (b) A portion of this work was presented at the 168th National Meeting of the American Chemical Society, Sept 8–13, 1974, Atlantic City, N.J., Orgn 100. (c) We are indebted to Dr. David Rosenthal and Mr. Fred Williams of the Research Triangle Institute for Mass Spectrometry (supported by NIH Grant RR 00330) for mass spectral determinations.

(2) (a) P. de Mayo, H. Takeshita, and A. B. M. A. Sattar, *Proc. Chem. Soc.*, 119 (1962); (b) P. de Mayo and H. Takeshita, *Can. J. Chem.*, **41**, 440 (1963).

(3) (a) P. de Mayo, *Acc. Chem. Res.*, **4**, 41 (1971). (b) P. G. Sammes, *Synthesis*, **3**, 636 (1970). (c) P. G. Bauslaugh, *Ibid.*, **3**, 287 (1970); (d) P. G. Sammes, *Quart. Rev.*, **24**, 37 (1970). (e) P. E. Eaton, *Acc. Chem. Res.*, **1**, 50 (1968). (f) For a particularly informative example of these complexities, see H. Nozaki, M. Kurita, T. Mori, and R. Noyori, *Tetrahedron*, **24**, 1821 (1968).

(4) (a) J. J. Partridge, N. K. Chadha, and M. R. Uskokovic, *J. Am. Chem. Soc.*, **95**, 532 (1973); (b) G. Büchi, J. A. Carlson, J. E. Powell, Jr., and L.-F. Tietze, *ibid.*, **95**, 540 (1973).

(5) (a) R. L. Frank and R. H. Varland, "Organic Syntheses", Collect. Vol. III, Wiley, New York, N.Y., 1955, p 829; (b) W. O. George and V. G. Mansell, *J. Chem. Soc. B*, 132 (1968); (c) R. P. Mariella, *J. Am. Chem. Soc.*, **69**, 2670 (1947); (d) L. Claisen and L. Meyerowitz, *Chem. Ber.*, **22**, 2373 3273 (1889).

(6) (a) E. W. Garbisch, Jr., *J. Am. Chem. Soc.*, **85**, 1696 (1963); (b) E. W. Garbisch, Jr., *ibid.*, **87**, 505 (1965); (c) E. W. Garbisch, Jr., and J. G. Russell, *Tetrahedron Lett.*, 29 (1967); (d) V. A. Glndin, I. A. Chripun, B. A. Ershov, and A. I. Kolstov, *Org. Mag. Resonance*, **4**, 63 (1972).

(7) NMR spectra were determined in CCl_4 solution at ambient temperature; only slight deviations were noted relative to solvolysis conditions (pentane solutions at −20°). The NMR absorption for the "aldehyde" hydrogen (δ 7.6–7.9) was used to calculate the position of the rapid equilibrium (A ⇌ B) assuming extreme values of δ 6.7 and 9.2 for tautomers A and B, respectively.[6a] The ratio concentrations of the tautomers A:B for **1a**, **1b**, and **1c** are 52:48, 52:48, and 64:36, respectively.

(8) New compounds gave satisfactory elemental and spectral analyses. Although the yields of the reactions reported here have not been optimized, they are generally in the range of 60–100% for the photolysis and 60–90% for the aldol cyclization.

(9) Careful analysis of the aldehyde region of the NMR spectra of the crude photoproducts permitted the assignment of structure **3 vs. 5**. These results are in accord with a similar analysis of the cyclized material, **4 vs. 6**. For instance, **3b** exhibited a singlet at δ 9.64 while **4b** showed a singlet at δ 6.05. Compounds **5b** and **6b** would be expected to show a triplet and double doublet, respectively, for the same two protons. Because we could detect no trace of the alternate absorptions, we feel justified in assigning a conservative value of >95% for the enol specificity in the photochemical cycloadditions.

(10) The location of the carbonyl group at C-2 of **8a**, and thus the specificity of this photoaddition, was verified by mass spectral determination of the extent of deuterium exchange in the dihydro derivative of **8a**.

(11) The identity of **8c** was verified by independent synthesis.

(12) (a) P. de Mayo, A. A. Nicholson, and M. F. Tchir, *Can. J. Chem.*, **47**, 711 (1969); (b) P. J. Wagner and D. J. Bucheck, *ibid.*, **47**, 713 (1969).

(13) The photolyses reported here were performed with an excess of alkene using a Hanovia 450-W medium-pressure lamp through Corex or Pyrex. The reactor was cooled to −20 to −30° during irradiation, a condition which afforded increased efficiency in product formation as well as cleaner reaction mixtures. Reaction times were generally between 1 and 2 hr for the complete conversion of 2–4 g of formyl ketone.

Paul M. Gross **S. W. Baldwin***
Chemical Laboratory **R. E. Gawley**
Duke University **R. J. Doll**
Durham, North Carolina 27706 **K. H. Leung**

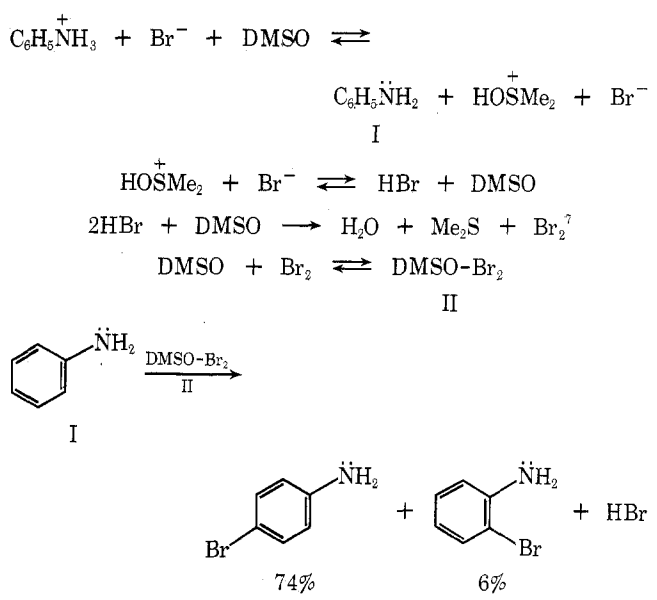
Received April 8, 1975

Indirect Bromination by Reaction of Aniline Hydrobromide with Dimethyl Sulfoxide

Summary: Indirect bromination of aniline can be achieved by reaction of the aniline hydrobromide salt with dimethyl sulfoxide to afford *p*-bromoaniline and *o*-bromoaniline in a 12:1 ratio. This simple indirect bromination proceeds with a high degree of regiospecificity to afford predominantly *p*-bromoaniline.

Sir: Fletcher and coworkers[1] have reported that 2-amino-3-bromofluorenone is obtained from the reaction of *tert*-butyl bromide and 2-aminofluorenone in dimethyl sulfoxide and from the reaction of 2-aminofluorenone with 48% HBr in dimethyl sulfoxide. We wish to report that the reaction of aniline hydrobromide with dimethyl sulfoxide at an elevated temperature (refluxed for 45 min) afforded predominantly the *p*-bromoaniline in 74% yield and only 6% *o*-bromoaniline. This indirect bromination process is summarized in Scheme I which depicts the DMSO–Br_2 adduct[2] II as the active brominating species.

Scheme I



The process depicted in Scheme I illustrates the selective indirect bromination of aniline by way of its hydrobromide salt to yield almost exclusively *p*-bromoaniline.[3] This result is somewhat surprising since direct bromination[3b] of aniline in most instances yields di- and trisubstituted derivatives.

Although the DMSO–Br_2 adduct has been depicted in Scheme I as the brominating species we have no direct evidence of its constitution. A second possible brominating agent is the Me_2S–Br_2 adduct;[4] dimethyl sulfide formed in the oxidation of hydrogen bromide could complex with free bromine. However the formation of both of the bromine adducts would be expected to be reversible processes, and it would be anticipated that the reaction conditions would favor the formation of the DMSO–Br_2 adduct (provided that the thermodynamic stabilities of the two adducts are not vastly different), since the reaction is normally carried out in the presence of a large excess of DMSO.

p- and o-Bromoaniline. Aniline hydrobromide (13.05 g, 0.075 mol) was added to 100 ml of dimethyl sulfoxide[5] and the resulting mixture was refluxed for 45 min. The reaction was allowed to cool to room temperature and poured into a dilute solution of sodium