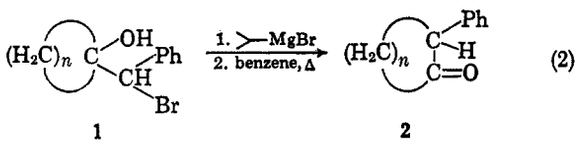


responding ring-enlarged ketones, **2** (eq 2). The results are presented in Table I. The structural assignments of the ketones, **2**, were based on infrared and nmr spectra and the 2,4-dinitrophenylhydrazones. It should be pointed out that the bromohydrins, **1**, were employed without purification since attempted distillation of the bromohydrin, **1** ($n=4$), resulted in extensive decomposition.

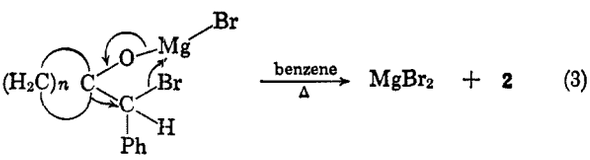
TABLE I

RESULTS OF THE DECOMPOSITION OF THE MAGNESIUM SALTS OF **1**

Compd 1, n	% yield of ketone, 2	2,4-DNP Mp, °C (lit.)	ν_{film}, cm^{-1}
4	80	136–137 (138–139)[a]	1700
5	72	171–172 (171–172)[b]	1700
6	70	153 (146)[c]	1695
7	60	162–163[d]	1705

[a] A. S. Hussey and R. R. Herr, *J. Org. Chem.*, **24**, 843 (1959). [b] C. D. Gutsche, *J. Am. Chem. Soc.*, **71**, 3513 (1949). [c] T. Weil and D. Ginsburg, *J. Chem. Soc.*, 1291 (1957). [d] Recrystallized twice from ethanol. *Anal.* Calcd for $C_{21}H_{24}N_4O_4$: C, 63.62; H, 6.10; N, 14.13. Found: C, 63.59; H, 6.19; N, 14.06.

Inspection of the results recorded in Table I reveals the excellent yields obtained by the use of this simple method. The use of nonpolar solvents in effecting the ring enlargement leads one to believe that an intimate ion pair or a concerted mechanism may be operating (eq 3).



Presently, research is underway in order to expand the synthetic utility, and investigate the mechanism, of the reaction.

Experimental Section[13]

1-Benzyl-1-cycloalkanols were prepared by procedures which were previously described: 1-benzyl-1-cyclopentanol according to Schaeffer,[14] mp 56–58° (lit.[14] mp 58–60°), 1-benzyl-1-cyclohexanol according to Pallos,[15] mp 59.5–61.5° (lit.[15] mp 61–62°), 1-benzyl-1-cycloheptanol according to Stach,[16] mp 47–48° (lit.[16] mp 46.5°), 1-benzyl-1-cyclooctanol according to Stach,[16] bp 152–156° (3 mm) (lit.[16] bp 138–142° 0.2 mm). The nmr spectra in CCl_4 indicated *two* benzyl hydrogens at τ 7.2–7.3.

1-(α-Bromobenzyl)-1-cycloalkanols were synthesized from the corresponding alkanols by employing 0.15–0.20 mole of alkanol, 200 ml of anhydrous carbon tetrachloride, an equivalent of N-bromosuccinimide, and 1 g of benzoyl peroxide. The mixture was brought to reflux with the aid of an oil bath. In a short time a vigorous reaction took place (0.5–1 hr) after which the mixture was refluxed an additional hour. The mixture was cooled in an ice bath and then the succinimide filtered off with suction. The carbon tetrachloride was removed under vacuum with a rotary evaporator. The residual light yellow oil was used directly in the ring enlargement reaction. The nmr spectra in CCl_4 showed one benzyl hydrogen at τ 4.9–5.1.

2-Phenylcycloalkanones.—To an ice-cooled solution of the bromohydrin dissolved in 300–350 ml of anhydrous benzene an equivalent amount of isopropyl magnesium bromide was added dropwise. The Grignard reagent was prepared in 50–75 ml of ether. After the addition the ice bath was removed and the resultant solution was refluxed (oil bath) for a period of 1–3 hr: for **1**, n = 4, 1 hr; n = 5, 3 hr; n = 6, 1 hr; n = 7, 1 hr. The brown solution was then cooled and added to an ammonium chloride solution in water. The benzene layer was separated and washed with 10% sodium carbonate followed by water. The benzene was then dried over magnesium sulfate and the solvent was subsequently removed under vacuum. The residue from **2**, n = 4, crystallized and was recrystallized from hexane, mp 56–58° (lit.[12] 59–60); n = 5, bp 105–107° (0.5 mm) (lit.[17] bp 94–96° (0.4 mm)); n = 6, bp 133–135° (1.7 mm) (lit.[18] bp 115° (0.4 mm)); n = 7, bp 113–115° (0.4 mm) (lit.[19] bp 115° (0.01 mm)). The nmr spectra revealed two doublets at τ 6.3–6.5 in CCl_4 for *one* benzyl hydrogen.

Registry No.—**2** (n = 4), 1444-65-1; **2** (n = 5), 14996-78-2; **2** (n = 6), 14996-79-3; **2** (n = 7), 14996-80-6; **2** (n = 7) 2,4-dinitrophenylhydrazone, 14996-81-7.

(13) All melting points are uncorrected. Infrared spectra were determined with a Perkin-Elmer Spectrocord infrared spectrophotometer. Nmr spectra were determined with a Varian A-60 instrument.

(14) H. J. Schaeffer and C. J. Collins, *J. Am. Chem. Soc.*, **78**, 124 (1956).

(15) L. Pallos, G. Zolyomi, Z. Budai, E. Komlos, and L. Petoez, Hungarian Patent 151,865 (1965).

(16) K. Stach and W. Winter, *Arzneimittel-Forsch.*, **12**, 194 (1962).

(17) C. D. Gutsche, *J. Am. Chem. Soc.*, **71**, 3513 (1949).

(18) T. Weil and D. Ginsburg, *J. Chem. Soc.*, 1291 (1957).

(19) E. Muller and R. Heichkeil, *Tetrahedron Letters*, 1023 (1962).

A Convenient Synthesis of N-Substituted 2,4-Diarylpyrroles

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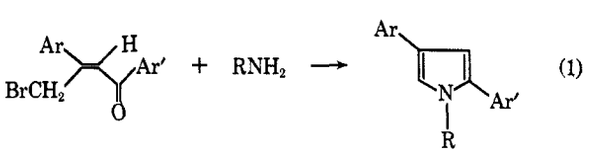
In the course of other studies in progress in this laboratory, we required a series of 2,4-diarylpyrroles with different substituents bonded to the nitrogen atom. The scarcity of literature on 2,4-diarylpyrroles can be ascribed to the difficulties encountered in attempts to prepare these compounds readily and in good yields.[1-4] We wish to report a convenient general route to these N-substituted pyrroles based on the cyclization of 1,3-diaryl-4-bromo-2-buten-1-ones with an appropriate primary amine[5] (eq 1). The advantage of the method



arises from the ease of preparation of the unsaturated bromo ketone and the high yields obtained in the cyclization step.

In a typical case, bromination of 1,3-diphenyl-2-buten-1-one with N-bromosuccinimide followed by

(1) A. H. Corwin, "Heterocyclic Compounds," Vol. I, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1950, p 277.

(2) H. Wasserman and J. B. Brous, *J. Org. Chem.*, **19**, 515 (1954).

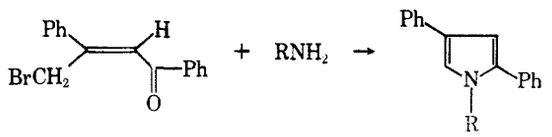
(3) K. Dimroth and U. Pintschovius, *Ann.*, **689**, 102 (1961).

(4) A. Treibs and R. Derra, *ibid.*, **589**, 176 (1954).

(5) A specific experimental case of this procedure was first reported by A. Padwa, R. Gruber, and L. Hamilton, *J. Am. Chem. Soc.*, **89**, 3077 (1967). Similar findings have been published since: R. Rodebaugh and N. Cromwell, *Tetrahedron Letters*, No. 30, 2859 (1967).

TABLE I

YIELD DATA FOR FORMATION OF DIARYLPYRROLES

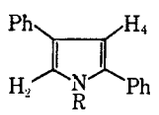


Compd	R	Reflux period, hr	% yield[a]	Mp	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
I	*t*-Bu	4	80	102–103	87.22	7.69	5.00	87.20	7.85	5.09
II	Ph	8	95	152–153[b]	89.46	5.80	4.74	89.12	5.83	4.56
III	C_6H_{11}	12	60	81–83	87.66	7.69	4.65	87.58	7.68	4.31
IV	$PhCH_2$	10	85	96–98	89.28	6.19	4.53	89.13	5.96	4.81
V	$PhCH_2CH_2$[c]	9	95	220 (0.1 mm)	89.12	6.55	4.33	88.97	6.73	4.25
VII[d]	(1-*t*-butyl-2,3-diphenylpyrrole)	6	60	128–129	87.22	7.69	5.00	86.55	7.63	4.85

[a] % yield of purified material. [b] Reported mp 151–152: G. K. Almstrom, *Ann.*, **400**, 131 (1913). [c] Clear oil. [d] Prepared from the cyclization of *t*-butylamine and 4-bromo-1,2-diphenyl-2-buten-1-one: R. Gruber, unpublished results.

TABLE II

PHYSICAL PROPERTIES OF DIARYLPYRROLES



Compd No.	Infrared spectra,[a] μ	Ultraviolet spectra,[b] λ_{max}	Nmr[c] chemical shift (J, cps) H_2	Nmr[c] chemical shift (J, cps) H_4
I	6.24; 8.22; 12.50	273 (15,500)	2.96 (2.0)	3.80 (2.0)
II	6.20; 8.10; 10.97	257 (32,000)		3.38 (1.9)
III	6.22; 8.20; 10.70	251; 282 (19,200; 18,900)	3.01 (2.2)	3.52 (2.2)
IV	6.24; 8.24; 10.70	251; 277 (21,200; 19,800)	3.10 (2.1)	3.54 (2.1)
V	6.24; 8.37; 10.77	256 (20,000)	3.20 (1.9)	3.62 (1.9)
VI[d]	6.24; 8.20; 13.08	254 (10,600)	3.18 (3.0)	3.79 (3.0)

[a] Infrared spectra were recorded on a Perkin-Elmer Infracord using carbon tetrachloride as a solvent. Most intense absorption bands. [b] Ultraviolet spectra were recorded on a Cary 15 recording spectrophotometer using 95% ethanol as solvent. [c] Nuclear magnetic resonance spectra were recorded in CCl_4 solution at 60 Mc on a Varian Associates A-60 nmr spectrometer. [d] In this case, $H_4 = H_5$.

cyclization of the resulting bromide[6] with benzylamine afforded the expected pyrrole, 1-benzyl-2,4-diphenyl pyrrole in 85% over-all yield. To delineate the usefulness of this synthetic scheme we carried out the typical reactions compiled in Table I.

Table I summarizes the yields obtained in the preparation of N-substituted pyrroles. If a large excess of amine was used the yield of pyrrole was high, but if the amine was reduced to only 1.2 moles/mole of bromide the yield of isolated product diminished. Although no attempts were made to optimize the conditions, yields of 60% were obtained in all cases when a fivefold excess of amine was used. The reaction was followed by both infrared spectroscopy and gas chromatography. When the amount of product leveled off, the reaction was cooled and the precipitated amine hydrobromide was removed by filtration and the product was isolated by crystallization. Table II presents physical properties of the pyrroles obtained. Conclusive evidence that the N-substituted pyrroles were indeed the products of the cyclization reaction was obtained by nmr spectroscopy (Table II). The cross ring or *meta* coupling constant ($J_{3,5}$) in the pyrrole system has a value of approximately 2.0 cps, in agreement with values reported in the literature.[7]

(6) H. H. Wasserman, N. E. Aubrey, and H. E. Zimmerman, *J. Am. Chem. Soc.*, **75**, 96 (1953).

(7) R. J. Abraham and H. J. Bernstein, *Can. J. Chem.*, **37**, 1056 (1959).

The exploratory reactions listed above indicate that this procedure offers an efficient method of synthesizing a wide range of N-substituted diarylpyrroles. In addition to the preparation of 2,4-diarylpyrroles, it is also possible to carry out a variation of this type of substitution–cyclization procedure which permits the synthesis of the isomeric 2,3-diarylpyrrole system.

Experimental Section

General Procedures.—The preparation of 1-*t*-butyl-2,4-diphenylpyrrole is shown below as a typical run. The other diaryl pyrroles were prepared in a similar manner.

A solution of 5.0 g of 1,3-diphenyl-4-bromobuten-2-one-1[6] and 20 g of *t*-butylamine in 80 ml of benzene was refluxed for 4 hr. After being cooled, the mixture was filtered from the amine hydrobromide and was then taken up in ether and extracted with 50 ml of 10% hydrochloric acid and washed with water. Drying and evaporation of the ether gave 11.2 g (80%) of a solid, mp 96–102°. Recrystallization from hexane–benzene gave colorless prisms, mp 102–103°. A sample of 1-*t*-butyl-2,4-diphenylpyrrole was heated in a sealed tube at 250° for 3 hr. Vacuum sublimation of the crude reaction mixture at 0.1 mm in a microsublimation apparatus gave crystals, mp 177–178°, which had an infrared spectrum identical in every detail with that of pure 2,4-diphenylpyrrole.

Acknowledgment.—The authors are indebted to the Public Health Service Grant GM13990-01 for generous support of this research.