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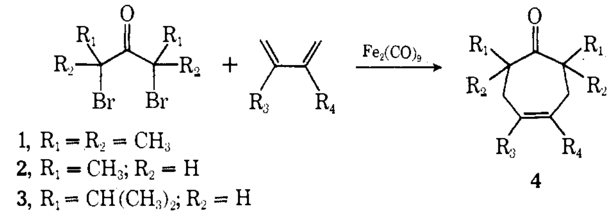
Reaction of α,α'-Dibromo Ketones with Iron Carbonyls in the Presence of 1,3-Dienes. A New Route to Troponoid Compounds

Sir:

Cycloadditions and cyclocondensations are the most widely used reactions for constructing the framework of organic molecules, and an enormous number of publications on these subjects have been presented. However, only a few examples are known of the formation of carbocyclic seven-membered rings by combining three- and four-carbon units.[1] We wish to describe a dehalogenation of α,α'-dibromo ketones with iron carbonyls in the presence of 1,3-dienes, which provides a novel, direct route to seven-membered cyclic ketones including troponoid compounds.

When a solution of 2,4-dibromo-2,4-dimethylpentan-3-one (**1**), diiron nonacarbonyl ($Fe_2(CO)_9$), and 2,3-dimethylbutadiene (1.0:1.2:9.0 mole ratio) in dry benzene was heated at 60° for 40 hr under nitrogen atmosphere, 2,2,4,5,7,7-hexamethyl-4-cycloheptenone (**4**, $R_1 = R_2 = R_3 = R_4 = CH_3$) was obtained in 71% yield after work-up.[2] The spectral data were in accord with the assigned structure: mass *m/e* 194 (M^+); nmr (CCl_4, TMS) δ 1.07 (s, 12 H, CH_3), 1.79 (s, 6 H, CH_3), and 2.25 (s, 4 H, $>CH_2$); ir (neat liquid) 1685 cm^{-1} (C=O) characteristic of di-*tert*-alkyl ketones.[3] Butadiene, isoprene, or cyclopentadiene as the diene component afforded similar adducts in moderate to good yields. Secondary dibromides **2** and **3** were also employable, but α,α'-dibromoacetone failed to give the corresponding cycloheptenones. Iron pentacarbonyl ($Fe(CO)_5$) could be used as the reducing agent, but less effectively. The use of the butadieneiron tricarbonyl complex (**5**)[4] in place of $Fe_2(CO)_9$ and free butadiene resulted in notably increased yields of cycloheptenones. Some examples of the new annelation reaction are summarized in Table I.



1, $R_1 = R_2 = CH_3$
2, $R_1 = CH_3$; $R_2 = H$
3, $R_1 = CH(CH_3)_2$; $R_2 = H$

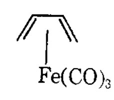
4

Table I. Reaction of α,α'-Dibromo Ketones with $Fe_2(CO)_9$ in the Presence of 1,3-Dienes

Dibromide[a]	Diene	Product	Yield,[b,c] %
1	2,3-Dimethylbutadiene	2,2,4,5,7,7-Hexamethyl-4-cycloheptenone	71
1	Butadiene	2,2,7,7-Tetramethyl-4-cycloheptenone	33 (84)
1	Isoprene	2,2,4,7,7-Pentamethyl-4-cycloheptenone	47
1	Cyclopentadiene	2,2,4,4-Tetramethylbicyclo[3.2.1]oct-6-en-3-one	82
2	Butadiene	2,7-Dimethyl-4-cycloheptenone	44 (55)
2	Isoprene	2,4,7-Trimethyl-4-cycloheptenone	36
2	2,3-Dimethylbutadiene	2,4,5,7-Tetramethyl-4-cycloheptenone	47
2	Cyclopentadiene	2,4-Dimethylbicyclo[3.2.1]oct-6-en-3-one	86
3	Butadiene	2,7-Diisopropyl-4-cycloheptenone	44 (77)
3	Isoprene	2,7-Diisopropyl-4-methyl-4-cycloheptenone	31
3	2,3-Dimethylbutadiene	2,7-Diisopropyl-4,5-dimethyl-4-cycloheptenone	50
3	Cyclopentadiene	2,4-Diisopropylbicyclo[3.2.1]oct-6-en-3-one	93

[a] Dibromo ketones **2** and **3** were used as mixtures of meso and *dl* isomers. [b] Isolated yield (preparative tlc on silica gel followed by distillation). [c] Yield obtained by the use of butadieneiron tricarbonyl (**5**) (dibromo ketones:**5** = 1:2, in benzene, 60–80°) is given in parentheses.

4-Cycloheptenones derived from secondary bromides and open-chain 1,3-dienes serve as potential intermediates for the synthesis of various seven-membered ketones, especially of troponoid compounds. For example, treatment of **4** ($R_1 = CH_3$, $R_2 = R_3 = R_4 = H$) with 4 equiv of pyrrolidone hydrotribromide in tetrahydrofuran (30°, 12 hr)[5] followed by dehydrobromination with lithium chloride in *N,N*-dimethylformamide (DMF) (140°, 1 hr) gave the known 2,7-dimethyltropone (**6**, $R_1 = CH_3$, $R_3 = R_4 = H$) in 64% yield, which was identified by comparison of the spectral data with those reported.[6] Bromination of **4** ($R_1 = CH_3$, $R_2 = R_3 = R_4 = H$) with 5.5 equiv of pyridine hydrotribromide in acetic acid (25°, 12 hr)[7] was followed by treatment with lithium chloride in DMF (130°, 1 hr) and hydrolysis of the resulting 4-bromo-2,7-dimethyltropone in a mixture of 48% $HBr-H_2O$–acetic acid (3:4:3) in a sealed tube (130°, 8 hr) to afford 2,7-dimethyl-γ-tropolone (**7**, $R_1 = CH_3$; $R_3 = H$) in 53% overall yield. Physical properties of troponoid de-



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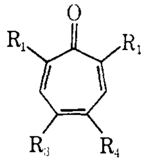

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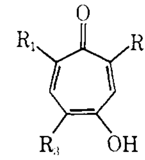

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(1) (a) R. A. Raphael, "Chemistry of Carbon Compounds," Vol. IIA, E. H. Rodd, Ed., Elsevier, New York, N. Y., 1953, p 249; E. S. Waight, "Rodd's Chemistry of Carbon Compounds," Vol. IIB, S. Coffey, Ed., Elsevier, New York, N. Y., 1968, p 347. (b) Cycloaddition of allyl cation to cyclic conjugate dines was recently reported: H. M. R. Hoffmann and D. R. Joy, *J. Chem. Soc. B*, 1182 (1968). (c) For the reaction of 1-diethylamino-1,3-butadiene with diphenylcyclopropenone, see J. Ciabattoni and G. A. Berchtold, *J. Amer. Chem. Soc.*, **87**, 1404 (1965).

(2) All new compounds gave correct elemental analyses and/or molecular peaks in mass spectra. Ir, nmr, and uv spectra were consistent with the structures assigned.

(3) J. Lascombe, P. Grange, and M. L. Josien, *Bull. Soc. Chim. Fr.*, 773 (1957).

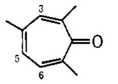
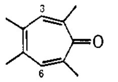
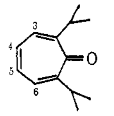
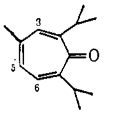
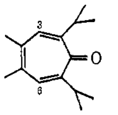
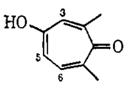
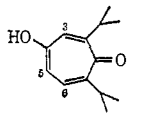
(4) R. B. King, *Organometal. Syn.*, **1**, 128 (1965).

(5) D. V. C. Awang and S. Wolfe, *Can. J. Chem.*, **47**, 706 (1969).

(6) G. L. Closs and L. E. Closs, *J. Amer. Chem. Soc.*, **83**, 599 (1961).

(7) C. Djerassi and C. R. Scholz, *ibid.*, **70**, 417 (1948).

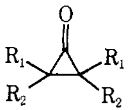
Table II. Physical Properties of New Troponoids

Compound	Yield,[a] %	Mp, °C	Uv, nm[b] (log ϵ)	Ir,[c] cm^{-1}	Nmr, δ[d,e]
	51	Oil	237 (4.19), 333 (3.89), 342 (3.86)	1559	2.29 (bs, 9 H, CH_3), 6.6–6.9 (m, 1 H, H_5), 7.1–7.3 (m, 2 H, H_3, H_6)
	66	88–89[f]	239 (4.25), 339 (3.76), 346 (3.76)	1553	2.28 (bs, 12 H, CH_3), 7.30 (bs, 2 H, H_3, H_6)
	63	Oil	238 (4.24), 243 (4.20), 325 (3.65), 340 (3.55)	1571	1.19 (d,[g] 12 H, CH_3), 3.1–3.8 (m, 2 H, >CH), 6.7–7.3 (A_2B_2 pattern, H_3, H_4, H_5, H_6)
	50	Oil	238 (4.31), 328 (3.80)[h]	1572	1.20 (d,[g] 6 H, CH_3), 1.22 (d,[g] 6 H, CH_3), 2.36 (s, 3 H, CH_3), 3.2–3.9 (m, 2 H, >CH), 6.6–6.9 (m, 1 H, H_5), 6.9–7.1 (m, 2 H, H_3, H_6)
	53	47–48[f]	240 (4.32), 334 (3.86)[h]	1563	1.19 (d,[g] 12 H, CH_3), 2.27 (s, 6 H, CH_3), 3.2–3.8 (m, 2 H, >CH), 7.00 (s, 2 H, H_3, H_6)
	55	168–170[i]	238 (4.34), 368 (4.28)[j]	1466[k]	2.03 (s, 3 H, CH_3), 2.13 (s, 3 H, CH_3), 6.66 (dd, 1 H, H_5), 7.62 (d, 1 H, H_3), 7.63 (d, 1 H, H_6)[l,m]
	46	160–161[i]	241 (4.31), 371 (4.29)[j]	1457[k]	1.08 (d,[g] 6 H, CH_3), 1.11 (d,[g] 6 H, CH_3), 3.0–3.6 (m, 2 H, >CH), 6.41 (dd, 1 H, H_5), 7.05 (d, 1 H, H_3), 7.12 (d, 1 H, H_6)[l,n]

[a] Isolated yield based on the 4-cycloheptenone. [b] Taken in H_2O unless otherwise stated. [c] Recorded in $CHCl_3$ except where otherwise indicated. Only the strongest band in the 1700–1400-cm^{-1} region is recorded. [d] Obtained in $CDCl_3$, unless a solvent is specified (60 MHz). [e] b = broad, s = singlet, d = doublet, m = multiplet. [f] From petroleum ether. [g] $J = 7.0$ Hz. [h] In MeOH. [i] From ethyl acetate. [j] In 0.1 *N* NaOH. [k] As Nujol mull. [l] In DMSO-d_6. The spectrum could also be interpreted as that of the tautomeric 3,5-dialkyl-γ-tropolone. [m] $J_{35} = 2.5$ Hz and $J_{56} = 10.5$ Hz. [n] $J_{35} = 2.0$ and $J_{56} = 10.0$ Hz.

rivatives obtained in a similar manner are given in Table II.

The annelation reaction which executed a key step of the new troponoid synthesis could *a priori* be accounted for by assuming the intervention of cyclopropanones **8**, allene oxides **9**, or the corresponding mesomeric zwitterions **10**,[8] produced by dehalogenation of dibromo ketones. However, free cyclopropanones add only to cyclic 1,3-dienes such as cyclopentadiene and furan, yielding bicyclic adducts, and *do not* react with acyclic conjugated dienes.[9] Furthermore, control experiments showed that reduction of the dibromo ketones **1**–**3** with zinc–copper couple in DMF, under which conditions formation of **9**[10] or **10**[11] would be expected, in the presence of 20-fold excess of 2,3-dimethylbutadiene, gives no trace of cycloheptenones. Thus mechanisms involving free **8**, **9**, or **10** seem unlikely. The reaction might proceed by way of the iron complexes bearing these species and diene as coordinated ligands. Alternatively, the coupling reaction might be achieved sequentially *via* iron enolates formed by an electron-transfer process,[12] or discrete σ-bonded organoiron compounds arising from oxidative addition[13] of the C–Br bond to iron carbonyl.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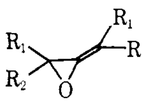
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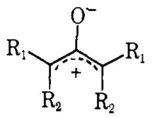
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(8) N. J. Turro, *Accounts Chem. Res.*, **2**, 25 (1969).

(9) N. J. Turro, S. S. Edelson, J. R. Williams, T. R. Darling, and W. B. Hammond, *J. Amer. Chem. Soc.*, **91**, 2283 (1969).

(10) H. M. R. Hoffmann and R. H. Smithers, *Angew. Chem.*, **82**, 43 (1970).

(11) (a) H. E. Zimmerman, D. Dopp, and P. S. Huyffer, *J. Amer. Chem. Soc.*, **88**, 5352 (1966); (b) H. E. Zimmerman and D. S. Crumine, *ibid.*, **90**, 5612 (1968); (c) T. M. Brennan and R. K. Hill, *ibid.*, **90**, 5615 (1968).

(12) Formation of nickel enolate was postulated in the reaction of α-bromo ketones and nickel carbonyl: E. Yoshisato and S. Tsutsumi, *ibid.*, **90**, 4488 (1968).

(13) J. P. Collman, *Accounts Chem. Res.*, **1**, 136 (1968).

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The Influence of Translational Entropy of Activation on Reaction Rates in Isotopic Solvents

Sir:

Hitherto, the influence of entropy has not been considered to be a major factor when different rates of reaction occur in isotropic solvents. In the case of water, pertinent discussions have emphasized the