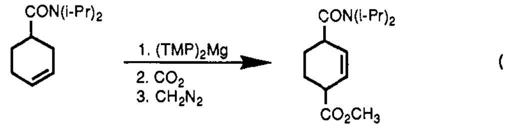
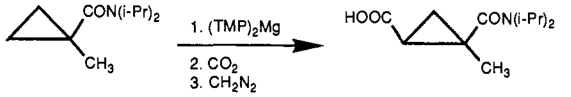
rather than the terephthalamide, we could even obtain some tetramethylpyromellitate (25%). However, in boiling THF some condensation between ester and intermediate amido-Grignard does occur, and this limits the yield of monomeric product.[19]

Ortho magnesiation is not restricted to aromatic systems. Similar to Beak's demonstration of remote lithiation,[7] we found that reaction of (*N*,*N*-diisopropylcarboxamido)cyclohex-3-ene with $(TMP)_2Mg$ gave, after carboxylation and esterification, the 4-carbomethoxy-2-ene in good yield (eq 4).



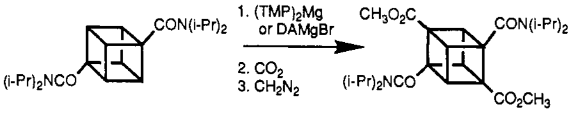
(4)

Following upon our earlier discoveries that ortho lithiation of amide-activated strained systems which have s-rich, acidity-enhanced C–H bonds,[8] we examined the behavior of cubane and cyclopropane derivatives toward amidomagnesium bases. This has been very successful. Reaction of 1-methyl-(*N*,*N*-diisopropylcarboxamido)cyclopropane with excess $(TMP)_2Mg$ followed by carboxylation and esterification gave the *cis*-2-carbomethoxy derivative in 85% yield, free of trans isomer (eq 5). Similar treatment of (*N*,*N*-diisopropylcarboxamido)cyclopropane, in which there is an acidic hydrogen α to the carbonyl group, gave both α- and β-carboxylation and some bis-carboxylation as well.



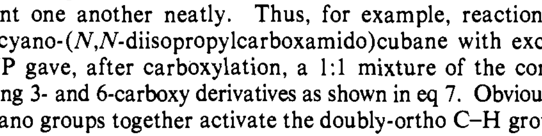
(5)

The cubane system behaves very well under magnesiation conditions. Reaction of 1,4-bis(*N*,*N*-diisopropylcarboxamido)cubane with excess $(TMP)_2Mg$ in refluxing THF, followed by carboxylation and esterification, gave directly the 1,4-diamide-2,7-diester derivative in better than 80% isolated yield (eq 6). DAMgBr worked as well in refluxing THF; at room temperature its reaction was controlled easily to give just monometalation and thus monocarboxylation.

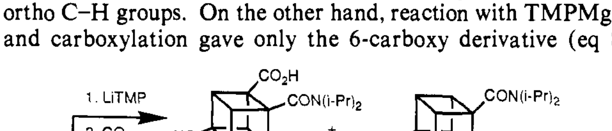


(6)

Ortho magnesiation and ortho lithiation reactions can complement one another neatly. Thus, for example, reaction of 2,4-dicyano-(*N*,*N*-diisopropylcarboxamido)cubane with excess LiTMP gave, after carboxylation, a 1:1 mixture of the corresponding 3- and 6-carboxy derivatives as shown in eq 7. Obviously, the cyano groups together activate the doubly-ortho C–H groups toward lithiation about as well as one amide group activates its ortho C–H groups. On the other hand, reaction with TMPMgBr and carboxylation gave only the 6-carboxy derivative (eq 8).



(7)



(8)

We are continuing our investigation of magnesium amide bases and will report soon on their structures and their utility for metalation in a variety of circumstances, on the uses of polymer bound magnesium amides, on optical induction from magnesium amides derived from chiral amines, etc. Similarly, we are expanding our work on amido-Grignard reagents.

Acknowledgment. We thank the National Institutes of Health (GM-36436), the Office of Naval Research, and the Technology Commercialization Center at The University of Chicago for support of this work. The National Science Foundation and the NIH, the latter through the University of Chicago Cancer Center (CA 14599), contributed significantly to the departmental instrument facility.

Registry No. $(TMP)_2Mg$, 117973-78-1; $(DA)_2Mg$, 23293-23-4; DAMgBr, 50715-01-0; TMPMgBr, 122357-95-3; TMP, 768-66-1; LiTMP, 38227-87-1; EtMgBr, 925-90-6; $PhCO_2Me$, 93-58-3; *p*-$MeO_2CC_6H_4CONEt_2$, 122357-96-4; *o*-$MeO_2CC_6H_4CO_2Me$, 131-11-3; 3,4-$(MeO_2C)_2C_6H_3CONEt_2$, 122357-99-7; 2,4-$(MeO_2C)_2C_6H_3CONEt_2$, 122382-43-8; dibutylmagnesium, 1191-47-5; diisopropylamine, 108-18-9; dimethyl terephthalate, 120-61-6; (*N*,*N*-diisopropylcarboxamido)cyclohex-3-ene, 87115-25-1; 1-methyl-1-(*N*,*N*-diisopropylcarboamido)cyclopropane, 106711-45-9; 1,4-bis-(*N*,*N*-diisopropylcarboxamido)cubane, 94161-36-1; 2,4-dicyano-1-(*N*,*N*-diisopropylcarboxamido)cubane, 122357-97-5; *N*,*N*-diethylbenzamide, 1696-17-9; *N*,*N*-diethylterephthalamide, 15394-30-6; 3,6-dicarboxy-*N*,*N*-diethylterephthalamide, 21761-77-3; 3,6-dicarbomethoxy-*N*,*N*-diethylterephthalamide, 122357-98-6; tetramethylpyromellitate, 635-10-9; 4-carbomethoxy-1-(*N*,*N*-diisopropylcarboxamido)cyclohex-2-ene, 122382-44-9; *cis*-2-carboxy-1-methyl-1-(*N*,*N*-diisopropylcarboxamido)cyclopropane, 122358-00-3; 2,7-dicarboxy-1,4-bis(*N*,*N*-diisopropylcarboxamido)cubane, 106711-44-8; 6-carboxy-2,4-dicyano-1-(*N*,*N*-diisopropylcarboxamido)cubane, 122358-01-4; 3-carboxy-2,4-dicyano-1-(*N*,*N*-diisopropylcarboxamido)cubane, 122358-02-5; 2,7-dicarbomethoxy-1,4-bis(*N*,*N*-diisopropylcarboxamido)cubane, 122358-03-6; *o*-carboxy-*N*,*N*-diethylbenzamide, 4166-52-3; *o*-carbomethoxy-*N*,*N*-diethylbenzamide, 26593-44-2; *o*-carboxymethylbenzoate, 4376-18-5.

Supplementary Material Available: Representative experimental procedures and spectral data (^{1}H NMR, ^{13}C NMR) (3 pages). Ordering information is given on any current masthead page.

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[19] This establishes that amido-Grignards under correct conditions are sufficiently nucleophilic to react with esters.

Carbonylative Cyclization via Intramolecular Trapping of Acylmetal Derivatives by Carbon Nucleophiles Catalyzed by Late Transition Metals[1]

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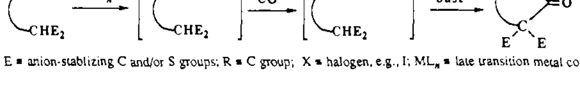
Received June 5, 1989

We wish to report a potentially general carbonylative cyclization methodology involving the use of catalytic amounts of late transition-metal complexes, in particular those of Cu, Ni, and Pd. The generalized scheme for the method is shown in eq 1.



(1)

E = anion-stablizing C and/or S groups; R = C group; X = halogen, e.g., I; ML_n = late transition metal complex.

Specifically, the dimethyl and diethyl esters of *o*-iodobenzylmalonic acids (**1a** and **1b**, respectively) were chosen as test substrates, and the feasibility of their carboxylative cyclization was examined, by using CO (600 psi), NEt_3 (1.0–2.0 equiv), and catalytic amounts of late transition-metal complexes containing Fe, Co, Ni, Cu, Ru, Rh, and Pd at the reaction temperature of 90–100 °C. As indicated by the results summarized in Table I, Li_2CuCl_4, $NiBr_2$, $NiBr_2$ treated in situ with *n*-BuLi (2 equiv) in the presence of 2 equiv of cyclooctadiene (COD), $Pd(PPh_3)_4$, and $Cl_2Pd(PPh_3)_2$ induced the desired carbonylative cyclization of **1** to produce **2** in high yields. Under comparable conditions, the use of $CpCo(CO)_2$ led only to a 40% yield of **2**, and the reactions

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[1] Metal-Promoted Cyclization. 29. Part 28. Swanson, D. R.; Rousset, C. J.; Negishi, E.; Takahashi, T.; Seki, T.; Saburi, M.; Uchida, Y. *J. Org. Chem.* **1989**, *54*, 3521.

[2] On leave from NKK Corporation, Japan.

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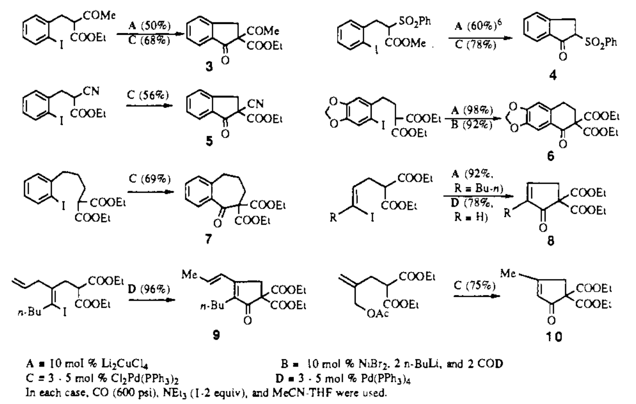
Table I. Carbonylative Cyclization of Esters of 2-(*o*-Iodobenzyl)malonic Acid (**1**)[a]

R of **1**	catalyst	amount, mol %	time, h	yield of **2**,[b] %	residual **1**, %
Et	Li_2CuCl_4	10	40	92 (91)	8
Et	$NiBr_2$	5	40	90	*c*
Me	$NiBr_2$, 2*n*-BuLi, 2COD	10	20	88 (77)	0
Et	$Cl_2Ni(PPh_3)_2$	3	30	92	0
Et	$CpCo(CO)_2$	20	24	40	54
Et	$Fe(CO)_5$	20	24	16	82
Et	$Pd(PPh_3)_4$	3	16	90	*c*
Me	$Cl_2Pd(PPh_3)_2$	5	16	85	*c*
Et	$ClRh(PPh_3)_3$	5	24	5	94
Et	$Cl_2Ru(PPh_3)_3$	5	24	5	94

[a] The reactions were carried out under an atmosphere of CO (600 psi) in the presence of 1–2 equiv of NEt_3 in MeCN at 90–100 °C. [b] GLC yield. The numbers in parentheses are isolated yields. [c] Not determined.

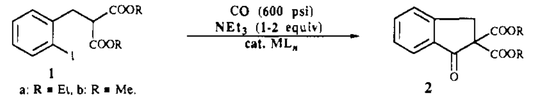
Scheme I



A = 10 mol % Li_2CuCl_4 B = 10 mol % $NiBr_2$, 2 *n*-BuLi, and 2 COD
C = 3 - 5 mol % $Cl_2Pd(PPh_3)_2$ D = 3 - 5 mol % $Pd(PPh_3)_4$
In each case, CO (600 psi), NEt_3 (1-2 equiv), and MeCN-THF were used.

promoted by $Fe(CO)_5$, $ClRh(PPh_3)_3$, and $Cl_2Ru(PPh_3)_3$ appear to be only stoichiometric. Although most of the reactions run so far have been carried out at the CO pressure of 600 psi, the carbonylation reaction of **1b** with 1 equiv of $NiBr_2$ which was treated in situ with 2 equiv of *n*-BuLi in the presence of 2 equiv of COD and 2 equiv of NEt_3 in refluxing MeCN proceeded smoothly even at 1.1 atm of CO to give **2b** in the 99% yield by GLC within 2 h. However, our brief attempts to use a catalytic amount (10 mol %) of the same Ni compound have not so far led to satisfactory results.

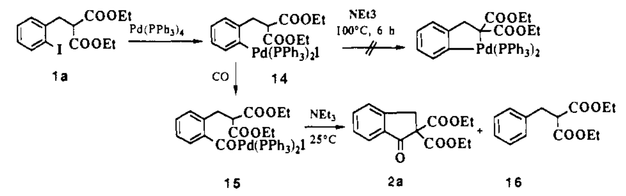
Various acylmetals generated via CO insertion of organotransition-metal derivatives are known to react with a wide range of heteroatom nucleophiles to form carbon–heteroatom bonds.[3] In contrast, the corresponding reactions with carbon nucleophiles to give carbon–carbon bonded species are rare, and those involving transition metals other than Pd[4] appear to be unknown. Furthermore, no carbonylative cyclization of this type appears to have been previously reported.

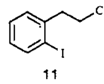


1
a: R = Et, b: R = Me.
2
(2)

The scope of the reaction with respect to the substrate structure appears to be reasonably broad, as indicated by the results summarized in Scheme I. Various precursors to doubly stabilized enolates participate in the reaction, as indicated by the synthesis of **2**–**5**. In the synthesis of **4**, the carbomethoxy group was lost during the carbonylation reaction prior to workup. The reaction is applicable to the synthesis of five-through seven-membered ketones, **6** and **7** being examples of six- and seven-membered ketones. It is noteworthy that, under the reaction conditions, known non-carbonylative cyclization[5] leading to the formation of indane and tetralin derivatives did not compete with carbonylative cyclization. In addition to aryl halides, alkenyl and allyl electrophiles also participate in the reaction, as in the synthesis of **8**–**10**. In the cases of **9** and **10**, the isolated carbon–carbon double bonds migrated into conjugation. Some limitations have also been noted. Thus, attempts to cyclize **11** using several bases including NEt_3 and KOBu-*t* have failed. With KOBu-*t* the major product isolated was **12**. The reaction of **13** using 5 mol % of $Cl_2Pd(PPh_3)_2$ has also failed to give the desired four-membered product.

Scheme II

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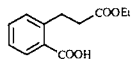
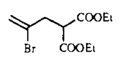

12


13

Although we have so far been preoccupied with the synthetic aspects of the methodology, a brief investigation of the Pd-catalyzed cyclization of **1a** has revealed the following. Treatment of **1a** with 1 equiv of $Pd(PPh_3)_4$ quantitatively gives **14**. Its treatment with CO (40 psi) in the absence of a base at 25 °C quantitatively produces the expected acylpalladium derivative **15**. Addition of 1 equiv of NEt_3 to **15** at 25 °C provides **2a** in 40% yield along with a 10% yield of **16**. Treatment of **14** with 1 equiv of NEt_3 in MeCN in the absence of CO does not induce cyclization or any other reaction even at 100 °C over 6 h. These results are in accord with the mechanistic path outlined in eq 1, even though the nature of the nucleophilic attack, e.g., Pd attack vs CO attack, remains to be unclear. A related study using Li_2CuCl_4 in place of $Pd(PPh_3)_4$ has not yielded useful mechanistic information due mainly to extensive broadening of the NMR signals of the reaction mixtures. Intermediacy of paramagnetic species may be suspected.

The following procedure for the conversion of **1a** into **2a** catalyzed by a Cu catalyst is representative. To a solution of **1a** (0.38 g, 1.0 mmol) in 3 mL of THF–CH_3CN (1:1) were added sequentially NEt_3 (0.28 mL, 2.0 mmol) and Li_2CuCl_4 (0.1 M in THF, 1 mL, 0.1 mmol). The mixture was placed in an autoclave, and CO (600 psi) was introduced. The mixture was heated to 100 °C and stirred for 40 h. After cooling, the mixture was worked up with ether and brine, washed with aqueous $NaHCO_3$, and dried over $MgSO_4$. Evaporation of volatiles (50 °C, 0.1 mmHg) followed by a short-path chromatography (silica gel) provided 0.276 g (91%) of **2a**: IR (neat) 1728 (s), 1590 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 1.28 (t, J = 7 Hz, 6 H), 3.82 (s, 2 H), 4.26 (q, J = 7 Hz, 2 H), 7.40 (t, J = 7 Hz, 1 H), 7.49 (d, J = 7 Hz, 1 H), 7.63 (t, J = 7 Hz, 1 H), 7.79 (d, J = 7 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.77, 36.01, 62.36, 67.08, 125.05, 126.12, 127.94, 134.14, 135.58, 151.72, 166.72, 194.35; high resolution MS calcd for $C_{15}H_{16}O_5$ 276.0997; found 276.0997.

Acknowledgment. We thank the National Institutes of Health (Grant No. GM 36792), the Petroleum Research Fund, administered by the American Chemical Society (Grant No. 18710-AC1), and NKK Corporation, Japan, for support of this research.

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[6] A 1:1 mixture of **4** and its 2-methoxycarbonyl derivative was obtained.

We also thank Johnson Matthey for a loan of Pd and Rh compounds.

Supplementary Material Available: Spectral data (IR, ^1H NMR, and ^{13}C NMR) for **1a**, **1b**, **2b**, **3–7**, **8a**, **8b**, and **9–15** (6 pages). Ordering information is given on any current masthead page.

Trihalomethyl Cations[1]

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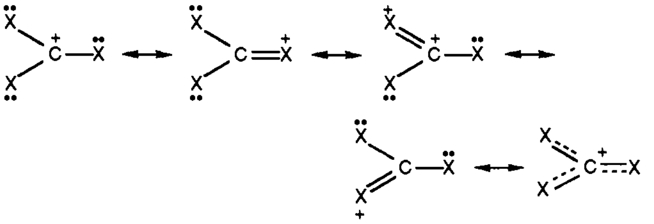
Received June 12, 1989

Although trialkyl,[2] halodialkyl,[3] and dihaloalkylmethyl[4] cations have been prepared and spectroscopically characterized under long-lived stable ion conditions in solution, the corresponding parent trihalomethyl cations have never been observed. Halogen atoms adjacent to a carbocationic center are inductively destablizing due to their high electronegativity. On the other hand, the nonbonded electron pairs on the halogen atom can stabilize the positive charge through back-donation (p–p interaction). The extent of stabilization is dependent on the electronegativity of the halogen atom and its size. Following the known electronegativity order F > Cl > Br > I,[5] fluorine should inductively destabilize the adjacent carbenium center the most. However, since fluorine is a small atom possessing 2p nonbonded electron pairs, the back-donation 2p–2p overlap is maximum, and in fact fluorine is an excellent stabilizer of adjacent positive charge. From previous studies[3] the order of the charge stabilizing effect of halogens on adjacent carbocationic centers has been found to be F > Cl > Br > I.

Consequently it was of interest to prepare stable trihalomethyl cations under superacid conditions and to probe the effect of three halogen atoms attached to carbocationic center. In principle the three halogen atoms should significantly stabilize the positive charge through back-donation involving several resonance structures. Such back-bonding resonance stabilization in guanidinum[6] and trihydroxycarbenium ions[7] is well-known.



Slow addition of a precooled solution of carbon tetrachloride in SO_2ClF to a stirred solution of 5-fold excess of SbF_5 in SO_2ClF maintained at −78 °C (dry/ice acetone bath) gave a clear colorless solution. The 50 MHz ^{13}C NMR spectrum of the solution obtained at −80 °C shows a single sharp resonance at $\delta^{13}C$ 236.3, deshielded from the progenitor signal by 139.6 ppm. The same

$$\underset{X = Cl, Br, I}{CX_4} \xrightarrow[-78\ ^\circ C]{nSbF_5/SO_2ClF} {}^+CX_3{}^-Sb_nF_{5n}X$$

ion (obtained from CCl_4) was also observed by the ionization with subsequent loss of SO_2 of trichloromethanesulfonyl chloride with SbF_5 under similar conditions. These data are indicative of the formation of the trichloromethyl cation.

$$CCl_3SO_2Cl \xrightarrow[-78\ ^\circ C]{nSbF_5/SO_2ClF} {}^+CCl_3{}^-Sb_nF_{5n}Cl + SO_2$$

To further confirm the observation of the trichloromethyl cation we also ionized trichloroacetyl chloride in SbF_5/SO_2ClF solution at −78 °C. Under the reaction conditions rapid CO gas evolution is observed with the formation of the identical trichloromethyl cation.

$$CCl_3COCl \xrightarrow[-78\ ^\circ C]{nSbF_5/SO_2ClF} {}^+CCl_3\ Sb_nF_{5n}Cl^- + CO\uparrow$$

In an attempt to observe the intermediate trichloroacetylium cation (CCl_3CO^+) we repeated the ionization experiment at −120 °C (ethanol/liquid N_2 slush bath). At this temperature trichloroacetyl chloride–SbF_5 undergoes rapid halogen exchange via the formed donor–acceptor complex. The complex showed two ^{13}C absorptions at $\delta^{13}C$ 194.8 (J_{C-F} = 120 Hz) and 92, with no discernible long-range fluorine coupling observed with the trichloromethyl carbon. Upon standing the complex even at this temperature decomposes to give the trichloromethyl cation.

$$CCl_3COCl + nSbF_5 \rightarrow CCl_3COF \rightarrow SbF_4Cl(Sb_{n-1}F_{5n-5})$$

The trichloromethyl cation is stable below −50 °C, above which it decomposes. Surprisingly, the $^+CCl_3$ ion coexists in the presence of excess carbon tetrachloride, and no evidence was obtained for the formation of bis(trichloromethyl)chloronium ion $(Cl_3C)_2Cl^+$. When a solution of the trichloromethyl cation was reacted with 3 equiv of benzene, the triphenylmethyl cation[8] was cleanly formed.

Carbon tetrabromide similarly ionizes in excess SbF_5/SO_2ClF solution at −78 °C giving the tribromomethyl cation. The ^{13}C NMR spectrum of the tribromomethyl cation shows a singlet at $\delta^{13}C$ 207. The extent of deshielding compared to its precursor carbon tetrabromide ($\delta^{13}C$ −28.5) is 235.5 ppm, consistent with the formation of tribromomethyl cation.

Even carbon tetraiodide undergoes clean ionization in SbF_5/SO_2ClF solution at −78 °C to give the triiodomethyl cation. The triiodomethyl cation exhibits a ^{13}C NMR chemical shift of 95 ppm, a deshielding of 387.3 compared to its progenitor carbon tetraiodide ($\delta^{13}C$ −292.3).[9]

All of our attempts to observe the trifluoromethyl cation were so far unsuccessful. Tetrafluoromethane (bp −128 °C) was found to be unreactive even in large excess SbF_5/SO_2ClF solution at −78 °C. Ionization of either trifluoroacetyl fluoride or trifluoromethanesulfonyl chloride with antimony pentafluoride, on the other hand, led to the formation of tetrafluoromethane. Further, trifluoroacetic acid in $FSO_3H{:}SbF_5$ (Magic Acid)/SO_2ClF solution gave the corresponding protonated acid, which was characterized by its ^{13}C NMR spectrum $\delta^{13}C$ 174.2 (J_{C-C-F} = 49.3 Hz), 112.4, (J_{C-F} = 283.7 Hz). Attempts to dehydrate the protonated acid to trifluoroacetyl cation (CF_3CO^+) and subsequently to trifluoromethyl cation ($CF_3{}^+$) were unsuccessful. When trifluoroacetyl chloride was reacted with benzene in the presence of $AlCl_3$ catalyst, besides trifluoroacetophenone the Friedel–Crafts trifluoroacetylation product, triphenylmethyl chloride was formed.[10] This is indicative of in situ decarbonylation of the trifluoroacetyl cation to the trifluoromethyl cation which

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(1) Stable Carbocations, Part 276. For Part 275, see: Olah, G. A.; Prakash, G. K. S.; Fessner, W.-D.; Kobayashi, T.; Paquette, L. A. *J. Am. Chem. Soc.* **1988**, *110*, 8599.

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